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PROCEEDINGS

of the 12th Annual

BIO-ASSAY and ANALYTICAL CHEMISTRY MEETING

held at Gatlinburg, Tennessee
October 13-14, 1966

Compiled By
C. M. West

UNION CARBIDE CORPORATION
NUCLEAR DIVISION
OAK RIDGE Y-12 PLANT
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Sponsored By

East Tennessee Chapter of the Health Physics Society

Oak Ridge Associated Universities
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Oak Ridge Gaseous Diffusion Plant
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INTRODUCTION

The Twelfth Annual Meeting on Bio-Assay and Analytical Chemistry was held at the Huff House, Mountain View Hotel, Gatlinburg, Tennessee.

The proceedings of previous meetings have been issued as AEC Reports NLCO-595 (1955), WASH-736 (1956), WASH-1023 (1958), TID-7591 (1959), TID-7616 (1960), ANL-6637 (1961), DP-831 (1962), TID-7696 (1963), CONF-727 (1964), CONF-651008 (1965). No proceedings were published for the 1957 meeting.

The conferences are held in order that AEC and AEC contractor personnel will have an opportunity to discuss procedures and problems associated with the collection, interpretation, and application of bio-assay and other pertinent health data.

CONTENTS

IMPROVED PROCEDURE FOR RADIOSTRONTIUM ANALYSIS OF HUMAN URINE*

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ABSTRACT

The procedure used routinely for radiostrontium analysis at Oak Ridge National Laboratory has been revised for greater efficiency and also for more extensive examination of an individual sample. An alkaline-earth-phosphate precipitation procedure is applied to co-precipitate both the alpha emitting actinide elements and radiostrontium. Improved efficiency for radiostrontium is attained by the addition of calcium, H_3PO_4, excess NH_4OH, and the exclusion of atmospheric CO_2 after precipitation. Revisions were made also in the cation exchange column separation of radiostrontium from calcium and magnesium using Na_4EDTA and citric acid. Use of these chelating and complexing agents reduces the time required for strontium analysis by about 50 per cent.

INTRODUCTION

The two methods most commonly used for estimating the body burden of ^{90}Sr are (1) measurement of the bremsstrahlung from internally deposited $^{90}Sr - ^{90}Y$ in a whole body counter with the use of a NaI(Tl) crystal and a gamma spectrum analyzer, and (2) analysis of urine for ^{90}Sr. The limit of detection by whole body counting is less than 10 per cent of the maximum permissible body burden, while the estimation of the body burden by urinalysis is limited by a prior knowledge of the relationship between the total body burden and the excretion rate as a function of time after exposure. In general, it is usually necessary to rely heavily on urinalysis in monitoring for ^{90}Sr for several reasons: (1) in some cases there is a need for surveillance of personnel at levels below the detection limit of whole body counting; (2) the bremsstrahlung from ^{90}Y gives a continuous spectrum only with no distinguishable peak relating to ^{90}Y per se, therefore, urinalysis may be necessary to identify the beta emitter present in the body; and (3) where a large number of persons or frequent sampling is required urinalysis is more practical and economical.

Although each nuclear installation may have problems of special interest in monitoring for internal radiation hazards, the alpha emitting actinide elements and ^{90}Sr are certainly of widespread interest, and at ORNL about 85 to 90 per cent of the urinalysis laboratory work load involves the analyses for these radionuclides. The analytical procedure for ^{90}Sr analysis, which was developed at ORNL and which has been in use since 1956, involves two

*Research sponsored by the United States Atomic Energy Commission under contract with the Union Carbide Corporation.

major steps: (1) the precipitation of the calcium and magnesium of the urine as phosphates with NaOH, and (2) the separation of radiostrontium from the calcium and magnesium on a cation exchange resin column with a solution of tetrasodium ethylenediaminetetracetic acid (Na_4EDTA) and citric acid as chelating and/or complexing agents.[1] Recently it became necessary to make some changes in the procedure in order to expedite the urinalysis program by using one precipitation step to concentrate both radiostrontium and alpha emitting actinide elements, thereby providing a method of analyses for several radionuclides in an individual urine sample. In addition, some changes were made in the resin column separation of radiostrontium from calcium and magnesium to provide a more efficient procedure.

ALKALINE EARTH PHOSPHATE PRECIPITATION

Experimental

In the procedure presently used at ORNL for analysis of actinide elements in urine, the initial step is the precipitation of urinary calcium and magnesium as phosphates with NH_4OH.[2] In order to co-precipitate metabolized plutonium from urine, 50 ml of concentrated HNO_3 is added per liter of urine and the sample is heated to 80° C and stirred for 1 to 2 hours. H_3PO_4 is added, then the alkaline earth phosphates are precipitated with NH_4OH.[3] In order that this precipitation may be used also as the initial step in concentrating radiostrontium, it was necessary to prove that quantitative recovery of radiostrontium can be achieved. In the developmental work ^{85}Sr (0.51 Mev gamma) was used to facilitate the study of solubility losses, since direct counting of liquid samples can be done with a NaI(Tl) crystal and a multichannel analyzer. During the exploratory tests on precipitation of alkaline earth phosphates with the use of NH_4OH it was found that rather large solubility losses of ^{85}Sr occurred, especially when dilute urine was used. When the precipitation was done with NaOH, however, the ^{85}Sr recovery was consistently about 98 per cent. The larger loss with NH_4OH may be due to the buffering action in urine at pH 7 to 8, thereby prohibiting the optimum pH for best recovery. Other factors affecting the larger solubility loss may be insufficient calcium and phosphates in dilute urine samples.

In an attempt to minimize solubility loss of ^{85}Sr in alkaline earth phosphate precipitation, studies were made to determine the effect of: (1) the addition of calcium; (2) added H_3PO_4; (3) the pH at which the precipitation is made; and (4) the exclusion of atmospheric CO_2 after precipitation until the sample is processed. For these studies, composite dilute urine was used (sp. gr. 1.007).

Results

The exclusion of the atmosphere by wrapping the beaker containing the sample with a plastic wrap increased the recovery of ^{85}Sr by an average of 3.6 per cent, therefore, this practice was followed in all subsequent studies. By exploratory experiments, it was found that the optimum conditions for precipitation of alkaline earth phosphates from urine with NH_4OH to give a final pH of >9. To show the effect of each of the three conditions for precipitation on recovery of ^{85}Sr, two conditions were held constant for maximum recovery while the third was studied.

The addition of calcium, when the pH is 9.2 and H_3PO_4 is 0.1 molar, improves the recovery from 80 per cent to about 95 per cent (Fig. 1). The addition of H_3PO_4, when the pH is 9.2 and calcium is 120 mg/liter, also improves recovery (Fig. 2). With optimum conditions of added calcium and H_3PO_4, it was shown that a large excess of NH_4OH must be added for optimum recovery (Fig. 3).

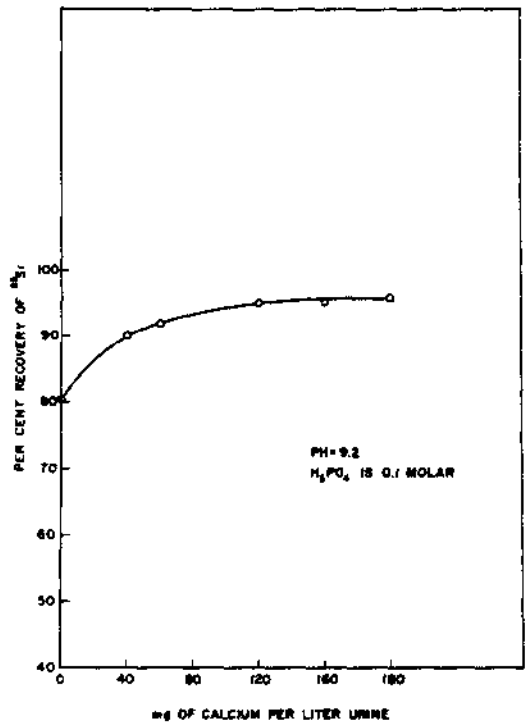

Fig. 1 Effect of added calcium on ^{85}Sr recovery.

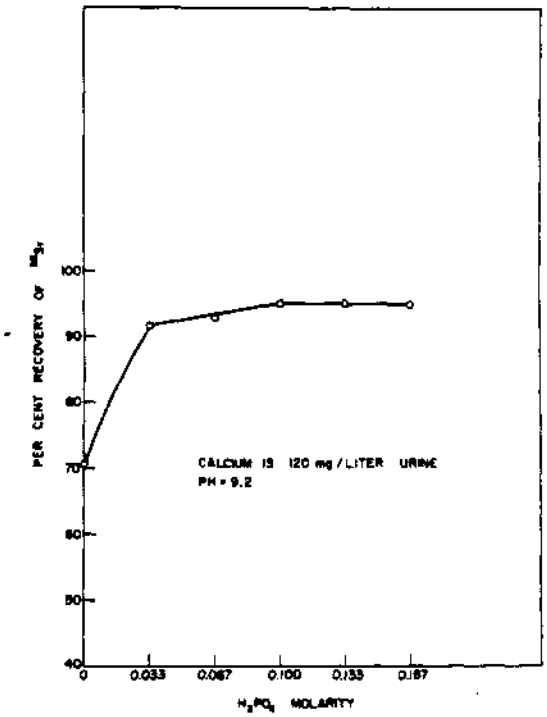

Fig 2. Effect of excess H_3PO_4 on ^{85}Sr recovery.

In summary, when using the optimum conditions for precipitation the average recovery of ^{85}Sr in 10 dilute urine samples of volumes ranging from 500 to 1500 ml was 94.9 % (± 0.4), while recovery in seven individual urines of volumes from 750 to 1500 ml and specific gravity from 1.007 to 1.015 was 96.5 % (± 0.5). Although the recovery of ^{85}Sr from urine using NH_4OH is about 1 to 2 per cent less than the recovery when NaOH is used, the precipitate is much more compact, which facilitates the subsequent washing and destruction of organic matter. The NH_4OH precipitation also provides better separation from ^{137}Cs and ^{40}K, two beta emitters commonly present in urine. The separation factor for both ^{137}Cs and ^{40}K in the precipitation step alone is 400.

RESIN COLUMN SEPARATION OF RADIOSTRONTIUM

In order to achieve maximum use of the alkaline earth phosphate precipitation for the analysis of urine for several radionuclides, the analytical scheme must provide for removal of some of the radionuclides without loss of others. Thus, in the procedure presently used for the analysis of Pa, Np, U and Pu, a strong HCl solution of the precipitate is passed through an anion exchange resin column, thereby removing these radionuclides.[2] The column effluent will contain many radionuclides of interest in a urinalysis program, chief of which are the trivalent actinides, radiostrontium, radiobarium and radium. If there is a need to analyze for the trivalent actinides as a group, the conventional $BiPO_4$ - LaF_3 precipitation procedure can be used. The radiostrontium can be recovered directly from the $BiPO_4$ supernate or from the column effluent by use of the resin column technique described below.

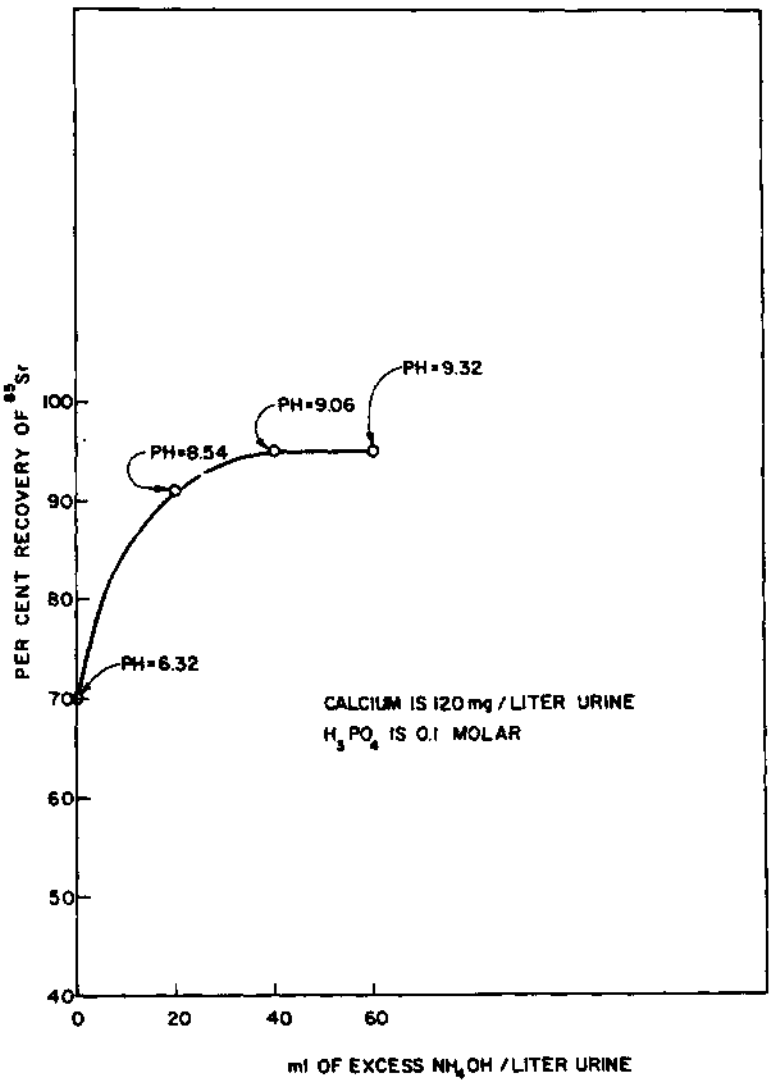

Fig. 3 Effect of excess NH_4OH on ^{85}Sr recovery.

Equilibrium Distribution Studies

In designing the resin column procedure, it was helpful to know the relative adsorption of radiostrontium, calcium and magnesium on Dowex resin in each step of the column separation. This can best be done by batchwise equilibrium distribution studies in systems containing a solution of radiostrontium, calcium, and magnesium, and Dowex 50-X12 at pH 5.00 with (1) Na_2H_2 EDTA only, (2) with citric acid only, and (3) a combination of both.

The results of batchwise equilibrium distribution coefficient studies with EDTA solutions at pH 5.00 containing Dowex 50-X12 (100 - 200 mesh), ^{85}Sr tracer, calcium (12 mg) and magnesium (12 mg) as a function of EDTA molarity are shown in Fig. 4. Strontium-85 is adsorbed on the resin by a factor of 100 over Ca(II) and 6.3 over Mg(II).

Citric acid is used in the feed solution to complex iron and is also a component of the wash solution to remove calcium and magnesium from the resin column. Distribution coefficient studies with solutions of citric acid at pH 5.00 containing Dowex 50-X12 (100 - 200 mesh), ^{85}Sr tracer, calcium (12 mg) and magnesium (12 mg) as a function of citric acid molarity are shown in Fig. 5. Strontium-85 is adsorbed on the resin by a factor of 4 over Ca(II) and 8 over Mg(II).

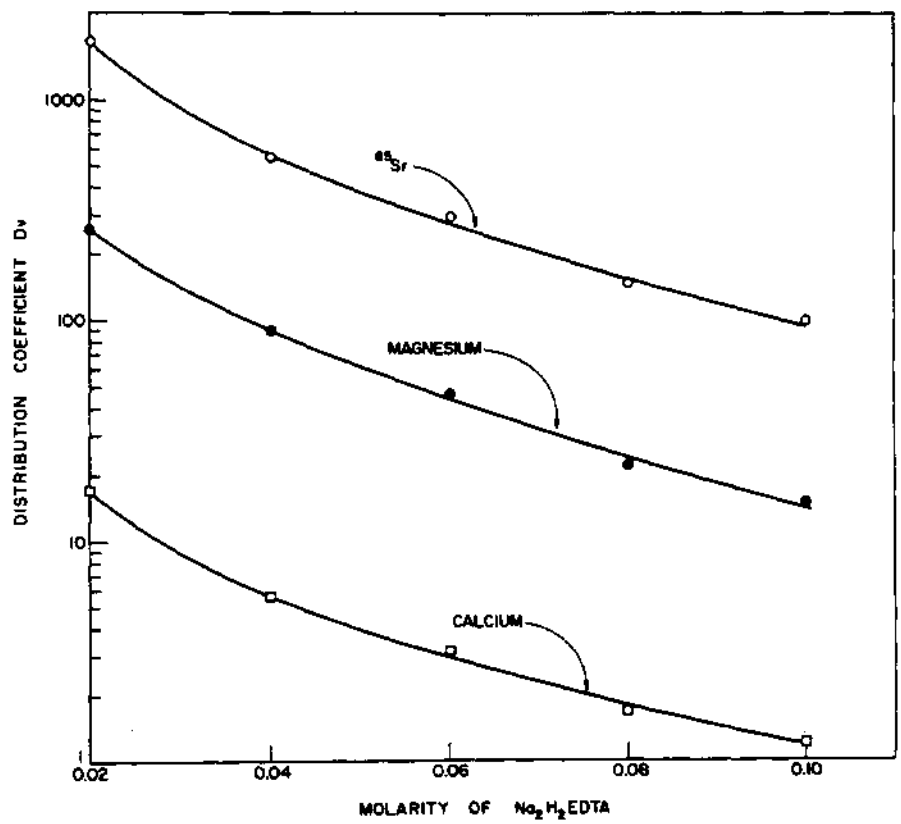

Fig. 4 Distribution coefficients of ^{85}Sr, Ca(II), Mg(II) in Na_2H_2EDTA and Dowex 50 resin at pH 5.00.

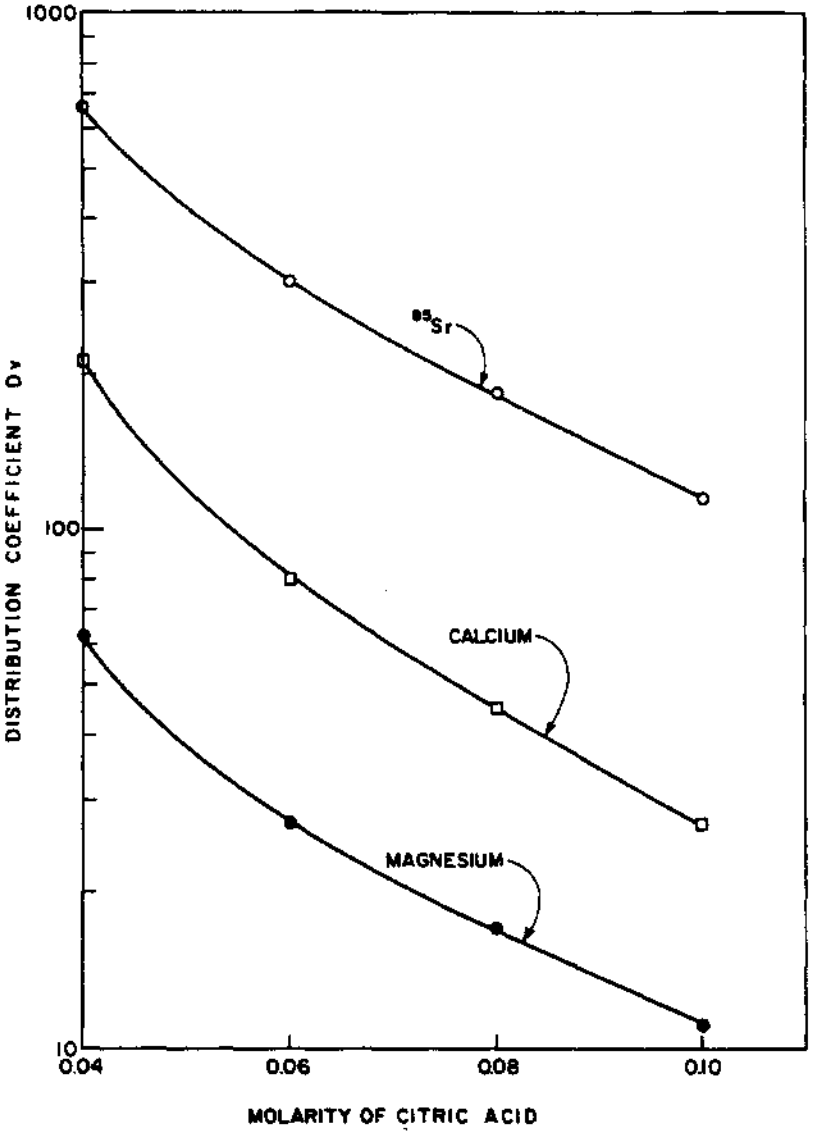

Fig. 5 Distribution coefficients of ^{85}Sr, Ca(II), Mg(II), in citric acid and Dowex 50 resin at pH 5.00.

Since the feed solution is made up of both EDTA and citric acid, distribution coefficient studies in which both are used in the same ratio as recommended for preparation of the feed solution show that ^{85}Sr is adsorbed on the resin by a factor of 45 over Ca(II) and 9.5 over Mg(II). In practice it has been found that when a sample is put through a cation exchange resin column, about 90 per cent of the calcium and 60 per cent of the magnesium will pass through the resin as the chelate. All of the radiostrontium is retained on the resin. Since only 20 per cent of the alkaline earths in the sample are retained on the resin, a much smaller column can be used, thereby decreasing the volumes of wash and eluting solutions.

Separation Procedure

The changes recommended in this revised procedure will reduce the time required for an analysis by about 50 per cent over the procedure previously used.[1] The changes include: (1) 100 - 200 mesh Dowex 50-X12 is used instead of 50 - 100 mesh; (2) the resin column is 1.6 cm I.D. instead of 1.8 cm; (3) the volume of resin has been reduced from 25 ml to 13 ml; (4) the pH of the feed solution is 5.00 instead of 5.50; and (5) citric acid is added to give a concentration of 0.25 per cent.

(a) The Resin Column

A cylindrical glass or plastic tubing 8 inches long and 1.6 cm I.D., fitted at the top with a funnel to serve as a reservoir for feed and wash solutions and a stopcock at the bottom to control the flow rate is filled with 13 ml (wet volume) of Dowex 50-X12 (100 - 200 mesh) which has been converted to the Na^+ cycle with NaCl. The resin bed is supported with glass wool at both bottom and top. The use of smaller size resin particles provides faster exchange rates and, most important, greater ease of removing radiostrontium with a smaller volume of HNO_3 elutriant.

(b) Preparation of Urine Sample

After removal of the actinide elements from the urine sample by either the anion exchange technique, the $BiPO_4$ precipitation, or a combination of both, the radiostrontium can be recovered from the effluent or supernate as follows: (1) the excess HCl in the anion resin column effluent must be removed by evaporation, (2) the residue is solubilized in H_2O and the volume brought to about 350 ml, (3) as the solution is stirred constantly, the electrodes of a pH meter are immersed and NaOH is added to bring the pH to about 10, (4) add a solution of technical grade Na_4EDTA until all of the alkaline earths are chelated as indicated by a color change from wine-red to blue of Eriochrome Black T, (5) add 10% excess Na_4EDTA, (6) add sufficient citric acid to make the solution 0.012 molar (0.25%), and (7) adjust the pH to 5.00 with HCl and/or NaOH. The concentration of the alkaline earths should not exceed 1 mg/ml. This solution is then passed through the cation exchange resin column at a maximum flow rate of about 8 ml/min (4 ml cm^{-2} min^{-1}) when the liquid height in the reservoir is about one foot above the resin. The column effluent, which will contain about 90 per cent of the calcium and 60 per cent of the magnesium, can be discarded.

(c) Removal of Ca and Mg from Resin Column

The residual calcium and magnesium are removed from the resin by passing 250 ml of wash solution made up of 0.75 % Na_4 EDTA and 1.00% citric acid, which is adjusted to a pH of 5.00, through the column at maximum flow rate. Discard the effluent wash.

(d) Removal of Na from Resin Column

The sodium, which was used to prepare the resin, can be removed by passing 250 ml of 0.5 N HCl through the resin at maximum flow rate. Discard the effluent wash.

(e) Elution of Radiostrontium

The radiostrontium is eluted from the resin with 60 ml of 6 N HNO_3 at a flow rate of 2± 0.5 ml/min (1.0 ± 0.25 ml cm^{-2} min^{-1}), Fig. 6. After evaporating the excess HNO_3, the radiostrontium is transferred to a suitable dish for counting the beta activity.

Separation from ^{40}K and ^{137}Cs

The above procedure provides excellent separation from ^{40}K and ^{137}Cs, two beta emitters commonly present in urine. By using ^{42}K tracer, the separation factor from potassium was found to be 7.2×10^4. A similar study with ^{137}Cs gave a separation factor of 1.7×10^4.

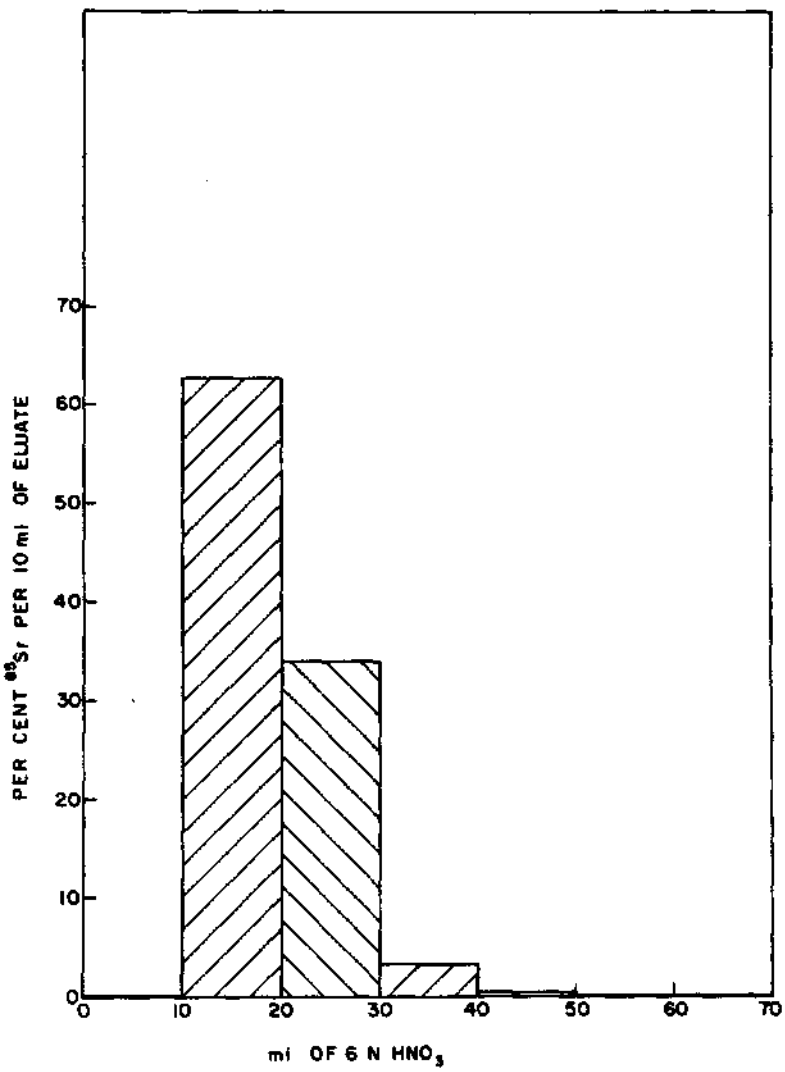

Fig. 6 Elution of ^{85}Sr from resin with 6 N HNO_3.

SUMMARY

The procedure described offers a way to utilize an individual urine sample for analysis for radiostrontium after removal of the actinide elements. Since the column operation is about 100 per cent efficient, only losses in alkaline earth precipitation need be considered. In routine operations, one person can tend 12 or more columns at one time. When only ^{90}Sr is present at low levels, it is possible to count the sample after growth of ^{90}Y to equilibrium thereby permitting greater accuracy with a longer counting time. The separation from ^{40}K and ^{137}Cs is excellent. The chief disadvantage is that both radiobarium and radium, members of the alkaline earth group with strontium, are likewise quantitatively recovered.

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RAPID DETERMINATION OF BERYLLIUM BY A DIRECT-READING ATOMIC ABSORPTION SPECTROPHOTOMETER

by

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ABSTRACT

A sensitive and specific analytical method for beryllium in air, wipe, biological, and packing material samples was developed. A single-beam atomic absorption spectrophotometer and high-temperature nitrous oxide - acetylene flame is used. The chemical technique for sensitivity enhancement and decontamination from radionuclides is described. Maximum time expenditure for an analysis is less than 30 minutes. Multiple samples may be run in the same time period. Sensitivity of the method is less than 0.04 parts per million of beryllium with a repeatability of approximately 2 percent of the amount present. Decontamination factors for uranium and transuranium elements were greater than 5000.

INTRODUCTION

As a result of its unique chemical and physical properties the use of beryllium in industry, especially in the nuclear and space industries, has been expanding rapidly in recent years. The fabrication and assembly of components made from beryllium produces a potential for exposure of workers to dust and fume of this toxic metal. Operations such as casting, machining, drilling, sawing, etching, grinding, heating, polishing, etc., may lead to exposures.

Since the recognition of beryllium as a serious occupational disease in the 1940's, engineering measures aimed at the reduction of personnel contact with beryllium materials have been effective in reducing the incidence of exposure. In 1949 the U.S. Atomic Energy Commission set the threshold limit value for beryllium at 2 ug/M^3 average air concentration per 40-hour workweek, with 25 ug/M^3 peak concentration for a single exposure, and 0.01 ug/M^3 for neighborhood concentrations. The low magnitude of these guidelines indicates the need for sensitive, accurate, and specific analytical methods for evaluating occupational exposure and as an aid in diagnosing beryllium poisoning. High efficiency methods for sampling beryllium dust and fume are readily available, but quantitative methods for determining low concentrations of

beryllium, especially in biologic materials, have tended to be complex and difficult. Substances present in atmospheric samples and biologic materials which interfere with colorimetric and fluorimetric methods necessitate separation and concentration procedures to eliminate their effects, and thus opportunities for losses are increased. The spectrographic method, while less disturbed by interferences, requires a trained operator of some experience. The use of an instrument which has sufficient dispersion to eliminate the imposition of lines from potential interferences involves considerable expense.

Hiser et al [1] have analyzed air samples for beryllium by a spectrophotometric method using p-nitrobenzene azoörcinol as colorimetric agent. Sensitivity is 0.5 micrograms of beryllium per milliliter. However, the method is applicable only to those samples containing a preponderance of beryllium and is subject to interference from many metals. Sill et al [2,3] reported a fluorimetric procedure for beryllium in air samples and biologic materials in which the fluorescent complex of morin with beryllium is measured. They report the astonishing sensitivity of 0.0002 microgram of beryllium per milliliter. A great number of steps and a highly developed technique is required to reduce the effects of a host of interfering substances. Keenan and Holst, [4] utilizing the "sustaining" a.c. arc, have reported their development of a spectrographic technique with a sensitivity of detection of 0.001 microgram of beryllium per analyzed aliquot of biological tissue, fluid, or atmospheric particulate sample.

While not attaining the level of sensitivity achieved by fluorimetric and spectrographic methods, the technique of atomic absorption spectrometry provides a very attractive and adequate method for a simple, rapid, sensitive and specific quantitative measurement of beryllium in atmospheric air samples and urine. With the nitrous oxide - acetylene flame the sensitivity, [5] defined as concentration for 1 percent absorption, is 0.03 microgram of beryllium per milliliter* with a detection limit of approximately 0.003 microgram of beryllium per milliliter* in aqueous solution. This sensitivity can be greatly increased with chemical concentration by solvent extraction.

Atomic absorption, in contrast to emission spectroscopy, is practically free of spectral or radiation interferences. For atomic absorption analysis the sample is reduced to the atomic state in a flame. Until recently beryllium was a member of the group of elements forming refractory oxides (e.g., aluminum, silicon, titanium) which could not be determined in the air - acetylene flame ordinarily used in this technique. In this flame dissociated beryllium atoms were immediately oxidized to a compound

* These values are for a double-beam instrument.

which would not dissociate further at the flame temperature. The oxygen-acetylene flame provided a high enough temperature to effect dissociation, but the burning velocity was too rapid for safe operation. Willis [6] solved this problem when he reported that the nitrous oxide and acetylene flame had a temperature almost as high as oxygen-acetylene with a burning velocity similar to air-acetylene.

INSTRUMENTATION

A Perkin-Elmer Model 290 atomic absorption spectrophotometer was used for this study. The Model 290 is a direct-reading a.c., single-beam instrument. The principles of its design have been described. [7,8] Working curves for this instrument are not needed since readout is linear in absorbence units. Ability to expand or contract the absorbence scale makes it possible to calibrate the scale to the concentration of metal in a standard solution and then read analyte concentration directly. The d.c. voltage level of the absorbence scale meter was monitored with a Hewlett-Packard Model 405-CR automatic d.c. digital voltmeter with additional damping provided by 300-mfd capacitance across the input terminals of the voltmeter. Zero and fullscale meter deflection on the Model 290 correspond to zero and 550 millivolts, respectively, on the voltmeter display.

Power to the instruments was regulated by a Sola constant voltage transformer. Since the acetylene flow rate to the Model 290 is preset and not adjustable, the fuel and oxidant flows are routed through a Perkin-Elmer Model 303 burner regulator. The Perkin-Elmer nitrous oxide burner head [9] was used with 3-inch slot length and 0.015-inch width. The hollow cathode lamp was manufactured by Atomic Spectral Lamps Pty. Limited; Melbourne, Australia.

REAGENTS

All reagents are analytical reagent grade. All solutions were prepared from distilled, deionized water.

Stock Beryllium Solution A solution containing 1000 micrograms of beryllium per milliliter is prepared by dissolving the appropriate weight of high purity beryllium metal* in a minimum amount of hydrochloric acid and diluting to volume. To prevent hydrolysis the pH of the solution should be 1 or less.

* New Brunswick Laboratories, New York. U.S. Atomic Energy Commission analyzed samples.

Beryllium Standard Solutions These solutions are prepared just before use by dilution from stock. Standard dilutions for smear analysis are prepared in synthetic smear paper solution which is 5 percent in hydrochloric acid.

Synthetic Smear Paper Solution This solution contains aluminum, calcium, nickel, magnesium, chromium, iron, and zinc in 5 percent hydrochloric acid in the average amounts that were found by atomic absorption on 20 smear samples taken at various locations in a beryllium working area.

Swipe and Air Filter Papers Whatman 41 filter paper is used for both air sampling and environmental swipes at Rocky Flats. Swipes are 1½ inches in diameter and air filters 47 mm. in diameter.

Smear Digestion Mixture A mixture used to effect solution of smear papers containing beryllium is made up of 30 percent concentrated nitric acid, 50 percent 27 N hydrofluoric acid, and 20 percent concentrated perchloric acid by volume. This mixture is stored in a polyethylene bottle.

Air Filter Digestion Mixture A solution composed, by volume, of 20 and 80 percent, respectively, of concentrated perchloric and nitric acids, is used to dissolve air filter papers.

EXPERIMENTAL PROCEDURES

Borosilicate glassware is used for all procedures. Each item is soaked in Alconox detergent immediately after use for 1 to 2 hours, rinsed with hot water, and then soaked in 6 N nitric acid overnight. The item is then rinsed in tap water followed by distilled water.

Filter Paper Smears

The smear paper is carefully folded into the bottom of a 15-ml. platinum crucible. Several drops of butyl acetate are placed on the filter paper and the paper ignited by the flame from an inverted Bunsen burner. The flame is allowed to quietly burn away a large portion of the organic material. Two to three milliliters of smear digestion mixture are added to the residue; the crucible is placed on an asbestos-covered hotplate at approximately 250° C. and the mixture is evaporated to dryness. The residue is brought into solution by warming with 2 ml. of 5 percent hydrochloric acid. The cooled 5 percent hydrochloric acid solution is then filtered into a 10-ml. volumetric flask and the flask brought to volume with repeated rinsings from the crucible with 5 percent hydrochloric acid.

Air Filters

The filter paper is placed in a 20- or 30-ml. Pyrex beaker and the paper wet down with 2 ml. of digestion mixture. The beaker is then placed on a hotplate at approximately 250° C. and the mixture evaporated until dense fumes of perchloric acid are evolved. The beaker is then removed and cooled. The contents are quantitatively rinsed into a 10-ml. volumetric flask and made up to volume with distilled water.

Urine

The methods used for urine are a modification of the procedure described by Keenan and Holst. (4)

An entire urine sample is transferred to a graduated cylinder and the volume recorded. (To prevent beryllium absorption on container walls, 10 ml. of concentrated nitric acid was added to the 500-ml. polyethylene sample bottles at the time of contribution.) The sample container is rinsed with a volume of concentrated nitric acid which is about 10 percent of the sample volume and the rinse added to the sample. The total volume of the mixture is recorded. The urine is then filtered, if necessary, and then either treated directly or wet-ashed.

Wet-Ashed Urine

A volume of urine mixture equivalent to 50 ml. of the original sample is transferred to a 250-ml. Erlenmeyer flask. Ten milliliters of nitric acid are added and the mixture is heated on a medium temperature hotplate (approximately 400° C.). A few drops of octyl alcohol are added if excessive foaming occurs. The mouth of the flask is covered with a ribbed watchglass and the sample evaporated just to dryness. After cooling, the evaporation is repeated with small quantities of nitric acid; the residue is baked briefly and then cooled between additions of acid until a light-colored or white ash remains. The ash is evaporated just to dryness three times with 10-ml. portions of 6 N hydrochloric acid to hydrolyze any pyrophosphate formed during ashing. The ash is then dissolved by warming with 10 ml. of 5 percent hydrochloric acid. The solution is quantitatively transferred to a 100-ml. beaker by rinsing down the walls of the flask with 25 ml. of distilled water.

Raw Urine

A volume of urine mixture equivalent to 50 ml. of original sample is transferred to a 100-ml. beaker and the sample treated according to the procedure outlined below under acetylacetone extraction.

Acetylacetone Extraction

For atomic absorption spectrometry it is unnecessary to isolate beryllium from the other substances present in atmospheric and biologic samples which would interfere with its determination by chemical or fluorimetric methods. However, for the sensitivity needed to detect the presence of submicrogram quantities, some type of concentration procedure is required. The neutral chelate resulting from reaction between beryllium ions and acetylacetone has been used extensively for quantitative solvent extraction of beryllium. (10)

The electrodes of a pH meter are immersed in the beaker containing the solution of urine ash or acidified raw urine. While stirring magnetically, ammonium hydroxide is added dropwise to adjust the pH of the solution to 1.5; 10 ml. of 10 percent disodium ethylenedinitrilotetraacetate (EDTA) and 0.5 ml. of acetylacetone are then added to the mixture and the pH raised to 7 by further addition of ammonia. The electrodes are then rinsed into the beaker and the beaker contents transferred quantitatively to a 125-ml. separatory funnel.

Four milliliters of methyl isobutyl ketone (MIBK) are added and the funnel thoroughly shaken for 5 minutes. After standing 5 to 10 minutes, the bulk of the lower layer is discarded, the last 10 to 15 ml. being passed, along with upper layer and interface emulsion, into a 30-ml. Fisher-Porter Ultramax centrifuge funnel. The funnel is centrifuged at 2,000 rpm for 5 minutes; the lower layer is carefully drawn off and discarded. The organic layer is then sprayed directly into the burner for measurement of its beryllium content. Quantitative recovery of the organic layer is not necessary since one is concerned only with the concentration of beryllium in it.

DETERMINATION OF BERYLLIUM

The instrument operating conditions for beryllium determination are given in Table 1. The zero end of the scale is set by aspirating a blank sample or low value standard solution while setting zero millivolts on the voltmeter with minimum concentration control. The high end of the scale is adjusted with the maximum control while aspirating a standard solution calibrated in any desired units (e.g., ppm, milligram percent, meq/liter). The hydrochloric acid solutions of ashed smear papers or air filters and the organic layer from acetylacetone extractions are aspirated directly into the flame. If the beryllium concentration in aqueous solution is less than 0.5 ppm, an aliquot of the sample is extracted with acetylacetone and MIBK. At the level of noise suppression used, approximately 15 seconds of aspiration time are required to obtain the millivolt reading on the voltmeter.

TABLE 1

SPECTROPHOTOMETER OPERATING PARAMETERS FOR BERYLLIUM ANALYSIS

Parameter	Aqueous Solution	Organic Solution
Wavelength (Å)	2348.6	2348.6
Select Element Setting	120.6	120.6
Slit	7A	7A
Lamp Current (ma)	15	15
Nitrous Oxide, flowmeter	9	8
Acetylene, flowmeter	Adjust to maximum absorption while aspirating standard	Adjust to maximum absorption while aspirating standard
Sample Uptake (ml/min.)	2.0 - 2.5	2.5
Nitrous Oxide Pressure (psi)	30	30
Acetylene Pressure (psi)	10	8

Beryllium in Smears and Air Filters

The amount of beryllium in an analyzed aliquot, X ug/ml, is obtained from the measured millivolt readings of standard $MV_{(s)}$, and sample $MV_{(x)}$ from the proportion

$$\frac{x}{\text{ug/ml (std)}} = \frac{MV_{(x)}}{MV_{(s)}}$$

Final calculation of total beryllium in the sample is determined by taking into account dilution factors and the size of the analyzed aliquot.

Beryllium in Raw and Ashed Urine

To one of two duplicate 50-ml. urine specimens is added 0.5 milliliter of a standard solution containing 10 milligrams of beryllium per liter.

The samples are then carried through the procedure for wet-ashing and extraction or the procedure for direct extraction of urine.

The concentration of beryllium in the urine, X mg/liter, is calculated from the measured millivolt readings $MV_{(1)}$ and $MV_{(2)}$ by the relation

$$\frac{x}{x + 0.1} = \frac{MV_{(1)}}{MV_{(2)}}$$

RECOVERY EXPERIMENTS

Beryllium Swipes

Table 2 shows the results from recovery experiments on 25 simulated smear samples which were produced by smearing a beryllium-free machine shop and adding from 10 to 100 micrograms of beryllium to each of the samples. From 94 to 103 percent of the added beryllium was recovered. Each value represents a group of five samples.

TABLE 2

RECOVERY OF BERYLLIUM ADDED TO SMEAR SAMPLES

Beryllium Added (µg)	Recovery	
	Micrograms	Percent
10	9.6 - 10	96 - 100
30	29.1 - 30.2	97 - 101
50	47.7 - 50.8	95 - 102
70	65.7 - 70	94 - 100
100	98.3 - 102.7	98 - 103

Raw and Ashed Urine

Beryllium was added to urine pooled from nonexposed personnel to obtain a beryllium content of 0.1 milligram per liter. Fifty-milliliter aliquots of this standard urine were treated as described in the sections covering ashing and extraction techniques.

Fifty-milliliter distilled water standards containing 0.0 and 0.1 milligrams of beryllium per liter were extracted in the same fashion as the urine samples and measured to determine the recovery efficiency from urine. These recoveries are shown in Table 3.

PRECISION

Air Filters

Nine Whatman 41 air filters were collected from air sample heads in a beryllium working area and treated as described in the section on digestion and solution of air filters. Results of four runs on each of the samples are given in Table 4. The determinations were made on consecutive days.

TABLE 3

PERCENT RECOVERY OF BERYLLIUM FROM RAW AND ASHED URINE

	Fresh Urine	Urine After 96 Hours	Urine After 168 Hours	Ashed Urine
	90.2	107.3	105.8	103.0
	93.5	104.2	101.1	97.6
	91.8	99.8	106.7	102.0
	92.7	102.5	100.8	99.4
Average	92.1	103.5	103.8	100.5
Standard Deviation	1.4	3.1	3.4	2.5

TABLE 4

BERYLLIUM ON AIR FILTERS (MICROGRAMS)

Run Number				Average	Standard Deviation	Coefficient of Variation (%)	
1	2	3	4				
94.5	100.7	100.0	98.2	98.4	2.8		2.8
124.3	115.6	116.3	117.1	118.3	4.0		3.4
117.1	114.2	--	115.0	115.4	1.2		1.0
121.5	116.4	119.3	118.2	118.8	2.1		1.8
100.0	100.0	100.0	100.3	100.1	0.1		0.1
117.4	114.5	115.3	115.8	115.7	1.2		1.0
10.2	10.0	10.5	10.3	10.3	0.1		1.0
71.6	78.4	77.1	74.4	75.4	3.0		4.0
45.0	48.0	47.6	46.7	46.8	1.3		2.8
						Mean	2.0

ACCURACY

Beryllium Swipe Samples

An experiment was carried out in which an attempt was made to ascertain the extent of agreement between the methods of emission spectroscopy and atomic absorption for analysis of beryllium in swipe samples. Approximately "duplicate" swipe samples of a contaminated area were obtained by single swipes of a limited area. Each swipe formed one leg of an X across the area. Agreement appears satisfactory when the limitations of the sampling procedure are considered. (See Table 5.)

TABLE 5

COMPARISON OF EMISSION AND ATOMIC ABSORPTION METHODS FOR DETERMINATION OF BERYLLIUM IN SWIPE SAMPLES

Specimen No.	Beryllium Content (micrograms)	
	Atomic Absorption Spectrometry	Emission Spectroscopy
S-184	7.7	< 10
S-185	5.0	< 10
S-186	120.0	100
S-187	100.0	90
S-188	10.0	20
S-189	57.0	80
S-190	4.2	< 10
S-191	1.9	< 10
S-192	6.0	< 10
S-193	7.9	< 10

Beryllium Air Filters

Replicate air filter specimens were obtained from a beryllium working area by utilizing a dual air head device in which the filters are mounted side by side. Table 6 shows that satisfactory agreement was obtained.

INTERFERENCES

Radioactive Contamination

Beryllium in environmental air filters and swipes which have become highly contaminated with radioactive materials must be efficiently isolated before analysis by atomic absorption. This is necessary because aspiration of radioactive solutions into

TABLE 6

COMPARISON OF EMISSION AND ATOMIC ABSORPTION METHODS FOR DETERMINATION OF BERYLLIUM IN AIR FILTERS

Specimen No.	Beryllium Content (micrograms)	
	Atomic Absorption Spectrometry	Emission Spectroscopy
A-117	6.5	9
A-118	22	30
A-119	77	80
A-120	70.5	70
A-121	22.5	10
A-122	109.7	90

the burner would contaminate the instrument and its environment and pose an exposure hazard to the operator. Modification[11] of the acetylacetone extraction procedure provided good removal of beryllium from actinides. The extent of decontamination from various materials was determined by ashing of the organic layer with nitric acid and measurement of the radioactivity of the nuclide present relative to the total activity added to the sample.

Decontamination

Two drops of phenol red indicator are added to the 5 percent hydrochloric acid solution of air or swipe sample ash contained in a 30-ml. Ultramax centrifuge funnel. The pH is adjusted to the endpoint with ammonia and then 2 milliliters of 2 percent disodium EDTA and 2 milliliters of 0.1 M sodium carbonate are added. Two milliliters of amyl acetate and 0.2 milliliters of acetylacetone are added and the mixture shaken thoroughly for 5 minutes. (It was determined that MIBK would extract U^{235} even with holdback chemicals present.)

The funnel was then centrifuged for 5 minutes at 2,000 rpm. The aqueous layer is then carefully discarded as radioactive waste. The organic layer is then washed with 10 milliliters of 0.1 M sodium carbonate and 10 milliliters of distilled water, the aqueous layers being discarded in turn. The average separation factors for several actinides are shown in Table 7. Each value represents the mean of four samples.

TABLE 7

SEPARATION FACTORS FOR BERYLLIUM EXTRACTION FROM VARIOUS ACTINIDES

Actinide	Separation Factor (Average)
U^{238}	5,848
Pu^{239}	5,423
Am^{241}	5,730

Ionization

The temperature reached with the nitrous oxide - acetylene flame is high enough to ionize a considerable portion of the atoms of many elements. Loss of ground state atoms to this effect, therefore, amounts to a form of interference since sensitivity would be diminished by this phenomenon. Fortunately, beryllium is exceptional[12] among refractory-forming elements in that no significant ionization of its atoms occurs in the nitrous oxide - acetylene flame.

Chemical

The loss of atoms which are bound in molecular combinations in the flame constitutes a form of interference often termed "chemical." Since beryllium is a member of the alkaline earth group of elements, several of the traditional chemical interferences were examined to determine their effect on beryllium absorption in the nitrous oxide - acetylene flame. Figure 1 shows absorptions for solutions containing 4 ppm of beryllium and various concentrations of aluminum, phosphorus, and silica. The presence of phosphorus as phosphoric acid had little effect on beryllium absorption except at concentrations above 100 ppm. The enhancement of absorption above this concentration was 3 to 4 percent. Aluminum and silica showed interference but the effect did not become serious until concentrations of these elements approached 1,000 ppm. Concentrations of sulfate (as sulfuric acid) up to 80,000 ppm showed no effect on beryllium absorption.

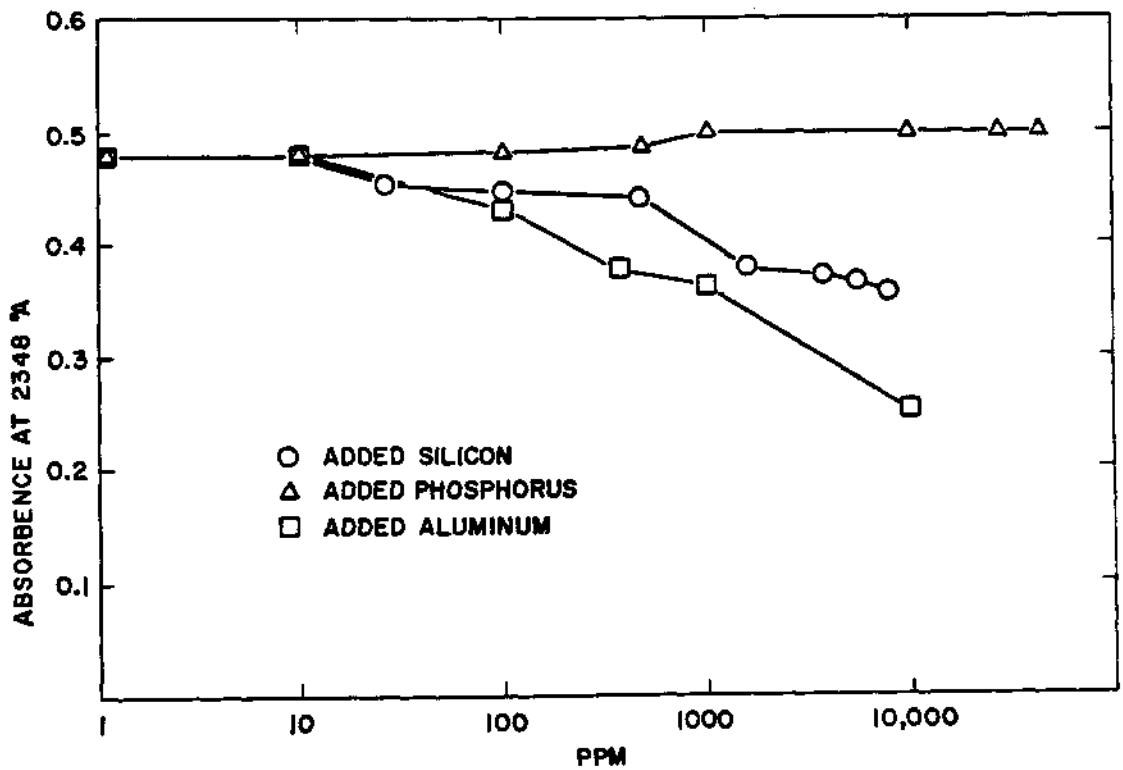

Fig. 1 EFFECT OF ADDITION OF ALUMINUM, PHOSPHORUS, AND SILICON ON THE ABSORBENCE OF A 4-PPM BERYLLIUM SOLUTION.

SUMMARY

A rapid and specific atomic absorption spectrophotometric method for the analysis of beryllium in urine and in environmental swipes

and air samples collected on filter paper has been presented. Beryllium is determined directly in swipe and air filter ash solutions without need for chemical separations. Solvent extraction procedures for separation and concentration of beryllium from radioactive contaminants and from urine have been described. The approximate sensitivity and detection limit for beryllium in aqueous and methyl isobutyl ketone solutions, respectively, are 0.04 ppm and 0.01 ppm. A beryllium content of 2 micrograms of beryllium per liter of urine can be detected. The method has the rapidity and sensitivity needed for advantageous use as a rapid monitoring procedure and could easily be adapted to determination of beryllium in tissue and other biologic materials.

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URANIUM LEVELS IN HUMAN DIET AND BIOLOGICAL MATERIALS

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Abstract

There has been increasing interest in accurately documenting the levels of natural radioisotopes in man, his diet and environment. The tri-city diet program, for the study of strontium-90 levels, presents an opportunity to measure the uranium content of foods, as monthly total diet samples are available from New York City, Chicago, and San Francisco. In addition to the diet, materials such as air, bone, lung, and water samples were analyzed from the New York area.

The data indicate uniform intake of uranium at the three sites examined. The values found were 1.3, 1.4, and 1.3 micrograms of uranium per day for New York City, Chicago, and San Francisco, respectively.

The urinary excretion levels for non-exposed individuals are reviewed and new data from the Chicago area indicate a range of values within the previously reported New York data of from 0.03 to 0.3 microgram of uranium per liter.

It has been previously reported in the literature[1][2][3] that trace quantities of uranium exist in man and his environment. The ICRP

currently accepts the estimate of Davis[4] that the daily intake of uranium is 2 micrograms per day. Klemont[5] cites Dudley[6] as having estimated that the general population has a daily intake of 1 microgram of uranium. The tri-city diet studies established for documenting strontium-90 levels at New York, Chicago, and San Francisco, were used to experimentally establish uranium intake levels.

Five grams of the dry ashed food material is weighed and transferred to a 250-ml beaker for analysis. A known aliquot of uranium-232 is added as tracer and residual organic material is destroyed by evaporation with nitric acid and hydrogen peroxide. Hydrochloric acid is added and the solution evaporated to dryness. The salts are dissolved in hydrochloric acid and passed through a conventional ion exchange column of pretreated Dowex 1 X-4 (100-200) mesh. The column is washed with hydrochloric acid and the uranium, along with iron, is eluted with hydrochloric acid. The eluate is evaporated to dryness, and the residue dissolved in a sulfuric acid solution and electrolyzed in a mercury cathode cell. The resulting solution is evaporated to dryness with dilute nitric acid. Triplicate 0.1-ml aliquots of the solution are dried and flamed on a platinum dish, fused with 100 milligrams of sodium fluoride, and the fluorescence measured by a HASL fluorimeter. An additional 0.1-ml aliquot, from the 5-ml volumetric flask, is pipetted on a platinum disc, dried, alpha phosphor added, and counted for tracer, uranium-232 recovery.

The method described is capable of determining 0.005 microgram of uranium per sample. Each analysis for the uranium content of food was preceded and followed by a blank determination using the same quality of reagents

outlined in the procedure. This blank varied slightly but averaged 0.007 microgram of uranium which is the same level of uranium found in one gram of reagent grade calcium phosphate.

The overall recovery indicated by the tracer technique varied in different food matrices but generally was above 80%. Several samples previously analyzed at HASL were shipped to Union Carbide Corporation for neutron activation analysis and a comparison of the results is shown in Table 1. The two methods are in general good agreement and the distribution seems random.

Table 1

COMPARISON OF NEUTRON ACTIVATION ANALYSIS AND FLUORIMETRIC METHODS FOR URANIUM DETERMINATION

Food	microgram Uranium/gram of ash	
	Neutron Activation Analysis	Fluorimetric
Bakery Products	.062	.066
" "	.074	.077
" "	.040	.070
Whole Grain Products	.052	.056
" " "	.043	.057
" " "	.045	.059
Fresh Vegetables	.080	.076
" "	.078	.080
" "	.220	.136
Blended Chicken Bone	.041	.050
Fresh Vegetables	.086	.076

Tables 2, 3, and 4 show the data obtained from the diet samples from New York, Chicago, and San Francisco, respectively. Foods and their annual consumption values are taken from the USDA's 1955 report. The values were grouped in 19 categories by Rivera and Harley[7]. These authors also reported the experimentally-determined figures for percent ash that

Table 2

ANNUAL URANIUM INTAKE

New York City

Category	Kg/yr	μg U / g ash	% ash	μg U/yr
Bakery Products	37	0.08	2.23 ± 0.11	66
Whole Grain Products	11	0.06	2.47 ± 0.05	16
Eggs	16	0.02	1.07 ± 0.03	3.4
Fresh Vegetables	43	0.08	0.73 ± 0.02	25
Root Vegerables	17	0.09	0.79 ± 0.03	12
Milk	221	0.01	0.71 ± 0.04	16
Poultry	17	0.02	0.82 ± 0.04	2.7
Fresh Fish	8	0.03	1.42 ± 0.10	3.4
Flour	43	0.11	0.49 ± 0.04	23
Macaroni	3	0.06	0.69 ± 0.04	1.2
Rice	3	0.32	0.60 ± 0.02	5.8
Meat	73	0.12	0.90 ± 0.02	79
Shellfish	1	0.60	1.59 ± 0.56	9.5
Dried Beans	3	0.04	3.78 ± 0.06	4.5
Fresh Fruit	68	0.18	0.62 ± 0.01	76
Potatoes	45	0.22	1.12 ± 0.04	111
Canned Fruit	26	0.05	0.31 ± 0.04	4.2
Fruit Juices	19	0.01	0.59 ± 0.03	1.1
Canned Vegetables	20	0.02	0.99 ± 0.01	4.0
SUM	674			463.8

1.3 μg U/day

are used in these tables. The data indicate that the daily indicate of uranium is constant at the three sites studied.

New York - 1.3 micrograms Uranium/day

Chicago - 1.4 micrograms Uranium/day

San Francisco - 1.3 micrograms Uranium/day

This is so in spite of variations of the uranium content of certain foods at different locations. For example, the yearly intake of uranium

Table 3

ANNUAL URANIUM INTAKE

Chicago

Category	Kg/yr	µg U/g ash	% ash	µg U/yr
Bakery Products	37	0.07	2.23 ± 0.11	58
Whole Grain Products	11	0.06	2.47 ± 0.05	16
Eggs	16	0.02	1.07 ± 0.03	3.4
Fresh Vegetables	43	0.08	0.73 ± 0.02	25
Root Vegetables	17	0.07	0.79 ± 0.03	9.4
Milk	221	0.02	0.71 ± 0.04	31
Poultry	17	0.06	0.82 ± 0.04	8.4
Fresh Fish	8	0.06	1.42 ± 0.10	6.8
Flour	43	0.07	0.49 ± 0.04	14
Macaroni	3	0.07	0.69 ± 0.04	1.4
Rice	3	0.07	0.60 ± 0.02	18
Meat	73	0.16	0.90 ± 0.02	105
Shellfish	1	1.80	1.59 ± 0.56	29
Dried Beans	3	0.10	3.78 ± 0.06	11
Fresh Fruit	68	0.18	0.62 ± 0.01	76
Potatoes	45	0.20	1.12 ± 0.04	101
Canned Fruit	26	0.08	0.31 ± 0.04	6.4
Fruit Juices	19	0.01	0.59 ± 0.03	1.1
Canned Vegetables	20	0.01	0.99 ± 0.01	2.0
SUM	674			522.9

1.4 µg U/day

from shellfish in New York is less than half of that in Chicago and San Francisco. Potatoes, meat, fresh fish and bakery products contribute more than 70 percent to the annual uranium intake. Milk in the San Francisco area is a major contributor of uranium but it is less so in Chicago and New York. Table 5 compares the annual intake of uranium for the three sites. In spite of these individual differences the total daily intake of uranium is strikingly similar at the sites tested.

Table 4

ANNUAL URANIUM INTAKE

San Francisco

Category	Kg/yr	µg U / % ash	% ash	µg U/yr
Bakery Products	37	0.07	2.23 ± 0.11	58
Whole Grain Products	11	0.06	2.47 ± 0.05	16
Eggs	16	0.02	1.07 ± 0.03	3.4
Fresh Vegetables	43	0.14	0.73 ± 0.02	44
Root Vegetables	17	0.09	0.79 ± 0.03	12
Milk	221	0.09	0.71 ± 0.04	62
Poultry	17	0.04	0.82 ± 0.04	5.6
Fresh Fish	8	0.04	1.42 ± 0.10	4.5
Flour	43	0.04	0.49 ± 0.04	8.4
Macaroni	3	0.09	0.69 ± 0.04	1.9
Rice	3	0.24	0.60 ± 0.02	4.3
Meat	73	0.07	0.90 ± 0.02	46
Shellfish	1	1.96	1.59 ± 0.56	31
Dried Beans	3	0.10	3.78 ± 0.06	11
Fresh Fruit	68	0.10	0.62 ± 0.01	42
Potatoes	45	0.20	1.12 ± 0.04	101
Canned Fruit	26	0.05	0.31 ± 0.04	4.0
Fruit Juices	19	0.03	0.59 ± 0.03	3.4
Canned Vegetables	20	0.02	0.99 ± 0.01	4.0
SUM	674			462.5

1.3 µg U/day

Recent data from Russian[8] publications have documented intake and excretion levels of uranium from two sites which differed in intake levels by a factor of more than 25. In these studies the water levels were the contributing factor since the population was consuming spring water with levels of uranium of 200 and 7 micrograms per liter, respectively. Vegetables and meat were measured at each of these sites but their contribution of uranium to the total diet was insignificant. Table 6 presents their data and

Table 5

COMPARISON OF ANNUAL URANIUM INTAKE

Category	micrograms of Uranium/year New York	Chicago	San Francisco
Bakery Products	66	58	58
Whole Grain Products	16	16	16
Eggs	3.4	3.4	3.4
Fresh Vegetables	25	25	44
Root Vegetables	12	9.4	12
Milk	16	31	62
Poultry	2.7	8.4	5.6
Fresh Fish	3.4	6.8	4.5
Flour	23	14	8.4
Macaroni	1.2	1.4	1.9
Rice	5.8	18	4.3
Meat	79	104	46
Shellfish	9.5	29	31
Dried Beans	4.5	11	11
Fresh Fruit	76	76	42
Potatoes	111	101	101
Canned Fruit	4.2	6.4	4.0
Fruit Juices	1.1	1.1	3.4
Canned Vegetables	4.0	2.0	4.0
SUM	463.8	522.9	462.5
	1.3 µg U/day	1.4 µg U/day	1.3 µg U/day

it is interesting to note that most of the uranium from both sites was eliminated in the feces. In both locations the total uranium eliminated was approximately 10 percent of the daily intake. At the site of high level uranium intake, 304 micrograms per day, 1% was eliminated in the urine and at the other site with an intake of 12.6 micrograms of uranium per day only 0.05% was excreted in the urine. If we use these figures to calculate the urinary excretion level for the three U. S. sites studied we should find

from .07 to 0.1 microgram of uranium eliminated per day in the urine, based on the intake values found of 1.3 micrograms of uranium per day. Using the average excretion value of 1500 ml of urine per day, the concentration of uranium per liter for the non-exposed population should range from 0.04

Table 6

MEAN AMOUNT OF URANIUM INTAKE AND ELIMINATED BY THE ORGANISM IN THE TWO SETTLEMENTS

	Uranium Intake (micrograms/day)				Uranium Elimination (micrograms/day)		
Settlement	With Water	With Plant Produce	With Animal Produce	Total	With Urine	With Feces	Total
Under Investigation	300	4.5	> .01	304	3.2	40	43
Control	12	0.6	> .001	12.6	0.05	1.2	1.25

to 0.08 microgram of uranium per liter of urine. Several publications[9][10][11] have reported excretion levels of uranium ranging from 0.012 to 26 micrograms of uranium per liter of urine.

A recent article[9] surveying the pre-employment urinary uranium levels of 1081 employees reports an average of 5 micrograms per liter of urine with a range of 5 to 7 micrograms. Using the calculated values of 0.05 to 1.0 percent excretion in the urine, an intake of 250 to 500 micrograms of uranium per day, must be assumed. These values are almost as much as our studies have found for annual intake. Table 7 reports the levels of uranium found in 11 subjects from the Chicago area. Each sample contained more than five liters of urine and the average concentration found was 0.09 microgram of uranium per liter of urine with a range of 0.04 to 0.18 within the range found in earlier work by the authors[1] in the New York City area of 0.03 to 0.3.

Table 7

URANIUM IN NON-EXPOSED PERSONNEL

(Chicago Area)

Name	microgram Uranium per Liter
O.H.	0.081
H.V.	0.043
D.W.	0.054
H.W.	0.076
R.S.	0.064
R.B.	0.082
B.T.	0.162
R.W.	0.083
D.S.	0.060
D.T.	0.054
B.M.	0.182
Average	0.09
Range	0.04 - 0.18

The concentration of uranium in tap water was inventigated in the New York area. Table 8 gives the sampling data and the levels of uranium found. These values are insignificant as far as total consumption is concerned and were not considered in our calculations. Deionized water from the laboratory contains a factor of ten less uranium per liter than New York City tap water.

Table 9 presents data obtained from the analyses of bone samples from the New York area. It seems that the uranium levels in bone are rather uniformily distributed throughout the skeleton with an average concentration of 0.20 microgram of uranium per gram of ash.

Some lung tissue available from the New York area was analyzed for uranium. Table 10 presents the data. The average concentration of uranium was one(1) nanogram per gram of wet tissue with a range of from 0.7 to 3 nanograms.

Table 8

URANIUM IN TAP WATER AND DEIONIZED WATER

Sample #	Collection Date		microgram Uranium per liter
Tap Water - New York City			
A8	10-22-63		.025
			.032
A55	11-19-63		.039
			.040
B44	2-18-64		.029
			.041
B62	6-11-64		.033
			.035
B67	7-14-64		.024
			.024
		Mean:	0.032 ± 0.2%
		Range:	0.024 - 0.040
Deionized Water			
A7	10-22-63		.0034
A54	11-19-63		.0024
B43	2-18-64		.0027
B61	6-11-64		.0018
B66	7-14-64		.0024
		Mean:	0.002 ± 0.2%
		Range:	0.0018 - 0.0034

Table 9

URANIUM IN HUMAN BONE

HASL#	Identification	microgram Uranium/gram ash
B1673	Hands and Feet	.027 ± .003
B1674	Skull	.026 ± .008
B1675	Vertebrae	.026 ± .003
B1676	Ribs	.023 ± .005
B1677	Long Bone (Shafts)	.011 ± .001
B1678	Long Bone (Ends)	.014 ± .001
B1689	Miscellaneous Bones (Pelvis, Clavacle Stem, Patella, Scapula)	.027 ± .011
B1708	$Ca_3(PO_4)_2$	.013 ± .001
B1710	Split of B1678	.013 ± .001
B1690	Hands and Feet	.011 ± .001

Several air samples consisting of more than 1200 m^3 of air, representing New York City air supply during January and February 1965, were analyzed for uranium. The average concentration was 0.4 nanogram per cubic meter.

Summary

Diet, urine, bone, lung, water, and air have been analyzed for uranium. The most complete picture is in the New York area. Diet figures available from New York, Chicago, and San Francisco are uniformily about 1.3 micrograms a day. This figure would infer a level of uranium excreted in the urine of approximately 0.08 microgram per liter. Recent data from the Chicago area show an excretion level of 0.09 microgram per liter. Bone and lung show low levels of uranium, and in bones the uranium is uniformily distributed throughout the skeleton.

Table 10

URANIUM IN HUMAN LUNG

HASL#	microgram Uranium/sample	Wet Weight (grams)	microgram Uranium / gram wet lung
X0911	0.11	97	0.001
X0912	0.10	138	0.0007
X0913	0.14	136	0.001
X0914	0.14	128	0.001
X0915	0.40	116	0.003
X0916	0.09	100	0.0009
X0917	0.14	99	0.001
X0918	0.07	74	0.0009
X0919	0.20	126	0.002
X0920	0.11	88	0.001
X0921	0.15	127	0.001

Average 0.001

Range 0.0007 - 0.003

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UPTAKE OF RADIOACTIVITY BY VEGETATION: A FOLLOW-UP STUDY ✱

by

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Abstract

To further evaluate the effect of time on the uptake of radioactivity due to soil contamination, a follow-up study was initiated. The same sub-plots were used. No additional radionuclides were added to the soil- and foliar-contaminated plots used the year before. In the follow-up study only corn, lettuce and tomatoes were planted. Lettuce and tomatoes were processed and analyzed as before, corn yielded four fractions: kernels, cobs, husks and stalks. Corn stalks were analyzed in this study to evaluate their uptake since stalks as well as the ears are used as cattle fodder.

In addition, a small section of each of the control plots (40' x 52') was roped off and before planting "spiked" with 0.5mCi each of Zn-65, Cs-137, Mn-54 and RuRh-106. The first three nuclides were used to confirm and further study the predominant species appearing in soil-contaminated crops in the first study; RuRh-106, to further elucidate the 0.51 Mev region. The same crops were planted in these sub-plots as in the others.

In general, the results follow the anticipated pattern. Levels of activity in the crops, due to uptake, decreased with time; with crops from the previously foliar-contaminated plots showing a significantly greater decrease. Again, crops grown on the non-fertile plots showed greater uptake than those grown on the fertile plots. However, several interesting deviations from the expected patterns have been noted throughout the experiment.

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Introduction

The second phase of a two year study to determine some of the parameters of uptake of radioactivity by growing vegetables is described herein.

The results of the first phase have been reported elsewhere[1]; however, a brief description of the original experimental design is in order.

Two half-acre plots about a half mile apart were used. One plot (non-fertile) had not been fertilized, cultivated, or used for crop growth within the past few years. The other plot (fertile) has been fertilized continuously with cow manure and lime and used for growing hay and fodder corn. Each plot was further divided into three sub-plots separated by large furrows. Five crops were planted on each sub-plot.

To determine the extent of uptake due to contamination of the soil prior to seeding, one sub-plot from each half-acre plot was sprayed with approximately 0.5 mc of each of 10 gamma emitting radionuclides chosen as typical of fallout and activation product nuclides.

The second sub-plot of each half-acre plot was sprayed exactly as the first, but not until the crops planted were in an advanced stage of growth. This maximized foliar uptake over that due to root absorption from soil. The remaining two sub-plots were not contaminated and were used as controls.

Second Phase - Experimental Design

In this second phase, two studies were conducted simultaneously: (a) Follow-up study: to evaluate the effect of time on radionuclide uptake due to previous soil contamination; and (b) Recontamination study: to confirm and further study the predominant nuclides that appeared in the soil-contaminated crops in the first phase study.

Follow-up Study

Smaller sections (40'x52') of the same sub-plots were used. No additional radionuclides were added either to the soil or foliar contaminated plots used the year before and only corn, lettuce and tomatoes were planted. Lettuce and tomatoes were processed as before, and corn yielded four fractions: kernels, cobs, husks and stalks; corn stalks, to evaluate their uptake, since they are used for cattle fodder. A 7 x 7 analytical matrix (Sb-125, RuRh-106, Cs-137, ZrNb-95, Mn-54, Zn-65 and K-40) was used to quantitate the results.

Recontamination Study

A similar section of each of the control plots was roped off and, before seeding, "spiked" with 0.5mCi each of Zn-65, Cs-137, Mn-54 and RuRh-106. The same crops were planted in these sub-plots as in the others.

Spraying Procedure

Since those portions of the control plots to be contaminated were too small to be sprayed using the tractor as before[1], hand spraying was indicated. Practice runs, using tap water, indicated the feasibility of using a 2-gallon sprinkling pail. The sprinkling pail was filled from a plastic-lined 55-gallon drum containing a dilute mixture of the four radionuclides. After the drum was emptied, it was filled again with tap water and the wash solution sprayed on the plots as before. Prior to spraying each plot area, six 7"x9" glass fiber filter webs, each backed by a 7-1/2" x 9-1/2" piece of absorbent paper, and six 7"x9" absorbent blotters, each backed by a 7-1/2"x9-1/2" piece of absorbent blotter paper were arranged on the plot as shown in Fig. 1. Subsequent gamma analyses of these specific area papers would indicate the concentration/sq. ft. of each radionuclide applied to the plot.

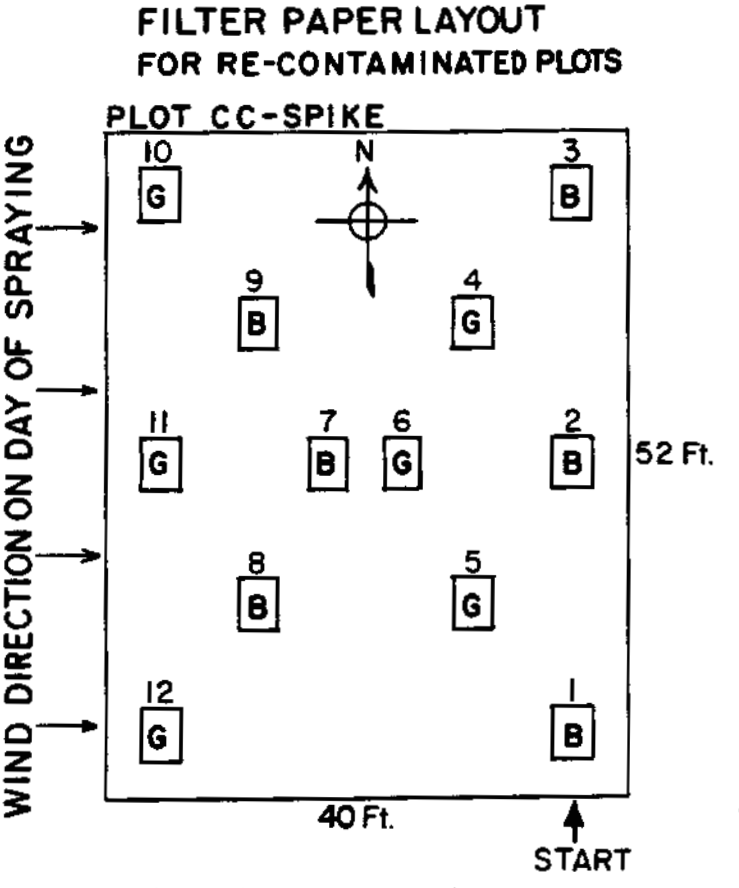

Fig. 1 Arrangement of filter and absorbent papers

All the filter pads and backing papers were removed from the plots and placed in individual plastic bags before the plots were sprayed with wash solution.

In addition, representative soil samples (16 from each plot) were taken, following the method of Greweling and Peach[2].

Sample Collection and Preparation

During the summer, the plots were continually tended. Due to the prevailing drought condition, the plants were hand-watered with water hauled or pumped from a nearby creek. The drought was temporarily relieved by a severe wind and rain storm which inflicted heavy damage to the growing crops. Over an inch of rain, accompanied by high winds and hail, fell in less than one-half hour.

The estimated damage to the crops was:

Lettuce	- 90 per cent lost - had to be replanted
Tomatoes	- 30 per cent lost
Corn	- 10 per cent lost

The crops were harvested daily at the end of the growing season, and prepared and analyzed as before.

Results and Discussion

Since this was a two-part study, the results of each part will be discussed separately.

Follow-up Study

In this phase, the effect of time on soil uptake was evaluated.

Lettuce

The averaged results for lettuce are presented in Table I. With the exception of ZrNb-95, and possibly Sb-125, uptake of all radionuclides is demonstrated. Soil uptake is fairly constant with apparently little difference between the previously-contaminated soil and foliar plots; an exception is noted for Zn-65 in the nonfertile plots, the previously foliar-contaminated plots showing about twice as much uptake as the soil plots. Soil fertilization, again, appears to be effective in reducing uptake of Zn-65 and RuRh-106, but remains unclear for the other radionuclides. High concentrations of RuRh-106 are seen in the nonfertile control plots. These are higher than any RuRh-106 activity from the contaminated plots and are due probably to the severe rain and windstorm described above.

In order to make a meaningful comparison of these with those obtained last year (1964), the averaged data from Table I and the 1964 lettuce results[1] were again averaged, by plot, to give a single annual

Table I

Uptake by Lettuce (pCi/kg)

Codes:
- P = Plot Type
- FC = Fertile Control Plot
- FF = Fertile Foliar Contaminated (1964) Plot
- FS = Fertile Soil Contaminated (1964) Plot
- NFC = Non-Fertile Control Plot
- NFF = Non-Fertile Foliar Contaminated (1964) Plot
- NFS = Non-Fertile Soil Contaminated (1964) Plot
- HD = Harvest Date
- * = Below Analytical Sensitivity
- NH = No Harvest or No Sample Collected
- ± = Error Value at 95% C. L.

	Zn-65					Cs-137				
P / HD	7/15-31	8/1-15	8/16-31	9/1-15	9/16-30	7/15-31	8/1-15	8/16-31	9/1-15	9/16-30
FC	*	*	*	*	*	*	25± 24	*	*	16± 12
FF	504± 82	420±94	347± 61	181± 88	313± 48	35± 29	83± 40	40± 24	*	40± 17
FS	490±195	268±68	233± 62	325±123	176± 52	107± 84	51± 24	40± 23	*	37± 23
NFC	NH	NH	NH	*	*	NH	NH	NH	*	*
NFF	NH	NH	1570±160	911±111	995±107	NH	NH	79± 33	34± 25	80± 25
NFS	NH	NH	507± 92	573± 84	486± 49	NH	NH	60± 34	33± 25	57± 16

	Mn-54					RuRh-106				
FC	*	*	*	*	*	60± 58	*	*	*	*
FF	38± 27	54±35	*	*	26± 22	240±147	435±191	156±117	*	108± 81
FS	*	*	*	*	*	460±402	222±136	*	128± 69	159±113
NFC	NH	NH	NH	*	*	NH	NH	NH	240±154	557±192
NFF	NH	NH	73± 35	52± 28	85± 27	NH	NH	415±193	217±127	434±144
NFS	NH	NH	58± 35	49± 28	41± 16	NH	NH	345±165		263± 79

	Sb-125					ZrNb-95				
FC	*	*	32± 29	*	22± 20	20± 11	*	*	*	20± 14
FF	67± 48	*	*	193± 69	*	*	*	*	*	*
FS	*	*	*	*	*	*	*	*	*	*
NFC	NH	NH	NH	*	*	NH	NH	NH	*	*
NFF	NH	NH	*	*	78± 42	NH	NH	*	*	*
NFS	NH	NH	52± 49	*	45± 23	NH	NH	*	*	*

average for each nuclide according to plot. This is shown in Table II. "No harvest" periods were not averaged, and an arbitrary value of 10 pCi/kg was assigned to all "below sensitivity" values for averaging purposes. Comparison for ZrNb-95 was not made since all results for Impact 65 were below sensitivity.

Table II

Effect of Time on Uptake by Lettuce

NOTE: "1964" indicates the average radionuclide concentration in lettuce grown on plots contaminated that year.

"1965" indicates the average radionuclide concentration in lettuce grown on plots contaminated the year before.

"Ratio 64:65" indicates the fraction of average radionuclide concentration seen in 1965 as compared with 1964.

"Expected Decay Ratio" is the fraction expected if the only process operating was radioactive decay.

FOLIAR CONTAMINATED

	Fertile Plots				Nonfertile Plots			
Nuclide	1964 (pCi/kg)	1965 (pCi/kg)	Ratio 64:65	Expected Decay Ratio	1964 (pCi/kg)	1965 (pCi/kg)	Ratio 64:65	Expected Decay Ratio
Zn-65	11633	353	1:0.03	1:0.36	4828	1159	1:0.24	1:0.36
Cs-137	9684	42	1:0.004	1:0.98	1908	64	1:0.03	1:0.98
Mn-54	9910	24	1:0.002	1:0.42	838	70	1:0.08	1:0.42
Sb-125	5729	58	1:0.01	1:0.77	606	33	1:0.05	1:0.77
RuRh-106	11134	190	1:0.02	1:0.5	1139	363	1:0.31	1:0.50

SOIL CONTAMINATED

	Fertile Plots				Nonfertile Plots			
Nuclide	1964 (pCi/kg)	1965 (pCi/kg)	Ratio 64:65	Expected Decay Ratio	1964 (pCi/kg)	1965 (pCi/kg)	Ratio 64:65	Expected Decay Ratio
Zn-65	788	298	1:0.38	1:0.36	1060	522	1:0.49	1:0.36
Cs-137	83	49	1:0.60	1:0.98	129	50	1:0.39	1:0.98
Mn-54	46	13	1:0.28	1:0.42	89	49	1:0.55	1:0.42
RuRh-106	166	172	1:1.05	1:0.50	239	275	1:1.15	1:0.50
Sb-125	85	10	1:0.12	1:0.77	27	36	1:1.33	1:0.77

Soil fertilization is apparently effective in reducing uptake by lettuce grown on plots contaminated the year before. The fraction of average radionuclide concentration seen in 1965 as compared with 1964, i.e., ratio 64:65, is, with one exception, always higher in the nonfertile plots. The exception, Cs-137 in the soil contaminated fertile plot, probably occurs because small numbers are being compared. Certain radionuclides, such as Cs-137, ZrNb-95 and Sb-125, are apparently rapidly fixed by this type of soil and are unavailable to the plant.

Antimony and zirconium have very limited solubility in soil and would not be available to the plant[3]. Cesium, particularly micro- or carrier-free amounts, is strongly fixed on clay minerals which accounts for its lower concentration in plants than in soils[4,5]. The removal of Cs-137 from soils and its

availability to plants is retarded by the strong absorptive forces in soil[6]. An increase in the amount of available potassium would tend to reduce these retentive forces thus making cesium more available to plants[7]. However, Auerbach and Crossley[8] found that in uptake of Cs-137 by corn, Cs-137 concentrations were not directly related to potassium concentration.

Addition of large amounts of labile Ca^{+2} to the soil would tend to free or solubilize less than 10 per cent of the added carrier-free Cs-137 and plants grown thereon would be expected to take up minimal amounts of the nuclide[5]. However, when organic matter is responsible for a large fraction of the total exchange capacity of the soil, the adsorption and consequent fixation of Cs-137 on the clay minerals are much reduced[9].

The relatively low solubility and/or unavailability of these nuclides is demonstrated by the comparatively low average specific activity from plots typical of soil contamination. For them, the important mode of uptake is foliar deposition. The other radionuclides, i.e., Zn-65 and RuRh-106, indicate the availability from the soil, although foliar deposition is still the major mode of uptake.

Uptake of Zn-65 and RuRh-106 is strongly influenced by soil pH, since they are most soluble, and therefore available to the plants under acid conditions[3,5]. As the pH of the soil increases, they will precipitate as hydroxides and would no longer be available. Complex ions such as nitrosylruthenium (RuNO) may be formed, and may result as the metal being present uncharged or as an anion and as such, would tend to be soluble and available[5].

Manganese would be expected to behave similarly to zinc and ruthenium. While non-fertile plots indicated somewhat greater uptake than fertile plots, reflecting the increased pH due to fertilization; overall, the uptake of Mn-54 was barely detectable.

If radioactive decay was the only effective uptake-reducing process, then it would be expected that the ratio 64:65 would always be equal to or, more often, less than the Expected Decay Ratio, since uptake from the soil is usually slow and selective. This is the case in the foliar plots.

However, it should be emphasized that only an unknown fraction of the original activity sprayed on the foliar plots was available to the soil. The only valid relationships that can be established with foliar plots are: (1) fertile plots: 3 per cent or less of the initial radionuclide concentration was observed after one year, and (2) non-fertile plots: as much as 31 per cent of the initial concentration was observed after one year. In all cases, the fraction of initial concentration observed one year later was always higher in the nonfertile plots.

The soil contaminated plots permit a direct comparison. In the non-fertile plots, Ratio 64:65 is higher than the Expected Decay

Ratio for Mn-54 and Sb-125. However, we are again comparing small numbers and the validity of such a relationship is doubtful. The fraction of Zn-65 and RuRh-106 concentration, observed one year later, is greater in both fertile and nonfertile plots than that expected, due to radioactive decay alone. For RuRh-106, it is greater by a factor of 2, while Zn-65 agrees closely with the expected fraction due to radioactive decay, at least in the fertile plot. This suggests some process in the soil influencing the biological half-life. We cannot speculate on what this may be; further study is required to determine possible mechanisms.

Tomatoes

Uptake by tomatoes for Impact 65, is shown in Table III. As before, Zn-65 is predominant; lesser concentrations of Cs-137 were also observed. Except for minimal amounts in the nonfertile plots, Mn-54 was not detectable. None of the other radionuclides were observed. The nonfertile plots again indicated higher concentrations than the fertile plots.

A single annual average for each nuclide, according to plot taken from the data in Table III and the 1964 tomato results is presented in Table IV. Only Zn-65 and Cs-137 are evaluated.

Table III

Uptake by Tomatoes (pCi/kg)

Code: As in Table I

	Zn-65			Cs-137			Mn-54		
P/HD	8/16-31	9/1-15	9/16-30	8/15-31	9/1-15	9/16-30	8/16-31	9/1-15	9/16-30
FC	*	*	91±11	23±12	*	14±4	*	*	*
FF	316±59	388±37	274±15	28±23	36±12	43±6	*	*	*
FS	309±54	352±55	265±15	33±22	*	28±5	*	*	*
NFC	115±25	*	11± 8	16±11	10± 9	8±4	*	*	*
NFF	NH	655±93	652±27	NH	66±33	71±7	NH	*	8±7
NFS	371±91	418±35	439±20	35±34	39±13	51±6	*	16±12	12±6
	RuRh-106			Sb-125			ZrNb-95		
FC	*	*	*	*	16±15	*	*	*	*
FF	*	*	*	*	*	*	*	*	*
FS	*	*	*	*	*	*	*	*	*
NFC	*	*	*	*	16±14	*	*	12±10	*
NFF	NH	*	*	NH	*	*	NH	*	*
NFS	*	*	*	*	*	*	*	*	*

Table IV

Effect of Time on Uptake by Tomatoes

Code: As in Table II

FOLIAR CONTAMINATED

	Fertile Plot				Nonfertile Plot			
Nuclide	1964 (pCi/kg)	1965 (pCi/kg)	Ratio 64:65	Expected Decay Ratio	1964 (pCi/kg)	1965 (pCi/kg)	Ratio 64:65	Expected Decay Ratio
Zn-65	2,307	316	1:0.14	1:0.36	2,988	654	1:0.22	1:0.36
Cs-137	2,008	36	1:0.02	1:0.98	3,955	68	1:0.02	1:0.98
SOIL CONTAMINATED								
Zn-65	1,216	309	1:0.25	1:0.36	2,185	409	1:0.19	1:0.36
Cs-137	38	24	1:0.63	1:0.98	152	42	1:0.28	1:0.98

No unusual relationships are observed here. In both cases the fraction of radionuclide concentration observed one year later is less than that expected due to radioactive decay alone, indicating no apparent influence on the biological half-life.

Corn

Uptake by the three corn fractions is shown in Table V. Zinc-65 again predominates in all three fractions. The nonfertile plots show the greater uptake, indicating the effectiveness of fertilization in reducing uptake from the soil. Smaller amounts of Cs-137 are also observed. The concentrations in the fertile plots are approximately equal to those in the control plots. It is difficult to tell whether this reflects normal fallout or is attributable to the windstorm of July 18. Minimal amounts of Mn-54 are seen in the nonfertile plots only; and, as before, no soil uptake of RuRh-106, Sb-125 or ZrNb-95 is observed.

A single annual average for each nuclide, in each corn fraction, according to plot, taken from the data in Table V and the 1964 corn results[1], is presented in Table VI. Only Zn-65 and Cs-137 are evaluated.

Considering the relationships for the previously foliar contaminated fertile plots, 7-15 per cent of the initial Zn-65 concentration was observed after the one year in all three fractions. Cesium-137 showed less than one per cent, possibly indicating fixation by the soil. The nonfertile plots showed 11-18 per cent of the initial Zn-65 concentration in all fractions, again indicating the effect of fertilization.

In the previously contaminated soil plots, the fraction of Zn-65 concentration observed one year later was greater, for all three corn fractions, than that expected due to radioactive decay alone, but only in the fertile plots. The nonfertile plots approached the expected decay ratio

Table V

Uptake by Corn Fractions (pCi/kg)

Code: As in Table 2

	Zn-65					Cs-137				
	KERNELS		COBS		HUSKS	KERNELS		COBS		HUSKS
P/HD	9/1-15	9/16-30	9/16-30	10/1-15	9/16-30	9/1-15	9/16-30	9/16-30	10/1-15	9/16-30
FC	NH	159±14	102±30	NH	221±30	NH	38± 5	44± 8	NH	39±12
FF	NH	1500±35	841±38	823±122	475±38	NH	34± 5	48±10	66±35	39±13
FS	NH	885±27	590±38	690± 84	345±36	NH	26± 6	40±13	42±23	42±14
NFC	NH	*	*	*	*	NH	29± 6	30±11	42±26	34±13
NFF	NH	3210±85	1900±63	NH	1200±50	NH	102±10	104±12	NH	86±14
NFS	1759±167	1570±58	1150±48	NH	728±40	90±32	79±11	71±12	NH	53±13
	Mn-54					RuRh-106				
FC	NH	15± 5	12± 8	NH	*	NH	*	*	NH	*
FF	NH	*	*	*	*	NH	*	*	*	*
FS	NH	*	*	*	*	NH	*	*	*	*
NFC	NH	*	*	*	*	NH	*	*	*	*
NFF	NH	*	*	NH	26±14	NH	*	*	NH	*
NFS	*	22±10	17±12	NH	21±13	*	*	*	NH	*
	Sb-125					ZrNb-95				
FC	NH	*	*	NH	*	NH	*	*	NH	*
FF	NH	*	*	*	*	NH	*	*	*	*
FS	NH	*	*	*	*	NH	*	*	*	*
NFC	NH	*	*	*	*	NH	*	*	*	*
NFF	NH	*	*	NH	*	NH	*	*	NH	*
NFS	*	*	*	NH	*	*	*	*	NH	*

but never exceeded it. Correspondingly, the fraction for Cs-137 was always greater in the fertile plots. Whatever process influencing the biological half-life was apparently affected by fertilization of the soil.

Recontamination Study

Upon reviewing the results obtained in this study, and comparing them with similar results from the 1964 study, it became apparent that the concentrations of Zn-65 and RuRh-106 in the crops were only equal to or lower than those obtained from the same crops grown on soil contaminated the year before[1]. Three possible reasons were assigned: (1) not all of the radionuclides were delivered to the plot during the spraying operation, (2) the vendor did not supply us with the correct amount of radionuclides, or (3) for some reason all three crops showed reduced soil uptake of Zn-65 and RuRh-106. Each of these possibilities was examined in turn.

Examination of the survey meter readings taken during the dilution, transfer and spraying operations, indicated that less than 5 per cent of the total gross activity was left behind on bottles, drum and spraying can.

The amount of each radionuclide actually delivered to the plots was determined by gamma analysis of the filter paper systems and soils. The concentration of each radionuclide per unit area was determined, then extrapolated to yield the amount of each nuclide delivered to the plot. These are given in Table VII.

Table VI

Effect of Time on Uptake by Corn Fractions

Code: As in Table II

Nuclide	Fertile Plot 1964 (pCi/kg)	Fertile Plot 1965 (pCi/kg)	Fertile Plot Ratio 64:65	Fertile Plot Expected Decay Ratio	Nonfertile Plot 1964 (pCi/kg)	Nonfertile Plot 1965 (pCi/kg)	Nonfertile Plot Ratio 64:65	Nonfertile Plot Expected Decay Ratio
				CORN KERNELS				
				Foliar Contaminated				
Zn-65	10,140	1,500	1:0.15	1:0.36	17,725	3,210	1:0.18	1:0.36
Cs-137	4,752	34	1:0.007	1:0.98	13,682	102	1:0.007	1:0.98
				Soil Contaminated				
Zn-65	1,412	885	1:0.63	1:0.36	5,332	1,664	1:0.31	1:0.36
Cs-137	65	26	1:0.40	1:0.98	255	84	1:0.33	1:0.98
				CORN COBS				
				Foliar Contaminated				
Zn-65	11,222	832	1:0.07	1:0.36	16,750	1,900	1:0.11	1:0.36
Cs-137	7,845	57	1:0.007	1:0.98	17,300	104	1:0.006	1:0.98
				Soil Contaminated				
Zn-65	1,093	640	1:0.59	1:0.36	5,818	1,150	1:0.20	1:0.36
Cs-137	76	41	1:0.54	1:0.98	294	71	1:0.24	1:0.98
				CORN HUSKS				
				Foliar Contaminated				
Zn-65	4,315	475	1:0.11	1:0.36	6,728	1,200	1:0.18	1:0.36
Cs-137	6,005	39	1:0.006	1:0.98	13,460	86	1:0.006	1:0.98
				Soil Contaminated				
Zn-65	519	345	1:0.66	1:0.36	2,298	728	1:0.32	1:0.36
Cs-137	70	42	1:0.60	1:0.98	198	53	1:0.27	1:0.98

Table VII

Radionuclide Concentration Deposited on Each Plot

Nuclide	Fertile Plot By Filter Paper Analysis	Fertile Plot By Soil Analysis	Nonfertile Plot By Filter Paper Analysis	Nonfertile Plot By Soil Analysis
RuRh-106	0.133 mc	0.179	0.088	0.186
Cs-137	0.511	0.451	0.441	0.501
Mn-54	0.462	0.391	0.448	0.476
Zn-65	0.141	0.134	0.110	0.131

Relative to each other, less Zn-65 and RuRh-106 was delivered to the plots. Based on this data, we were convinced that the amount of Zn-65 and RuRh-106 we received was low by factors of 3 to 5.

Lettuce

Results for uptake by lettuce from contaminated soil for Impact 64 and 65 are compared in Table VIII. Results below sensitivity were assigned an arbitrary value of 10 pCi/kg. "No harvest" periods were not averaged, neither were the error values for Impact 65.

Table VIII

Lettuce: Comparison Impact 64 and 65

(pCi/kg)

Code: P = Plot Type
HP = Harvest Period

P / HP	1	2	3	4	5	6	Average	Ratio 64:65
			Zn-65					
FS-64	224	244	NH	NH	2310	373	789	1:0.36
FS-65	402	142	269	213	402	NH	286	
NFS-64	844	346	1240	1650	1220	NH	1060	1:1.05
NFS-65	965	947	552	869	2240	NH	1115	
			Cs-137					
FS-64	103	77	NH	NH	141	*	83	1:3.89
FS-65	600	300	236	138	340	NH	323	
NFS-64	85	87	158	207	108	NH	129	1:5.45
NFS-65	460	477	542	473	1570	NH	704	
			Mn-54					
FS-64	69	49	NH	NH	57	*	46	1:8.08
FS-65	697	280	277	217	587	NH	372	
NFS-64	*	*	109	186	131	NH	89	1:11.92
NFS-65	909	683	652	722	2340	NH	1061	
			RuRh-106					
FS-64	177	105	NH	NH	253	129	166	1:0.59
FS-65	148	114	103	44	80	NH	98	
NFS-64	198	168	202	323	303	NH	239	1:0.72
NFS-65	347	198	158	145	*	NH	172	

Averaged uptake of Zn-65 and RuRh-106 were lower by factors of 1.5 to 3, for Impact 65, than in Impact 64. Only Zn-65 in the nonfertile plots showed equal averaged uptake for both years. Surprisingly, however, both Cs-137 and Mn-54 levels were substantially higher for Impact 65, i. e., Cs-137 by factors of 4-5 and Mn-54 by factors of 8-12. In fact, Mn-54 which was barely detectable in the fertile soil plot in 1964, was very much in evidence in 1965. This is more typical of the predicted behaviour of the Mn-54 under these conditions. It is possible that this is due to a drastic change in soil pH during Impact 65, but this is unlikely since the type and amounts of fertilizer used were the same for both years. Since we are reasonably sure of the amounts of Cs-137 and Mn-54 delivered to the plots in 1965, one may only speculate as to the accuracy of the radionuclide standards used for Impact 64.

In general, the patterns observed were similar for both phases. The nonfertile plots showed substantially higher concentrations of all four radionuclides than did the fertile, confirming the effectiveness of fertilization in reducing uptake by lettuce. In the fertile plots, Mn-54, Cs-137 and Zn-65 were the dominant nuclides. Zinc-65 and Mn-54 were the principal nuclides appearing in the nonfertile plots, with Cs-137 also showing considerable activity. Ruthenium Rhodium-106 was also present in lettuce from both plots, but in lesser concentrations. Interestingly, a peaking effect was noted in the Impact 65 nonfertile plots with Zn-65, Cs-137 and Mn-54 during the last harvest period, but not for RuRh-106.

Tomatoes

A similar comparison for tomatoes is made in Table IX.

Table IX

Tomatoes: Comparison Impact 64 and 65

(pCi/kg)

Code: As in Table VIII

P/HP	1	2	3	4	Average	Ratio 64:65
			Zn-65			
FS-64	1280	903	1340	1340	1216	1:1.52
FS-65	NH	3055	655	NH	1855	
NFS-64	3460	2020	1910	1350	2185	1:0.42
NFS-65	1329	676	787	NH	931	
			Cs-137			
FS-64	*	*	64	67	38	1:6.10
FS-65	NH	399	66	NH	232	
NFS-64	170	137	129	171	152	1:10
NFS-65	201	106	145	NH	151	
			Mn-54			
FS-64	*	*	*	*	10	1:3.0
FS-65	NH	*	50	NH	30	
NFS-64	*	*	*	*	10	1:3.0
NFS-65	*	42	38	NH	30	
			RuRh-106			
FS-64	105	56	*	*	45	1:0.22
FS-65	NH	*	*	NH	10	
NFS-64	42	*	*	*	18	1:0.55
NFS-65	*	*	*	*		

As in Impact 64, only Zn-65 and, to a lesser extent, Cs-137 showed uptake from soil. Average concentrations of Zn-65 and Cs-137 in tomatoes were variable in comparing Impact 64 to 65. No definite pattern could be established.

Soil fertilization does not appear to be effective in reducing uptake by tomatoes. The reverse was observed in Impact 64. This apparent anomaly may be due to a possible concentration peak observed in the fertile plots only; no such effect was noted in Impact 64. Furthermore, the short harvest period for tomatoes in the fertile plots, two periods in Impact 65 as opposed to four in Impact 64, tend to make the effect of fertilization uncertain.

Corn

The averaged results of corn fraction uptake for Impact 65 are given in Table X to indicate the extent of uptake by stalks which were not sampled during Impact 64.

Corn stalks showed the greatest uptake with all four radionuclides. The predominant nuclide was Zn-65, and approximately 50 per cent of the Zn-65 activity in the corn was concentrated in the stalk. Cesium-137 and Mn-54 showed little activity in the other fractions, but definite concentration in the stalks (more than 65 and 90 per cent respectively, of the total activity). The stalks alone showed concentration of RuRh-106.

TABLE X

Impact 65, Corn Results

Codes: P = Plot Type
HD = Harvest Date

	KERNELS		COBS		HUSKS	STALKS
P / HD	9/1-15	9/16-30	9/16-30	10/1-15	9/16-30	10/1-15
			Zn-65 (pCi/kg)			
FS	NH	885±27	590± 38	690±84	345±36	1960±401
FS	NH	838±31	549± 29	NH	295±33	1530±222
NFS	1759±167	1570±58	1150± 48	NH	728±40	4130±385
NFS	NH	1520±85	1070±128	NH	445±47	2130±293
			Cs-137 (pCi/kg)			
FS	NH	26± 6	40± 13	42±23	42±14	242±131
FS	NH	43± 7	66± 9	NH	58±13	1020±110
NFS	90±32	79±11	71± 12	NH	53±13	320±100
NFS	NH	262±23	289± 46	NH	138±20	694±117
			Mn-54 (pCi/kg)			
FS	NH	*	*	*	*	175±151
FS	NH	39± 8	30± 9	NH	47±14	1100±123
NFS	*	22±10	17± 12	NH	21±13	572±132
NFS	NH	188±23	159± 48	NH	144±21	1420±171
			RuRh-106 (pCi/kg)			
FS	NH	*	*	*	*	852±684
FS	NH	*	*	NH	*	600±423
NFS	*	*	*	NH	*	734±503
NFS	NH	*	*	NH	*	579±499

The average uptake by corn fractions, from contaminated soil for Impact 64 and 65 are compared in Table XI. Stalks are not included.

Table XI

Corn: Comparison Impact 64 and 65 (Averages only)

Plot	Kernels Average	Ratio 64:65	Cobs Average	Ratio 64:65	Husks Average	Ratio 64:65
			Zn-65			
FS-64	1412	1:0.59	1093	1:0.50	519	1:0.56
FS-65	838		549		295	
NFS-64	5332	1:0.28	5818	1:0.18	2298	1:0.19
NFS-65	1520		1070		445	
			Cs-137			
FS-64	48	1:0.89	76	1:0.86	70	1:0.82
FS-65	43		66		58	
NFS-64	255	1:1.02	294	1:0.98	198	1:0.69
NFS-65	262		289		138	
			Mn-54			
FS-64	10	1:3.9	10	1:3.0	10	1:4.7
FS-65	39		30		47	
NFS-64	10	1:18.8	10	1:15.9	10	1:14.4
NFS-65	188		159		144	
			RuRh-106			
FS-64	10	1:1.0	10	1:1.0	10	1:1.0
FS-65	10		10		10	
NFS-64	10	1:1.0	10	1:1.0	10	1:1.0
NFS-65	10		10		10	

The average concentration of Zn-65 was, as expected, lower by factors of approximately 2 for the fertile plot and 5 for the nonfertile. The ratios for each fraction were quite consistent with each other. Cesium-137 showed approximately equal concentrations in both phases. Definite uptake of Mn-54 was observed for Impact 65, particularly in the nonfertile plots, whereas no uptake was noted during Impact 64. Uptake of RuRh-106 was not observed in either year.

The nonfertile plots again showed higher concentrations of all four radionuclides, confirming the effectiveness of soil fertilization in reducing uptake by corn.

Conclusions

Considering the two sub-phases as part of one overall study and the uncertainty of the accuracy of the radionuclide standards used, the following conclusions can be made:

1. Soil uptake is slower and more selective. Only Zn-65 and Cs-137 showed appreciable concentration in all the crops. Manganese-54 and RuRh-106 were not seen to any great extent except in lettuce and corn stalks.

2. Stalks, sampled and analyzed during Impact 65 only, showed the greatest uptake of all the corn fractions. Approximately 50 per cent of the Zn-65 activity in corn was concentrated in the stalk. The other nuclides showed little or no activity in the other corn fractions but definite concentration in the stalk.

3. In general, fertilization of the soil is quite effective in reducing uptake due to soil contamination. Most fertilizers tend to increase soil pH reducing the solubility of ions such as zinc, ruthenium and manganese and making them less available to the plant.

In modern agriculture, three inorganic fertilizer elements are commonly added to soils. These are nitrogen, potassium and phosphorus. Potassium is added as a salt that will furnish soluble K^+ in soils; nitrogen may be added either as the cation, NH_4^+, or as the anion, NO_3^-.

Considering the complementary ion effect, it would be expected that NH_4^+ or K^+ ion would liberate a considerable amount of fixed Cs-137 into a labile form. If, however, nitrogenous fertilizer is added as $Ca(NO_3)_2$, this fertilizer would be expected to have little effect on the fixed Cs-137.

On this basis it could be predicted that the addition of $Ca(NO_3)_2$ fertilizer would have little effect on the uptake of Cs-137 by plants. If the nitrogen is supplied as $(NH_4)_2SO_4$, considerable increase in uptake of Cs-137 might be expected. From the same considerations, it could be expected that if K^+ is added as K_2SO_4 in the same amounts as the NH_4+, the added K+ would increase the uptake of Cs+ to about the same degree as would NH_4+.

These considerations take into account only inorganic soil chemical principles. They do not consider the possible effects of microbiological oxidation of NH_4+ to NO_3- nor do they take into account possible ion competition in plant uptake by the root[5].

4. Lettuce, and perhaps corn stalks, appear to be excellent indicators of gamma-emitting contamination in the environment. Both sample types showed concentration of all radionuclide species used.

5. In the case of a contaminating event, foliar deposition would be the important mode of uptake if it took place when the crops were in some advanced stage of growth. Assuming no further contamination, then vegetables grown on those plots a year later will show only a fraction of the original activity. This will depend on the type of crop, radionuclide species and extent of fertilization. Crops grown on fertile plots showed

from <1-15 per cent of the original activity a year later; while the same crops grown on nonfertile plots showed from 25-65 per cent of the original activity.

Should deposition occur on the soil only, i.e., before seeding, the initial radionuclide concentration of crops grown on those plots will be substantially smaller than if the mode of deposition were foliar. Nor, will the reduction in activity in crops grown a year later be as great because of the continued availability of the radionuclides from the soil.

6. The difficulties encountered in establishing the reliability and accuracy of radionuclides used point very definitely to the need for establishing laboratory competency in standardization of radionuclides.

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HIGHLIGHTS OF THE Y-12 BIOANALYSIS LABORATORY OPERATION

R. H. Kent

INTRODUCTION

For those who have not had the opportunity to visit the Oak Ridge Y-12 Plant,[a] an overall view is given in Figure 1. Perhaps not as well known as our sister plant, the Oak Ridge National Laboratory, it has approximately 4500 employees working on a rather wide range of projects. A large portion of these projects involve materials which, with indiscriminate handling, could create a toxicological or radiological health problem. In order to assure ourselves that no one is being subjected to hazardous conditions, the Health Physics and Industrial Hygiene Departments at the Y-12 Plant maintain a close check on all Plant personnel, and the Bioanalysis Laboratory, in support of these groups, analyzes a rather large number and variety of samples. Table I gives a list of the more common types of analyses performed by this group. Rather than concern you with a description of each type of analysis, I want to discuss only three. These procedures have been chosen because of their low cost and the short time involved.

ENRICHED URANIUM IN URINE

A few years ago, the Y-12 Bioanalysis Laboratory was analyzing approximately 800 urine samples per week for enriched uranium. This number is more than most laboratories analyze in a two-month period. Because of this large volume, a method of analysis had to be developed that was both rapid and inexpensive while, at the same time, reliable. Electroplating was chosen as the method of analysis because it offered the best possibilities for meeting these requirements. After operating for several years with a manually adjusted system, a semiautomatic apparatus was developed. This system, shown in Figure 2, consists of a bank of 24 plating cells. Each cell is individually controlled by a servo mechanism which maintains a constant current and voltage during the thirty-minute plating time. Twenty-milliliter aliquots are used that require no previous treatment, such as digesting with acid or pH adjustment. The high current density (230 milliamps/cm^2) is sufficient to give a consistent recovery of 73 ± 5% on a 1.3 d/m/spike. Comparisons of this method with other methods indicate that any complexes being formed in the urine which might inhibit plating are broken up in the electroplating operation. The big advantage in this method of urinalysis is that the cost of analysis is very low since only 12 minutes of the analyst's time per analysis are required and nontechnical personnel can be used.

(a) Operated for the US Atomic Energy Commission by the Union Carbide Corporation-Nuclear Division.

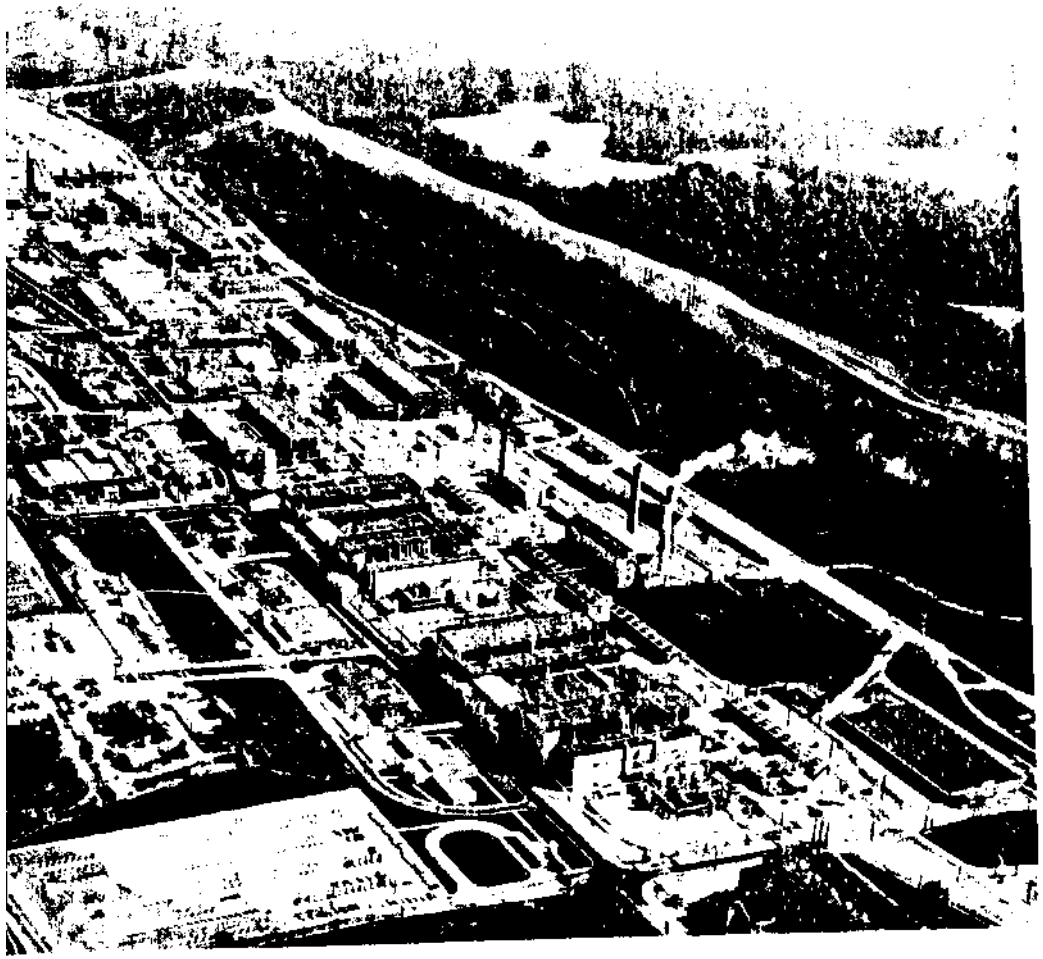

Figure 1

Table I

SOME COMMON TYPES OF ANALYSES PERFORMED BY
THE Y-12 BIOANALYSIS LABORATORY

Urine Samples			
U-234	U-238	Pb	Sr
U-235	Hg	Pu	Po-210
Feces Samples			
	U-234	Po-210	
Reactor Samples			
U-232	Pu-238	Np	Cm
Th-238	Pu-239	Am	
Process Solutions			
	U-235	Np	
	U-238		
Miscellaneous Samples			
H-3 & Hg in Half Heavy Water		Hg in Zinc	
Hg in Lithium Compounds		H-3 in Gases	
Fission Products (Zr-Nb, Ru-Rh, Pa)		Po in Blood	
Tc-99 in Pellets			

MERCURY IN URINE

One of the Laboratory's most successful analyses is that for mercury in urine and other solutions. The mercurometer and filtering equipment we use in the analysis are shown in Figure 3. Our limit of error with this method is ± 9.0% at the 0.4 ppm level, with a lower limit of detection of 0.01 μg/ml. This limit is lower by a factor of 100 than can be obtained by atomic absorption methods. The method of operation for urine is as follows (other solutions which may require a lower sensitivity are handled in the same manner except that a 100-milliliter aliquot instead of 10 milliliters is used):

The samples are filtered through a material which consists of asbestos fibers that have been heated to 800° C in a muffle to destroy any combustible material and then mixed with cadmium sulfide. A small pad of this material is placed in the bottom of a Gooch crucible attached to a vacuum manifold. The sample is allowed to filter through this pad. Any mercury present is trapped as the mercuric sulfide by exchange with the cadmium. The pads are washed with water, then alcohol, and finally dried for approximately twenty minutes. The pads must be thoroughly dry so that no water vapor enters the instrument. Known standards are prepared at the same time using 0.1 to 0.8 μg/ml solutions of mercuric nitrate. The crucible containing the sample is then placed in a down-draft furnace connected to a General Electric instantaneous mercury vapor detector. Since the furnace is maintained at 1200° F, any mercury present readily volatilizes and is detected by the vapor detector. An integrating device is attached to the vapor detector which gives the result in counts per four minutes. (Four minutes is the amount of time required to completely vaporize and detect any

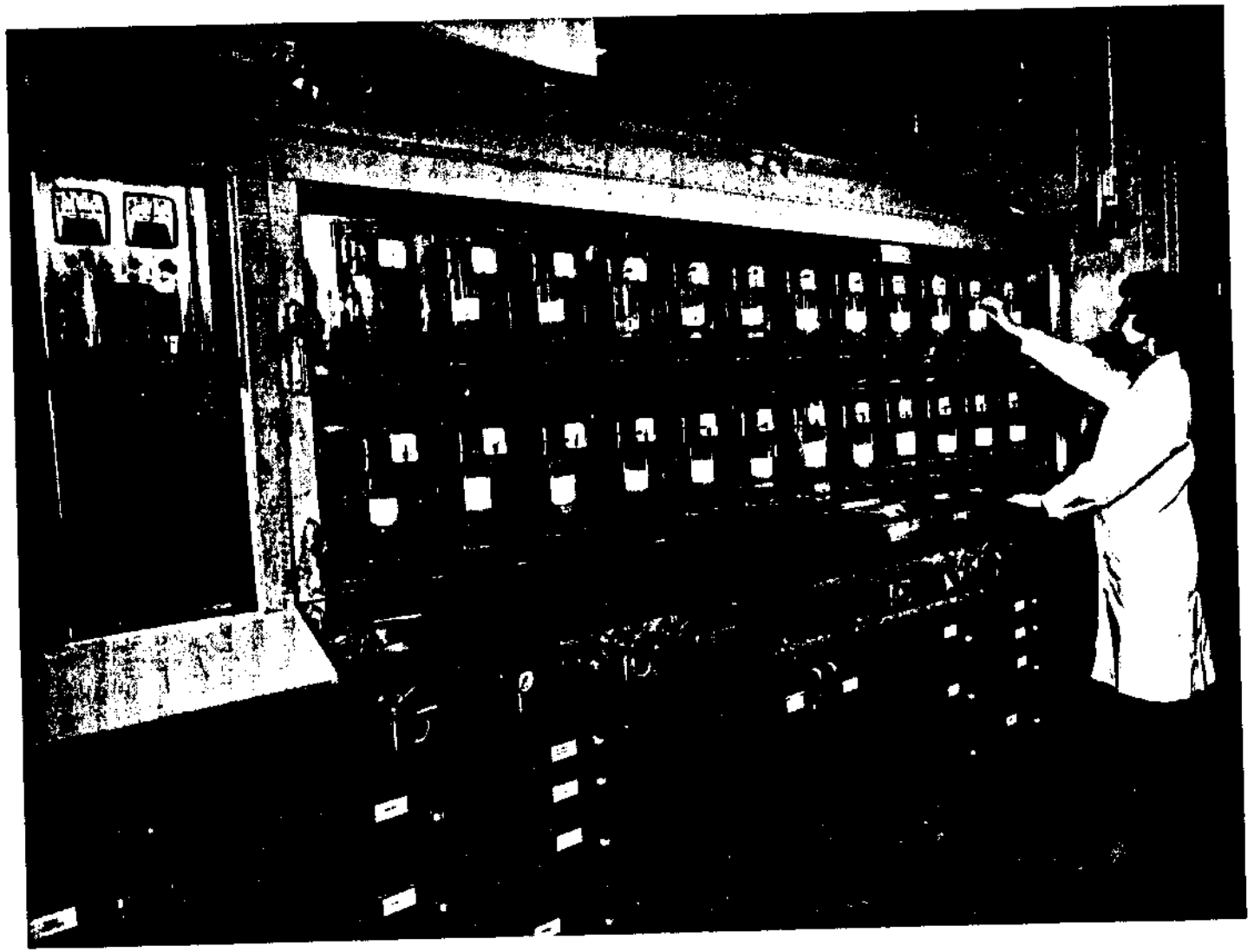

Figure 2

mercury present.) A factor, using this count rate on the standards, can readily be made for use on the unknowns. The Y-12 Quality Control Department routinely sends in spiked urine samples at these levels bracketing the maximum permissible level (0.3 ppm) plus a blank under fictitious names. These values are reported monthly and results over the years have been quite good. We have had very little trouble with this instrument and it also lends itself very readily to the analysis for mercury in plant effluents, lithium compounds, and presently on core drillings for zinc mine explorations. This method of analysis was originally brought to our attention by an article in the December 1956 issue of "Industrial Hygiene Quarterly of Workmen", Moffett and Doherty.

Recently the procedure has been refined as to the method of sample introduction and readout. Approximately four samples can be analyzed per hour with our present equipment. Our experience with employees known to be excreting mercury does not indicate that there is any advantage in a pretreatment of the urine. Use of a muffle furnace rather than a bunsen burner gives a better control of the temperature and, consequently, a more reproducible rate of mercury volatilization from sample to sample. The vapor detector, also seen in Figure 3, is installed in a hood. This precaution is advisable since a large number of samples are run and this prevents contamination of the laboratory.

POLONIUM-210 IN URINE

Recently the Bioanalysis Laboratory had occasion to analyze urine for polonium-210. This job seemed to involve a simple procedure since much has been written in the literature on this analysis. We decided to use a spontaneous-deposition method on nickel foil at an elevated temperature. This method is similar to that described by Feldman and Frisch at the University of Rochester.[b] Spiked solutions gave recoveries of approximately 98% which are certainly acceptable except that we soon found out that samples which required both a polonium analysis and a uranium analysis by electroplating gave higher counts by electroplating than spontaneous deposition, and when these urines were analyzed chemically for uranium the difference could not be completely accounted for. Flaming of the electroplated discs reduced the count, which was another indication that polonium was plating on the nickel disc and not uranium. This discrepancy indicated that for some reason certain urines had polonium complexed in such a manner that it would not spontaneously plate, although when spikes were added to raw, unexposed urine, the recovery indicated that the procedure was workable. Table II shows the difference observed between spontaneous deposition and electroplating of urine from five different subjects. Nickel foil was used for plating, the solution was stirred at a medium speed, and the temperature of the water bath in which the plating cells were placed was maintained at 90° C. Plating continued for two hours with the sides of the cell flushed down after one hour.

An experiment was designed to determine what effect ascorbic acid would have on these urines since the literature indicated that polonium was inhibited by iron when analyzing

(b) Anal Chem, p 2024; December 1956.

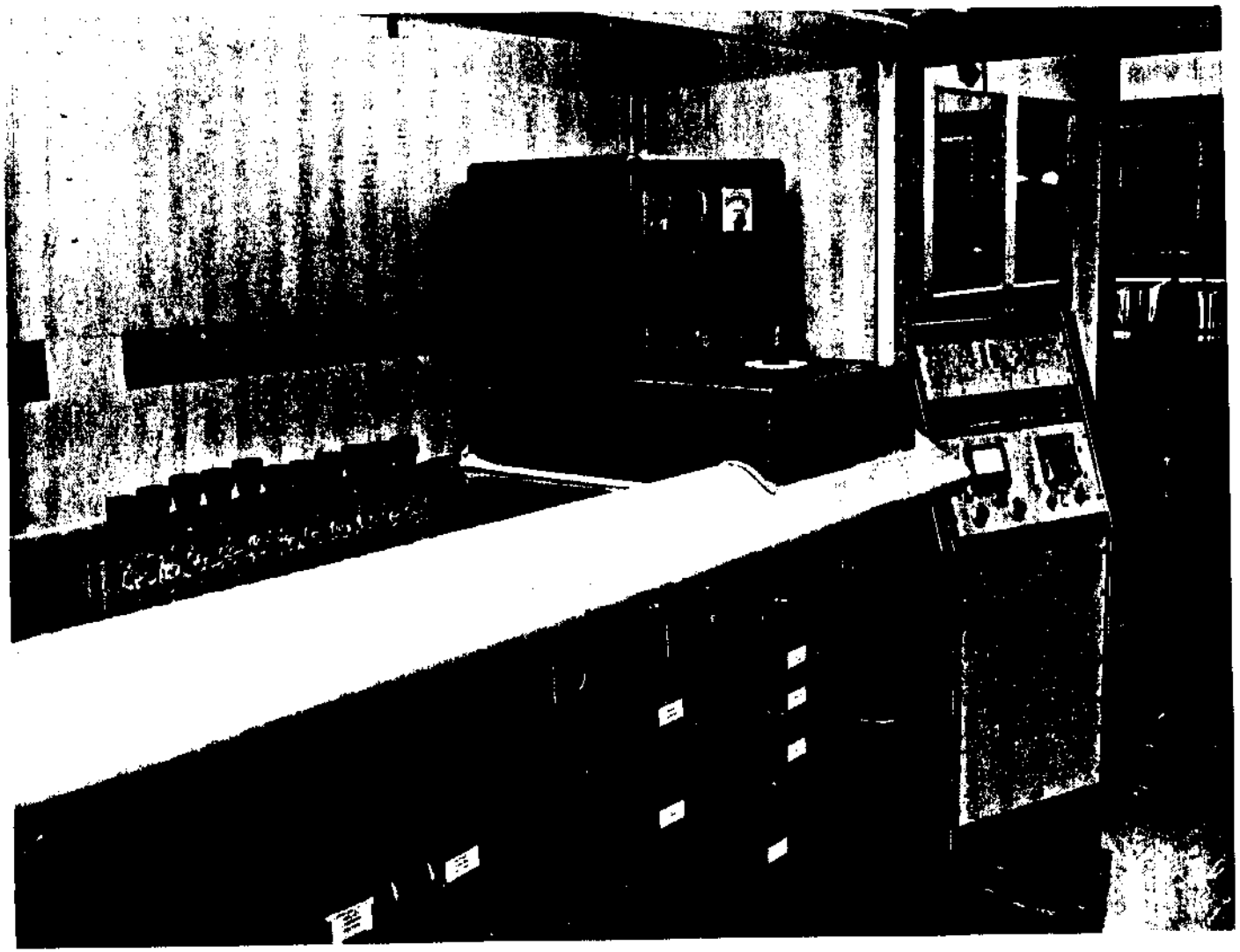

Figure 3

Table II

COMPARISON OF METHODS OF ANALYSIS FOR POLONIUM-210 IN URINE

Specimen	Date	Concentration (d/m/24 hours) Electroplated	Raw Spontaneous Deposition	Digested Spontaneous Deposition
L	3-6	49.6	37.9	63.1
S	3-7	135.8	40.4	142.0
P	3-6	91.0	44.2	92.3
K	3-20	4.0	5.4	8.0
P	3-20	10.4	25.8	42.4
M	3-21	9.6	9.6	29.6

tissue and fecal matter. The procedure used in this experiment was to take a 24-hour voiding from a subject known to be excreting polonium. Seven aliquots were taken from this 24-hour voiding and the results determined. The results are summarized in Table III.

Table III

EXPERIMENTS TO DETERMINE EFFECT OF ASCORBIC ACID ON POLONIUM ANALYSIS

Experiment	Sample Treatment	Results (c/30 min)
1	Raw urine - electroplated by enriched uranium plating method.	90
2	Raw urine - no ascorbic acid - no digestion - 0.5 N HCl - volume adjusted to 100 mls.	40
3	Raw urine - 200 mgs ascorbic acid - 0.5 N HCl - volume adjusted to 100 mls.	31
4	Digested with HNO_3 and $HClO_4$ - neutralized - 200 mgs ascorbic acid - 0.5 N HCl - volume adjusted to 100 mls.	62
5	Digested with HNO_3 and $HClO_4$ - neutralized - no ascorbic acid - 0.5 N HCl - volume adjusted to 100 mls.	86
6	Repeat of Experiment 5.	73
7	Digested with HNO_3 and $HClO_4$ - neutralized - 200 mgs ascorbic acid - 0.5 N HCl - volume only adjusted to 50 mls.	61
8	Residue from Experiment 2.	48

With the exception of Experiments 1 and 7, all aliquots were made to 100 milliliters. The result in Experiment 1 was adjusted to that of a volume of 100 milliliters. The data indicate that ascorbic acid did not improve the recovery and that much greater recovery could be obtained by digesting the urine specimen first. As a further check on whether the polonium was remaining in solution, the remaining solution in Experiment 2, after two hours of plating, was removed, digested, and the acidity adjusted to 0.5 N in HCl (Experiment 8). As indicated, 48 counts were obtained. This number added to the 40 obtained the first time gave 88 counts, which is comparable to Experiment 5. This result, to us, indicated that unless specimens were predigested to physically break up any complexes existing, there was the possibility of reporting exposures too low and that although there may be some ion in these solutions that is inhibiting the plating, ascorbic acid for one is not sufficient to complex

this ion. It should be pointed out that not all urines we analyzed showed this discrepancy between digested and nondigested urine, which might indicate that this phenomenon is a product of the individual's diet. Unfortunately, or fortunately depending on which way you look at it, we did not have but a few people excreting measurable amounts of polonium and these for only a few weeks. Thus, we were prevented from getting as much data as we would have liked. When looking at the results indicated in Table III, it would seem that a preferable way to analyze for polonium would be by electroplating and thereby eliminate the time involved in digesting the urine. In plants where the only exposure potential is polonium this would probably be true, but where there is also uranium present, the uncertainty of whether it is polonium or uranium removes this method as a possibility.

In conclusion, I would like to point out that the analytical methods here are not unique but do offer the advantage of economy. The cost of performing the mercury and uranium analyses in urine is lower by a factor of approximately 20 from that of such other methods as solvent extraction or ion exchange, while at the same time accuracy has not been sacrificed. In addition, only a small aliquot of urine is needed for these analyses which allows specimens to be taken on the job rather than subjecting the employee to the inconvenience of a 24-hour collection. Finally, it appears that metabolized polonium may behave differently than ordinary polonium which is added as a spike and, therefore, gives a false indication of recovery efficiency.

A PRÉCIS OF THE PROPOSED LUNG MODEL

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The lung model currently used by the International Commission on Radiological Protection[1] and other groups to estimate radiation dose from inhaled radioisotopes is well known for its simplicity and general utility. It has served a very important need of the health physicist.

In relationship to the information available on dust deposition and clearance, air sampling techniques and instrumentation, and on radioactive hazard evaluation generally, it became apparent that this simple model did not utilize this knowledge to any important degree. In order to bring about an increased utilization, a new model of greater flexibility and complexity was indicated. Since dust sampling is so fundamental to health physics and to environmental assay in particular, it seemed appropriate to build a model around this basic procedure. Of course, this would have its main effect on considerations of deposition.

Clearance, on the other hand, had to be described in terms of the different regions of the respiratory tract and the major redistribution pathways and mechanisms in order to bring this portion of the model up to the same level of sophistication. The ambiguity of "soluble" and "insoluble" dusts had to be eliminated but the basic concept that the physical-chemical properties of the dust are important in clearance needed expansion so as to emphasize the importance of this factor in retention. Finally, it was recognized that some cognizance of the variable nature of respiratory performance under different work loads was needed. With these general ideas in mind, Committee 2 of the ICRP created a Task Group to undertake the creation of a new lung model and the following discussion will briefly describe the essence of the Task Group report[2].

Deposition Model

The experimental data and the theoretical treatments of dust deposition were critically reviewed. From this, a group of experimental studies emerged as being the most carefully controlled and least equivocal with respect to deposition measurements and assessment of the aerosol utilized. From the theoretical work, Findeisen's respiratory model[3] was selected mainly because of its simplicity, but the method of calculating diffusion deposition was modified[4] and a respiratory pattern based on several pneumotachographic studies in man was used[5].

These two bodies of information were found to be similar in their size-deposition relationships. They tended to differ somewhat from several descriptions in the literature in one important respect, namely, they indicated a relatively greater role of the nasal passages as a deposition site and a less important role for the tracheobronchial tree. The overall prediction of respiratory tract deposition was not greatly different, however.

The selected data on nasal deposition are summarized in the first figure (Figure 1) in which the experimental results of Landahl and co-workers[6] are portrayed in relation to an empirical deposition curve obtained by Pattle[7] using monodisperse aerosols. In the figure, N is the fractional deposition of particles with an aerodynamic diameter D_a, and F is the air flow rate (l/min.). The different symbols denote studies with different substances some of which were hydroscopic (dark triangles) and some not (inverted open triangles). The agreement seems to be generally good. The Pattle curve was used for all calculations of nasal deposition in the subsequent descriptions.

The theoretical deposition curve for the lower respiratory tract was based upon a modification of Findeisen's model as already noted. On the basis of nasal breathing at a 1450 ml tidal volume and a respiratory frequency of 15 respirations per minute, the curves depicted in Figure 2 were obtained.

Selected experimental data are compared to theoretical curves in Figure 3: these curves are for mouth breathing (upper) and nasal breathing (lower), respectively. Wilson and LaMer[8] effectively eliminated nasal-pharyngeal (N-P) deposition by breathing through a tube. Their deposition data corrected for the hygroscopic growth of their aerosol is depicted by the dotted line in the upper figure. The lower curve shows Hatch's estimate of the deposition data of Brown and co-workers[9] using nasal breathing. In both curves the solid line is derived from Findeisen's model.

There is some question about the actual deposition compartment in the case of Brown's study as it is based primarily on the CO_2 levels of the respired air. In the case of the Wilson and LaMer data, there is also a complication due to the hygroscopic nature of the aerosol; here the question of the precise relative humidity is profoundly important. Nevertheless, both sets of data seem to fit the theoretical values reasonably well. No experimental data were available on particles of submicroscopic size nor on tracheobronchial deposition alone so it was necessary to rely on theory in these cases. Also variations in deposition induced by changes in tidal volume were estimated on theoretical grounds.

In order to incorporate dust sampling information into the model, it was clear that some way had to be found whereby dust distributions could be described and utilized conveniently. Assuming most distributions can be successfully described as log normal, several approaches were developed. For example, using the basic deposition curve already alluded to, e.g., Figure 2, and working with various distributions, i.e., different count median aerodynamic diameters and different degrees of heterogeneity expressed by geometric standard deviations (σ_g) from 1.0 to 5.0, deposition curves for each distribution were calculated. See Figure 4.

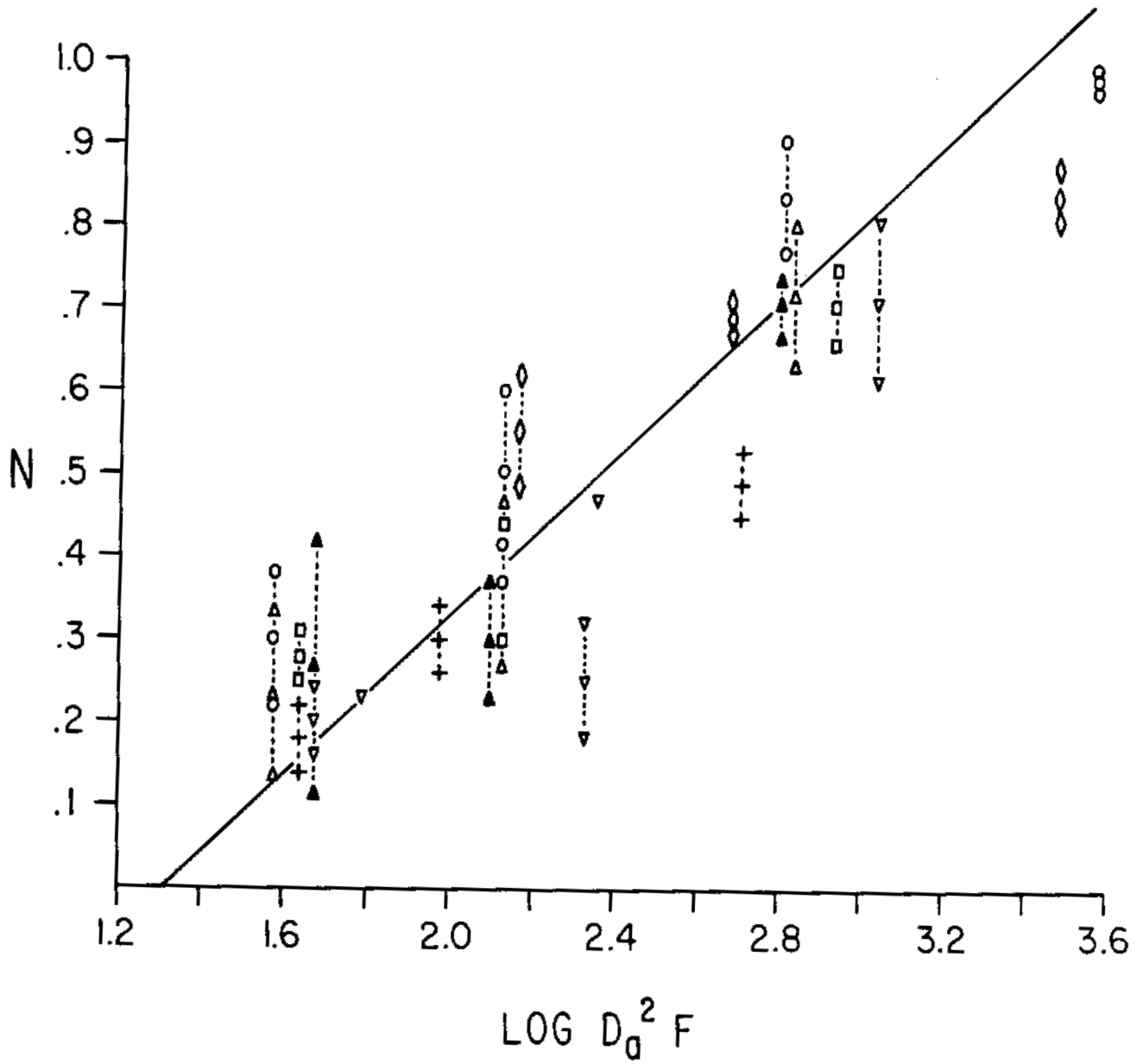

Figure 1: The empirical data of Pattle are represented by the straight line. The symbols have the following meaning: + methylene blue - 17 1/min; o glycerol - 17 1/min; Δ bismuth subcarbonate - 17 1/min; □ tyrosine - 17 1/min; ▽ corn oil - 29 1/min; bismuth subcarbonate ◇ - 60 1/min; ▲ tricalcium phosphate - 17 1/min.

Ultimately it was found that the median aerodynamic diameter of the activity or mass distribution could, within practical limits, describe the activity or mass deposition potential of the entire dust distribution. Stated another way, it was found that one parameter, the MMAD or AMAD, gives an adequate indication of the overall deposition of the entire dust cloud in various regions of the respiratory tract, irrespective of the heterogeneity of the distribution. See Figure 5.

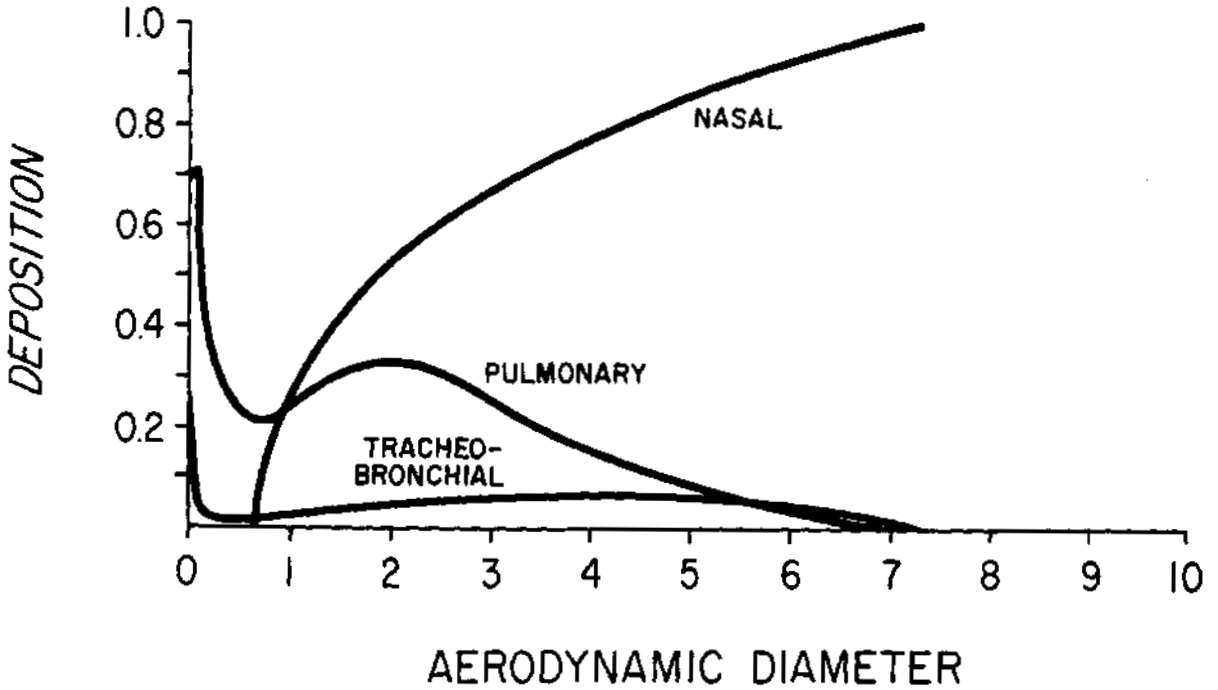

Figure 2: These curves were computed by a method similar to that used by Findeisen. A 4 second respiratory cycle was assumed with a 0.2 second pause, 1.74 second inspiratory phase and a 2.06 second expiratory phase. The tracheobronchial estimates were corrected for an additional 50 cm^3 representing the first part of the rebreathed air which is considered free of dust particles.

It was determined on theoretical grounds that doubling or tripling the tidal volume, so as to double or triple minute ventilation, did not produce an important shift in the mass deposition pattern (percentage deposition in each compartment). Rather, it appeared that such a change in respiratory performance mainly alters the amount of dusty air breathed and provides a direct proportionality between minute ventilation and the absolute mass deposition.

Finally, a convenient and simplified graphic description of the deposition relationships for the two respiratory regions was created. (Figures 6 and 7). While for the third, the T-B region, a constant deposition value of 8 percent was assigned. Note the constancy of T-B deposition in Figure 5.

Clearance Model

A review of the literature revealed (a) very little attention had been given to the study of clearance in the nasal passages, (b) information regarding tracheobronchial clearance tended to produce two widely different views of ciliary transport kinetics and (c) little quantitative information and few lucid qualitative descriptions were available on phagocytosis and lymphatic drainage, the dominant clearance processes serving the pulmonary region. The Task Group concluded however that a group of values (including

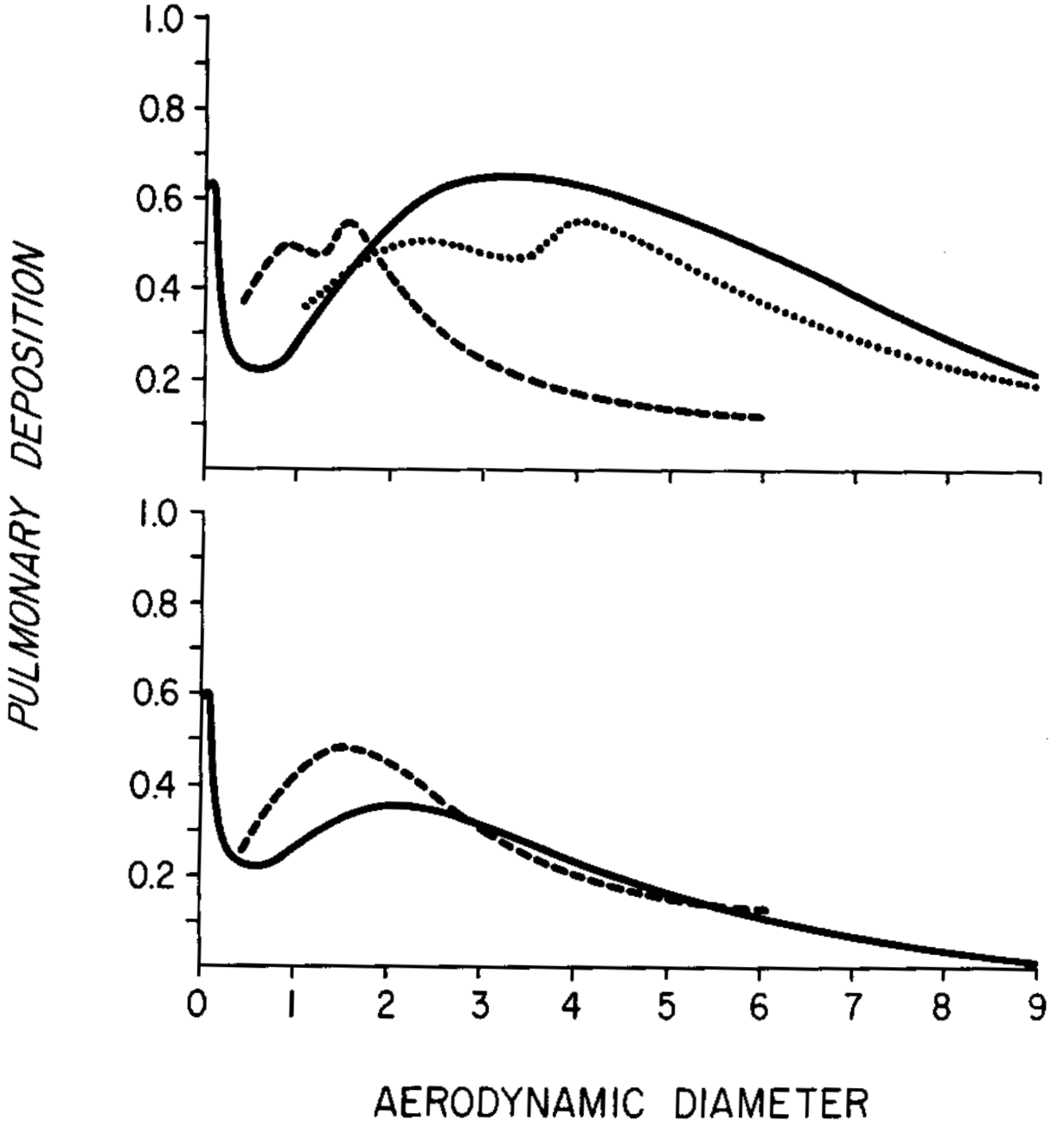

Figure 3: The upper curves are for mouth breathing. The solid line is theoretical; the dashed line gives the data of Wilson and LaMer; and the dotted line indicates the change in the Wilson and LaMer data at 99.5 percent relative humidity. The lower curves are for nasal breathing. The solid line is theoretical and the dashed curve is based on Hatch's estimate of the Brown et al deposition data.

many educated guesses) could be compiled which appeared to be consistent with the best available data. The information employed came from widely diverse sources, such as the endocytotic studies in the amoeba; studies of flagellates

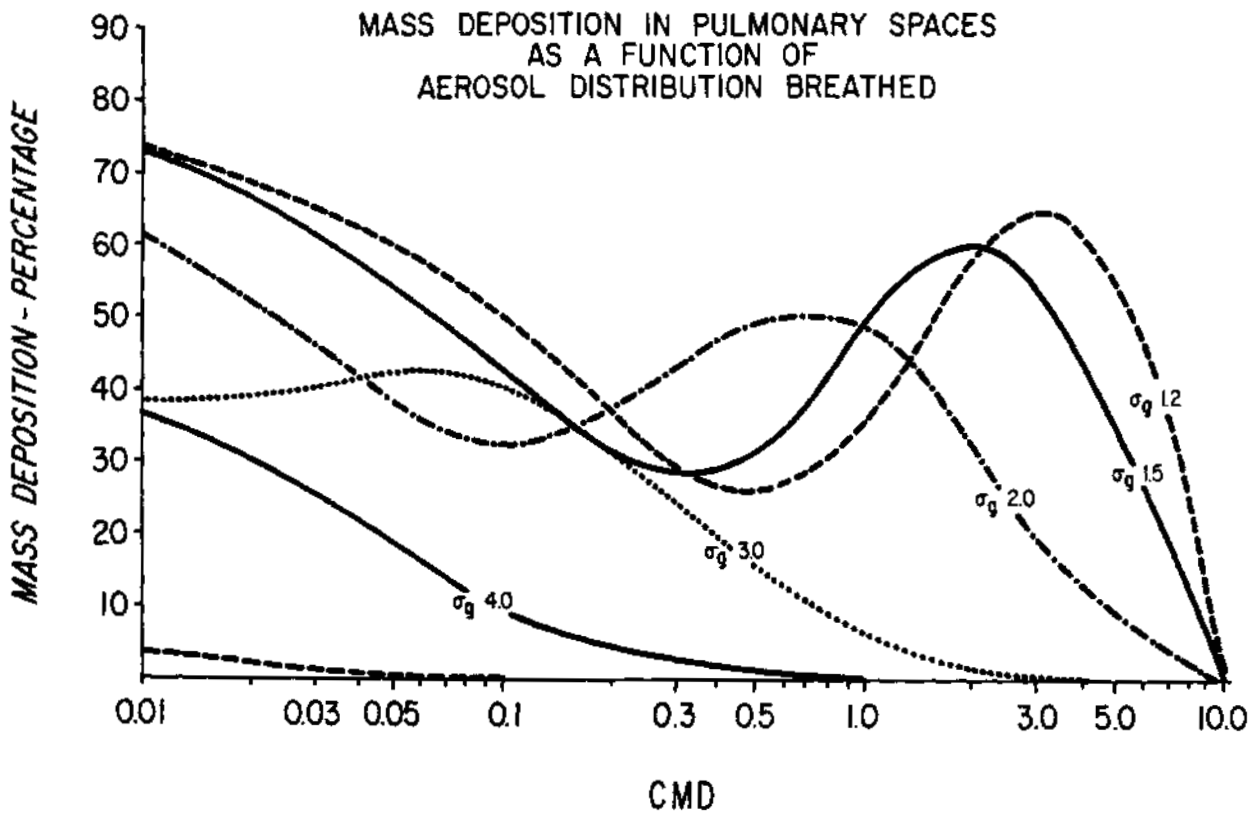

Figure 4: The mass deposition predictions for various aerosol distributions are depicted. For example, at a count median aerodynamic diameter of 0.5 μ, the mass deposition in the pulmonary region for distributions having geometric standard deviations (σ_g) of 1.2, 1.5, 2.0, 3.0, 4.0 and 5.0 is predicted to be 25, 32, 48, 16 and 3 percent, respectively.

and the cilia of mollusks; measurements of mucous flow in tracheal preparations, usually in rodents; measurements of dust clearance from the respiratory tract of man; in vitro studies of phagocytosis, usually employing peritoneal macrophages, gastrointestinal absorption and reticuloendothelial blockade studies in mammals; measurements of lymphatic flow in experimental animals; transport of monomeric and polymeric metals across membranes; cell turnover studies, etc. By utilizing these kinds of information, some aspects of all the known clearance mechanisms and pathways serving the respiratory tract were brought together into a working model schematically presented as Figure 8.

It seemed inexcusable to use any model to the exclusion of the available relevant data which have been obtained rather directly. This was especially

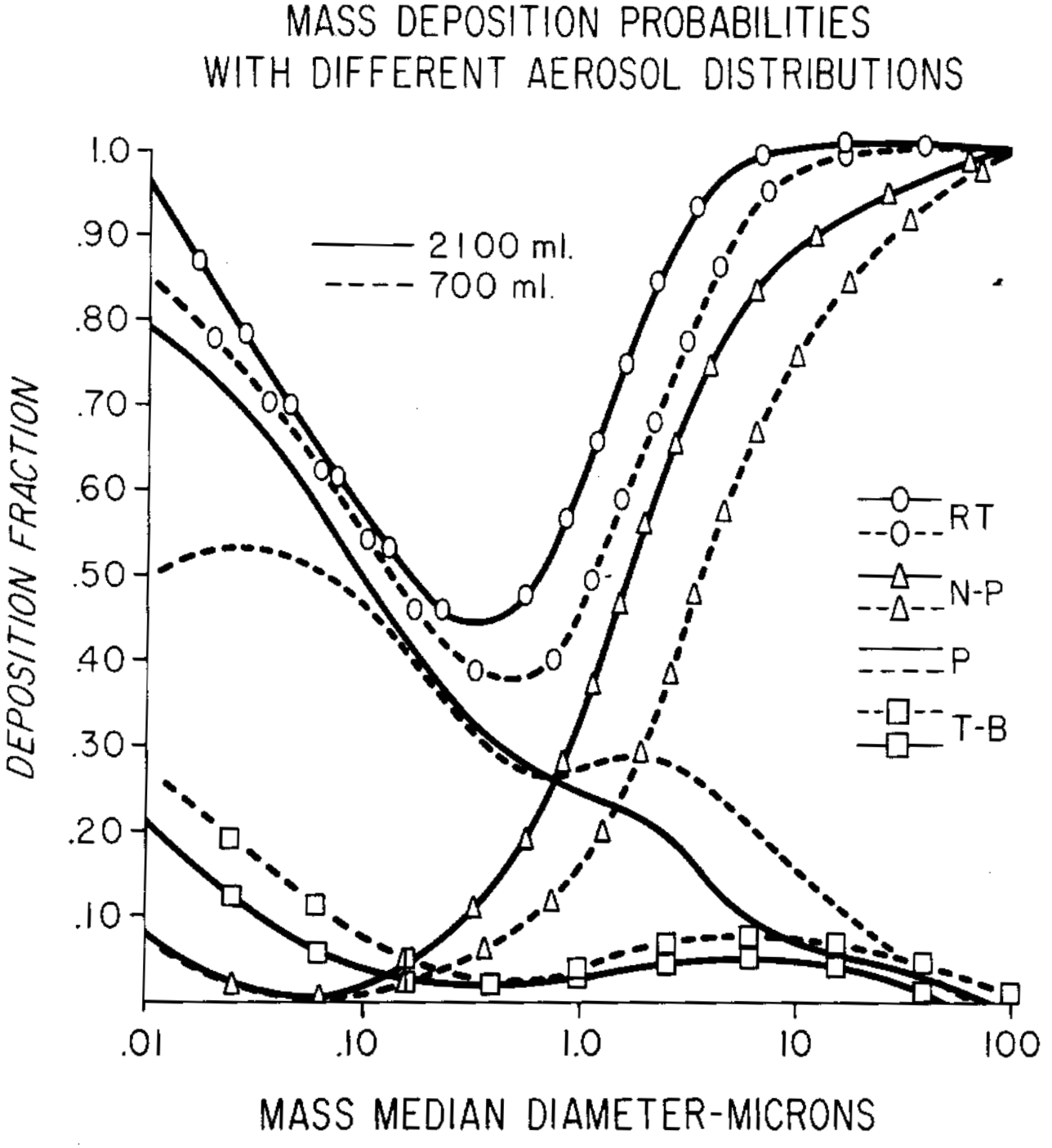

Figure 5: Mass deposition predictions are given for various distributions represented solely by their mass median aerodynamic diameters. RT, N-P, P and T-B, signify the total respiratory tract, nasopharyngeal, pulmonary and tracheobronchial regions, respectively. For each region the effects of modifying the tidal volume from 700 to 400 ml are indicated.

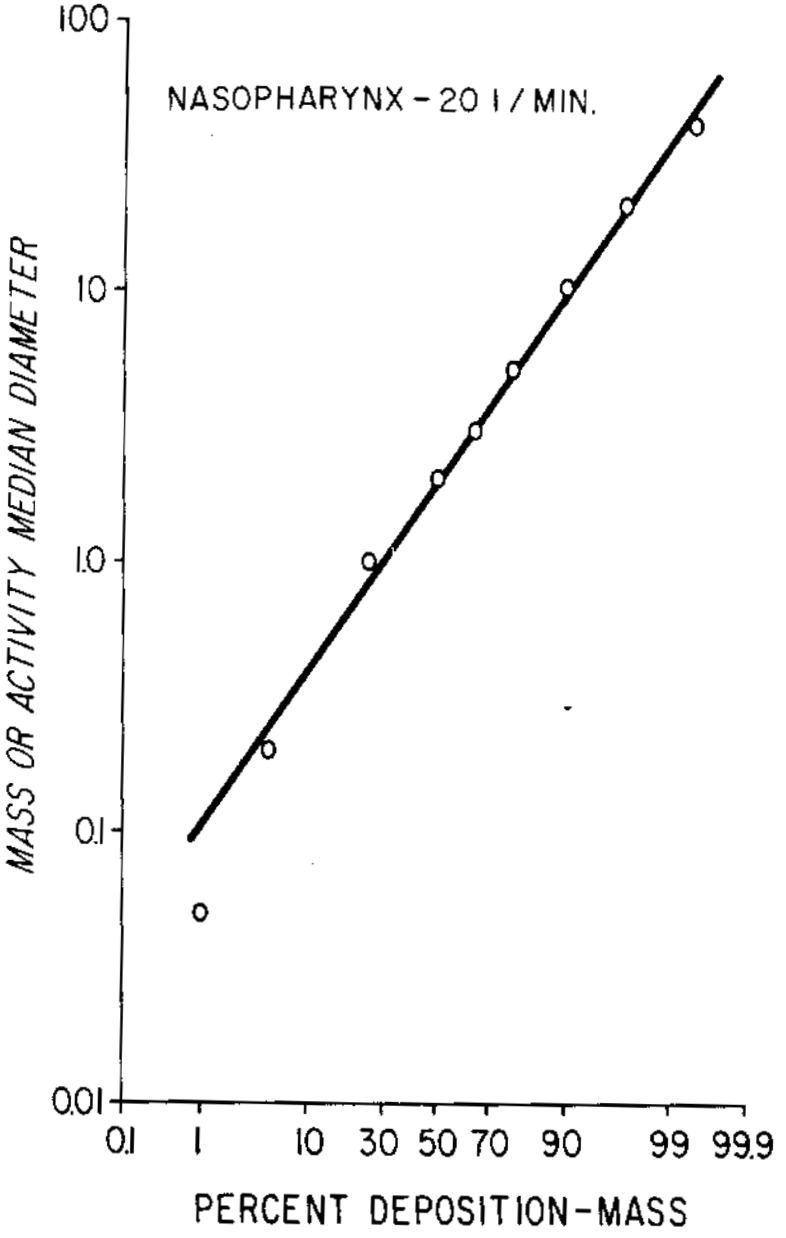

Figure 6: This graph depicts the average nasopharyngeal deposition curve (evident in Figure 5) replotted on log-probability paper. This provides a convenient linear form of the relationship.

true in the case of clearance data so the proposed clearance model utilizes two types of clearance information, viz., estimated values which are largely based on analogies are used for "untested" substances, and measured values taken from various experimental and biomedical sources, including accidental human exposures, are used wherever applicable. The latter have priority over

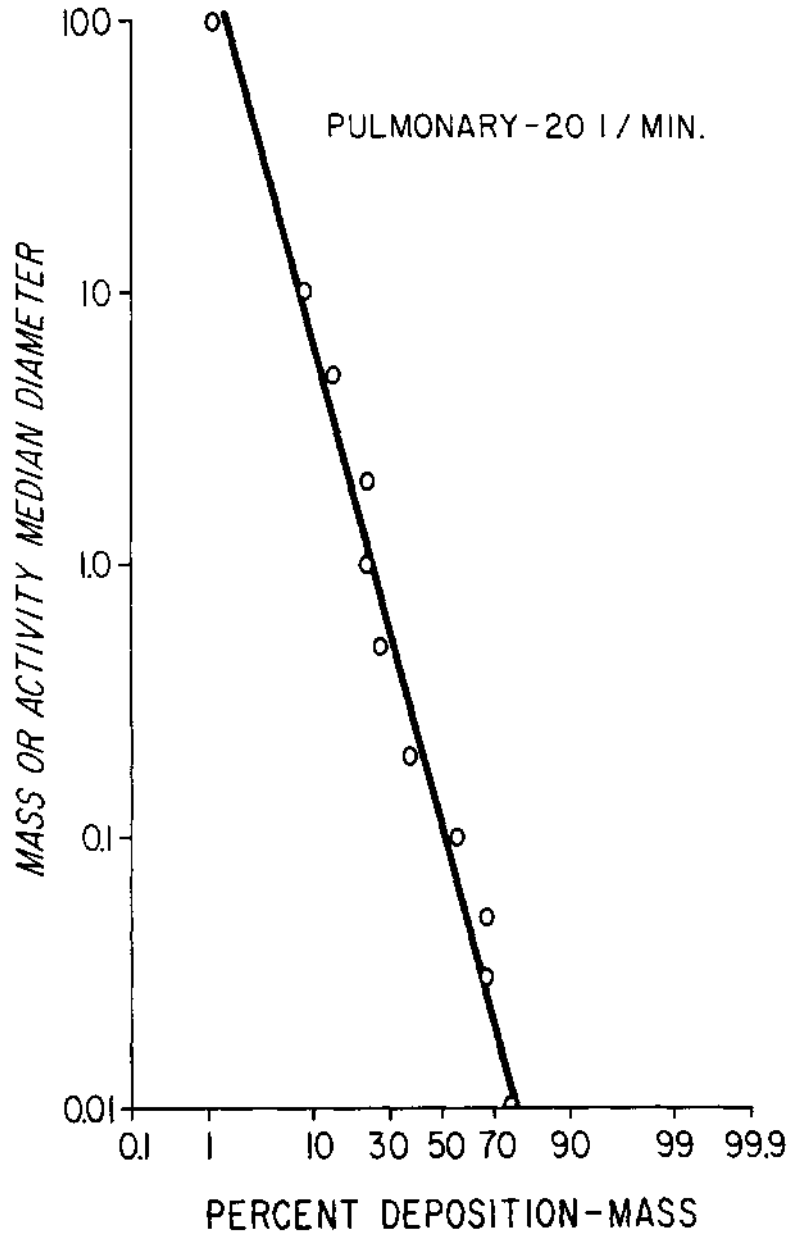

Figure 7: The average pulmonary deposition relationship implicit in Figure 5 has been replotted on a log-probability graph in order to obtain a convenient linear form.

the former in every instance. In both cases, a series of exponentials was advocated for describing and reporting clearance information. Generally, one or more fast phases were regarded as being dominantly but not exclusively associated with the clearance of the ciliated areas of the respiratory tract (N-P and T-B) and usually one slow phase is associated with the pulmonary compartment, but this exponential was regarded as the net expression of several clearance mechanisms having essentially the same kinetics. See Table 1.

RESPIRATORY TRACT CLEARANCE MODEL

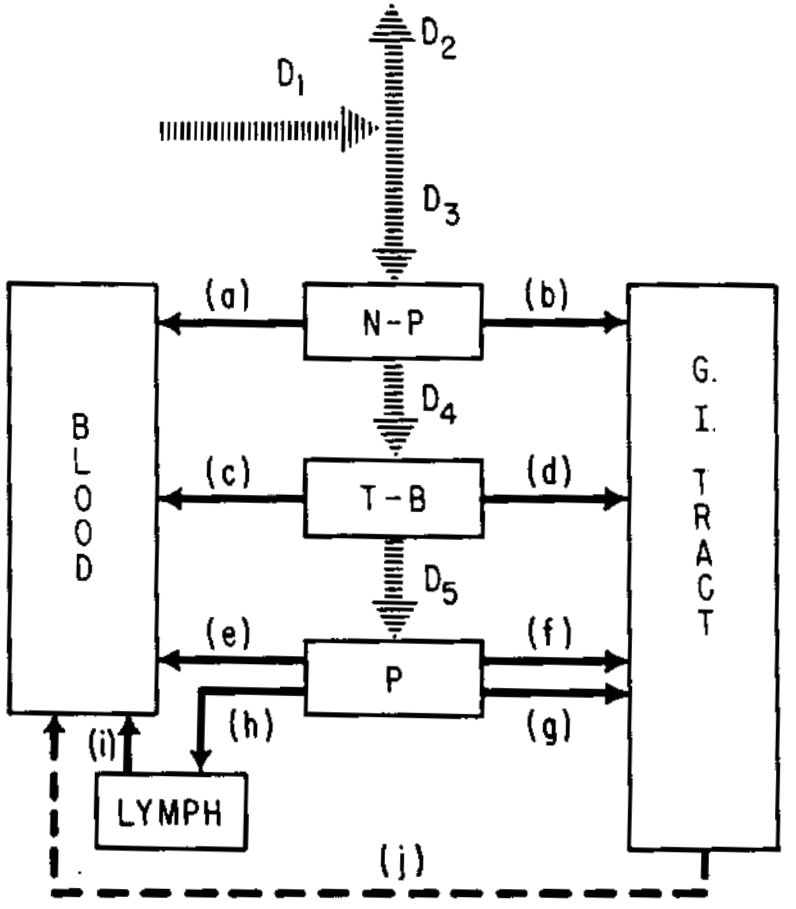

Figure 8: The D notations signify the aerosol inspired (1), expired (2), deposited in compartments N-P (3), T-B (4) and P (5), respectively. The letters a, c and e denote absorption from different respiratory compartments into the systemic circulation. The letters b, d, f and g are ciliary mucous transport pathways, with f and g special cases in which phagocytosis precedes the ciliary process. The influx and efflux of material from the lung parenchyma to the lymph nodes is denoted by h and i, respectively. An important redistribution process indirectly associated with respiratory tract clearance, i.e., gastrointestinal absorption, is termed "j".

Table I. Constants For Use With Clearance Model*

		Class (D)	Class (W)	Class (Y)
N-P	(a)	4 min/0.50	4 min/0.10	4 min/0.01
	(b)	4 min/0.50	4 min/0.90	4 min/0.99
T-B	(c)	10 min/0.50	10 min/0.10	10 min/0.01
	(d)	10 min/0.50	10 min/0.90	10 min/0.99
P	(e)	30 min/0.80	90 days/0.15	360 days/0.05
	(f)	n.a.	24 hr/0.40	24 hr/0.40
	(g)	n.a.	90 days/0.40	360 days/0.40
	(h)	30 min/0.20	90 days/0.05	360 days/0.15
Lymph	(i)	30 min/1.00	90 days/1.00	360 days/0.10

* The first value in each pair is the biological half-time of the particular compartmental process; the second value is the fraction of the material within the compartment which follows the half-time value.

The last step in creating the clearance model required the compilation of common compound forms of the important radionuclides. These materials were in turn classified according to their predicted retention in the pulmonary region. Realizing that lung clearance half-times vary from hours to years, it was felt that the older clearance format was unable to deal with the most rapid and slowest clearance situations, especially the latter (except for plutonium and thorium which were treated as special cases). This led to the decision to create three clearance classifications with one classification (Y) for materials of prolonged retention represented by a 360 day half-time. The rapid (D) and intermediate (W) clearance classifications are similar to those proposed by the older model (Table I) except for the much shorter half-times assigned the N-P and T-B regions.

Perhaps the best way to indicate the use of the models is to work through a hypothetical case. Imagine a man under comparatively normal working conditions being acutely exposed to an aerosol of enriched uranium dioxide (95 percent U^{235}), with a concentration of 10^{-6} microcuries per liter, meaning the maximum permissible concentration in air for a 40 hour week has been exceeded ten fold[1]. The AMAD was found to be 5.6 microns with a geometric standard deviation of 2.8. According to the deposition model, 80 percent of the U^{235} is expected to deposit within N-P region, 8 percent in the T-B area and approximately 10 percent in the pulmonary region. Refer to Figures 6 and 7.

From the clearance point of view we utilize the class Y constants in Table I except that 120 days is used for the clearance half-time of the P region. This value is based upon actual measurements in man and experimental animals which are summarized in Appendix 1 of the Task Group Report[2]. Turning

our attention to 10 percent of the U^{235} activity breathed now deposited in the lung parenchyma, we estimate 40 percent of this will be removed with a half-time of 24 hours to the gastrointestinal tract and the balance will be cleared with the 120 day half-time, i.e., 5 percent of that breathed. With this particular example, the clearance half-time is identical to that used in the older model, but we can judge from the difference in the deposition that the 10X MPC exposure is only about a half to a third as effective in producing the long-term lung burden as the older model would predict.

It would be easy to create examples with enormously different circumstances in which the newer approach would give a much higher estimated hazard compared to that given by the older model. The main point to be made is that the newer model does not ipso facto increase or decrease the permissible exposure levels. It attempts to make use of the information and opportunities usually available to the health physicist so that he can work with some of the realities of the situation and not be compelled to deal with a completely arbitrary scheme. Both Dr. Snyder and Dr. Mercer will consider other aspects of these models in the matters of dosimetry and implementation of sampling.

The final point which has been left until last on purpose is certainly most difficult to discuss at this time and certainly most fluid in the view of the Task Group and Committee 2; this concerns the questions of lymphatic drainage and the general kinetics associated with material moving into and out of the lymphatic tissue. There is evidence that lymphatic system and especially the lymph nodes serving the lungs can on occasion be the critical organ. In fact, according to the model that we are discussing, there are possibilities that the lymph node dose can be so significant as to overshadow the lung dose in the setting of standards. Our concern should not suggest we are attempting to squirm out of a difficult situation because it looks so bad for the lymph nodes - but we do want to be more certain about the dust buildup in and clearance from the lymph nodes serving lungs and learn more about the nature of the lymphatic system itself. Also of special importance are views on lymphatic tissue turnover (presently a highly controversial field), the radiosensitivity of lymphatic tissue and the risk to the individual from suppressed lymphatic function. I will conclude by saying that a great deal of thought is being given to these topics at this time, perhaps some commentary from Drs. Morgan and Snyder will be forthcoming at this meeting since they have just returned from a session on this topic. In any event, I will not attempt to discuss this interesting question further at this time because of its complexity and unsettled nature.

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THE USE OF THE LUNG MODEL FOR ESTIMATION OF DOSE*

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Abstract

Using the lung model developed by the ICRP Task Group on Lung Dynamics, one easily obtains estimates of the μCi-days of residence of inhaled radioactive aerosols in three regions or compartments of the respiratory tract, namely, the nasopharynx (N-P), the trachea and bronchial tree (T-B), and the pulmonary compartment (P). The report also provides an estimate of deposition and retention in the lymph of the respiratory system (L). Formulas for the μCi-days of residence in each compartment are developed in terms of the parameters used in the report to define the model and to characterize the aerosol. The dosimetric problems involved are discussed and formulas developed for expressing the dose to each of the compartments and to the lung as a whole. Adjustment factors are given to take account of the activity median aerodynamic diameter of the aerosol. For alpha emitters and beta rays of short range, say, less than 20 μ, the dose to the N-P and T-B regions is computed by considering the radioactive material as a surface deposit. For photons and beta rays of greater range, much of the energy is absorbed outside the region of deposition, and the dose estimate is an average for the lung as a whole. Following years of continuous exposure, the lymph of the respiratory system will contain a significant fraction of the total lung burden according to the present lung model. Thus the model does predict high concentrations and doses in lymphatic tissue as has been observed experimentally and as a result of human exposures.

The lung model used by ICRP to estimate values of $(MPC)_a$ [1,2] was revised recently by a task group created to advise ICRP Committee 2 concerning lung dynamics. The report of the task group[3] specifies a more realistic and quantitative scheme for the deposition and clearance of particulate matter from the respiratory tract than did the previous model. However, it does not discuss the actual computation of dose to the various compartments of the lung or to the lung as a whole. Additional information needed for the estimation of dose to various portions of the lung is discussed here, and methods of obtaining the dose estimates are presented.

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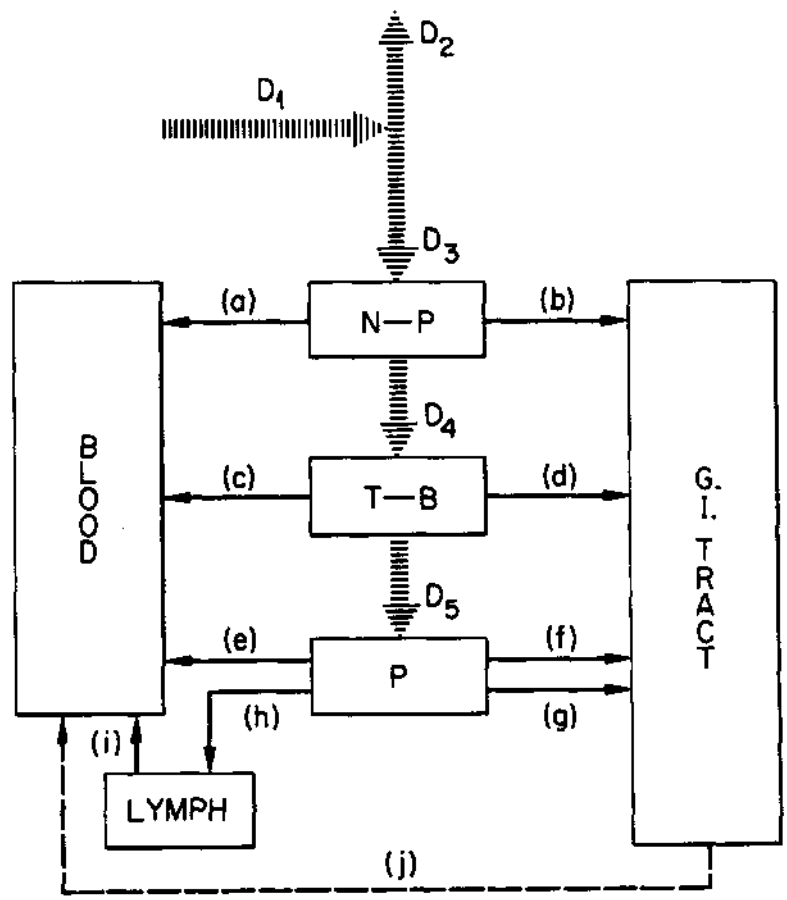
The model respiratory tract, as described by the task group, consists of three compartments: the nasopharynx (N-P), beginning with the anterior nares and extending back and down to the level of the larynx; the trachea and bronchial tree (T-B), including the terminal bronchioles; and the pulmonary (P) compartment. The schematic portrayal of these compartments, together with the associated deposition and clearance processes as shown in the report[3] of the task group, is reproduced in Fig. 1. The letters D_1 through D_5 indicate the fractions of the inhaled aerosol which are either exhaled or deposited in each of the compartments. The task group finds that these fractions vary with the activity median aerodynamic diameter (AMAD) of the aerosol, and graphs are provided in the report to show this variation. In the diagram the letters "a" through "j" indicate clearance pathways from the compartments into blood, GI tract, and/or lymph. It should be noted that the pulmonary region is not a simple compartment in the usual sense of uniform mixing and elimination, since each pathway clears a prescribed fraction of the material which is deposited, and this fraction varies depending upon the solubility of the material deposited.



Respiratory Tract Clearance Model.

Figure 1.

Both the amount of material following a particular route and the rate at which it is cleared are assigned on the basis of three classes of aerosols, as shown in Table 1. Class D material is cleared in < 1 day to 10 days, Class W in a matter of days or months, and Class Y material over a period of months to years. The values of the deposition factors $D_1 \ldots D_5$ and the corresponding clearance rates are given in the report of the task group.[3]

Table 1. Clearance Classification

Class D, Rapid	Class W, Intermediate	Class Y, Slow
< 1 da to 10 da	10 da to 100 da	> 100 da

Using this model, it is a straightforward matter to calculate the μCi-days of residence in each of the three regions for a given intake of a specified aerosol. Formulas follow for dose to the three compartments of the respiratory system during the first t days following a single intake of an aerosol:

For the nasopharynx region

$$D_{rems} = \frac{I \times 51 \times \mathcal{E}}{M} \times D_3 \left(f_a \frac{1 - e^{-\lambda_a t}}{\lambda_a} + f_b \frac{1 - e^{-\lambda_b t}}{\lambda_b} \right) \quad (1)$$

For the tracheobronchial region

(1) Dose from inhaled material deposited in region

$$D_{rems} = \frac{I \times 51 \times \mathcal{E}}{M} \times D_4 \left(f_c \frac{1 - e^{-\lambda_c t}}{\lambda_c} + f_d \frac{1 - e^{-\lambda_d t}}{\lambda_d} \right) \quad (2)$$

(2) Dose from material cleared from P region through the T-B region to the GI tract

$$D_{rems} = \frac{I \times 51 \times \mathcal{E} \times t^*}{M} \times D_5 \left(f_f \lambda_f^b \frac{1 - e^{-\lambda_f t}}{\lambda_f} + f_g \lambda_g^b \frac{1 - e^{-\lambda_g t}}{\lambda_g} \right) \quad (3)$$

For the pulmonary region

$$D_{rems} = \frac{I \times 51 \times \mathcal{E}}{M} \times D_5 \left(f_e \frac{1 - e^{-\lambda_e t}}{\lambda_e} + f_f \frac{1 - e^{-\lambda_f t}}{\lambda_f} + f_g \frac{1 - e^{-\lambda_g t}}{\lambda_g} + f_h \frac{1 - e^{-\lambda_h t}}{\lambda_h} \right) \quad (4)$$

where

I = intake at time zero (μCi)

51 = dis/day x g-rad/Mev

$\mathcal{E}$ = effective energy/dis (Mev)

M = mass of region considered (g)

D_3, D_4, D_5 = fraction of the inhaled aerosol deposited, respectively, in the N-P, T-B, and P regions

t^* = time of passage through the T-B region of material cleared from the P region to the GI tract (da)

f_a, f_b, etc. = fractions cleared by pathways a, b, etc.

λ_a, λ_b, etc. = effective elimination constants for pathways a, b, etc.

λ_f^b and λ_g^b = biological elimination constants for pathways f and g.

If the fraction $51\mathcal{E}/M$ is deleted from these formulas, they then represent the μCi-days of residence in each compartment during the first t days following the intake of I μCi. As mentioned earlier, these formulas follow directly from the definition of the new lung model except for the two factors $\mathcal{E}$ and M, the effective energy absorbed per disintegration and the mass of the particular tissue under consideration, respectively. As will be seen, it is not an entirely simple matter to decide on appropriate values for either of these parameters.

Figure 2 shows the accumulated dose to the pulmonary region from an instantaneous intake of 1 μCi of a standard aerosol, i.e., one having an AMAD of 1 μ; but in order to be perfectly general, the effective energy has been taken as 1 Mev. Thus, this graph is universally applicable for any aerosol considered in the report of the task group; one need only select the longest effective half-time for elimination from the P region, read off the ordinate for the desired time, and multiply by the appropriate effective energy. In computing these

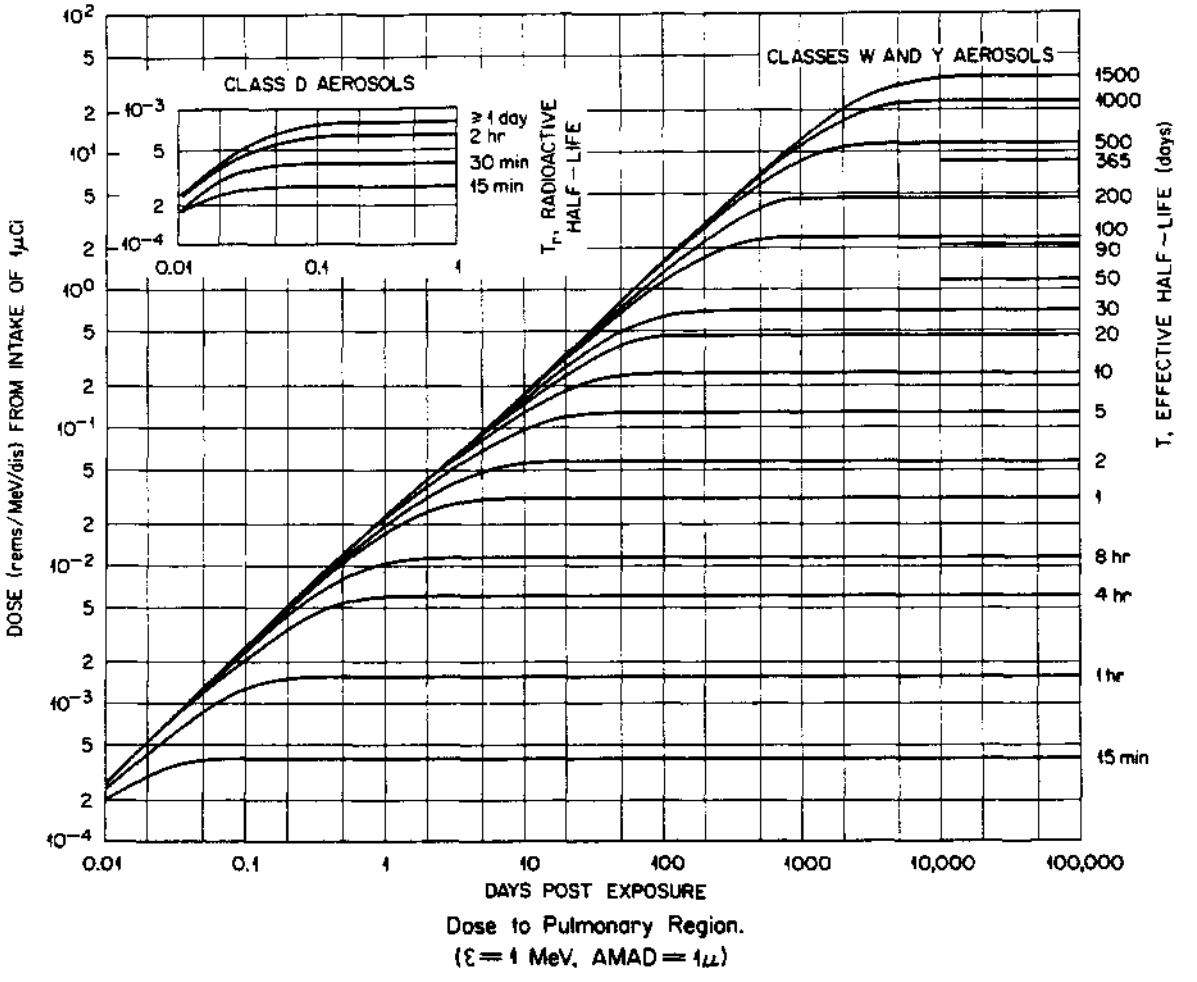


Figure 2.

doses, the mass of the pulmonary region is taken as 500 g, which must be considered to include the capillary, or trapped, blood that is present there. Of course, the doses could be changed by proportion for any other mass one might prefer to use.

The curves for aerosols of Class W or Class Y in Fig. 2 are labelled with the effective half-time, T, of the long-term component of the retention function, i.e.,

$$0.693/T = \lambda_g = \lambda_g^b + \lambda_r = 0.693/T_g^b + 0.693/T_r$$

with T_r as the radioactive decay half-time and T_g^b representing the long-term biological elimination half-time as given in Table 4 or in the appendix of the report. In all cases $T_g^b \geq 10$ days. For example, the curve corresponding to T = 1 day represents quite a number of different radionuclides; namely, all of those whose radioactive half-lives, together with the half-lives of the long-term pulmonary retention given in the report, are such that the effective half-time is 1 day, i.e., $1/T = 1/T_r + 1/T_b$. The terms of the formula corresponding to pathways of short elimination time probably would not be the same for all of

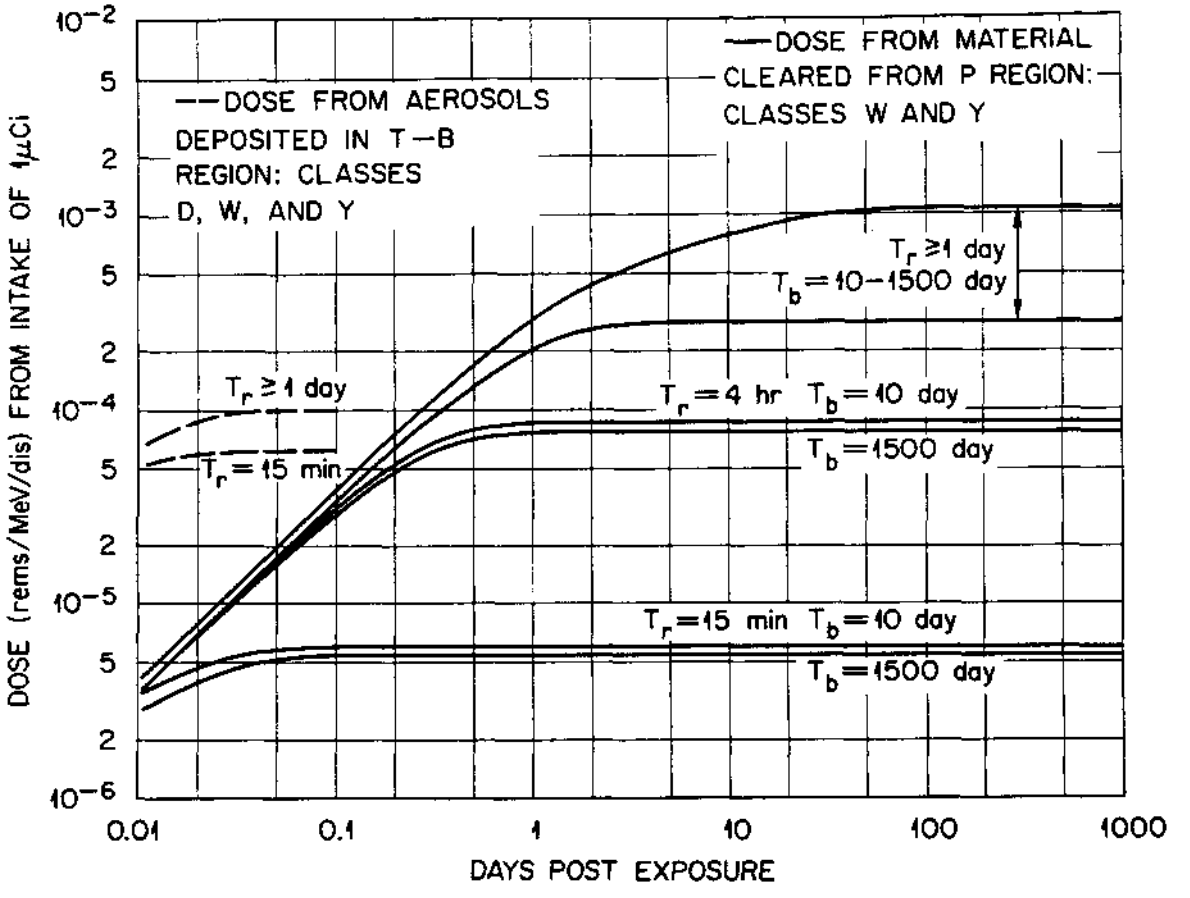
these radionuclides, but the use of a single curve for all of them does not involve an inaccuracy of more than 4%, and this inaccuracy is considered as negligible in this context. This error estimate is derived in the appendix.

With very few exceptions, the elimination half-times for an aerosol of Class D do not exceed 30 minutes; see the values given in Table 4 of the report of the task group. Thus, with these very few exceptions, the dose is substantially independent of T_r except when $T_r < 1$ day. The dose to the pulmonary region from an aerosol of Class D is given as an insert in Fig. 2, and it includes all cases except those where the report of the task group indicates a value of T_b, the biological half-time, which is substantially greater than 30 minutes. There are a few such cases listed in the appendix of the report.

The estimation of dose to the tracheobronchial region involves more novelty. The tracheobronchial tree consists of the trachea and branching bronchi down to the terminal bronchioles. It is essentially a branching tubular network. The aerosol material is carried by the mucus over the surface of these tubes as the material is cleared by ciliary action. The mass of this region is taken as 400 g which is arrived at on the basis of estimates of volume given by Weibel[4] and others and on values for the density. Because of the intricate geometrical configuration, a significant portion of the energy released will be absorbed in neighboring tissues. This is true even in the case of an alpha emitter. For example, estimates of the surface area of the T-B region vary from 10 to 20 m^2. If one takes a layer of tissue based on this surface which is 45-μ thick, i.e., the range of an alpha particle having an energy of about 5 Mev, he obtains 450 to 900 g. This is far more mass than the T-B region should have according to most estimates and indicates that a significant portion of the energy is absorbed in the surrounding tissue. The mass of 400 g is used here as an estimate of the mass of tissue lying within range of the alpha particles originating in the T-B region. The estimated dose to the T-B region from an aerosol deposited there is shown in Fig. 3 by the dashed curves.

In addition to this dose, material cleared from the P region to the GI tract must traverse the T-B region, and hence this material contributes dose during its passage through the region. The estimated dose to the T-B region from this source is shown in Fig. 3 by the solid curves. The other assumptions are as before, *i.e.*, a standard aerosol with the effective absorbed energy taken as 1 Mev. Estimates for the time of passage of the material cleared from the P region through the T-B region differ rather widely. Estimates based on observation of the movement of the material at certain sites led to estimates of a half-time for clearance of about 15 minutes, but this estimate may favor the more rapid elimination routes which are more readily observed. Other estimates based on gamma spectrometry indicate clearance times of 2 hours or more, but these estimates may be influenced somewhat by the presence of the pulmonary deposits. Although the present dose estimate, using $t^* = 1/24$ da, involves this uncertainty, it is clear that material passing from the P region to the GI tract makes a very significant contribution to the total dose received by the T-B region.

The N-P region consists essentially of the nasal passages and pharynx down to the level of the larynx. The aerosol merely deposits on these surfaces and is removed by the movement

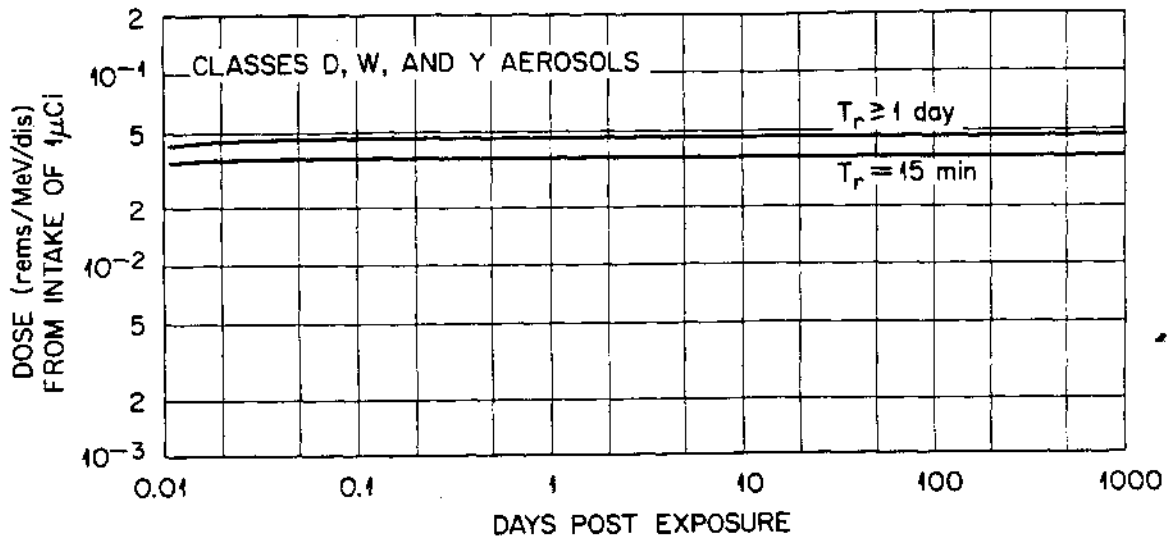


Dose to Tracheobronchial Region.
($\mathcal{E}$ = 1 MeV, AMAD = 1μ)

Figure 3.

of the mucus. Thus a surface distribution of the material seems appropriate as a model for estimation of dose. The N-P region has about 300 cm^2 of surface, and the proposed lung model assigns a half-time of 4 minutes for removal of the deposited material. There is evidence that the material accumulates to a greater degree and resides longer at certain sites than at others, but in this calculation the dose is averaged over the tissue. The dose has been computed primarily for an alpha emitter, and so the dose has been averaged over a layer which is 45-μ thick. This is the range of an alpha particle having an energy of about 5 Mev. Figure 4 shows this dose for a standard aerosol with an effective energy of 1 Mev. Because of the short clearance time for this region, the radioactive half-life makes little difference in the dose, and essentially all of the dose is delivered within the first half-hour following intake.

A certain fraction of the inhaled material is transported to the lymph nodes. For very insoluble dusts, such as those of Class Y, the proposed lung model allows 10% of this material to be eliminated from the lymph nodes with a rather long half-time of 100 to 1500 days,



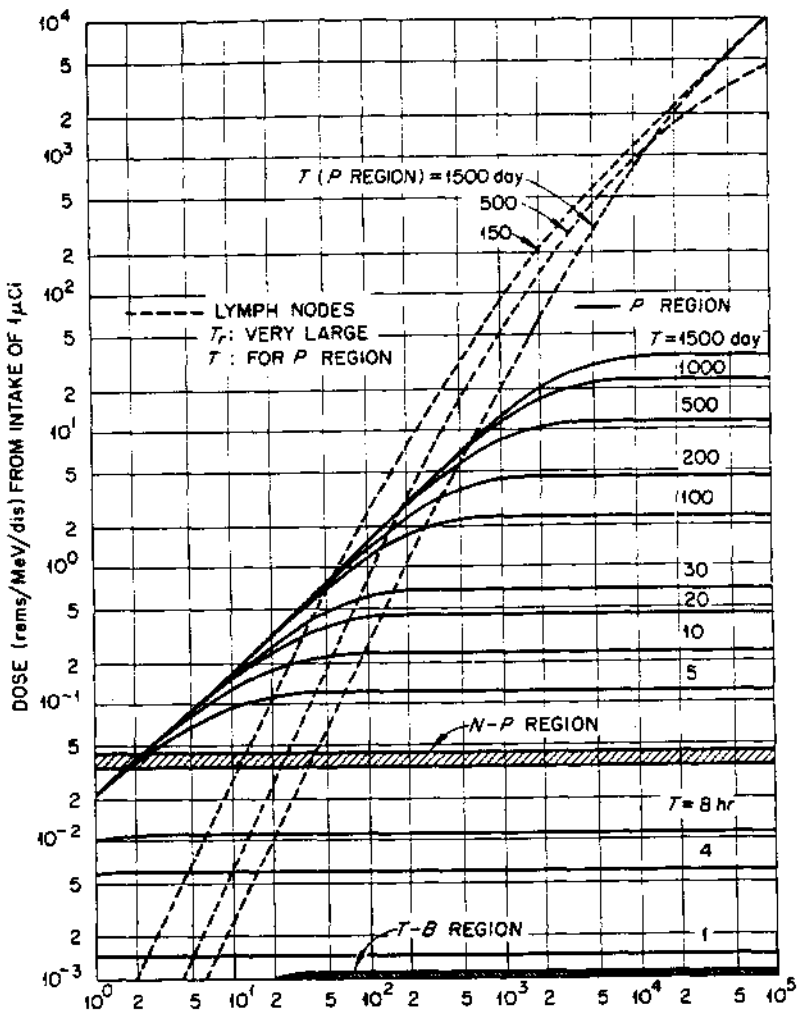
Dose to Nasopharyngeal Region.
($\mathcal{E} = 1$ MeV, AMAD $= 1\mu$)

Figure 4.

depending on the solubility of the dust. The other 90% remains in the lymph nodes indefinitely, being subject only to radioactive decay. The dose to the lymph nodes has been computed using 15 g as the weight of these respiratory lymph nodes, a value given by Pochin[5] for the tracheobronchial lymph glands. The total mass of lymphatic material in the lung is probably larger than this and the dose averaged over this mass somewhat smaller than that computed here. As discussed by Pochin,[5] the problem of migrating lymphocytes complicates the problem, and the facts are not in hand which might serve as the basis for a more accurate dose estimate to individual lymph nodes or lymphocytes.

Figure 5 shows a composite of all these calculations for a very insoluble material. The curves apply to any radioactive aerosol of Class Y which has the indicated AMAD and effective half-times in the P region. The effective energy per disintegration has been taken as 1 Mev. It is clear that the total dose to lymph nodes is greater than to any of the other three regions of the lungs. Even if one averages the dose over the entire lymphatic system of the body (which is not done here), the dose to the lymph predominates, but not by such a large factor.

In computing the dose curves given in Figs. 2-5, the AMAD has been taken as 1 μ. Since D_3 and D_5 occur as factors in the dose formula, it is possible to give a factor which corrects these curves for aerosols of other AMAD. Since $D_3 = 30$ and $D_5 = 25$ for AMAD = 1 μ, the required correction factors for the N-P and P regions are $D_3/30$ and $D_5/25$, respectively. The proposed lung model gives a constant deposition factor for the T-B region, and so factors for the pulmonary region and the N-P region are the only ones shown. It is clear that the doses vary greatly with the AMAD—the dose to the P region decreasing and that to the N-P region increasing as AMAD increases.



Dose to the Respiratory Tract.
($\mathcal{E}$ = 1 MeV, AMAD = 1 μ)

Figure 5.

In the foregoing formulas and graphs, the effective energy has been taken as 1 Mev. Thus each value must be multiplied by the effective energy absorbed per disintegration of the isotope in order to obtain the actual dose in rem. In the case of alpha particles, it seems sufficiently accurate to take the effective energy as the total energy of the alpha particles, for the thickness of the various tissues considered will be at least of the order of the range of the particle. While individual bronchioles may have a diameter this small, these smaller ones are quite closely spaced. This is indicated clearly by considerations of surface area as noted above.

It is clear that not much of the energy of photons will be absorbed near the point of origin of the photon, and hence it seems reasonable to average the dose from photons over

the entire lung. A Monte-Carlo-type code has been written to obtain the absorbed fraction of energy for photons of various energies which originate uniformly within the volume occupied by the lungs.[6] This code has been used to estimate the fraction of energy absorbed in lungs from a gamma emitter uniformly distributed in lungs, and the results are given in Table 2. A similar study has been made for a surface distribution of photons, and, as would be expected, the fraction of energy absorbed in a layer of 45-μ thickness is generally quite small.

Table 2. Absorbed Fraction for a Uniform Distribution of a Gamma Source in the Lungs of a Tissue Phantom

Energy of Gamma (Mev)	Absorbed Fraction, A.F.
0.01	0.97
0.05	0.27
0.1	0.17
0.5	0.16
1	0.15
2	0.13

Beta emitters clearly are somewhere between these two extremes. For a beta such as the tritium beta, one may use the model for local absorption; and for a beta of long range—say, 1 cm—the model averaging over the entire lung seems more appropriate. However, it is clear that further studies of the problem are indicated, but a more detailed consideration of the morphology of these regions of the lung than we have been able to find in the literature seems to be required.

Appendix

The lung model described in the report[3] provides that $\lambda_e = \lambda_g = \lambda_h$ and that $f_e + f_g + f_h = 0.6$ for all aerosols of Classes W or Y. Thus it is possible to simplify the notation of Eq. (4) and write

$$D(t) = \frac{I \times 51 \times \mathcal{E} \times D_5}{M} \left\{ 0.4 \frac{1 - e^{-\lambda t}}{\lambda} + 0.6 \frac{1 - e^{-\tau t}}{\tau} \right\} \qquad (5)$$

for aerosols of these two classes. In Eq. (5), $0.693/T = \tau = \lambda_e = \lambda_g = \lambda_h$ and $\lambda = \lambda_f$, T being the long-term effective elimination half-time of the pulmonary region which is used as index on the curves of Fig. 2. Thus $\tau = \mu + \lambda_r = 0.693/T_b + 0.693/T_r$ with T_r as the

radioactive half-time of the radionuclide and T_b as the half-time for biological elimination via routes e, g, or h of the lung model. Values of T_b are given as 90 days or 360 days in Table 4 of the report, but values of T_b ranging from 10 days to 1500 days are recommended for a variety of compounds in the appendix.

It is clear that the specification of τ, or T, does not determine the value of T_r or of $\lambda = \lambda_f$. Several radioactive aerosols might have the same T but different values of T_r. In that case λ_f will have different values also since the half-time for biological elimination via pathway f is fixed at 1 day. In preparing Fig. 2, the maximum value of T_b compatible with the value of T and with the lung model was used, i.e., in the relation $1/T = 1/T_r + 1/T_b$, $T_b = 1500$ days was used to determine T_r. This choice only affects the calculation through the parameter $\lambda = 0.693\,(1 + 1/T_r)$ and makes the dose estimates provided by Fig. 2 slightly smaller than might be the case if other values of T_r and T_b compatible with the chosen value of T were used. It will be seen that the difference cannot exceed 4% in any case, and the values as calculated indicate the difference is much less than this in all the numerical cases computed.

Assume, then, that (5) is the formula as computed for a specified value of T with $T_b = 1500$ days and that in an actual case the appropriate value is T_b'. In this case $1/T = 1/T_r' + 1/T_b'$ since we are supposing this aerosol has a long-term effective elimination half-time of T. Then the value of λ in (5) for the actual isotope will be given by

$$\lambda' = 0.693\,(1 + 1/T_r') < 0.693\,(1 + 1/T_r) = \lambda$$

and

$$\lambda - \lambda' = 0.693\,(1/T_r - 1/T_r') = 0.693\,(1/T_b' - 1/T_b) < 0.693/10.$$

Let $D'(t)$ be the dose corresponding to the use of the primed values in (5), i.e., the actual aerosol. Then the fractional error in using the computed curve is given by

$$\frac{D'(t) - D(t)}{D'(t)} = \frac{\dfrac{1 - e^{-\lambda' t}}{\lambda'} - \dfrac{1 - e^{-\lambda t}}{\lambda}}{\dfrac{1 - e^{-\lambda' t}}{\lambda'} + 1.5\,\dfrac{1 - e^{-\tau t}}{\tau}} . \qquad (6)$$

Note that the numerator satisfies the relation

$$\frac{1 - e^{-\lambda' t}}{\lambda'} - \frac{1 - e^{-\lambda t}}{\lambda} = t \int_{\lambda' t}^{\lambda t} \frac{1 - e^{-x} - x e^{-x}}{x^2}\, dx$$

$$\leq t\,(1 - e^{-\lambda t} - \lambda t\, e^{-\lambda t}) \int_{\lambda' t}^{\lambda t} \frac{dx}{x^2} = \frac{(1 - e^{-\lambda t} - \lambda t\, e^{-\lambda t})\,(\lambda - \lambda')}{\lambda\,\lambda'} \tag{7}$$

$$\leq \frac{(1 - e^{-\lambda t})^2\,(\lambda - \lambda')}{\lambda\,\lambda'} .$$

The above inequalities follow readily from the facts that $1 - e^{-x} - xe^{-x}$ is an increasing function of x for $x > 0$ and that $1 - e^{-x} - xe^{-x} \leq (1 - e^{-x})^2$. Both of these properties are easily established.

Consequently, we can substitute in (6) and obtain

$$\frac{D'(t) - D(t)}{D'(t)} \leq \frac{(1 - e^{-\lambda t})^2\,(\lambda - \lambda')}{\lambda\,\lambda'\left(\frac{1 - e^{-\lambda' t}}{\lambda'} + 1.5\,\frac{1 - e^{-\tau t}}{\tau}\right)} . \tag{8}$$

The right member of (8) may be rearranged to obtain

$$\frac{D'(t) - D(t)}{D'(t)} \leq \frac{1 - e^{-\lambda t}}{1 - e^{-\lambda' t}} \times \frac{(1 - e^{-\lambda t})\,(\lambda - \lambda')}{\lambda + \frac{1.5\,\lambda\lambda'}{\tau} \times \frac{1 - e^{-\tau t}}{1 - e^{-\lambda' t}}} . \tag{9}$$

It is not difficult to show that if $x > y$ one has

$$\frac{y}{x} \leq \frac{1 - e^{-y}}{1 - e^{-x}} < 1. \tag{10}$$

Substituting τ/λ' for $(1 - e^{-\tau t})/(1 - e^{-\lambda' t})$ and λ/λ' for $(1 - e^{-\lambda t})/(1 - e^{-\lambda' t})$ in (9) further increases the right member, and one obtains

$$\frac{D'(t) - D(t)}{D'(t)} \leq \frac{(1 - e^{-\lambda t})\,(\lambda - \lambda')}{2.5\,\lambda'} < \frac{0.1\,(1 - e^{-\lambda t})}{2.5\,(1 + 1/T_{r'})} < 0.04\,(1 - e^{-\lambda t}) \tag{11}$$

since $0 < \lambda - \lambda' < 0.693/10$ and $\lambda' = 0.693\,(1 + 1/T_{r'})$.

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Air Sampling Problems Associated with the Proposed Lung Model

by

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Abstract

Air sampling requirements introduced by the new lung deposition model proposed by the Task Group on Lung Dynamics are considered in relation to available sampling techniques. It is shown that present techniques for determining the activity median aerodynamic diameters of hazardous dusts are sometimes not applicable in practice. The alternative technique offered by size selective samplers is discussed and recommendations are made for relating "respirable dust" concentrations to the new lung model. Certain limitations of the deposition model are briefly discussed.

INTRODUCTION

I doubt that the problem of air sampling was uppermost in the minds of any of the members of the Task Group on Lung Dynamics during the preparation of the report on deposition and retention models. Once the deposition model had been defined in terms of particulate aerodynamic diameters, it became apparent that the problem facing the health physicist in the field would be that of determining the activity distribution of hazardous airborne particles as a function of their aerodynamic diameters. Since techniques for making such determinations have been available for some time, and since, in any event, air monitoring was not a responsibility of our Task Group, it did not appear necessary to consider the sampling problem in detail. A more pressing matter was that of relating deposition to the parameters of the various activity distributions that might be encountered. It appeared at first that it might be necessary to provide curves of deposition as a function of activity median aerodynamic diameter (AMAD) for a wide variety of geometric standard deviations. (σ_g). When the deposition curves were applied to hypothetical aerosols having log-normal activity distributions, however, it was found that the predicted deposition in each of the three compartments could be related to the median diameter of the distribution almost independently of the geometric standard deviation. Although differences in the latter introduced some uncertainty into the deposition value at at given AMAD, it appeared sufficiently small to warrant using an average curve for the range of distribution parameters normally encountered in air sampling. On the basis of these results, the Task Group recommended that air sampling be done to determine activity median aerodynamic diameters.

Superficially, then, the deposition model does not present any new sampling problems since, as I have already pointed out, techniques for making the necessary measurements are well known. However, when the activity distributions and concentrations that might be encountered in practice are compared with the capabilities of the sampling techniques actually available, it becomes apparent that there are real situations in which the Task Group's recommendation will be difficult to follow. Moreover, there are limitations on the lung model itself, arising from the fact the aerodynamic diameter is not invariably the particle characteristic of greatest significance in deposition, which might possibly introduce significant errors into the prediction of deposition for certain radioactive dusts of industrial significance if this prediction is based on an estimate of the AMAD. In the following discussion, therefore, I am going to review first how AMAD's are measured and what are the shortcomings of available instruments for doing so; then consider the alternative technique offered by size selective samplers; and finally take up the limitations of the lung model when activity is associated with very small particles.

THE MEASUREMENT OF AMAD'S

There are a number of devices which separate particles on the basis of their aerodynamic diameters and which conceivably could be adapted to the determination of the AMAD's. Most of them, however, are more suited to laboratory work than to routine air sampling. It is my own opinion that at the present time the only practical method for determining AMAD's in the field is one which employs May's technique of cascade impaction (1).

For the benefit of any who are not familiar with the cascade impactor it might be well to point out that it is a sampling instrument consisting of a series of impaction stages followed by a filter paper. At each stage, air flows through one or more jets to impinge normally on an adhesive-coated collecting plate. Particles of sufficient inertia are thrown out of the air stream onto the collecting surface. The jets at a given stage are constructed so that the velocity of the air stream is greater than it was at the preceding stage and the particles collected at successive stages become progressively smaller. After a sample is collected, the activities on each plate and on the back-up filter are analyzed and the data used to estimate the distribution parameters. With proper calibration, one of these parameters will be the AMAD.

In the past, many people felt that it was necessary to calibrate the instrument for whatever dust was to be sampled in order to relate the results to some linear dimension as measured by means of a microscope. I think it is generally recognized, now, however, that it is a real advantage to be able to calibrate the instrument using spherical particles of known density to obtain curves of collection efficiency as a function of aerodynamic diameter for each impaction stage. The diameter corresponding to a collection efficiency of 50% is then taken as an effective cut-off aerodynamic diameter (ECAD). In all subsequent interpretations of impactor data it is assumed that all particles collected at a given stage, regardless of shape or density, have aerodynamic diameters larger than the cut-off diameter for that stage. Couchman (2) has demonstrated the validity of the relationship between collection efficiency and

aerodynamic diameter for spheres for densities up to 19 gm/cm^3. The relationship is given added support by Laskin's data (3) for irregularly shaped UO_2 particles. It is reasonable to assume that particles will impact in accordance with their aerodynamic diameters except, perhaps, in the event that their shapes are quite extreme.

In principle, then, the cascade impactor can be used to provide the measurement of activity median aerodynamic diameter necessary in establishing the predicted deposition in the respiratory tract. What can be achieved in practice, however, will depend on the operating characteristics of the particular instrument chosen. The characteristics of a cascade impactor that are important in the determination of AMAD are the sampling flow rate, the effective cut-off aerodynamic diameters of the various stages, the wall losses, i.e., the relative amount of the material entering the impactor which is deposited on surfaces other than those of the collecting plate or the back-up filter, and the area covered by the deposited material at each stage. The first three of these characteristics are summarized in Table I for some typical impactors. I have chosen as examples three instruments which are commercially available but which are quite different in design. The Casella (May) impactor (4) has four impaction stages of rectangular jets; the Batelle impactor (5) has six stages of single round jets; the Andersen impactor (6) has six stages, each containing 400 round jets.

Table I. Calibration Data for Typical Impactors

	Casella (1)	Batelle (5)	Andersen (8)
ECAD Stage 1	12.0 μm	16.0 μm	7.5 μm
ECAD Stage 2	3.9	7.9	5.1
ECAD Stage 3	1.5	3.9	3.5
ECAD Stage 4	0.5	1.9	2.0
ECAD Stage 5	-	0.9	1.0
ECAD Stage 6	-	0.4	≈ 0.6
Flow Rate	17.5 L/M	12.5 L/M	28.3 L/M
Wall Losses	6-42% (2)	6% (5)	30-45% (2)

The cut-off diameters in Table I correspond to the indicated flow rate. A calibration for one particular flow rate can be extended to other flow rates simply by multiplying the observed effective cut-off diameters by the factor $(F_o/F)^{\frac{1}{2}}$, where F_o is the flow rate at which calibration was made and F is the flow rate for which cut-off diameters are needed. Extending the calibration in this way should give valid results as long as the Reynolds number of flow in any jet does not fall below about 100 (7). Moreover, there is no need to make one's own calibration of any of the impactors included in Table I; it is sufficient merely to verify that jet dimensions are as specified.

Wall losses reduce the reliability of impactor data in that there is no way of knowing if the activity actually analyzed had the same size distribution as that entering the impactor. Wall losses in the Casella and Andersen impactors may not be as discouraging as Table I indicates. Couchman (2), whose data are quoted in that table, found that most of the wall losses in the Andersen impactor were due to impaction of particles on the top of the first jet stage. The inlet

cone of this impactor functions somewhat like a single round jet of poor collection characteristics. May (8), whose data indicated an effective cut-off aerodynamic diameter for this process of roughly 15 μm, redesigned the inlet and first two stages of the Andersen to offset the inlet wall losses. With this modification, wall losses should be less than ten percent. The wide range of wall loss data for the Casella is, I believe, the result of size distribution effects combined with overloading of some stages. When radioactive aerosols in low mass concentrations were used, the wall loss figure of six percent was observed.

What I have said so far may have given the impression that determining AMAD's does not pose any real problem. However, a consideration of the flow rates at which these impactors normally operate will raise some serious doubts on this point. To detect MPC levels of some airborne contaminants, for instance, it may be necessary to sample many cubic meters of air to collect enough activity to yield statistically valid data. Not only may this require very long sampling periods, but the inevitable nuisance dust may overload some collector plates, leading to rebound of impacting particles and re-entrainment of deposited particles. Both of these effects should be scrupulously avoided, since they not only contribute to wall losses, but affect the collection efficiencies on which calibration is based.

In Table II, the quantity which I have labelled "loading capacity" has been introduced in an effort to put some numbers on the limits imposed by the requirement that rebound and re-entrainment be avoided. For stages other than the first, the loading capacity is merely the product of the total cross-sectional area of the jet orifices at a given stage and the average between its effective cut-off diameter and that of the previous stage. For the first stage, it was necessary to use its own effective cut-off diameter, so its loading capacity is relatively lower than those of other stages. Thus the loading capacity is approximately equal to the mass of material of unit density contained in a deposit when it covers the jet area with a layer one particle deep. As such, it is a rough estimate of the mass, active or otherwise, that can be collected before rebound and re-entrainment become a problem. The tabulated values, incidently, should be multiplied by the square root of the density of the material being collected.

While it would not be wise to give too much credence to the absolute values of these numbers, their values relative to one another should allow some reliable comparisons. Some interesting points are brought up by Table II, I think. First, under most circumstances a reliable sample will include only a few milligrams of material; second, when the AMAD is less than about five microns, the

Table II. Loading Capacities* for Typical Impactors

Stage	Casella	Batelle	Andersen
1	1.6 mg	2.3 mg	3.3 mg
2	0.24	0.70	1.7
3	0.05	0.14	0.69
4	0.006	0.03	0.25
5	-	0.005	0.05
6	-	0.001	0.016

*For unit density material.

size of a reliable sample will be governed by loading at the narrower jet stage and will be correspondingly restricted; and third, the multi-jet instrument has a marked advantage over the single jet instrument in the matter of tolerable deposit on each stage. For a given flow rate and cut-off diameter, the loading capacity increases with the cube root of the number of holes in the stage. Thus, a given stage of the Andersen impactor can safely collect perhaps seven times as much material as a stage of a single jet impactor having the same collection characteristics.

The factors of low flow rate and small loading capacity conspire to put severe limitations on applying instruments such as these to the air sampling problem. It is only fair to point out, of course, that the instruments I have discussed were not designed with this particular problem in mind. That the necessary instrumentation could be designed is indicated, I think, by the development of high flow rate samplers, such as those described by Lidwell (9) and by McFarland and Zeller (7), and the "centripeter", a sampler of essentially limitless loading capacity, described by Hounam and Sherwood (10). For the present, however, it seems to me that the Task Group's recommendation to determine AMAD's can be followed only when the activity concentration is sufficiently high that a statistically useful amount of activity can be collected while accumulating a few milligrams of total particulate material. When this is not the case other methods will have to be adopted.

SIZE SELECTIVE SAMPLERS

One of the most significant advances in air monitoring in recent years has been the development of size selective samplers. These are usually two-stage instruments in which the first stage removes particles that would be unlikely to penetrate to the pulmonary regions of the lung if inhaled. The second stage collects all particles passing the first, thus providing a sample that permits calculation of the air concentration of what has often been termed "respirable dust". A variety of collection mechanisms, including sedimentation (11), centrifugation (12,13), impaction (14), and filtration (15), have been applied in designing the first stages of such samplers. I am going to discuss the collection characteristics of three samplers, each representative of a different collection mechanism, in relation to the lung deposition model. The three I have chosen are the British horizontal elutriator (11), the HASL cyclone (12), and the May-Druett preimpinger (14).

Since two-stage samplers do not provide an estimate of AMAD's, it is apparent that some other method will have to be used to relate the data they provide to the deposition model. When a size selective sampler is used to monitor an atmosphere containing a contaminant having an activity median aerodynamic diameter, AMAD, and a geometric standard deviation, σ_g, we would like the second stage to collect a fraction, $C(AMAD, \sigma_g)$, of the total airborne activity, such that

$$P(AMAD,\sigma_g) = K \cdot C\ (AMAD, \sigma_g) \qquad (1)$$

where P is the fraction of the same contaminant which would be deposited in the pulmonary region and K is a constant for all values of AMAD and σ_g. This can be rigorously true, I think, only if

$$P(AD)/C(AD) = K \qquad (2)$$

i.e., the ratio of the probability that a given particle could deposit in the pulmonary regions to the probability that it would penetrate to the second stage of the sampler is a constant for all aerodynamic diameters.

That this relationship does not hold for any of the three instruments under consideration is apparent from Figure I, in which the ration, P(AD)/C(AD), calculated for the pulmonary deposition at a tidal volume of 1450 cm^3, has been plotted for each sampler. On the other hand, the manner in which the value of the ratio fluctuates with aerodynamic diameter suggests that when size distributions are considered, the average ratios may show less variation. To test this, predicted deposition was calculated as a function of the fraction of airborne activity penetrating the first stage. Log-normal activity distributions were assumed and the calculations were made for six values of σ_g between 1.5 and 4.0. For penetration values below about 0.15, the range of σ_g values that were included in the calculations diminished progressively. All three tidal volumes - 750 cm^3, and 1450 cm^3, and 2150 cm^3, - were included. The results are shown in Figures 2 - 4. Average values are shown for a tidal volume of 1450 cm^3, together with the extreme values for all three breathing patterns.

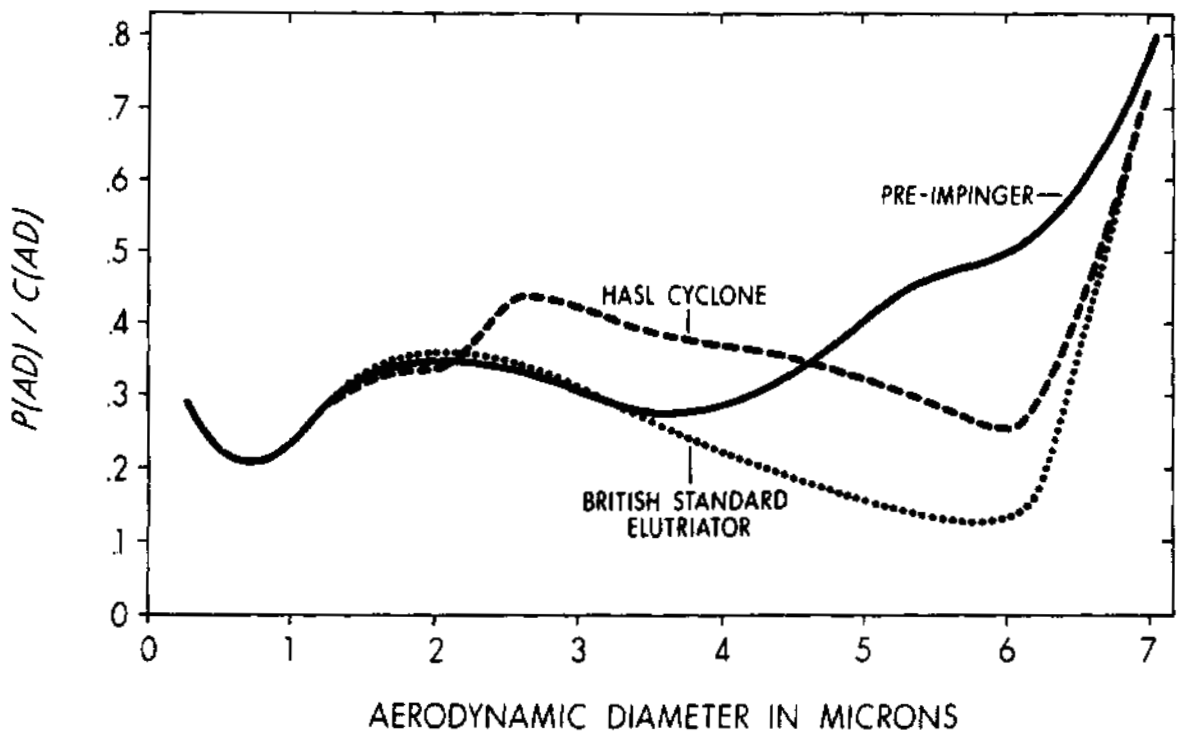

Figure 1. Ratio of predicted pulmonary deposition to first stage penetration as a function of aerodynamic diameter

Since the Task Group recommended the use of the average deposition curves at 1450 cm^3, when sampling for AMAD's, it seems reasonable to make a similar recommendation with respect to the use of size selective samplers, as far as pulmonary deposition is concerned. At that tidal volume, the extreme values of de-

position at a given penetration value do not differ from the average by more than ten percent when the latter lies between 0.1 and 0.9. For activity distributions penetrating the first stage to the extent of 30 percent or more, deposition estimates based on AMAD's show an even smaller range of values and extend to distributions which have penetrations close to one hundred percent. However, the size selective sampler requires fewer analyses and is probably more convenient to use.

Size selective samplers possess an interesting, although probably not very significant, advantage due to the fact that for penetration values between about 0.1 and 0.9 their deposition-penetration curves can be represented as

$$P(AMAD, \sigma_g) = a + b \cdot C(AMAD, \sigma_g) \qquad (3)$$

If an activity distribution is not itself log-normal but can be expressed as the summation of several log-normal distributions, each of which contributes a fraction, F_i, to the total amount penetrating the first stage, and if the penetration, C_i, of each individual distribution lies in the range for which equation 3 is valid, then the total predicted pulmonary deposition is

$$\begin{aligned} P(\text{total}) &= \Sigma\, P_i \cdot F_i = (a + b\, C_i)F_i \\ &= a\, \Sigma\, F_i + b \cdot \Sigma\, F_i C_i \\ &= a + b \cdot C\ (\text{total}) \end{aligned}$$

and equation 3 is valid for any activity distribution satisfying the conditions described above.

I have not discussed the operational characteristics of any of these samplers, because I have preferred to look at them as examples of different collecting mechanisms. They can be designed to operate at different flow rates (loading capacity should never be a problem) while maintaining approximately the same collection efficiency curves. Figures 2 - 4 show that essentially the same results are obtained with samplers having somewhat different efficiency curves. In this connection, calculation of deposition-penetration curves for a few other selective samplers show similar results.

SOME LIMITATIONS ON THE LUNG DEPOSITION MODEL

I pointed out earlier that the deposition model was defined in terms of aerodynamic diameters. The reason for this, of course, lies in the fact that the processes of sedimentation and impaction, which are responsible for most of the deposition of particulate mass in the respiratory tract, are both functions of aerodynamic diameter. The only other processes accorded any significant role in deposition are interception and diffusion due to Brownian motion, the first of which is independent of density, while the second is not only independent of density, but varies inversely with particle size. Since the deposition model was actually calculated for unit density spheres it was apparent that labelling the abscissa "aerodynamic diameter" could lead to erroneous applications when large particles of extreme shape or very low density or very small particles of large density are encountered. I think the former problem can be safely ignored, but there are practical situations that may make the latter problem significant.

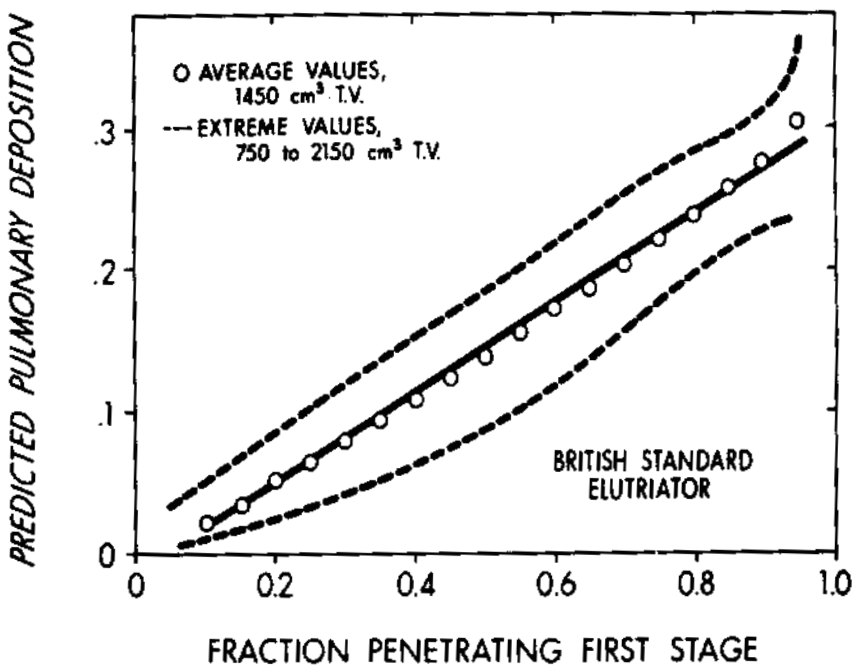

Figure 2. Predicted pulmonary deposition as a function of first stage penetration for British Standard elutriator

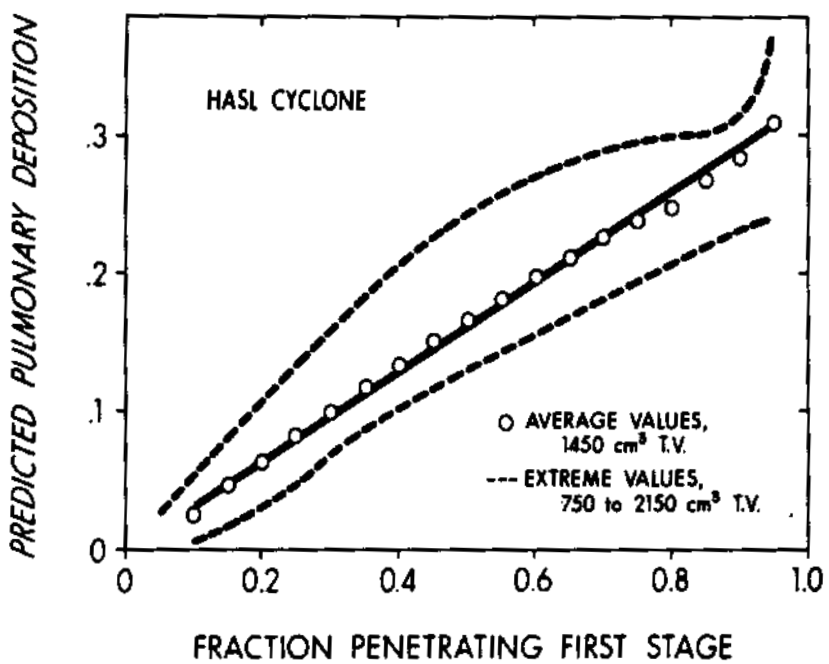

Figure 3. Predicted pulmonary deposition as a function of first stage penefor HASL cyclone

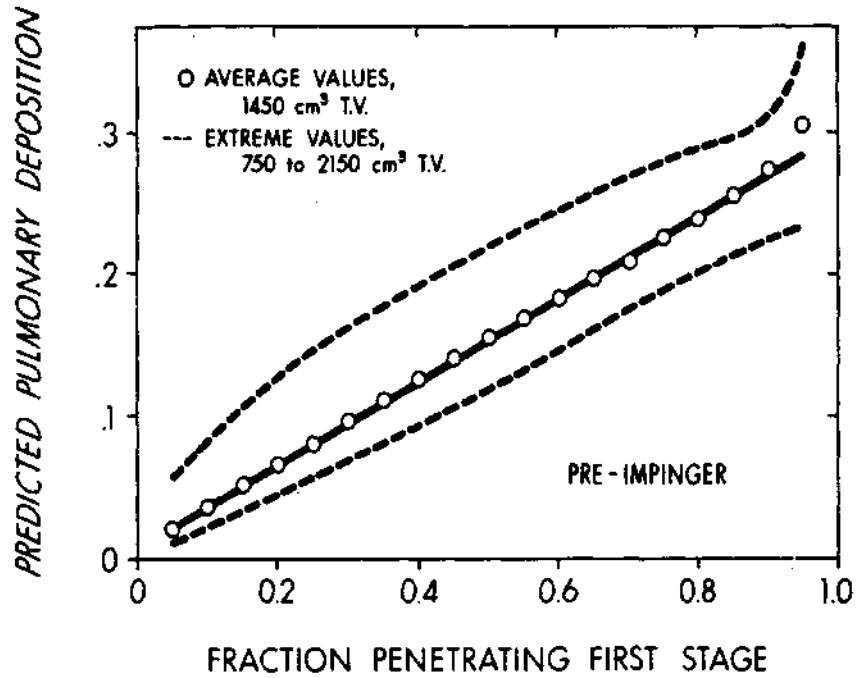

Figure 4. Predicted pulmonary deposition as a function of first stage penetration for the Pre-impinger

A spherical particle of density, ρ_p, and aerodynamic diameter, D_p, has a geometric diameter, D_p, given by

$$D_p = \left(\frac{C_u}{C_p \rho_p}\right)^{\frac{1}{2}} D_u$$

where C_u and C_p are slip factors. A particle having an aerodynamic diameter of 0.3 μm and a density of 11 gm/cm³, for instance, has a geometric diameter of about 0.05 μm and its proper predicted pulmonary deposition is at least twice the value assigned to it on the basis of the deposition curves. As geometric diameters approach molecular dimension an additional complication arises in that nasal deposition may again become significant.

I am not sure to what extent these limitations may prove important in practice. Certainly they raise questions concerning air sampling in certain mine environments where the decay products of radon are a prime hazard. Data on activity distributions in mine atmospheres (16,17) indicate that dust-borne radon decay products are predominantly on particles having aerodynamic diameters probably below 0.5 μm. When the methods described above are used to sample distributions of this sort, the data on AMAD or first stage penetration of a size selective sampler will be in the region of lowest reliability. Moreover, their interpretation will be complicated by the possible presence of unattached decay products.

SUMMARY AND CONCLUSIONS

The Task Group on Lung Dynamics has recommended that air monitoring be directed toward determining the activity median aerodynamic diameter of air-borne hazards. The capabilities of available sampling techniques, however, are such that the recommendation can be followed only when the activity concentration is sufficiently high that an adequate amount of activity can be collected while accumulating only a few milligrams of total particulate material.

For pulmonary deposition, size selective samplers provide a convenient alternative to determining AMAD's. The efficiency curves of the first stage of the British elutraitor, the HASL cyclone, and the May-Druett pre-impinger, each of which employs a different collection method, are such that a simple relationship exists between the predicted pulmonary deposition at a tidal volume of 1450 cm^3 and the fraction of air-borne activity penetrating the first stage, regardless of the parameters of the activity distribution. For penetration values between about 0.1 and 0.9, the relationship is essentially linear.

Because the deposition model has been defined in terms of aerodynamic diameters, its application in circumstances in which activity is associated primarily with very small particles of dense material may lead to erroneous conclusion.

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DEPOSITION AND CLEARANCE OF RADIOACTIVE PARTICULATES IN THE TRACHEOBRONCHIAL TREE OF RATS*+

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INTRODUCTION

The tracheobronchial tree serves two major roles in minimizing the retention of inhaled particles. The tree acts as a filtering network which protects the deep lung, and it serves as the final pathway in the removal of particulates which are carried to it from the lower respiratory tract[1,2]. Such particulates following transport to the mucociliary epithelium are carried by this mechanism to the tracheal orifice and the oropharynx, from which point they are usually swallowed or may be expectorated.

The rates of removal of particles from the tracheobronchial system are inadequately characterized. Direct measurements of the velocities of movement of particles deposited on the tracheal surface have been shown to range up to 30 mm per minute. In addition, two bronchial velocities have been reported[3] but no data are available on the rates of clearance from the finer bronchioles.

Studies in this laboratory have resulted in the development of an esophageal collection technique for directly measuring tracheobronchial clearance in rats[4]. The technique involves the placing of a tight fitting tube into the esophagus of the rat and carrying the tube down through

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the stomach and abdominal wall into a collection bottle. The tube contents are flushed into the collection bottle by the normal drinking of the animal or the system can be flushed with saline solution at any designated time by introducing a blunted needle into the tube via the mouth. The esophageal collection technique permits the collection of all material cleared from the pulmonary system of the rat through the tracheal orifice at time intervals ranging from minutes to days. Subsequent studies, in which comparisons of clearance measurements obtained by fecal analysis and esophageal collections were made, have shown no detectable alteration of mucociliary clearance dynamics over a five day period[5]. The esophageal collection method results in the direct measurement of clearance rates, i.e., the absolute amount of material removed from the pulmonary system through the tracheal orifice over the period of the designated collection interval. It should be noted that clearance and clearance rates are functions of both a specific deposition pattern of particles along the tracheobronchial tree and the velocities with which particles are swept to the tracheal orifice (escalator velocity). This is best demonstrated by two extreme but simple analogies.

Consider an anatomical compartment of the tracheobronchial tree where deposited material is swept toward the tracheal orifice by the mucociliary escalator at a constant velocity. This is represented by the conveyor belt shown in Figure Ia. Particles are assumed to be deposited on the conveyor belt (ciliated epithelium) in a specific, non-uniform pattern as shown. If all the material leaving the conveyor (pulmonary) system is collected in the collection bottle (clearance) and the bottle is changed every 20 minutes, then the contents of each

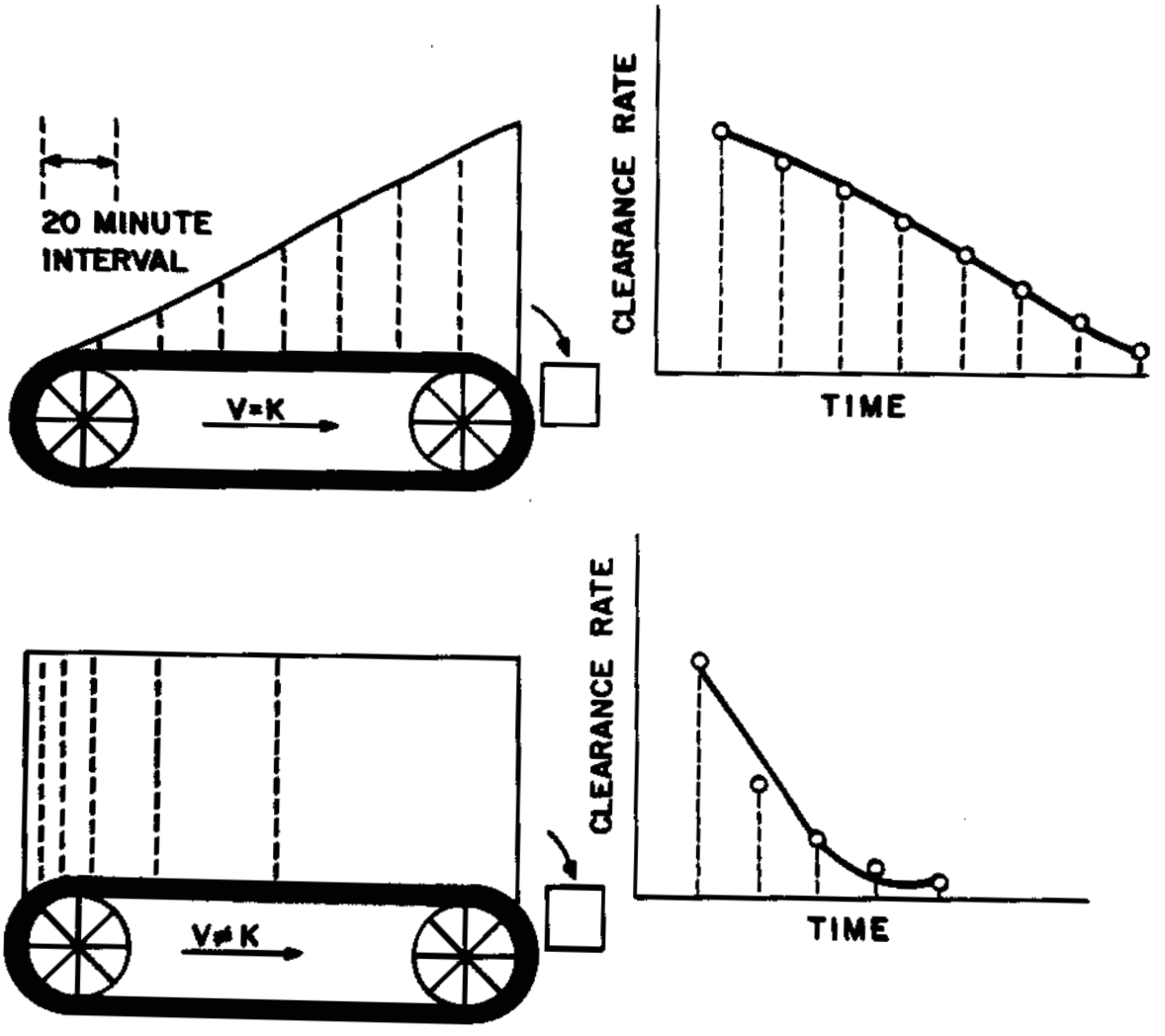

FIGURE 1

Analogy representing the tracheobronchial clearance of particles assuming:

(top) (A) A constant escalator velocity and a non-uniform deposition of particles, and

(bottom) (B) A uniform deposition of particles and varying escalator velocities.

bottle represents a clearance rate, i.e., the amount of material removed from the system per unit time. A plot of the amount of material in each bottle (clearance rates) gives a mirror image of the original deposition

pattern of material in the system. Under these conditions, the variation in clearance rates is determined primarily by the deposition pattern of the particles in the tracheobronchial tree.

At the other extreme, deposition on the conveyor belt (ciliated epithelium) is assumed to be uniform but the velocity of the conveyor belt (mucociliary escalator) varies (Figure 1b). This is analogous to the situation where the escalator velocity may vary depending on location in the lungs (primary or tertiary bronchioles) or as a result of the effect of stress on the system. If the clearance rates are plotted, any variation in clearance rates would reflect the varying velocities of the mucociliary escalator mechanism(s).

From the above, it is obvious that the interpretation of clearance and clearance rate data requires a knowledge of the specific deposition patterns associated with a technique of producing a pulmonary burden of particulates, as well as a knowledge of the biologic escalator velocities along the tracheobronchial tree. The present experiments were undertaken to determine the kinetics of removal of insoluble particles from the lungs of rats during the time period ranging from immediately after deposition to 5 days after exposure using the esophageal collection technique. The particles were administered to the animals by intratracheal injection. Two modifications in the positioning of the rats during and immediately following injection were utilized in an effort to alter the deposition pattern of the particles along the tracheobronchial tree.

MATERIALS AND METHODS

(1) Esophageal Collection Procedure. Adult male rats of the Wister

strain, weighing between 350 and 500 gm, were prepared surgically for esophageal collection as described previously[4]. The surgical procedure was performed under sodium pentobarbital (Nembutal) anesthesia on animals fasted for 48 hours. The animals were not restrained during the experiment and were given injections of 10 cc of glucose plus saline twice daily to avoid dehydration.

Experiments were initiated 24 hours after surgery. Collection intervals of less than 24 hours were achieved by introducing a blunted, 18 gauge needle into the esophagus via the mouth and flushing the tube system with 2cc of saline solution. For collection intervals of 24 hours, the spontaneous drinking of the animals served to flush the collection tubes. The collection bottles were changed at designated intervals for measurements of their particulate content.

(2) Particles. The particles used for clearance measurements consisted of a saline suspension of microgranular ceramic particles labeled with cesium^{134} (specific activity, 1mc/gm). A detailed description of this material has appeared (5). The particle size distribution of the suspension as determined by measuring the maximum horizontal diameters with a Filar micrometer had a log-normal distribution with a geometric mean and geometric standard deviation of 1.9 microns and 1.5 microns, respectively. Prior to removing a sample from the stock suspension for use, the suspension was routinely subjected to a 5 minute ultrasonic treatment to disperse the particles.

(3) Exposure Technique. Two methods of intratracheal injection were utilized in an effort to alter the deposition of the particles in the lungs. The first method, subsequently referred to as the Vertical Injection Tech-

nique, involved the injection of 0.2 cc of the particle suspension through a blunted, 18 gauge needle just above the level of the corina with the trachea in a vertical position. The rat was subsequently held in this vertical position for 5 minutes. With the second method, referred to below as the Semihorizontal Injection Technique, the particulate suspension was injected as above with the trachea in a semihorizontal position. Immediately following injection, the rat was placed in a prone position and was unrestrained. The intratracheal injections were given while the rats were anaesthetized lightly with ether. The animals were awake and active within 2 minutes following the injection.

(4) Analysis of the Data. The particulate content of the material present in the collection bottles and in the lungs, the esophagus, and the tube system at sacrifice was measured by counting the 605 Kev gamma photon of cesium^{134} with a single channel gamma ray spectrometer. The delivered dose to each animal was obtained by summing the above measurements (Previous studies have shown that these particles are insoluble in the body and are not distributed to any tissues other than those analyzed during a 10 day period after exposure[5]. These results were confirmed in the experiments reported below.) For groups of animals, the mean and standard error of the statistic has been reported.

The clearance rate curves have been described in terms of Clearance Rate Intervals, i.e., the time intervals during which clearance rate variations can be characterized by a simple mathematical relationship.

RESULTS

(1) Mucociliary clearance rates determined at ten minute intervals. A preliminary experiment using six surgically prepared animals was performed

to determine the optimal sampling interval for esophageal collection. The vertical injection technique was used to expose the rats and esophageal collections were made at ten minute intervals over a five hour period. Table 1 summarizes the results which are plotted in Figure 2. Figure 2 also shows the basic experimental data from Table 1 aggregated to simulate collection intervals of twenty minutes and one hour. Total clearance over

TABLE 1

CLEARANCE RATES FOR TEN MINUTE COLLECTION INTERVALS ON RATS EXPOSED BY THE VERTICAL INJECTION METHOD*

Rat Number	Time Post Exposure, Minutes														
	10	20	30	40	50	60	70	80	90	100	110	120	130	140	150
1	.89	1.05	.18	.22	.12	.03	.10	.14	.11	.11	.25	.02	.24	.18	.05
2	.02	.50	.20	1.07	.40	1.35	1.66	1.96	.53	1.04	.34	.13	.13	.50	.07
3	8.10	1.01	1.00	.88	.15	.23	.29	.48	.26	.07	.17	.02	.02	.10	.30
4	.46	.03	2.16	.64	4.63	1.30	.27	.17	.21	.11	.13	.25	.04	.13	.07
5	2.78	7.11	4.76	1.30	.03	.33	.40	.35	.12	.33	.34	.18	.19	.28	.06
6	.30	.75	.98	2.30	2.25	.92	.12	.69	.22	.31	.33	.22	.07	.02	.17
Mean Clearance Rate	2.09	1.90	1.55	1.08	1.24	.69	.37	.63	.24	.33	.26	.14	.12	.20	.12
Mean Cumulative Clearance	2.09	3.99	5.54	6.62	7.86	8.55	8.92	9.55	9.80	10.12	10.38	10.52	10.63	10.84	10.95

Rat Number	Time Post Exposure, Minutes														
	160	170	180	190	200	210	220	230	240	250	260	270	280	290	300
1	.05	.05	.09	.20	.03	.40	.18	.09	.24	.15	.14	.03	.13	.07	.14
2	.37	.39	.09	.09	.17	.19	.15	.19	.24	.08	.19	.14	.07	.07	.08
3	.03	.10	.03	.03	.05	.01	.04	.03	.02	+	+	+	+	+	+
4	.04	.26	.17	.69	.23	.12	.03	.17	.05	.12	.25	.12	.10	.12	.02
5	.05	.11	.07	.05	.10	.19	.12	.08	.04	.06	.18	.45	.15	.25	.09
6	.09	.20	.06	.19	.14	.12	.14	.07	.03	.20	.05	.15	.09	.14	.31
Mean Clearance Rate	.11	.19	.09	.21	.12	.17	.12	.11	.11	.12	.16	.18	.11	.13	.13
Mean Cumulative Rate	11.06	11.25	11.33	11.54	11.66	11.83	11.95	12.07	12.18	12.30	12.46	12.64	12.75	12.88	13.01

*Clearance rates are expressed as the percent of the initial lung burden.
+Animal died.

the 5 hour period equalled 13.% ± 1.9% of the delivered dose. From zero time to 150 minutes following exposure the variation in clearance rates can be approximated by a single decreasing exponential function with a one-half time ($T_{1/2}$) of 30 minutes. During this interval 11.0% of the initial burden was cleared. We designate this period of time as the first

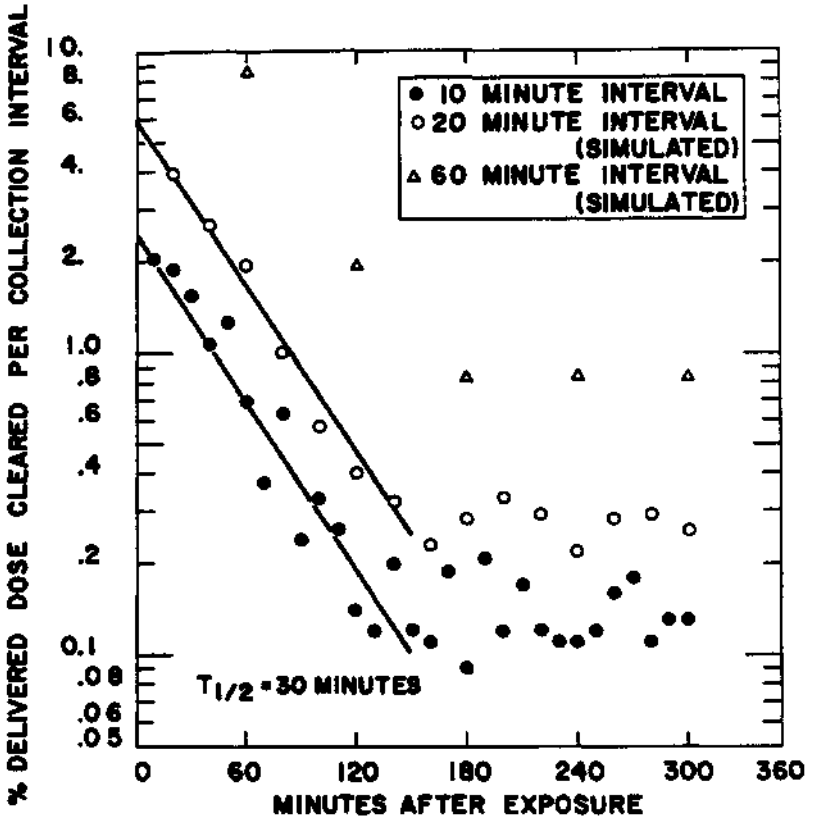

FIGURE 2.

Mucociliary clearance rates determined at ten minute intervals with the data aggregated to simulate twenty-minute and hourly collection intervals (see Table I).

clearance rate interval. Subsequently no definite trend can be seen. These data show that twenty minute sampling intervals are satisfactory to delineate the first clearance rate interval. Subsequently, hourly collection intervals would be adequate.

(2) Mucociliary clearance rates of particles administered by the vertical injection technique. Twenty four surgically prepared rats were injected intratracheally using the vertical method. The esophageal collection system of each animal was flushed at 20 minute intervals for a six hour period. Table 2 summarizes the data which are plotted in Figure 3.

TABLE 2

CLEARANCE RATES FOR TWENTY MINUTE COLLECTION INTERVALS ON RATS

EXPOSED BY THE VERTICAL INJECTION METHOD

Rat Number	Time Post Exposure, Minutes																		
	20	40	60	80	100	120	140	160	180	200	220	240	260	280	300	320	340	360	Total
1	6.48	1.70	1.72	.57	.15	.09	.15	.04	.10	.14	.43	.07	.13	.54	.45	.17	.37	.19	13.49
2	11.92	7.32	5.95	1.09	.10	.21	.75	.46	.07	.01	.88	.15	.63	.71	.23	.22	.24	.32	31.10
3	.19	.09	.69	1.63	.67	.23	.82	.54	.46	.39	.06	.20	.04	.05	.03	.04	.04	.03	5.24
4	1.41	.46	.18	.21	.14	.07	.20	.24	.21	.16	.03	.16	.03	.05	.05	.02	.02	.05	3.75
5	.19	.25	.75	.22	.11	.05	.11	.15	.08	.05	.02	.11	.05	.33	.38	.67	.39	.13	3.55
6	.87	1.55	1.04	.21	.15	.47	.29	.17	.15	.05	.03	.21	.30	.11	.10	.12	.10	.08	5.80
7	2.50	1.76	3.79	.54	4.65	3.17	.27	1.09	1.21	1.99	.26	1.13	.47	.43	.61	.12	.20	.21	24.53
8	2.57	1.73	.25	.10	.05	.05	.04	.12	.11	.06	.05	.03	.03	.03	.02	.10	.08	.32	5.54
9	2.69	1.09	.59	.32	.73	.23	.16	.23	.14	.21	.55	.41	.49	.23	.22	.17	.13	.14	8.55
10	1.48	.05	.24	.15	.11	.26	.47	.17	.11	.10	.09	.12	.12	.16	.09	.11	.11	.12	4.10
11	.05	.09	.27	.17	.12	.10	.11	.19	.11	.12	.11	.09	.05	.11	.11	.07	.03	.05	3.28
12	1.29	.73	.39	.52	.07	.03	.07	.09	.04	.09	.03	.10	.04	.05	.05	.04	.05	.05	3.64
13	1.70	.53	.21	.13	.09	.07	.14	.11	.07	.05	.03	.10	.05	.06	.03	.05	.10	.14	4.13
14	1.33	1.54	.37	.11	.09	.10	.09	.14	.47	.10	.05	.05	.05	.11	.10	.15	.04	.03	5.37
15	3.29	.16	.10	.09	.11	.07	.07	.05	.03	.07	.09	.07	.05	.07	.05	.05	.05	.03	4.09
16	.99	.05	.12	.14	.16	.20	.03	.15	.09	.10	.36	.21	.32	.50	.05	.24	.05	.10	2.85
17	.49	.25	.10	.22	.17	.13	.16	.09	.20	.15	.09	.09	.09	.10	.18	.15	.11	.09	2.05
18	.35	.11	.09	.17	.09	.25	.18	.15	.03	.10	.12	.12	.11	.13	.13	.12	.33	.28	3.51
19	1.30	2.84	.87	.03	.55	.39	.26	.35	.13	.13	.21	.13	.21	.17	.17	.27	.09	.15	9.05
20	4.03	.96	.77	1.45	.79	1.02	1.12	1.17	1.20	1.21	.99	.97	.89	.77	1.11	.86	.76	.76	20.74
21	.71	1.67	.46	.18	.19	.19	.15	.25	.42	.19	.30	.10	.20	.21	.16	.19	.24	.10	5.91
22	3.88	.59	.33	.40	.23	.39	.14	.25	.45	.35	.35	.24	.23	.12	.33	.15	.13	.12	8.74
23	2.06	.48	.23	.29	.55	.26	.50	.25	.32	.32	.20	.10	.22	.29	.29	.11	.16	.17	6.97
24	.49	.16	.31	.23	.12	.11	.16	.11	.14	.17	.14	.20	.17	.15	.15	.16	.14	.13	3.25
Mean Clearance	2.21	1.10	.85	.40	.42	.34	.28	.29	.27	.26	.23	.22	.21	.23	.22	.18	.18	.16	
Cumulative Clearance	2.21	3.32	4.17	4.51	4.99	5.33	5.61	5.90	6.17	6.43	6.66	6.87	7.08	7.31	7.53	7.71	7.89	8.05	

*Clearance rates are expressed as the percent of the initial lung burden.

Total clearance over six hours equalled 8.1% of the delivered dose. A single decreasing exponential function approximates the variations in clearance rates from zero time to 140 minutes following exposure. A one-half time ($T_{1/2}$) of 47 minutes was found for the first clearance rate interval. From 140 minutes to 6 hours following exposure, a decreasing exponential trend in clearance rates with a $T_{1/2}$ of 3.9 hours is apparent. This second clearance rate interval is not completely defined in this experiment since the trend may persist beyond 6 hours.

(3) Comparison of mucociliary clearance rates using the vertical and semihorizontal injection techniques. Twenty-seven rats were injected intratracheally using the semihorizontal injection technique. Table 3

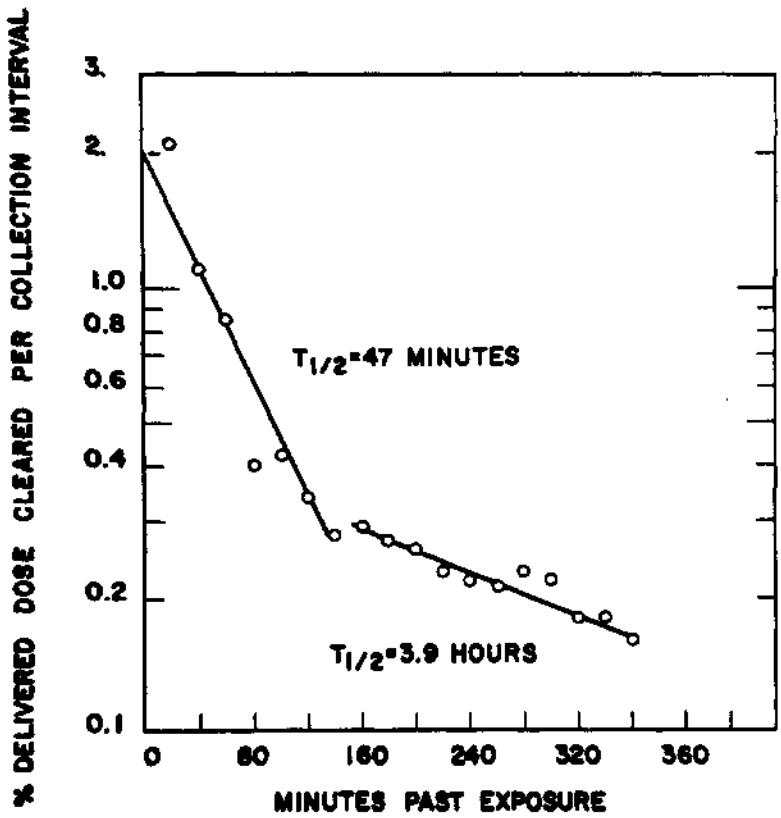

FIGURE 3.

Mucociliary clearance rates following the vertical injection of particles (see Table 2).

shows the experimental data at hourly collection intervals. The clearance rates are plotted in Figure 4. The hourly clearance rates obtained from the vertically injected animals in the previous experiment (Table 2) are shown for comparison.

Total clearance in the semihorizontally injected rats over 6 hours equalled 32.7% ± 3.4% of the delivered dose, as compared to the 8.1% ± 1.5% of the delivered dose cleared in 6 hours in the vertically injected animals. The difference in total clearance is significant by the Student t test ($P<<0.01$). The individual hourly clearance rates also differ

significantly ($P<0.1$). In both instances hourly clearance rates variations can be approximated by single exponential functions from approximately 2 hours following exposure to the termination of the experiments. In the animals injected semihorizontally, the $T_{1/2}$ of this clearance rate interval was found to be 2.8 hours, as compared with 3.9 hours found in the vertically injected rats.

TABLE 3

CLEARANCE RATES FOR HOURLY COLLECTION INTERVALS ON RATS EXPOSED BY THE SEMI-HORIZONTAL INJECTION METHOD*

Rat Number	Time Post Exposure, Hours								
	1	2	3	4	5	6	7	8	Total
1	1.39	1.63	.02	.39	.25	.38	.08	.07	4.21
2	27.13	93	4.11	7.37	3.35	1.49	.35	2.77	47.50
3	26.91	2.96	7.91	2.37	1.38	.46	.40	.33	42.22
4	14.47	4.72	.89	.96	.71	.69	1.04	1.01	24.48
5	36.89	3.30	4.18	2.71	3.34	1.05	1.01	.59	53.07
6	9.99	2.75	2.86	1.05	3.39	.58	.91	.20	21.73
7	13.38	.85	.42	.48	.34	.18	1.70	1.07	18.42
8	4.80	.15	.08	.16	.45	1.77	1.13	1.67	10.21
9	59.77	1.84	.97	.98	.98	.97	.85	.32	66.68
10	16.43	2.01	1.24	.35	.34	.64	.19	.14	22.14
11	16.19	2.59	2.15	.55	.96	.57	.92	.42	24.35
12	18.45	4.00	1.07	1.01	.98	1.27	.48	.23	28.16
13	21.29	5.62	1.79	2.92	.95	.47	.23	.33	33.60
14	7.30	.80	2.28	.39	1.48	1.10	1.03	.71	15.09
15	24.38	7.21	1.58	.83	.80	.95	.48	.21	36.44
16	18.21	3.97	2.78	.85	1.55	.11	.16	.14	27.77
17	62.91	6.36	1.50	.52	.45	.24	.65	.04	72.67
18	11.84	5.02	2.36	.96	.50	.42	.33	.29	16.57
19	1.76	9.77	2.74	2.98	.84	.65	.50	.55	19.79
20	39.88	3.38	1.10	1.20	.09	1.76	.44	.18	48.03
21	10.77	5.52	6.29	2.47	1.71	2.61	1.55	1.08	32.00
22	53.19	3.94	2.47	2.80	.54	.52	.46	.21	64.13
23	5.49	2.69	.66	.56	2.01	.88	1.43	.35	14.07
24	43.36	13.13	5.20	1.10	.26	.23	.17	.03	63.48
25	17.57	2.37	1.15	1.20	2.75	2.17	.84	.65	28.70
26	8.83	9.43	.84	.53	.15	.22	.07	.10	20.17
27	29.65	5.11	2.21	.53	.09	.87	.34	.52	39.32
Mean Clearance	22.29	4.18	2.27	1.42	1.13	.87	.69	.53	
Cumulative Clearance	22.29	26.47	28.74	30.16	31.29	32.16	32.85	33.74	

* Clearance rates are expressed as the percent of the initial lung burden.

(4) Clearance rates over 17 hours post exposure. To investigate the second clearance rate interval noted in the previous experiments, seven surgically prepared rats were exposed using the semihorizontal injection technique and followed at hourly intervals for 17 hours

following exposure. Table 4 gives the experimental results which are plotted in Figure 5. Total clearance over 17 hours equalled 27.1% ± 3.8% of the delivered dose. These particles were cleared from the lungs with clearance rates decreasing in a logarithmic manner. The $T_{1/2}$ from 2 hours following exposure to the termination of the experiment was 2.6 hours.

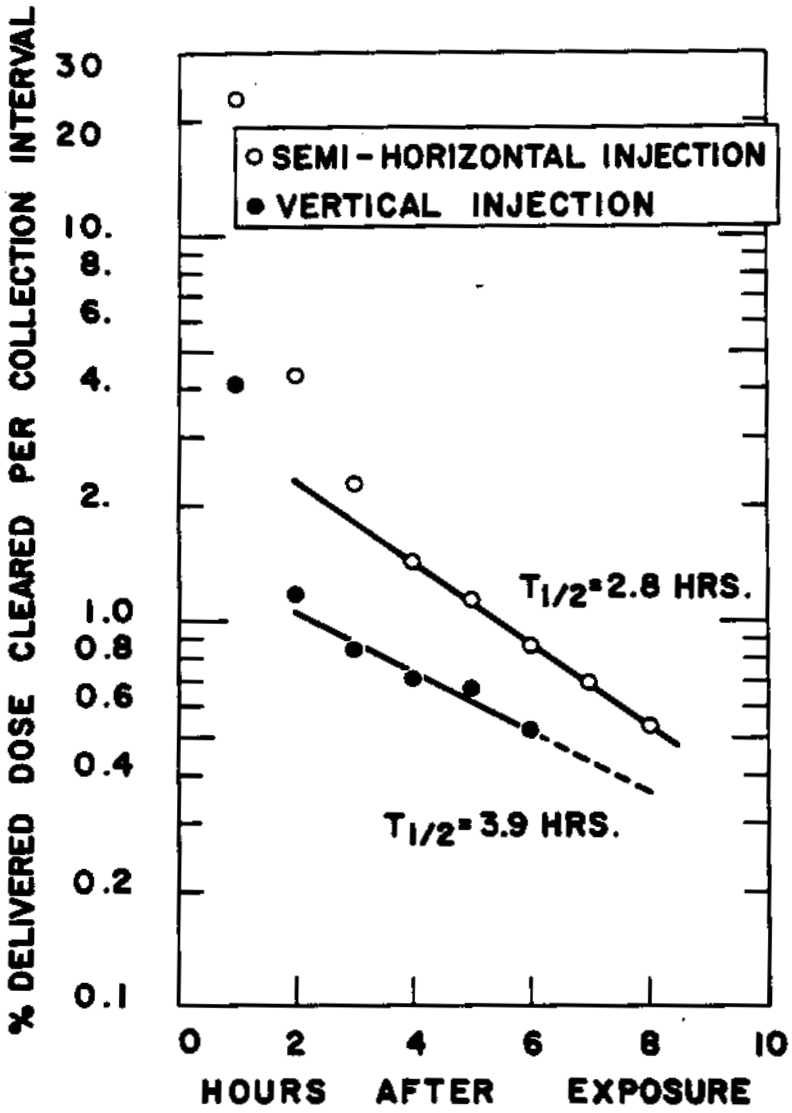

FIGURE 4.

Comparison of mucociliary clearance rates following the vertical and the semi-horizontal injection of particles (see Tables 2 and 3).

TABLE 4

CLEARANCE RATES FOR HOURLY COLLECTION INTERVALS ON RATS

EXPOSED BY THE SEMI-HORIZONTAL INJECTION METHOD*

Rat	Time Post Exposure, Hours																	
Number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	Total
1	1.94	.05	2.93	4.19	4.62	1.09	.35	.49	.88	.61	.83	.30	.24	.24	.14	.16	.08	19.96
2	8.63	4.23	4.14	15.57	1.50	1.45	1.68	1.72	1.47	.88	.37	.29	.22	.08	.07	.03	.03	42.36
3	3.63	.09	.47	.49	2.68	.38	.35	.37	.29	1.83	.18	.13	.16	.10	.07	.13	.09	11.49
4	19.03	5.23	2.52	2.09	1.86	1.10	.83	.65	.25	.09	.18	.11	.05	.03	.11	.03	.07	34.28
5	6.67	1.75	.84	.66	2.27	.68	.41	.90	.35	.20	.17	.27	.01	.11	.09	.06	.04	15.48
6	30.11	1.09	.66	.63	.86	.06	.11	.12	.07	.35	.19	.10	.05	.04	.03	.02	.01	35.10
7	19.46	6.86	.71	.30	.20	.47	.35	.21	.93	.73	.05	.30	.09	.15	.18	.24	.03	31.26
Mean Clearance	12.79	2.96	1.76	3.42	2.00	.75	.58	.64	.61	.67	.28	.21	.12	.09	.10	.10	.05	27.13
Cumulative Clearance	12.79	15.75	17.51	20.93	22.93	23.68	24.26	24.90	25.57	26.18	26.46	26.67	26.79	26.88	26.98	27.08	27.13	

* Clearance rates are expressed as the percent of the initial lung burden.

(5) Clearance rates from 1 day to 5 days following exposure. Seventeen rats were injected using the vertical injection technique and daily clearance rates were determined over five days (Table 5). The results are shown in Figure 6. The total clearance over 5 days equalled 21.5% ± 2.1% of the delivered dose. During the first 24 hours, 14.2% ± 1.8% of the delivered dose was cleared, presumably following the kinetics of the first and second clearance rate intervals found above. The remaining 7.3% ± 0.7% of the delivered dose was cleared from the lungs during the subsequent 4 days. The clearance rates in Figure 6 can be approximated by a single exponential function having a $T_{1/2}$ of 1.5 days.

COMMENT

Our findings suggest that mucociliary clearance rate variations over five days following intratracheal exposure of rats can be characterized by a sequence of exponential functions. We have introduced the term

"clearance rate interval" to designate a limited time interval over which clearance rate variations can be expressed by a simple mathematical relationship. The experimental data indicate that three distinct logarithmic clearance rate intervals are needed to describe clearance rates over five days following the intratracheal injection of particles.

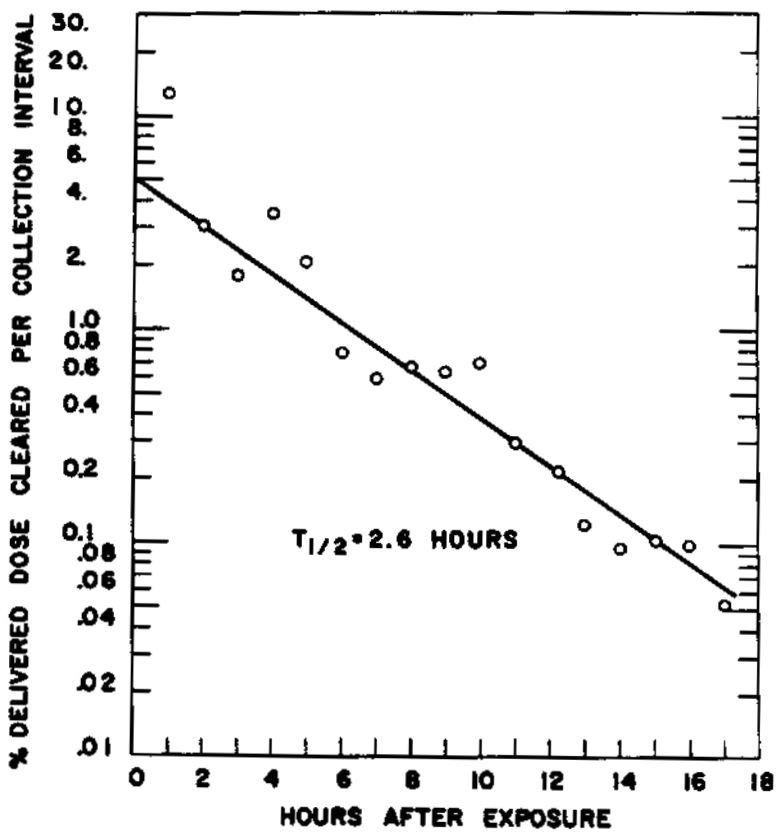

FIGURE 5.

Mucociliary clearance rates following the semi-horizontal injection of particles (see Table 4).

A deliberate attempt to alter the deposition pattern of the injected particles along the tracheobronchial tree was made in these experiments by changing the position of the rat during and immediately following the intratracheal injection. It was assumed that the gravitational effects

TABLE 3

CLEARANCE RATES FOR DAILY COLLECTION INTERVALS ON RATS EXPOSED BY THE VERTICAL INJECTION METHOD*

Rat Number	Time Post Exposure, Days					
	1	2	3	4	5	Total
1	11.49	2.66	1.48	.28	.08	15.99
2	11.80	1.83	.33	.31	.18	14.45
3	15.15	3.87	2.66	3.36	x	25.04
4	16.88	3.05	3.22	1.60	2.53	27.28
5	5.97	.69	1.40	.85	.80	2.61
6	21.67	.67	.98	1.31	1.52	26.15
7	19.23	3.03	.87	.24	9.15	23.52
8	11.60	7.50	.29	.26	x	19.65
9	13.30	4.40	1.10	2.08	1.53	22.41
10	3.30	2.97	1.45	.64	.30	8.66
11	14.92	5.62	2.05	1.21	.39	24.19
12	10.58	1.96	1.30	1.00	1.35	16.27
13	24.29	2.93	.02	6.90	.02	34.16
14	3.10	1.54	4.97	2.12	2.11	13.84
15	32.49	6.04	5.37	.36	.49	44.75
16	16.59	2.41	1.10	2.74	.17	23.09
17	8.76	3.42	2.66	.28	.25	15.37
Mean Clearance	14.18	3.21	1.84	1.51	.80	
Cumulative Clearance	14.18	17.39	19.23	20.74	21.54	

* Clearance rates are expressed as the percent of the initial lung burden.

x Collection lost.

on the particle suspension would result in a deeper penetration of the pulmonary system when the animals were positioned vertically. The total clearance over a 6 hour period in the vertically injected rats was significantly lower than the total clearance in the semihorizontally injected rats, i.e., 8.1% vs 32.7%, respectively, (Tables 2 and 3), and the individual hourly clearance rates between the two groups also differed significantly (Figure 4). Since the variations in the injection technique would not be expected to produce a difference between the two groups in the functioning of the mucociliary escalator, these data suggest that the variation in the injection technique results in an altered deposition pattern of the particles. The change in the distribution of the particles was reflected in the changes noted in total clearance and hourly clearance rates. The experimental method, therefore, is capable of assessing the effects of altering the particle deposition pattern even though the specific

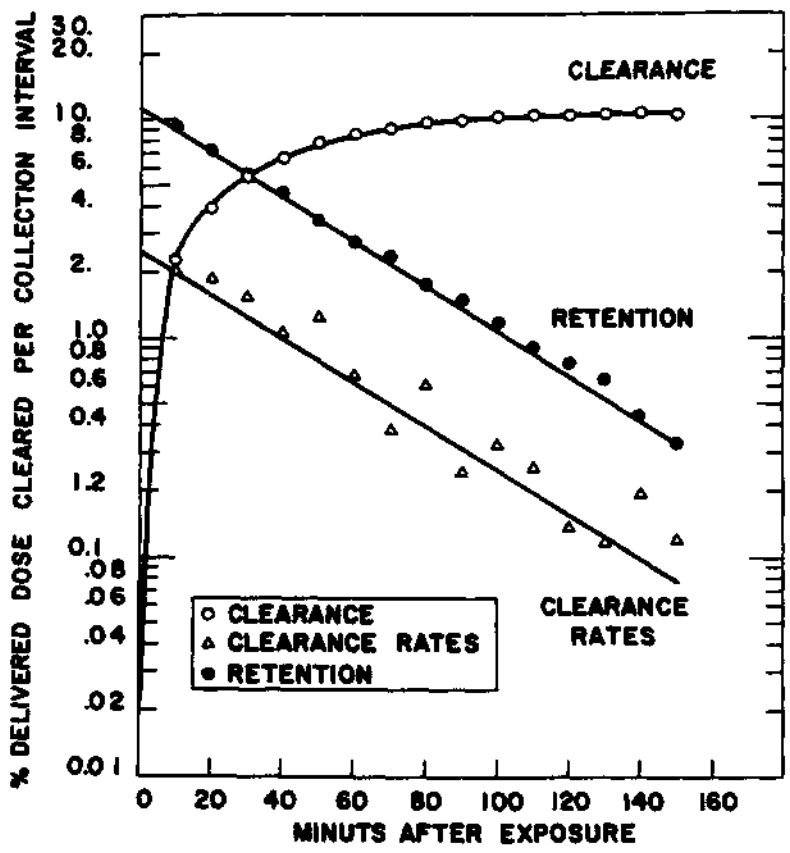

FIGURE 6.

Comparison of the empirical data (points) with the mathematical formulation (solid lines) of the clearance-rate-interval of Figure 1 (see text).

distributions of the particles along the tracheobronchial tree remains unknown.

Although we were able to influence clearance dynamics by varying particle deposition distributions, the data is inadequate to determine whether or not a change in the duration of the clearance rate intervals was produced. If further experiments utilizing modes of exposure which would give different particle deposition patterns, such as aerosol inhalation, produce the expected variation in clearance dynamics but show the same duration of the clearance rate intervals, a definite anatomic compartment or a specific physiologic clearance mechanism might be suspected.

The first clearance rate interval having a $T_{1/2}$ of 47 minutes and extending from zero time to 150 minutes following exposure probably results from particles deposited on, and rapidly cleared from the mucociliary epithelium of the upper tracheobronchial tree. The specific anatomic or physiologic basis of the second clearance rate interval extending from 2.5 hours following exposure to less than 24 hours and having a $T_{1/2}$ of 2.8 to 3.9 hours is less certain. This also applies to the third clearance rate interval extending from one day to at least five days following exposure and having a $T_{1/2}$ of 1.5 days. For clearance rate intervals in which the clearance rates decrease logarithmically the mathematical expression of clearance rates, clearance and retention would be as follows:

Clearance Rates

$$R = R_o e^{-kt} \qquad (1)$$

$$t_1 \leq t \leq t_2$$

R = clearance rate

R_o = initial clearance rate

k = clearance rate constant = $\frac{0.693}{T_{1/2}}$

$t_1 + t_2$ time of onset and end of clearance rate interval

t = time post exposure between limits t_1 and t_2

Retention. The total amount of material (D_o) cleared during a defined clearance rate interval may be considered as the total amount of material initially retained (or deposited) in some subsection of the pulmonary system. It follows from the definition of clearance rate that $R = \frac{dD}{dt}$ at time t where D is the amount of material retained in the pulmonary subsection. From this it can be shown that

$$R_o = -kD_o \quad (2)$$

Hence retention D can be written

$$D = D_o\, e^{-kt} \quad (3)$$

Cumulative Clearance. Since cumulative clearance (C) of material during a defined clearance rate interval is equal to D_o-D at any time t, it can be shown that

$$C = D_o\, (1-e^{-kt}) \quad (4)$$

In Figure 7 the solid lines are constructed by assuming that the prior mathematical formulation applies to the first clearance rate interval of Figure 3, where t_1 = 0 minutes, t_2 = 150 minutes; $T_{1/2}$ = 30 minutes and D_o (corrected) = 11.28% of the delivered dose. The experimentally determined data derived from Table I are plotted. It should be emphasized that retention refers not to total lung retention but only to the fraction of material remaining to be cleared during the clearance rate interval.

CONCLUSIONS

The determination of the general relevance of our findings must await comparison with data based on inhalation experiments. As emphasized above the study of clearance kinetics cannot be divorced from the effects of particle deposition distributions. These experiments demonstrate a method in the rat of determining clearance and clearance rate data in the immediate post exposure period. The technique permits the assessment of the effects on mucociliary clearance of variables or stresses which may influence either the deposition of particles or the mucociliary escalator mechanism.

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UPTAKE OF ^{125}I IN THYROID OF SEVEN INDIVIDUALS FOLLOWING INHALATION INCIDENT

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Seven individuals employed at an industrial firm in the greater Pittsburgh area were inadvertently exposed to vapors of ^{125}I the morning of April 15, 1966. The vapors had escaped from an open beaker containing 100mc of the isotope. The incident was first noted when local radiation monitors indicated excessive levels of radioactivity present in the laboratory. After Health Physics surveys of the exposed individuals showed presence of contamination, they were brought to the Radiation Medicine Department of Presbyterian-University Hospital. Further surveys with a geiger counter indicated excessive activity in the thyroid region of all seven personnel and swipe surveys of the nasal area indicated the presence of contamination. After decontamination by showering, all personnel were counted with a 2" x 2" NaI(Tl) crystal assembly utilized for detecting the 28 kev K X-rays of ^{125}I. This unit was connected to a 400 channel TMC analyzer with the detector placed for two measurements per individual at distances 10.5cm and 42.5cm from the isthmus of the thyroid on the initial day.

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The individuals were covered with lead aprons to eliminate activity other than that from the neck region. Prior to counting them, the detector was calibrated with the only available ^{125}I source, an oleic acid diagnostic test capsule containing 34.1μc of ^{125}I. The capsule was placed in a plastic "thyroid phantom." Included in further post-exposure measurements was a thin xtal [0.1cm NaI(Tl)] detector. Different measurement techniques were utilized with the various detectors and excellent agreement was obtained.

As of this writing (140 days post-exposure), follow-up studies of the biodecay have been performed on five of the individuals, using a collimated assembly on the 2" x 2" crystal. To obtain a true background count of activity present, other than in the thyroid, a 2mm thick copper absorber was placed over the individuals' thyroids. A least-square analysis of the biodecay data, assuming an exponential fit, has been performed and an estimated half-life for ^{125}I has been found to be 38-45 days with an average of 41 days $\pm$ a standard deviation of 2 days. Effective half-lives of 36 and 45 days were found for those two individuals refusing follow-up after the third measurement. These results are significantly different (by a factor of 50%) than the effective half-life of 27 days quoted in the literature.[1] One individual administered KI for the first month following the incident indicated an effective half-life of approximately 25 days during this period, but since stopping the treatment, has indicated an effective half-life of 38 days. Extrapolation of the biodecay back to zero time revealed thyroidal uptakes of 0.23 to 22μc. Neglecting the initial rapid drop off between days 0-4,

1. H. Endlich, P.V. Harper, et al: Am. J. Roentgenol. Rad. Therapy and Nucl. Med., 87, 148 (1962).

internal dosimetry calculations based on these uptakes and under the assumption of a unit density, 20 gram thyroid, gave dose (∞) values of 1.1 to 114 rads.

INITIAL THYROIDAL UPTAKES AND DOSE (∞) VALUES[a]

Employee	Extrapolated Initial Uptake (uc)	C_o (uc/gm)	T_{eff} (days)	D_T (∞) rads
A	22.1	1.11	45	114
B	3.20	0.160	38	14
C	2.44	0.122	39	11
D	0.228	0.0114	43	1.1
E	(4.00); 1.36	(0.200); 0.068	(25); 38	14 (8 + 6)
F	8.70	0.435	45	45
G	2.70	0.135	36	11

[a] Doses based on equation D_T (∞) = 2.29 T_{eff} C_o except for modification in case of Employee E. The dose is considered negligible during the initial rapid fall-off between days 0-4.

The Detection of Insoluble Alpha Emitters in the Lung

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Introduction

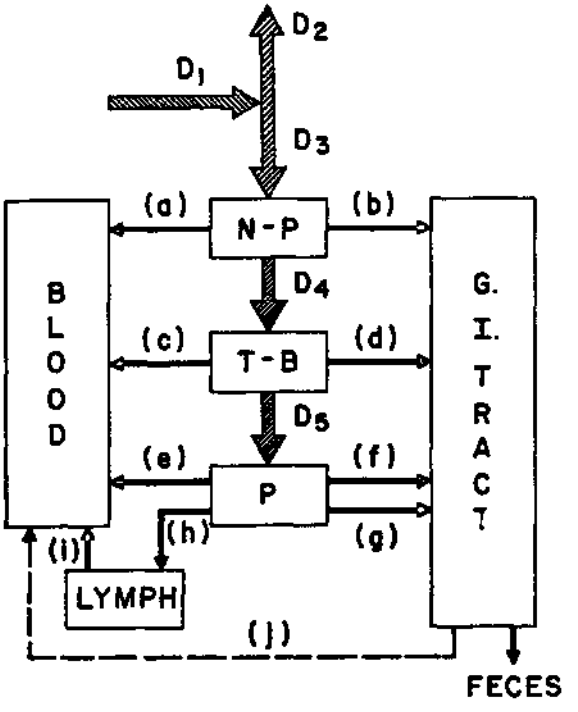
The pulmonary lung is the critical organ for many industrial exposures to radioaerosols. This is because the oxides of the actinide elements are cleared very slowly from the pulmonary compartment[1]. As little as 0.5 microcurie of $^{239}PuO_2$ has produced a high percentage of lung cancers in beagles[2]. And studies on uranium miners from the Colorado Plateau[3] show no human immunity to radiation induced lung disease.

If we designate the lung as a critical organ, then it is necessary to estimate accumulated lung burden in occupationally exposed workers. This paper will show that fecal sampling is the only satisfactory method for estimating lung burdens of insoluble alpha emitters. These insoluble alpha emitters are those actinide compounds classified as Class Y in the new lung model. The most important are $^{239}PuO_2$, $^{241}AmO_2$, $^{234}UO_2$ and $^{232}ThO_2$.

I. The Deficiencies of Urinalysis and In-vivo Counting for Class Y Actinides

In 1964 Sill[4] pointed out the errors in using urinalysis as a routine monitoring method for internal radioactive contaminants. In his experience, radioactivity measured by whole body counting could not be detected in the urine. He found however that in all cases fecal samples showed measureable quantities of the radio nuclide.

This can be easily understood if we consider the new ICRP deposition and retention model shown in Figure 1. Inhaled particles are deposited in three regions of the respiratory tract, the nasal-pharynx, tracheo-bronchial



ICRP DEPOSITION AND RETENTION MODEL

Figure 1.

and pulmonary compartments. Almost 100 per cent of the insoluble alpha emitters deposited in the N-P and T-B regions are removed by ciliary mucous transport to the G.I. Tract in a matter of minutes. This rapidly eliminated fraction, represented by (b) and (d), together with a similarly rapidly removed pulmonary fraction (f) make up an early clearance phase (Phase I). All Phase I insoluble alpha activity is eliminated in the feces. A second clearance phase with a half time of one year or greater from the pulmonary part of the lung is represented by (e), (g) and (h). Only about 5 per cent of the Class Y material originally deposited in the pulmonary compartment is absorbed (e) into the circulating blood. Another 15 per cent is removed to the lymph system (about 10% of which is later transferred to the blood).

The remainder is eliminated by endocytosis and the ciliary escalator through the G.I. Tract to the feces.

Dolphin and other UKAEA workers have suggested that lung burdens of PuO_2 can be estimated by urine sampling. The disadvantage of this technique is obvious in light of this new lung model. Only a twelfth of the long term lung burden is absorbed into the blood and subsequently deposited on the bone and other organs. The plutonium thus deposited will be excreted very slowly. The maximum urinary excretion from a maximum permissible lung burden (16 nc) would be less than 0.2 d/m/day. This maximum would occur several months after the deposition.

On the other hand easily measured quantities of plutonium are excreted in feces. This is demonstrated in Figure 2. A fecal excretion reference level is derived. Elimination from the pulmonary lung is by way of the blood, lymph and G.I. Tract. Three basic assumptions are made:

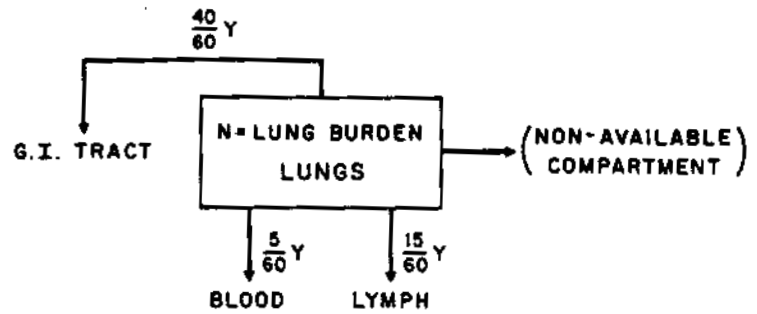
1) the half time of elimination from the pulmonary lung is 500 days. This is the recommended value in Appendix I of the Lung Dynamic Task Group's report.

2) The daily elimination from the Lung (Y) is proportional to the current burden N. This is a collary of the first assumption.

3) The original burden No is equal to the sum of the daily elimination from t = 0 to infinity.

The calculation shows that 49 d/m/day is eliminated from a 16 nc lung burden, 32 d/m by way of the feces. One tenth this value, or 3.2 d/m/day would be a suitable reference level. Persons excreting safely below this level could be safely assumed to have non-hazardous lung burdens.

PHASE II FECAL EXCRETION REFERENCE LEVEL



I. TASK GROUP DEFINITION, PuO_2:

$$N = N_0 e^{-\frac{.693}{500} t \text{ (days)}}$$

DAILY LUNG ELIMINATION (Y) α N

$$Y = Y_0 e^{-\frac{.693}{500} t}$$

II. $$N_0 = \int_0^\infty Y dt = Y_0 \int_0^\infty e^{-\frac{.693}{500} t} dt$$

$$= Y_0 \left[\frac{e^{-\frac{.693}{500} t}}{-\frac{.693}{500}} \right]_{t=0}^{t=\infty}$$

$$= Y_0 \left[0 + \frac{500}{.693} \right]$$

$$N_0 = \frac{Y_0 500}{.693}$$

III. $MPN_0 = 16\,nc = 3.5 \times 10^4$ d/m

$$Y_0 = \frac{.693\,(3.5 \times 10^4 \text{ d/m})}{500 \text{ days}}$$

$$= 49 \text{ d/m/day}$$

IV. DAILY FECAL EXCRETION $= \frac{40}{60} Y$

$$= 32 \text{ d/m/day}$$

Figure 2.

The non-available compartment represents possible retention of activity in the lung which is not available for elimination. This could occur by inclusion in scar tissue, etc. and would invalidate burden estimation by fecal sampling unless the fraction retained were known. This phenomenon can be seen in Sill's data[4] and a case by Saxby[10] where fecal excretion half times were shorter than chest burden elimination half times.

In-vivo or whole body gamma counting has demonstrated excellent results for the accurate assay of many radionuclides in the human body. The only requirement is the presence of an energetic gamma emitted with reasonable abundance from the radionuclide of interest.

Unfortunately, the actinide elements are not blessed with abundant energetic gamma radiation. ^{235}U is detected to levels as low as 7 NC.(6). ^{232}Th can be detected by gammas from its daughters, but redistribution of these daughters make evaluation difficult(7). Recent advances(8)(9) by using thin NaI crystals have improved the detection of ^{241}Am and ^{239}Pu. 2 nc of ^{241}Am and 16 nc of ^{239}Pu can be detected in the lung. The detection of ^{239}Pu depends on the ^{241}Am present.

There are two basic shortcomings of present In-vivo counting methods for actinide elements. Adequately shielded and sensitive whole body counters are expensive (>$250,000) and suitably inexpensive counters cannot usually detect lung burdens smaller than permissible.

II. Fecal Sampling Experience at the NUMEC Plutonium Laboratory

Fecal sampling has been carried out at NUMEC's Plutonium facilities since January, 1966. It is used to accomplish three goals: (1) the early detection of acute inhalation exposures, (2) the estimation of detected lung burdens, and (3) the screening of potential chronic exposures.

The Early Detection of Acute Inhalation Exposures

The value of fecal sampling for the early detection of inhalation exposures is illustrated in Figure 3. This shows the excretion data for an acute inhalation exposure following a glove box explosion. The glove box, filled with propane gas from a leaking Bern-z-matic torch, exploded when

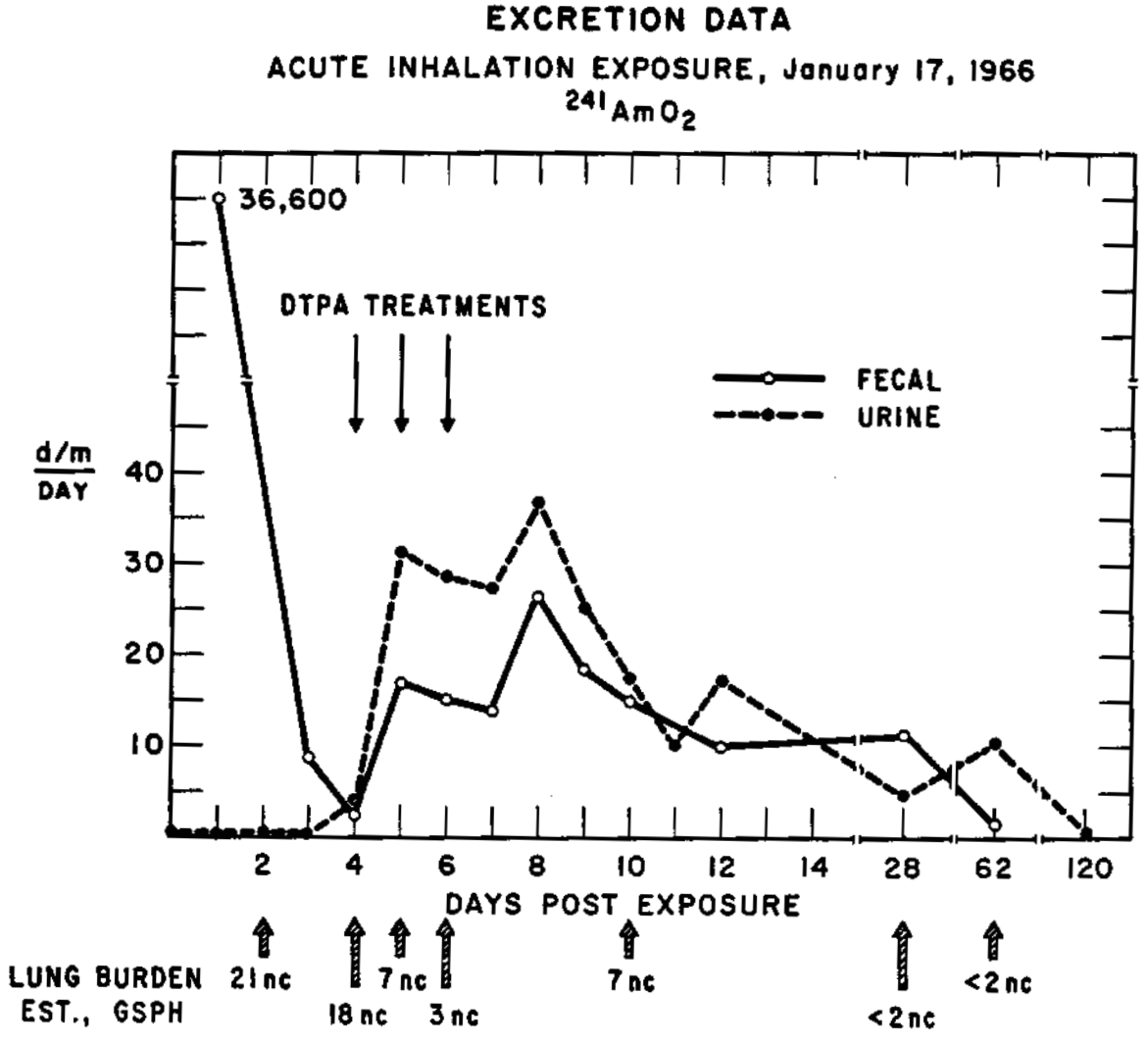


Figure 3.

the technician struck the lighter. $^{241}AmO_2$ was the main contaminant. Urine samples collected from the time of the accident through the third day showed negligible quantities of ^{241}Am. However, the first fecal sample, comprising the bulk of the Phase I clearance, contained more than 16 nc. This fact plus positive indications from whole body counts on the second day prompted medical consultants to perform chelation treatments the fourth, fifth and sixth days. The urine excretion level rose to more than 30 d/m/day and fell off over

the next 100 days to normal levels. The fecal level also rose, repeating the pattern of urine excretion. More than 2 nc were eliminated.

Lung burden estimates were made by thin crystal counting at the Presbyterian Hospital Whole Body Counter operated by Pitt GSPH personnel. These counts were performed on the second, fourth, fifth, sixth, tenth, twenty-eighth and sixty-second days past exposure. The indicated elevated counts on the second and fourth day are suspect, since residual external contamination was found on the patient's chest. When this was removed, the count dropped off by a factor of three. This decrease cannot be attributed to DTPA treatment, since less than 100 d/m were excreted in the interval. If it were true, then the value of the DTPA administration could be in doubt, since only 2 nc were ultimately excreted and several nanocuries should have been transferred from the lung to the bone.

The important point is that only the initial positive fecal sample gave a clear indication that an inhalation exposure had occurred. If only urinalysis had been used, it would have been concluded that no exposure had occurred. No DTPA treatment would have been prescribed and the technician would have unknowingly retained a lung burden of insoluble alpha emitters.

It is gratifying to learn that DTPA can effectively remove AmO_2 and PuO_2 from the lung. This possibility has been suggested by Tombropoulos[11]. He also indicated that the heat treatment history of the aerosol particles might alter the effectiveness of DTPA for removing PuO_2 from the lung. Perhaps this is the reason, Rocky Flats has reported a lack of success with similar chelation treatment[8].

Estimating Lung Burdens

The potential of fecal sampling for estimating plutonium lung burdens is illustrated in Figure 4. When routine fecal sampling was commenced in

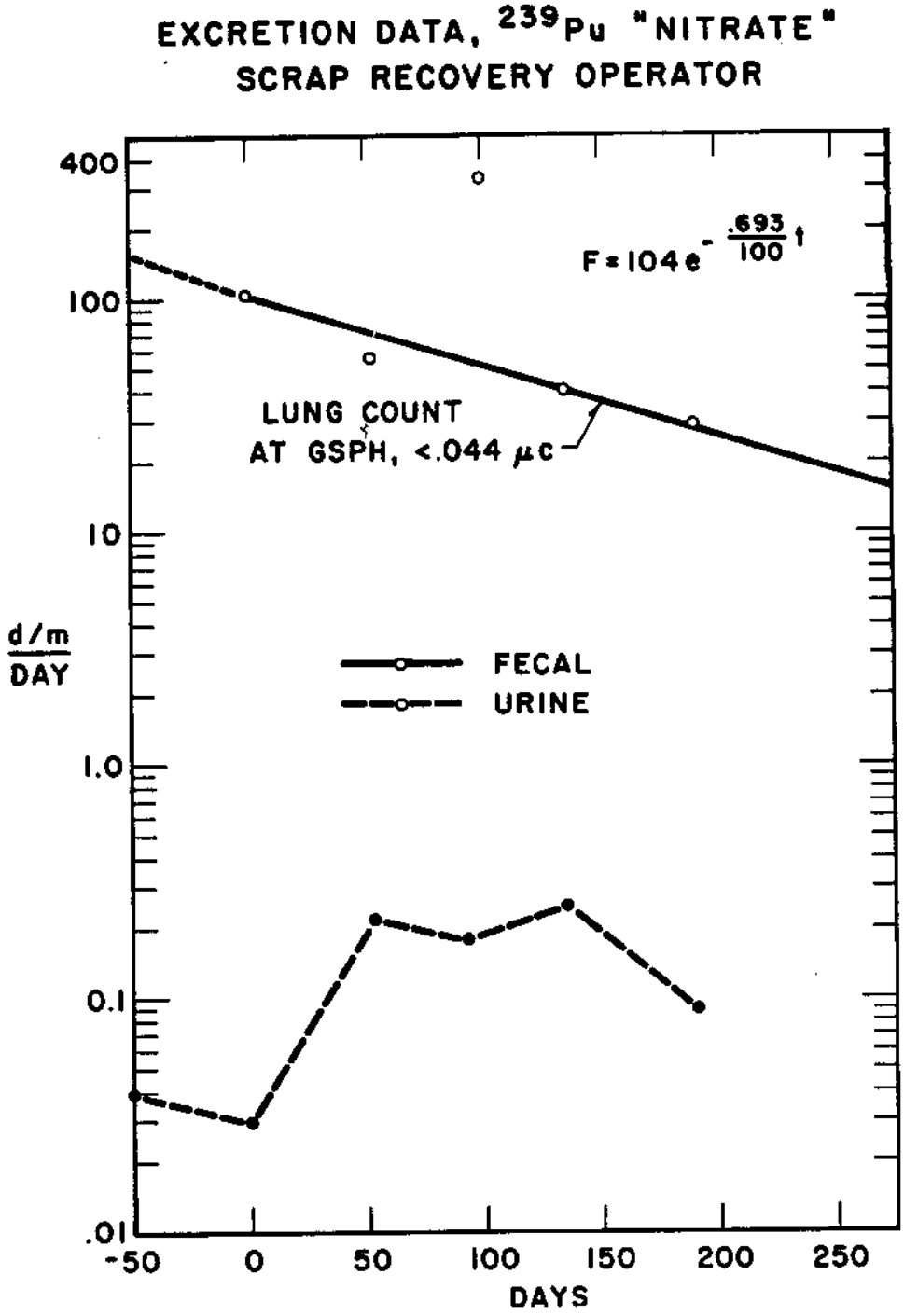


Figure 4.

early 1966, we discovered that some individuals were excreting ^{239}Pu in their feces from previously undetected exposures. These excretion data show that the fecal to urine excretion ratio may be large even for other chemical forms of plutonium. An investigation into this operator's exposure revealed that his principal exposures occurred during clean up of plutonium nitrate solution leakage from external piping. The actual chemical form of the aerosol in such cases is in doubt. However, the lung clearance seems to have a shorter half time, 100 days. The corresponding urine excretion rate seems to be about what would be expected for transferral from lung to bone.

The estimated lung burden at the time of the first fecal measurement is 7 nc.

I would like to discuss the third fecal datum point. Ordinarily, one takes stray bioassay data, records them and marks the deviation off to the vagaries of human metabolism. However, we discovered that the operator had been freshly exposed the day prior to submitting the sample. The high result probably is due to Phase I clearance from a low level exposure. We have learned that fecal sampling must be done after a person has been away from exposure for at least two days.

Routine Monitoring of Chronic Plutonium Exposures

Figure 5 shows the importance of routine fecal sampling in a plutonium bioassay program. The excretion rates via feces and urine are plotted against each other for all cases where samples were collected the same day. The UKAEA reference level is set at 0.2 pc. Exposures below this are given no further consideration. The derived fecal reference level was given earlier. It is at 1.5 pc.

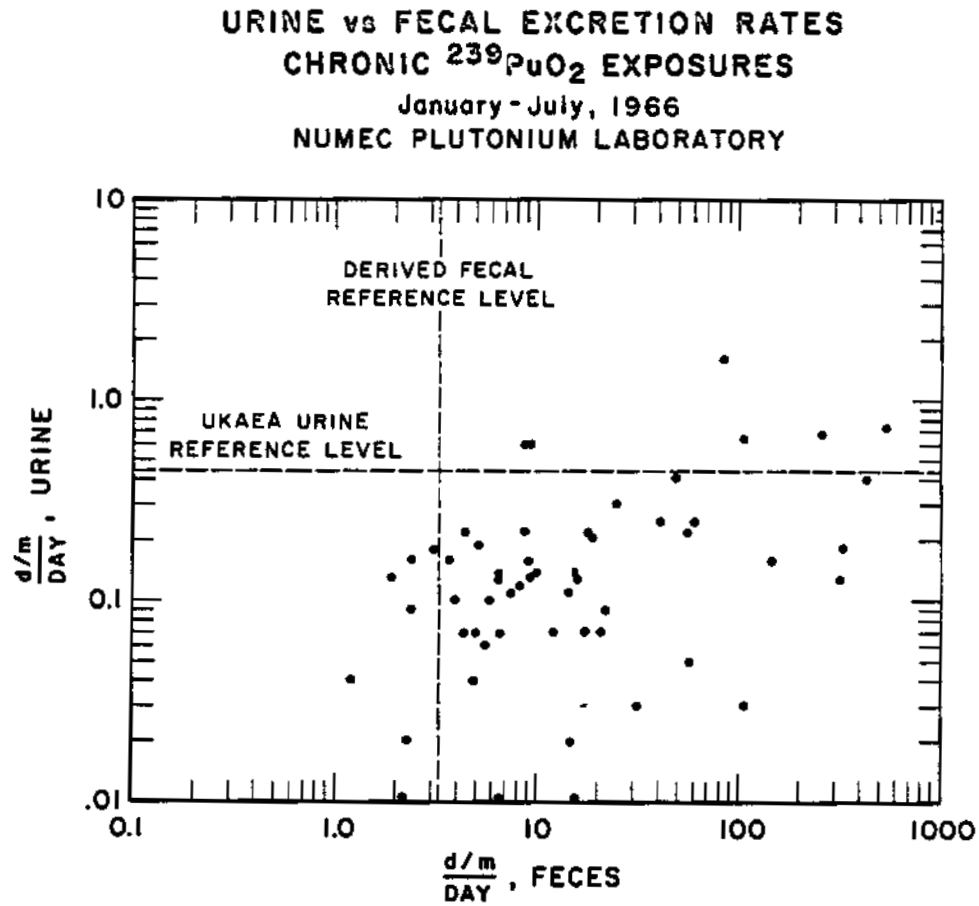


Figure 5.

Many of the fecal data undoubtedly represent Phase I clearance and are not necessarily important. However, it is obvious that urinalysis gives false assurance on the adequacy of environmental control. The information presented here caused us to investigate and correct conditions of which we had been unaware. Breathing zone sampling and fecal analysis will jolt any established plutonium facility out of its comfortable routine.

The Mechanics of Fecal Sampling

Fecal sampling is generally considered objectionable. We have found, given proper indoctrination and sampling technique, that our employees have

been as cooperative with the fecal sampling programs as they are with urine sampling.

We give the employee a quart plastic refrigerator carton, a small roll of tape, a paper bag and a written set of instructions. He takes this home to submit the sample. We have found it necessary to do home-only sampling to avoid low level contamination of samples. After depositing the sample in the carton, he replaces the lid and seals it with the tape. The carton is placed in the paper bag and brought back to the laboratory to await shipment to the Bioassay Vendor. No fuss, no smell, no messy handling problems. We even add formaldehyde, as requested by one vendor, by injecting the carton with a large hypodermic syringe. The resulting hole is sealed with plastic adhesive.

III. Prelimary Results from Uranium Fecal Sampling

Fecal sampling was begun on a large scale at NUMEC's Uranium plant in June, 1966. Generally we have found that uranium is easily detected in the urine, but that the feces is the principal route of excretion.

One interesting set of early bioassay data following exposure to a small release of enriched UF_6 is shown in Figure 6. Here the fecal excretion rate continues to increase until the fifth day before falling off. UO_2F_2 is the inhaled product during "hex" releases. This is generally considered to be highly absorbed into the blood from the lungs. Perhaps the delayed fecal excretion rate peak is an indication of elimination of systemic uranium via the feces. The urine curve ends the second day since the sequence of succeeding urine data is in doubt.

The last figure (No. 7) shows three groups of selected fecal to urine ratios. The ratios were selected from 126 cases to eliminate data where

EARLY BIOASSAY DATA
ENRICHED UF_6 EXPOSURE
August 10, 1966

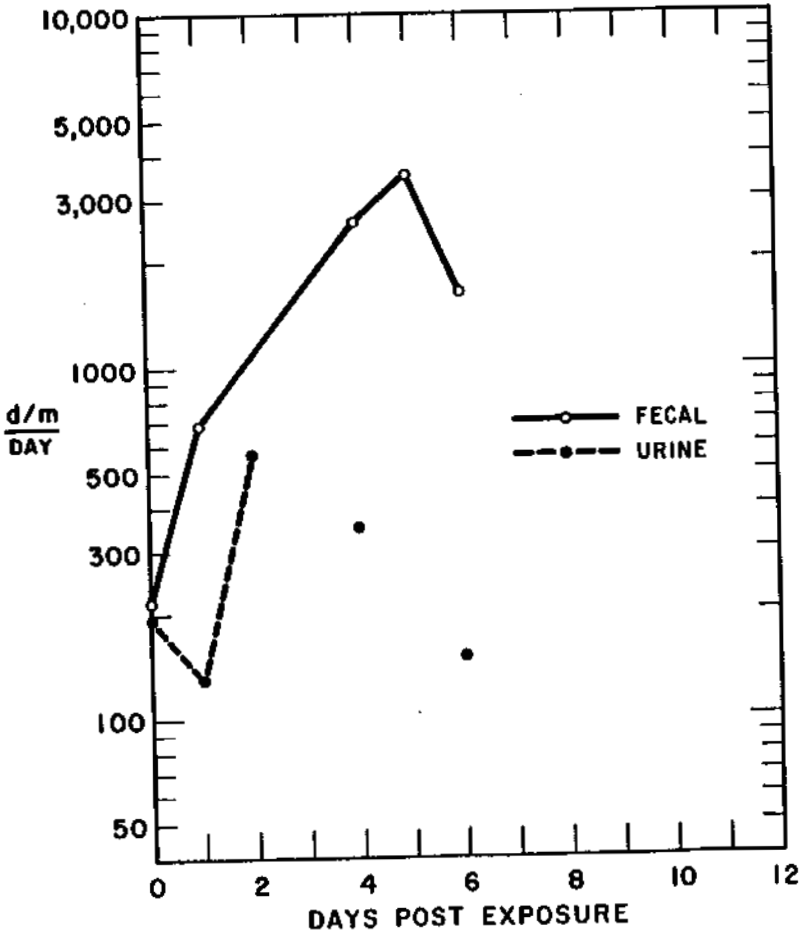


Figure 6.

FECAL/URINE RATIOS
CHRONIC $^{234}UO_2$ EXPOSURE
July, 1966

GROUP 1	GROUP 2	GROUP 3
2.6	13.7	58.7
1.8	16.2	76.7
1.2	18.6	45.0
2.7	16.5	
0.6	11.1	
3.1	7.1	
4.1		
3.5		
1.0		

DATA SELECTION RULES:

1. BOTH SAMPLES COLLECTED SAME DAY
2. OFF WORK AT LEAST TWO DAYS
3. EXPOSURE ONLY TO UO_2

— DATA SELECTED FROM 126 CASES

Figure 7.

fecal and urine samples were not collected simultaneously, where Phase I clearance will mask the long term retained excretion and where exposures to compounds other than UO_2 are possible.

The resulting 18 ratios fall almost magically into three well defined groups: Group I has nine ratios whose mean is about 2.3, Group II's 6 cases average 14 and Group 3, 60 for 3 cases. The study is continuing and whether this log-normal distribution will remain is problematical. However, it is obvious that at least some UO_2 exposures are poorly detected by urinalysis. Whole body counting is effective for enriched uranium lung burdens greater than 7 nc. But fecal sampling is necessary for the estimation of smaller fractions of the permissible lung burden.

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EVALUATION OF THE PUQFUA METHOD OF CALCULATING BODY BURDENS

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Abstract

Data on urinary excretion of plutonium following pulmonary deposition were obtained from five cases of depositions from plutonium dioxide and from one case of deposition from a mixture of more soluble compounds of plutonium. The PUQFUA system of J.N.P. Lawrence was used to estimate body burdens for these cases. An evaluation of the calculated body burdens for various time periods after exposure shows an exponential movement of plutonium from the lungs to the systemic circulation. The average half-time for the five cases was estimated to be 240 days, while the half-time for the exposure from more soluble compounds was 29 days. Through the use of the 240-day half-time, body burden estimates were made by an integration method and by a lung model urinary excretion curve method. These values agreed with the PUQFUA calculated body burdens and justifies the use of the PUQFUA system in calculating body burdens received by transfer from the lungs to the systemic circulations.

INTRODUCTION

The problems of assessing plutonium body burdens in man continues to be a subject of much concern to the health physicist. Variables such as particle size, chemical form, solubility, route of entry, acute or chronic exposure are all quite pertinent to the data evaluation process. Seldom are all of these factors known in cases of human involvement, and as a result most of the human data of record have been extremely difficult to evaluate. Even animal data which are generated under controlled conditions have not conclusively determined the physiological distribution of plutonium.

*Mound Laboratory is operated by Monsanto Research Corporation for the U. S. Atomic Energy Commission under Contract AT-33-1-GEN-53.

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Acknowledgments

I wish to express my appreciation for the past and continuing help I have received from the faculty of the Graduate School of Public Health, University of Pittsburgh, in particular Drs. N. Wald, A. Brodsky and J. Sayeg. The whole body counting data in this paper was received from them.

Eberline, Inc. performs NUMEC Plutonium urine and fecal analysis. They also do our uranium urinalysis. The quality of their work and the cooperation of Radiological Sciences Manager, Eric Geiger is greatly appreciated.

The preparation and analysis of the uranium bioassay data was done by Mr. Edward Schnell of the Uranium Plant Health and Safety Staff.

One of the major difficulties in the evaluation of human exposures has been the presence of unabsorbed reservoirs of material in the body which are released to the circulatory system at various rates depending on the location and solubility of the material.[1] This situation produces many elimination patterns and complicates evaluation processes based on urine assays; many of the plutonium exposure cases reported have been complicated by these reservoirs and therefore do not fit any simple model of elimination.[2]

Several computer programs have been developed to relate urine assay data to body retention.[3,4] These programs have used the systemic model of urinary elimination reported by Langham.[5] There has been a general use of these computer codes in routine monitoring programs even though doubt has been expressed on their ability to determine body burdens in cases where unabsorbed reservoirs of material exist.[1,6]

Healy in 1957 documented urinary curves from human exposure cases resulting from pulmonary depositions.[7] He suggested that a slow transfer from the lungs to the blood was taking place to produce the urinary elimination pattern observed. This type of elimination, quite different from that of a soluble uptake, has been observed and reported several times since. Beach and Dolphin have recently published urinary elimination curves based on both an exponential and a power function rate of removal from the lungs to the systemic circulation.[8]

The exposure cases reported here, with one exception, resulted from the inhalation of relatively insoluble plutonium dioxide. The urinary elimination pattern observed resembles very much that observed by Healy and others. The evaluation of the urine data to establish the systemic body burden has been done by a system based on the systemic model for acute exposure to soluble material. No attempt has been made to estimate the remaining lung burden nor the translocation sites of the material reaching the blood.

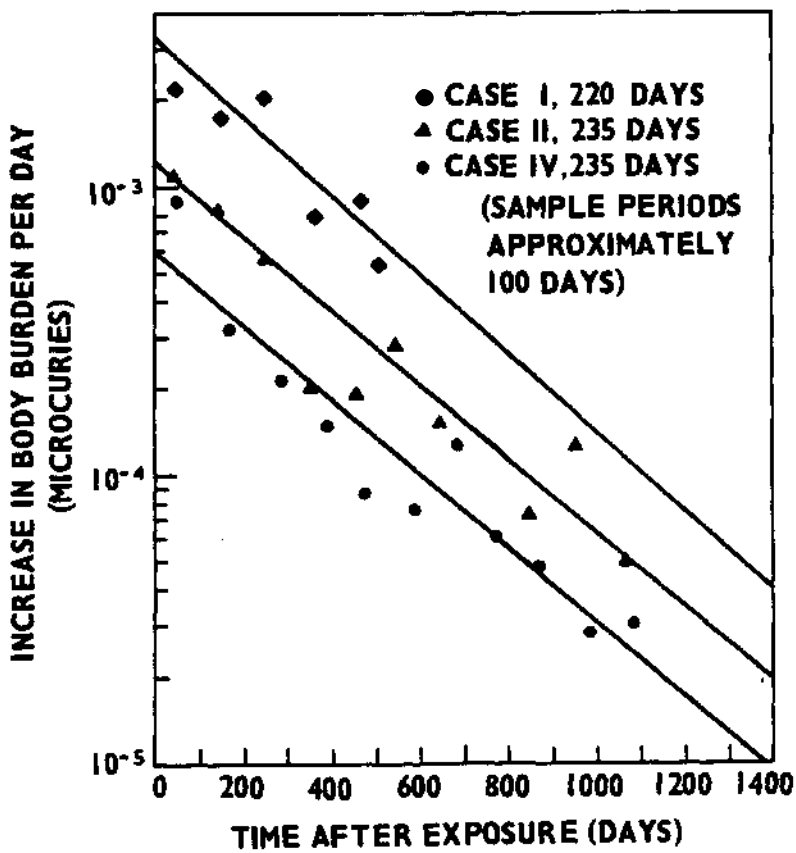
The object of this report is to show that existing methods can be used to determine the systemic burden in the more common types of exposures that occur in industrial operations.

BODY BURDEN CALCULATIONS AND INTERPRETATIONS

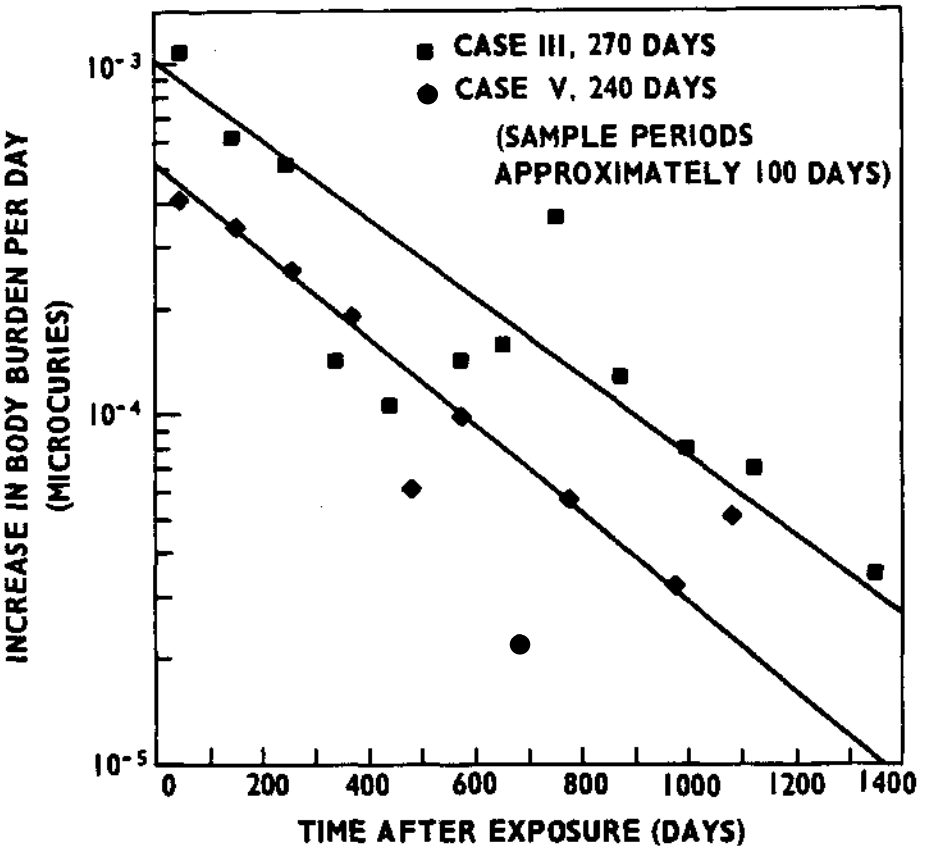
An accidental release of plutonium-238 oxide resulted in five cases of significant pulmonary deposition. The initial samples, though showing uptake, did not indicate, according to the Langham power function for excretion rate, that any of the cases had absorbed more than one tenth of the RPG (Radiation Protection Guide) of 0.04 μc. Subsequent sampling however, did not follow the excretion rate according to the power function, indicating that there had been additional uptake to the system. As a pulmonary deposition appeared to be feeding the systemic circulation with a continual transfer, the PUQFUA[3] method of calculating chronically received body burdens was adopted to perform these body

burden calculations. The method was felt to be reliable even though the assumed continuous release to the system is treated as an acute exposure midway between urine sampling dates.

With the rising excretion of plutonium, the PUQFUA calculations showed an increase in body burden for the five exposure cases. After a period of time, the rate for the movement of material to the systemic circulation was established by comparing the calculated body burdens at various times. Through this comparison the average increase per day for different periods of time past exposure was determined. Various spans of time were used for this evaluation. Since the rate of change of the increase was similar for each span chosen, only the 100-day calculations are shown in Figures 1 and 2. The translocation half-times, (hereafter simply half-times) shown for the five cases, demonstrate that the quantity moving to the system is depreciating exponentially with time by a half-time on the average of 240 days. The differences in the half-times of the five cases are considered to result from the method of their calculation, rather than individual variation. The average value is used for this reason. Individual values are listed in Table I along with the initial transfer value obtained through extrapolation of the curves of Figures 1 and 2 to Day One.



1. Average μc Increase in Body Burden/Day vs. Time (100 Day Time Period)



2. Average μc Increase in Body Burden/Day vs. Time (100 Day Time Period)

TABLE I

Determined Translocation Half-Times and the Initial Days Transfer

CASE	TRANSLOCATION HALF-TIME (days)	INITIAL TRANSFER DAY 1 (μc/day)
1	220	3.3×10^{-4}
2	235	1.22×10^{-4}
3	270	1.02×10^{-4}
4	235	0.60×10^{-4}
5	240	0.51×10^{-4}
AVERAGE	240	

BODY BURDENS THROUGH INTEGRATION

The total plutonium transferred from the lungs to the system can be calculated from the equation

$$\int_{1}^{2000} (I.T.)\, e^{-\lambda_s t}\, dt = D_t$$ (Total transferred to system, Systemic or Body Burden)

where (I.T.) = Initial Transfer,
$\lambda_s = 0.693/240$

The integration was completed to 2000 days to obtain a comparison with the PUQFUA method through the same time period. The equation reduces to

$$D_t = \frac{0.994\ (I.T.)}{\lambda_s}$$

The initial transfer fractions for Cases 1 - 5 are taken from Table I.

The retention fraction (R_t) is found by the equation:

$$R_t = \frac{\text{Total transfer - Total excretion}}{\text{Total transfer}}$$

$$R_t = \frac{\int_1^{2000} (I.T.)\ e^{-\lambda_s t}\ dt - \sum_{n=1}^{n=2000} (I.T.)\ e^{-n\lambda_s} \int_1^{2001-n} .0079\ t^{-0.94}\ dt}{\int_1^{2000} (I.T.)\ e^{-\lambda_s t}\ dt}$$

where $(I.T.)\ e^{-n\lambda_s} \int_1^{2001-n} .0079\ t^{-0.94}\ dt$ = the integrated[9,10] total excretion to day 2000 for the quantity $(I.T.)\ e^{-n\lambda_s}$ which moved into the systemic circulation on day n. The sum of this expression evaluated from n = 1 to n = 2000 gives the total excretion. The equation reduces to $R_t = 0.927$.

The retention fraction is further reduced by the physical decay of plutonium-238 on 2000 days (5.5 yrs), or

$$R_t = (0.927)\ e^{-\frac{(0.693)(5.5)}{90}} = 0.89$$

Therefore the systemic burden retained (D_R) is found by:

$$D_R = D_t\ R_t = \frac{0.994\ (I.T.)}{\lambda_s}(0.89) = 308\ (I.T.)$$

Table II lists these D_R values and PUQFUA calculations.

Table II

Comparison of the Integration Method and PUQFUA Method of Body Burden Calculations

CASE	INTEGRATION @ 2000 DAYS (μc)	PUQFUA @ 2000 DAYS (μc)
1	10.2×10^{-3}	9.1×10^{-3}
2	3.8×10^{-8}	4.0×10^{-3}
3	3.1×10^{-3}	3.6×10^{-2}
4	1.8×10^{-3}	2.4×10^{-2}
5	1.5×10^{-8}	1.8×10^{-3}

Case 1 received treatment with diethylenetriaminepentaacetic acid (DTPA) which effected an increased removal of 0.01 μc. This value was calculated by totaling urine excretion above the normal level prior to treatment. The integration method values for all cases except Case 1 are lower than the PUQFUA estimate. However, by subtracting the 0.01 μc removed through treatment, the body burden estimate of Case 1 should be adjusted to 9.2×10^{-3} μc which is in closer agreement with the PUQFUA estimate. This indicates that the PUQFUA method is capable not only of estimating body burdens received through inhalation of insoluble compounds but also of correcting for the loss of body burden resulting from DTPA administration.

Closer agreement between the integration and PUQFUA calculation can be achieved if consideration is given to the fact that other employees, who have had urine sampling for a comparable period of time with no known acute uptake, have an average of 0.003 μc body burden (PUQFUA estimate). If this value were taken as a background for the PUQFUA method of calculation over a 5 year period and was subtracted from the PUQFUA calculated body burdens of Cases 1 - 5; the corrected values would be as listed in Table III.

TABLE III

Comparison of Three Methods for Evaluating Body Burdens

CASE	BODY BURDENS BY EXTRAPOLATION (μc)	BY CORRECTED PUQFUA (μc)	BY INTEGRATION (μc)
1	9.0×10^{-3}	8.9×10^{-3}	9.2×10^{-3}
2	3.7×10^{-3}	3.7×10^{-3}	3.8×10^{-3}
3	3.5×10^{-3}	3.3×10^{-3}	3.1×10^{-3}
4	2.0×10^{-3}	2.1×10^{-3}	1.8×10^{-3}
5	1.5×10^{-3}	1.5×10^{-3}	1.5×10^{-3}

LUNG MODEL URINARY EXCRETION CURVE

With the assumptions that the 240-day translocation half-time for plutonium moving to the systemic circulation is correct and that the translocated plutonium is excreted according to Langham's systemic model, an equation for the rate of urinary excretion was derived.

With an initial transfer fraction, (I.T.), coming from a source which enters the blood stream with an exponential decrease, the rate of urinary excretion can be expressed as:

$$U_n = 0.002\ (I.T.) \sum_{t=1}^{t=n} e^{-\lambda_s t} \cdot (n-t+1)^{-0.74} \qquad (1)$$

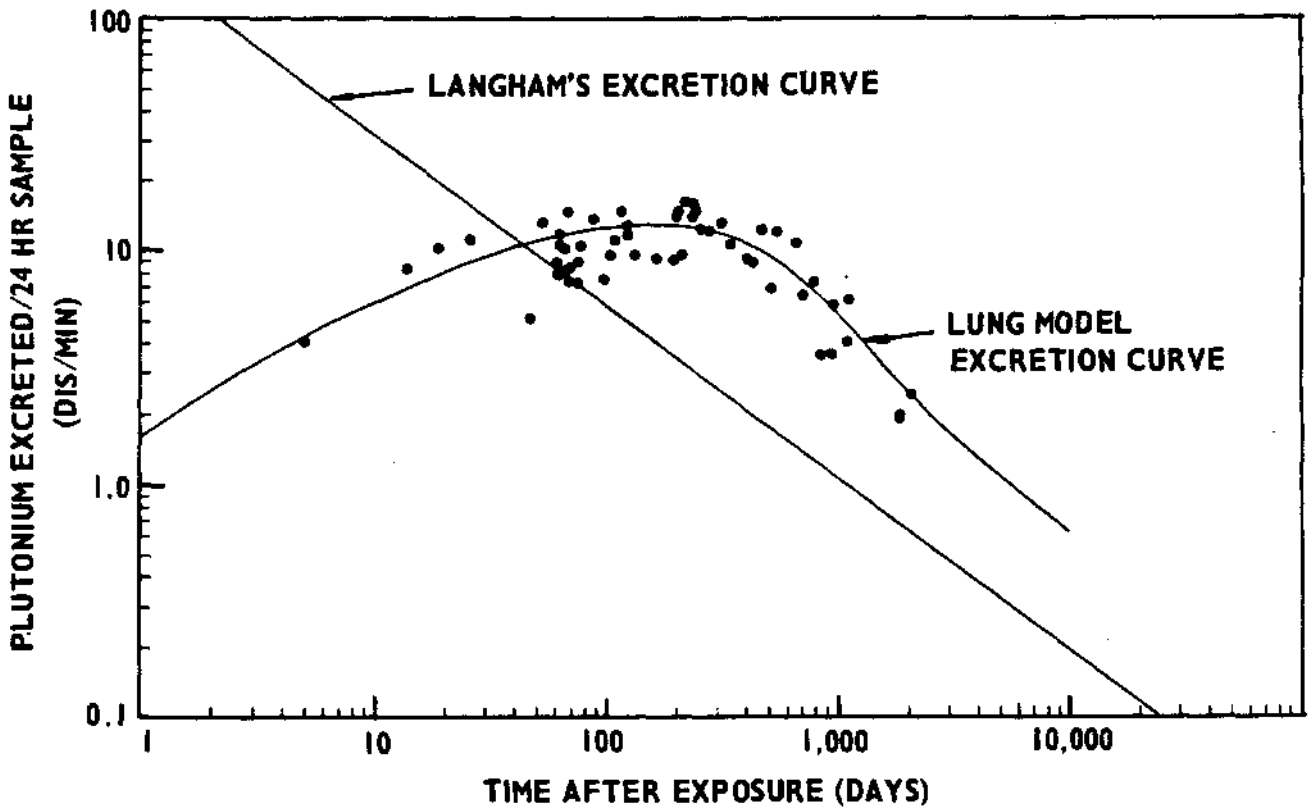
where U_n = The urinary excretion of plutonium for any day n, and
λ_s = Rate of movement to systemic circulation.
This can also be expressed by the equation

$$U_n = 0.002\ (I.T.) \int_1^n e^{-\lambda_s t}\ (n-t+1)^{-0.74}\ dt. \qquad (2)$$

Healy[7] developed a similar equation in an attempt to evaluate lung burdens from urinary excretion. Healy's equation

$$U_n = 0.002\ \lambda_s Q_o \int_0^n e^{-\lambda t}(n-t)^{-0.74}\ dt \qquad (3)$$

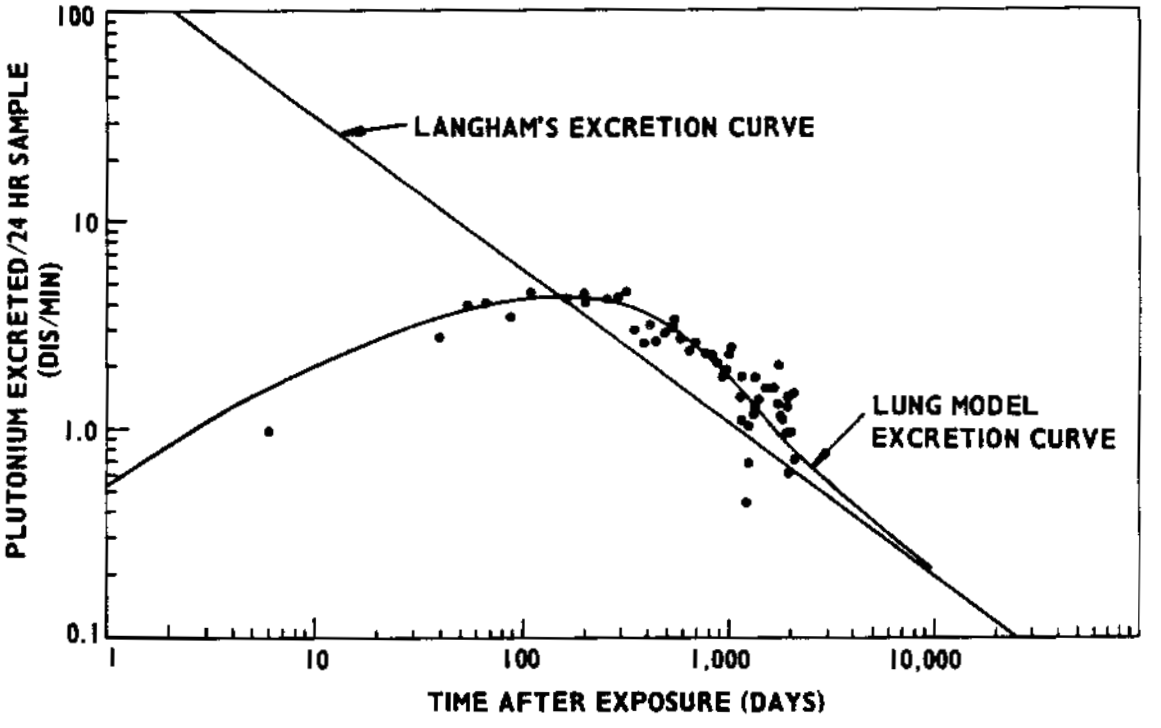
contained two unknowns, Q_o (total fixed quantity in the lungs) and λ (the overall rate of removal of the fixed quantity from the lungs), and hence the integral could be evaluated only by equating $\lambda = \lambda_s$. These two unknown variables are eliminated by dealing with a measured λ_s and an educated estimate of the initial transfer. This does not relate urine excretion to a total lung burden; it does relate measured transfers from the lungs to an expected urinary excretion rate. This establishes the pattern to be expected. The theoretical pattern (Equation 2) was then fit to the observed excretion rates (Figures 3-7).



3. Case #1 Daily Urinary Plutonium Excretion

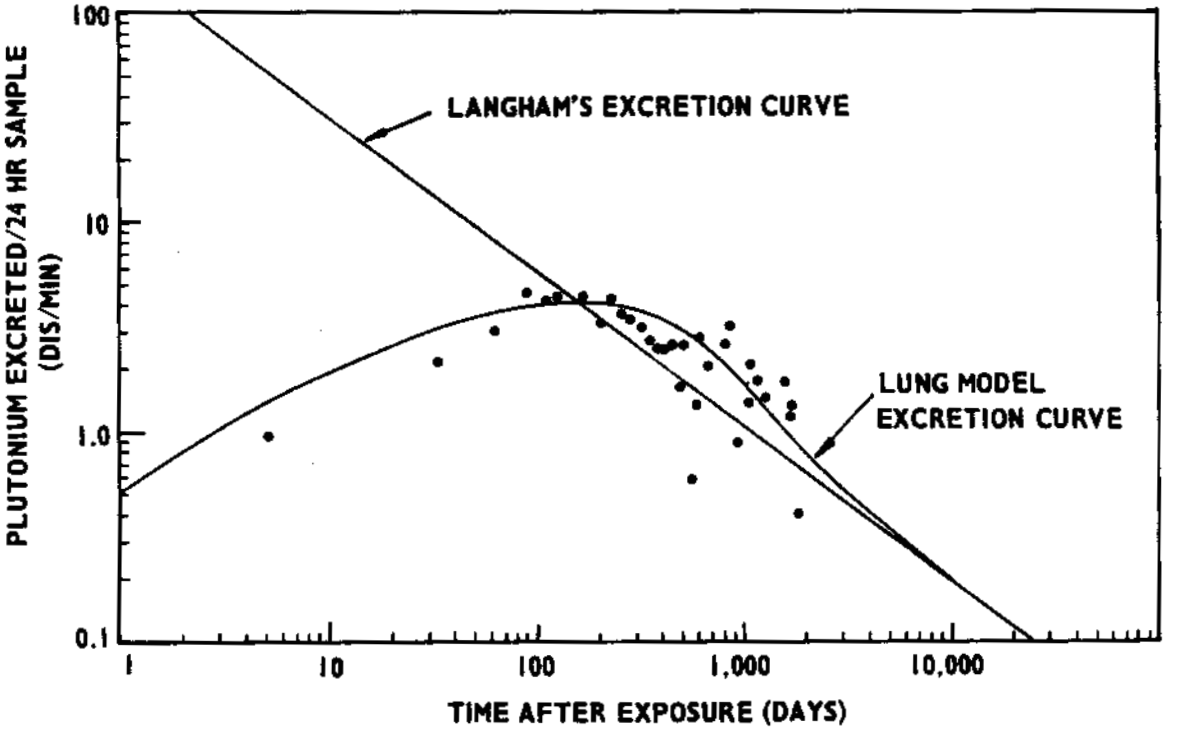
POWER FUNCTION APPLICATION AFTER AN EXTENDED TIME PERIOD

After 10,000 days the curve begins to follow the single power function of Langham and can be extrapolated back to estimate the body burden. The

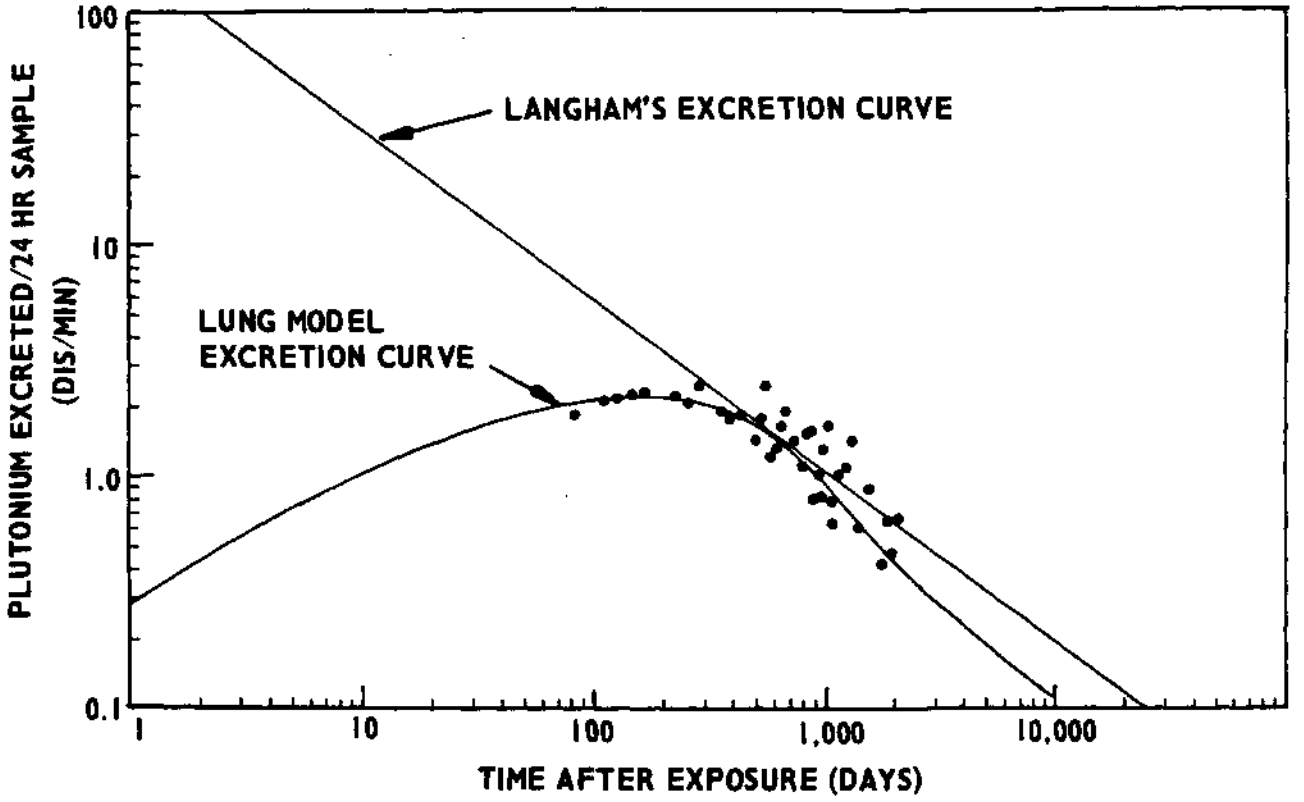


4. Case #2 Urinary Plutonium Excretion

body burden estimates by the extrapolation method are listed in TableIII with the PUQFUA and integration estimates for comparison.



5. Case #3 Urinary Plutonium Excretion



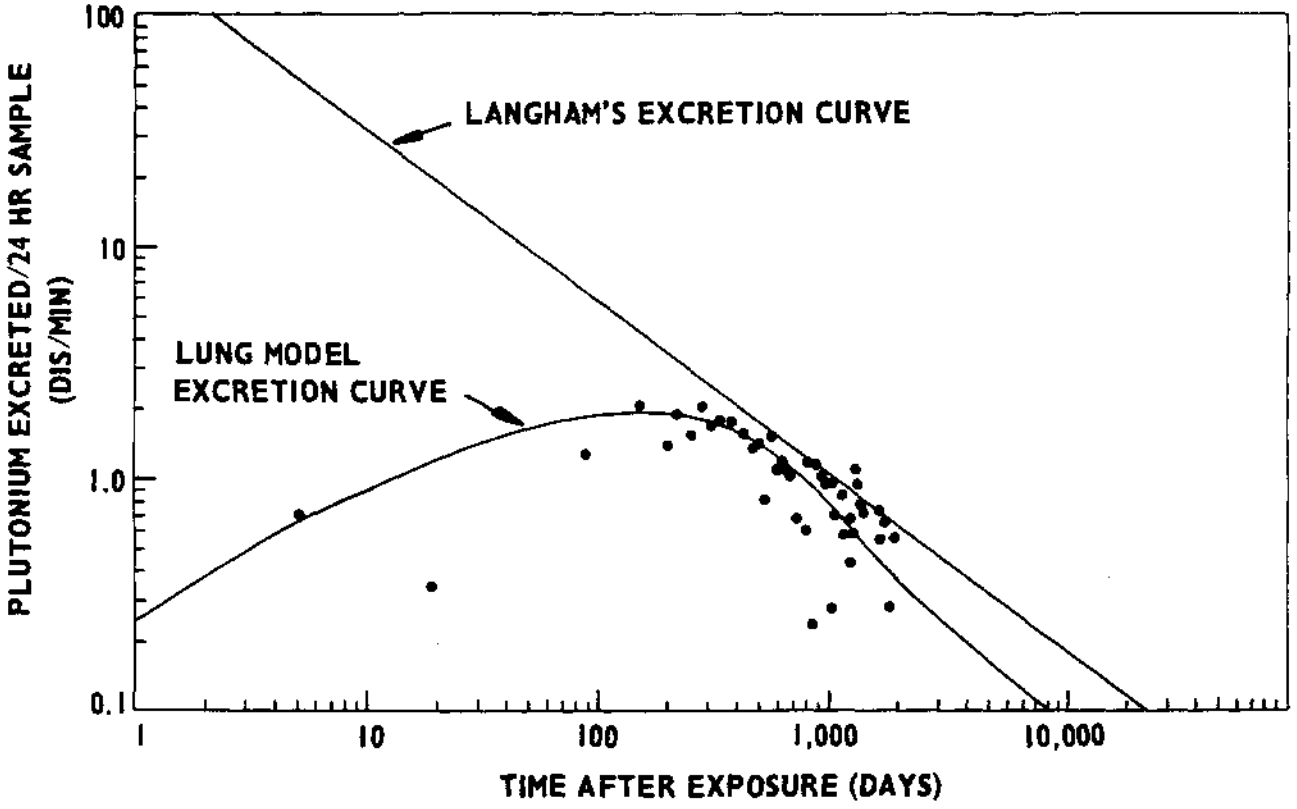
6. Case #4 Urinary Plutonium Excretion

PERFECT DATA CALCULATIONS

Additionally, the model curve was used to obtain data to be evaluated by the PUQFUA method. Values at 30 day intervals were taken from the curve for Case 2, from which a perfect data body burden was calculated. This calculation was completed through 1250 days and gave a body burden of 3.4×10^{-3} μc. At this time, 1250 days, approximately 96% of the plutonium has moved to the systemic circulation based on the 240 day half-time. Therefore, an estimate of the total transfer is obtained by: 3.4×10^{-3} μc/0.96 = 3.6×10^{-3} μc. This is in close agreement with the corrected PUQFUA calculation.

UPTAKE AT A FASTER RATE

To demonstrate the flexibility of the PUQFUA system and to show its independence from a precise translocation rate from the lungs such as the 240-day translocation half-time, another exposure case is presented. Case 6 received a pulmonary deposition exposure from a mixture of plutonium compounds, principally plutonium fluoride and oxalate. The body burden calculated by PUQFUA is 0.185 μc. An analysis of the calculated body burden as a function of time as in Cases 1 - 5, demonstrates a removal from the lungs to the system with a 29-day translocation half-time.



7. Case #5 Urinary Plutonium Excretion

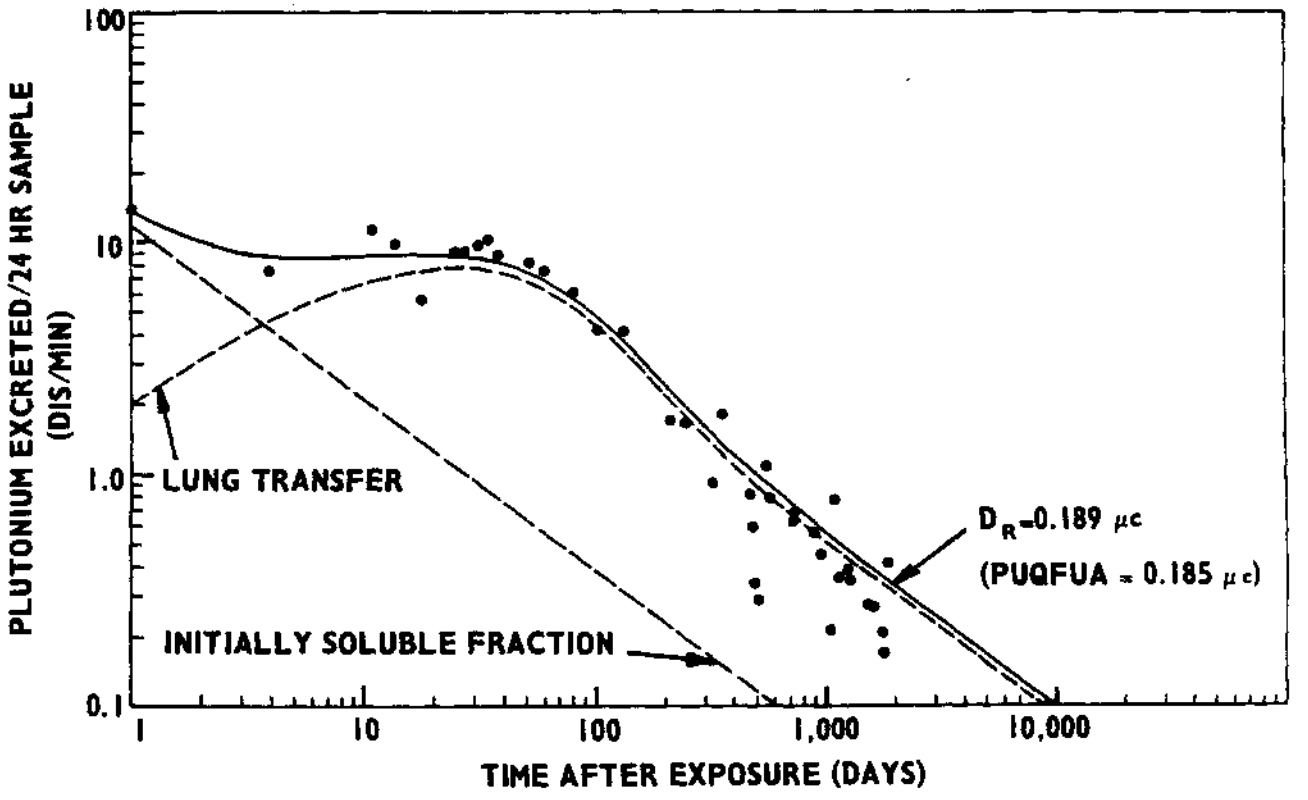
It can be seen in Figure 8 that the excretion rate after a period of time begins to follow the Langham curve. This time period is different from the previous five cases and is dependent on the rate of transfer from the lungs. The body burden estimate made from urinalysis data after it begins to follow the Langham curve, is 0.189, which is in close agreement with the PUQFUA calculated body burden.

SUMMARY

Data from those cases which received systemic burdens through solubilization of a reservoir of plutonium oxide do not demonstrate individual variation in the excretion pattern. (In the absence of particle size and relative solubility evaluations on the released material it is assumed that similar excretion patterns result from exposures to compounds of plutonium of comparable physical and chemical characteristics.)

The evaluations of the body burden calculations made by the PUQFUA method show that plutonium entering the systemic circulation through solubilization of a pulmonary deposition will exit the system according to W. Langham's equations, provided complexing agents such as DTPA are not used. These evaluations also show that the PUQFUA method is capable of estimating body burdens for different translocation half times of material transferring from the lungs to the systemic circulation.

The analysis of the evaluations of the body burden calculations led to the development of a urinary excretion curve for plutonium resulting from lung burdens of plutonium oxide. This model curve facilitates a more rapid estimation of a projected systemic burden which will result from lung burdens, but does not estimate the total lung burden itself. Simply, urinalysis data are related to systemic burdens and are used to extrapolate with the use of the lung model curve the fraction of the lung burden which will ultimately become the systemic burden.



8. Case #6 Urinary Plutonium Excretion

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A Review of Plutonium Exposure Cases at Los Alamos

Abstract

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Since it has been suggested (Health Physics 12, 1671 (1966)) that routine urine sampling programmes might be advantageously modified to yield urinary assay results of mathematically greater dependability, the experience at Los Alamos is reviewed in the hope of deriving some idea of the constancy of plutonium excretion by individuals.

On the basis of admittedly limited data, derived from the analysis of serial 24-hour urine samples from cooperative individuals known to excrete plutonium, it is suggested that altering the present Los Alamos sampling program would not necessarily result in the generation of more dependable estimates either of body burden or of exposure.

BIOASSAY ASPECTS OF A UF_6 FUME RELEASE

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ABSTRACT

About 3800 pounds of uranium as UF_6 escaped from a heated 10-ton cylinder. This paper describes the cause of the release as determined by an investigation team, emergency actions taken, consequences of the release, and several urinary uranium excretion patterns exhibited by exposed employees.

SUMMARY

On February 14, 1966, there was a major release of uranium hexafluoride in the Pilot Plant of the Feed Materials Production Center at Fernald, Ohio. A valve was accidentally removed from a heated 10-ton UF_6 cylinder, and approximately 3800 pounds of uranium, as uranium hexafluoride (UF_6) gas, escaped before the opening was plugged. The cylinder,

The work reported herein was performed for the U. S. Atomic Energy Commission under Contract No. AT(30-1)-1156.

installed in a vaporizer chest, was ready to provide feed to a UF_6-to-UF_4 reduction process. An operator attempting to open the cylinder valve inhaled enough of the escaping gas to develop pulmonary edema. He was hospitalized for 6 days.

Eight other operators involved in the incident were given oxygen as a precautionary measure in the plant dispensary. Two hundred and eighty National Lead and AEC employees submitted over 1,000 urine samples which were analyzed chemically for uranium and clinically for albumin, cells, mucus, protein, sugar, pH, and specific gravity.

Most of the UF_6 that escaped from the cylinder was absorbed in spray from fire hoses that were kept trained on the escaping gas.

DESCRIPTION OF EQUIPMENT AND PROCESS

The cylinder, shown in Figure 1, was one of the standard 10-ton-capacity vessels used by the diffusion plants for storage and shipment of uranium hexafluoride. When used in our UF_6-to-UF_4 reduction process the cylinders are cradled in a movable vaporizer chest. A length of copper tubing is attached to the cylinder valve to conduct the UF_6 gas to the process equipment. The cylinder is heated by steam introduced through two perforated pipes which extend along the length of the vaporizer hood.

Figure 2 is a schematic drawing of a UF_6 cylinder in the movable vaporizer chest. The copper tubing connecting the cylinder to the process

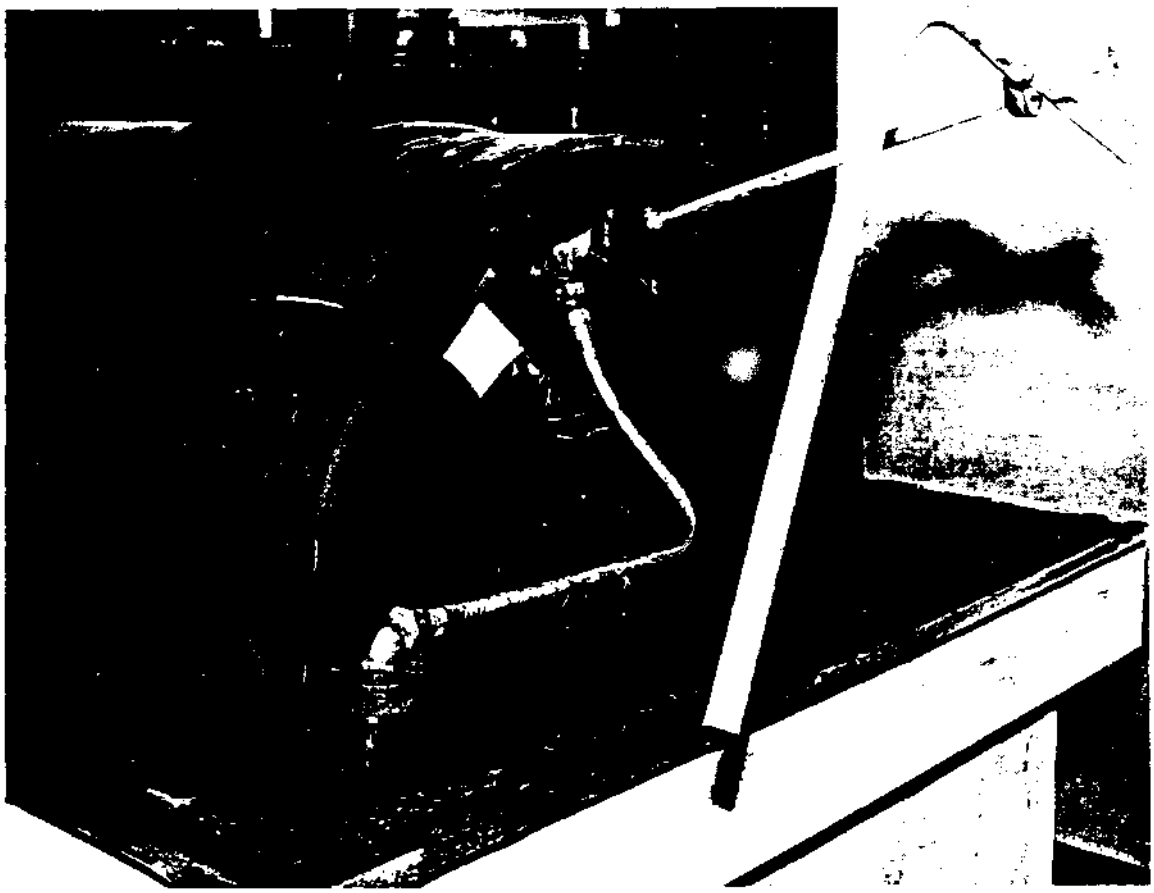

FIGURE 1 UF_6 Cylinder

feed line can be bent to accommodate slight variations in the positioning of the chest.

DESCRIPTION OF THE INCIDENT

The incident occurred during the normal Monday start-up operations. The cylinder had been used briefly on the previous Friday without trouble. At the end of the second shift on Friday the steam was shut off, and the cylinder valve was closed. The steam valve was "cracked" open to prevent freezing of condensate in the steam line.

At 7:00 a.m. on Monday the steam valve was opened to heat the contents of the cylinder. At 8:40 a.m. an operator attempted to open the valve

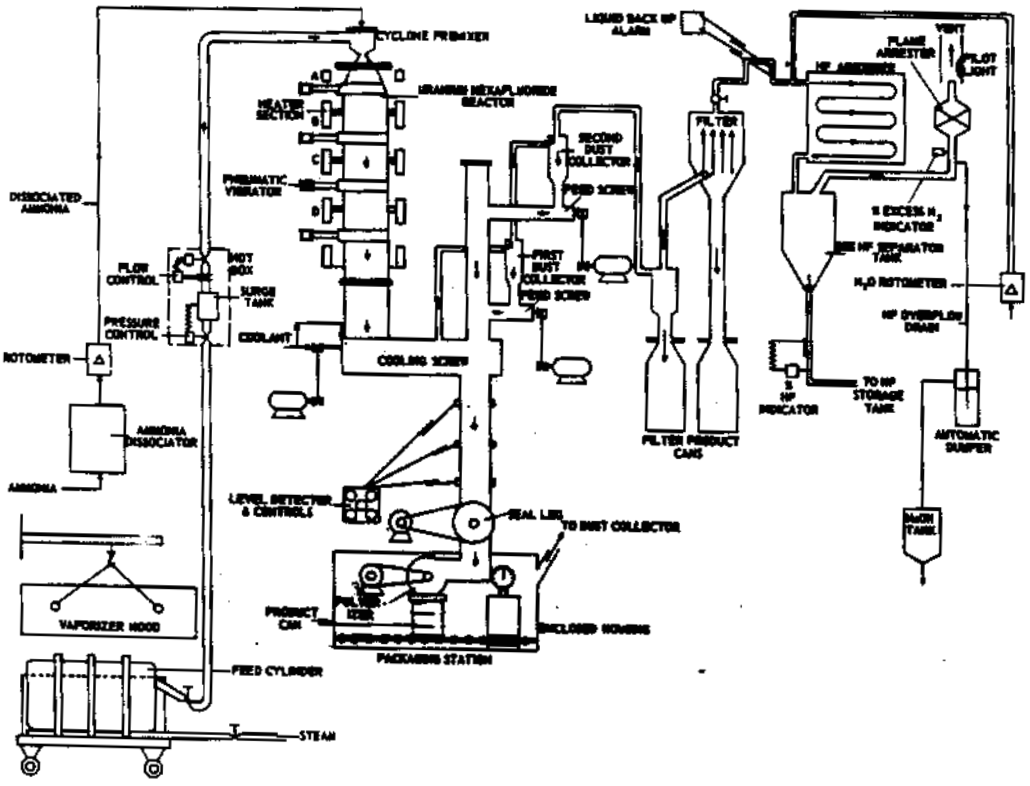

FIGURE 2 Flow Sheet UF_6 to UF_4

by turning a wrench stem which projected through an opening in the vaporizer hood. The wrench would not turn at his first attempt. He then applied more pressure and the wrench began to turn. He made less than one complete turn, felt a sharp movement, and then less resistance to turning. Unknown to the operator, the entire valve assembly had begun to turn. Then the copper tubing broke, allowing the valve assembly to unscrew completely from the cylinder.

The operator was immediately engulfed in the escaping cloud of UF_6. Two other operators nearby helped him to escape the building. There was an immediate request by a nearby security patrolman for an ambulance, and a disaster alarm signal was sent from the building. The fire truck and

fire brigade were also requested and were immediately sent to the building. Health and safety personnel also responded. The operator was taken by ambulance to the dispensary where he was given emergency treatment, including oxygen. Within a short time he developed rales in his chest, and it was believed that he was developing pulmonary edema. He was then taken to a hospital where he was given oxygen until the next day. He remained hospitalized for 6 days for observation. The two chemical operators who accompanied the man to the dispensary were also given oxygen but were not hospitalized.

The water deluge and spray system which was installed in the chest for controlling leaks is manually operated. An attempt was made to activate this system as soon as the leak was discovered but it failed to function for a few minutes. It is not known if this was due to equipment failure or if the operator, in his excitement, pushed the lever in the wrong direction.

Immediately upon their arrival, the fire brigade connected the fire hoses and began to direct a spray into the cloud near the place where it was leaving the chest. The vaporizer hood was then raised and a direct water stream was applied to the end of the chest so that it rebounded against the cylinder at the valve opening. Continued application of water for about an hour finally cooled the cylinder and reduced its pressure sufficiently to permit a wooden plug to be driven into the valve opening. This stopped the leak.

The escaping gas was carried by the wind in a southeasterly direction over a laboratory building and the administration building. Personnel from these buildings were evacuated to a location north and east. All employees were instructed that if they had noticed any peculiar odor or had any reason to believe they may have inhaled some of the material they should report to the dispensary. All involved in the emergency actions were also asked to report to the dispensary. Urine samples were collected from all of these individuals within a few hours of the incident. Follow-up urine samples were collected at the beginning of the work day for several days after the incident.

ACTIVITIES OF THE BIO-ASSAY LABORATORY

There was no need for evacuation of the Health and Safety Building since it and the site of the UF_6 release are on opposite ends of the project. Most of the personnel of the Bio-Assay Laboratory continued their routine duties during the release.

Urine samples began arriving soon after the release was stopped. During the week following the incident, 280 employees and 4 visitors submitted 1024 urine samples which were analyzed for uranium by a fluorometric technique. In the usual procedure, samples are analyzed in triplicate, and one technician can analyze 60 to 80 samples per 8-hour day. Because of the large sample load and the need for rapid results, the procedure was changed to duplicate analyses.

In our normal program, each urine specimen submitted for analysis is accompanied by a data slip identifying the sample. After analysis, the

uranium result is added to the slip which is then sent to the data processing group for the preparation of monthly, quarterly, and annual reports. Each of the incident samples was processed in similar fashion. Results were recorded on the data slips as the analyses were completed. For the early samples, data were typed and distributed to those members of the Health and Safety Division who required the information. Later, short data processing reports were prepared.

The typed information sheets and the data processing reports were helpful, but inadequate. In many cases, we needed to know if certain employees had submitted samples which were still waiting to be analyzed. To find out, we had to go through the stack of data slips for samples awaiting analysis. If information was desired before the preparation of a typed sheet or data processing report, the stack of completed data slips had to be checked.

In future emergencies of this sort we will use the incoming data slips to prepare a file card for each employee who submits a sample. One person will be assigned the task of recording all incoming samples on the file cards. In this way we will have an up-to-the-minute record, for each employee, of samples which have been analyzed and of samples awaiting analysis. Information sheets could be prepared from the cards; or personnel who required the information could call the recorder who would then read off data from the card. The cards would also be available for review, and copies could be made with an available copier. Com-

pleted data slips could be sent to the data processing group as soon as the slip information was recorded on the file card.

RESULTS OF URINALYSES

Six employees voided urine samples in which the uranium concentration exceeded 1 mg/l. Their exposures and results are briefly discussed below. No albumin was found in any samples from these employees. There was no clinical evidence that any employee suffered damage as a result of his uranium exposure.

Elimination of uranium was rapid. During the first few hours after exposure, the biological half-life for most employees was 4-6 hours. After 24 hours, most employees had dropped to their pre-incident level.

Employee A - The first urine sample from the hospitalized chemical operator was collected 2-1/2 hours after his exposure. For a period of 8 days, during his 6-day hospital stay plus 2 days at home, total urine voidings were collected and analyzed for uranium. During this 8-day period, only two voidings, at t = 83.8 hours and t = 96.3 hours, were not collected (t = time interval, in hours, following the incident).

Concentration of uranium in the first urine sample (at t = 2.5 hours) was 1.8 milligrams per liter. At t = 25.5 hours, the concentration was down to 0.055 mg/l. For this period of rapid decline, the biological half-life is about 5 hours. From t = 25.5 to t = 35.9 hours, the concentration dropped from 0.055 mg/l to 0.026 mg/l. Concentration increases occurred at t = 40.5 hours (0.049 mg/l) and at t = 65.6 hours (0.033 mg/l).

These increases occurred while the employee was confined in the hospital. Prior to the first increase, he was given oxygen, terramycin, and sedatives. There is no apparent correlation between his therapy and the two peaks in his excretion curve.

The graph in Figure 3 presents data up to t = 72.3 hours. From this point on until the end of the sample collection, fifty additional voidings were collected and analyzed. The highest uranium concentration in this group was 0.018 mg/l; most concentrations were below 0.010 mg/l. Normal concentration for this employee prior to the incident was 0.01 mg/l. Total uranium excreted was 3.36 mg after 25.5 hours and 3.65 mg after 211.6 hours when the collection was stopped.

The employee's condition improved rapidly during the first few days in the hospital. He stayed for 6 days, primarily for observation. He returned to work, fully recovered, 9 days after the accident. While he was in the hospital, 41 of his urine voidings were analyzed for protein. All results were negative. Since his return, three urine voidings have been analyzed by our Medical Lab for albumin, mucus, cells, protein, sugar and pH. No clinical abnormalities were found.

Employee B - One other Pilot Plant employee exhibited a pattern of urinary uranium which was similar to that of the hospitalized worker. This employee is a member of the Water Treatment Department, and during the release he helped man the fire hoses. His exposure differed from that of Employee A. Employee B was exposed for a longer period

of time but was exposed to lower concentrations. The first urine voiding, collected 2 hours after the start of exposure, contained 1.3 mg U/l. A second voiding 5 hours later contained 1.2 mg U/l. After this voiding the uranium concentration dropped rapidly, with a half-life of about 4.5 hours. Results are graphed in Figure 4.

Employee C - This employee of the local AEC office closely followed the efforts to halt the release. His first urine sample was collected 2.1 hours after the start of release. See Figure 5. The excretion pattern is similar to that of Employees A and B.

Employee D - This Pilot Plant employee was involved in efforts to halt the flow of UF_6. For 7 hours after his exposure his urinary uranium concentration decreased from 1.1 mg/l to 0.43 mg/l, with a half-life

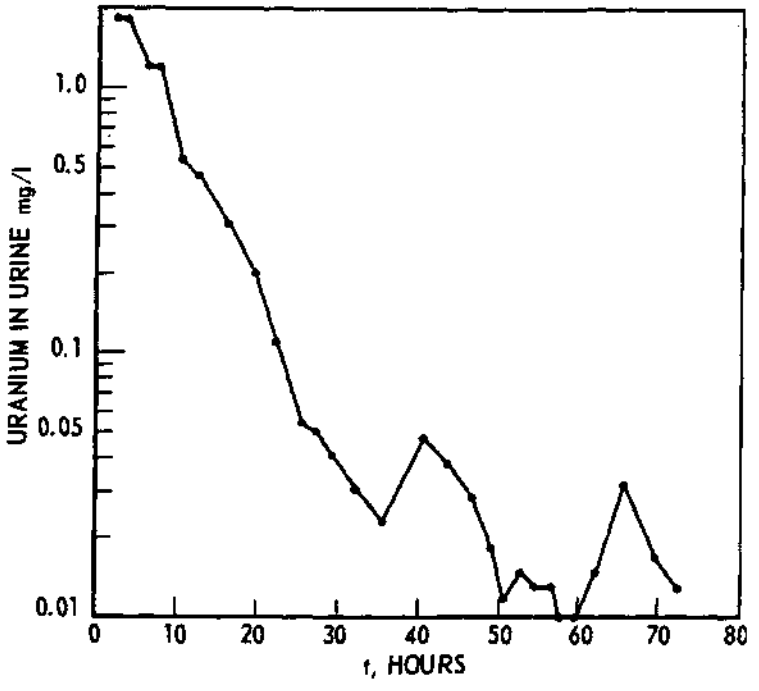

FIGURE 3 Employee A

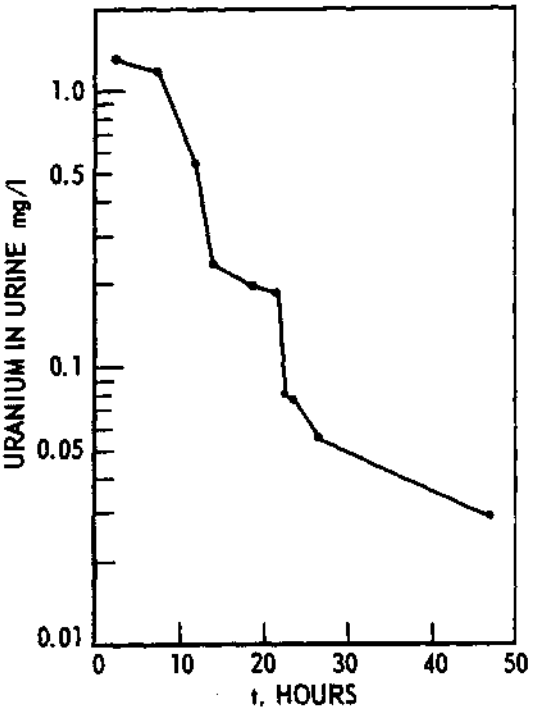

FIGURE 4 Employee B

of about 4.5 hours. After this, however, the elimination pattern becomes erratic. Later urine specimens contained 1.6 mg/l (t = 9.3 hours), and 1.9 mg/l (t = 17.8 hours). See Figure 6.

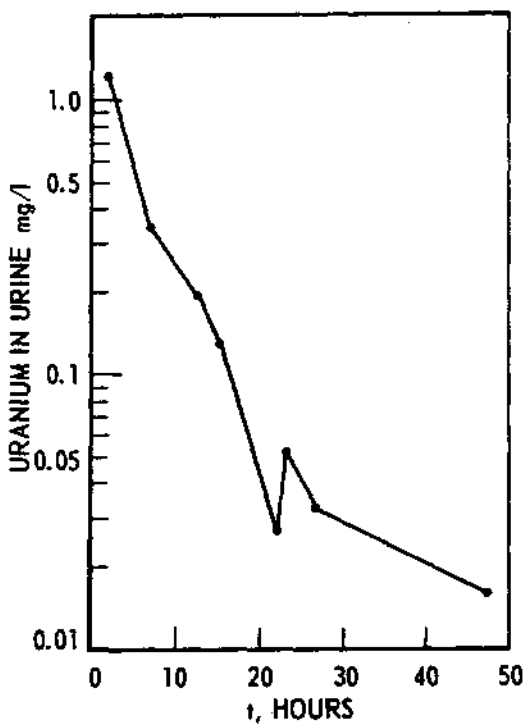

FIGURE 5 Employee C

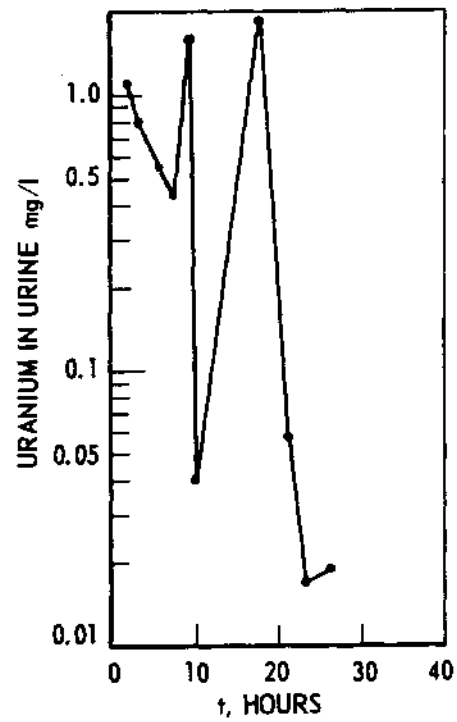

FIGURE 6 Employee D

This employee usually consumes large amounts of liquids. After his exposure, during the remainder of the workday, he and several Pilot Plant employees were kept in the Health and Safety Building for observation by the Medical staff. Only water and liquids from the Cafeteria and dispensing machines were available. It was during this period of inactivity that his urinary uranium concentration decreased in a "straight-line" pattern. His habit after work, when the pattern became erratic, is to drink other liquids, including beer, in modest quantities.

Employee E - After evacuating the Pilot Plant, this employee helped move fire hose to an area near the cylinder. He directed the nozzle of one hose, trying to cover the men who were trying to plug the cylinder. He worked without a respirator for 20 to 30 minutes and said that during this period he felt some effects of the fume in his throat. After obtaining an air pack he continued to man a fire hose and remained in the area until the UF_6 cylinder was plugged. See Figure 7.

The excretion curve in Figure 7 shows a definite decline, then a rise several hours after exposure, and then a further decline. As in the case of Employee A, we have no explanation for this behavior. Peaks of this type have been noted in other UF_6 exposure cases.

Employee F - This employee was at the reduction process panel board. He looked through an observation window just as the injured operator passed, in a cloud of fumes. He notified a supervisor that there was a UF_6 release and then tried, unsuccessfully, to activate the deluge system. When the fire brigade arrived, he helped man a fire hose. His first urine voiding was collected 3.3 hours after the start of the release. See Figure 8.

Other Employees - Sixty other employees submitted urine voidings which had uranium concentrations between 0.1 and 0.9 mg/l. Some of these employees were not near the release site, but walked through the light fog of steam and hydrolyzed UF_6 which drifted near the Laboratory and Administration buildings. A urine sample from one female office

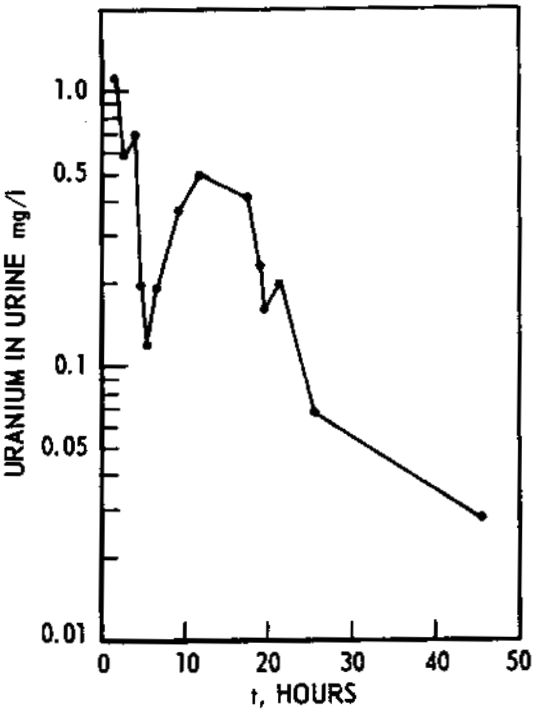

FIGURE 7 Employee E

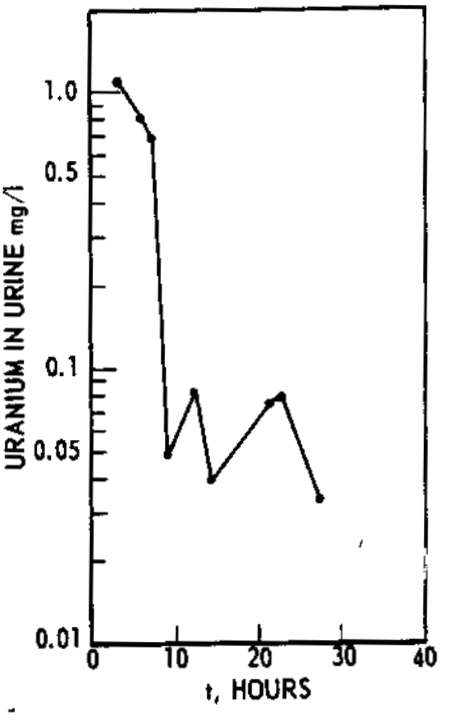

FIGURE 8 Employee F

worker, at t = 8.2 hours, contained 0.3 mg/l. A second voiding at t = 23.3 hours contained 0.006 mg/l.

The Medical Department Clinical Laboratory analyzed almost all urine samples for clinical abnormalities before the samples were analyzed for uranium. No abnormalities were found which could be attributed to exposures resulting from the UF_6 release.

PROBABILISTIC METHODS OF APPRAISING COVERAGE OF BIOASSAY SAMPLING PROGRAMS*

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INTRODUCTION

In a bioassay program, urine and other excreta are analyzed to determine how effectively current protection practices prevent assimilation of radionuclides by employees. A basis is needed to determine how often these samples must be collected from employees to provide adequate coverage at minimum cost. The method of West and Reavis[1] statistically evaluates recent past data to establish sampling frequencies. However, this method assumes no change in working conditions or effectiveness of protective measures.

Two probabilistic methods are presented which are based on a program of sample collection rather than past data, and avoid these assumptions. In these methods, coverage is defined as the probability of a single assimilation of a specific quantity of a radionuclide being detected by urinalyses. One method gives the probability of detecting by a program of urinalyses an assimilation by anyone in a group of individuals. The other gives the probability of detecting an individual's assimilation by analyzing a given sample of his urine.

*The information contained in this article was developed during the course of work under Contract AT(07-2)-1 with the U. S. Atomic Energy Commission.

METHOD I - GROUP CONSIDERATION

If an assimilation of a radionuclide occurs in a group, the probability of detecting this assimilation, P(GP), can be derived by considering two periods of time (Figure 1). There will be a time, T, when the rate of excretion is above the limit of detection, during which the assimilation can be detected if a urine sample is collected from the individual. By sampling the group at regular intervals, I, there will be a period of time, mI (where m = [T/I] or the number of whole integers in T/I, e.g., for $3 \leqslant T/I < 4$ then m = 3.), when detection is certain if the individual is sampled. When T > mI there will also be a probability of detecting the assimilation during an additional period T-mI. If A is the event of an individual being sampled and an assimilation being detected at least once during the period mI and B is the event of an individual being sampled and an assimilation being detected during the period T-mI, the probability of these two events are

$$P(A) = P(S)_A \cdot P(D|S)_A$$

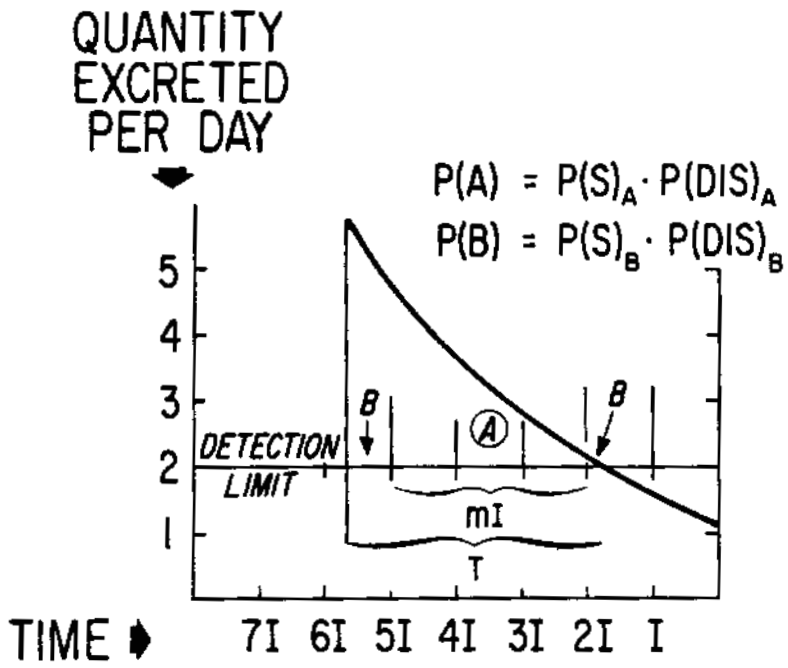

FIG. 1 THE PROBABILITY OF DETECTING AN ASSIMILATION IN A GROUP

and

$$P(B) = P(S)_B \cdot P(D|S)_B$$

where S is the event of sampling at least once, and $D|S$ is the event of detecting an assimilation, given that a sample had been taken. If F is the fraction of the group sampled, then

$$P(S)_A = [F + (1-F)F + (1-F)^2F + \ldots + (1-F)^{m-1}F]$$

and

$$P(D|S)_A = 1,$$

or taking the sum of a geometric series of m terms gives

$$P(A) = 1-(1-F)^m. \qquad (i)$$

Assuming that the probability of an assimilation occurring at a particular time between urinalyses is the same as for any other time during the interval,

$$P(B) = F\cdot\left(\frac{T-mI}{I}\right). \qquad (ii)$$

The probability of detecting an assimilation in a group P(GP) can now be expressed as the sum of the probabilities of detecting the assimilation either during the first or second period or during both periods

$$P(GP) = P(A\bar{B}) + P(\bar{A}B) + P(AB)$$

where $P(A\bar{B})$ is the probability of event A occurring and event B not occurring, etc. Since A and B are independent, this equation can be written

$$P(GP) = P(A)\cdot P(\bar{B}) + P(\bar{A})\cdot P(B) + P(A)\cdot P(B).$$

Substituting

$$P(\bar{A}) = 1-P(A)$$

and

$$P(\bar{B}) = 1-P(B)$$

in the above equation gives

$$P(GP) = P(A) + [1-P(A)]\cdot P(B)$$

or

$$P(GP) = 1-(1-F)^m + (1-F)^m \cdot F \cdot \left(\frac{T-mI}{I}\right).$$

Rearranging this gives

$$P(GP) = 1-(1-F)^m\left[1-F\left(\frac{T}{I}-m\right)\right]. \qquad \text{(iii)}$$

It should be noted that there are no restrictions upon this relationship. If $\frac{T}{I} < 1$, then m=o and $P(GP) = F\,\frac{T}{I}$. This is true even when F=1, since

$$\lim_{F \to 1} (1-F)^0 \to 1.$$

The values of P(GP) for various values of T/I and F are plotted in Figure 2.

METHOD II - INDIVIDUAL CONSIDERATION

If we select one individual from a group, the probability [P(IN)] of detecting a single assimilation of a specific quantity of a radionuclide by analyzing a given sample of his urine can be determined with this method. Since a sample of his urine has been collected, the probability of collecting it need not be considered. In order to apply the probability to anyone in the group, no knowledge of the individual's past sampling history is assumed. Rather, the collection values for I, F, and T for the "group consideration" can be used to calculate the probability, P(IN). This probability is the product of the probability of an interval of a certain length occurring between two consecutive urinalyses, P(L), and the probability of detecting a single assimilation occurring during the interval, P(M), summed over all possible intervals,

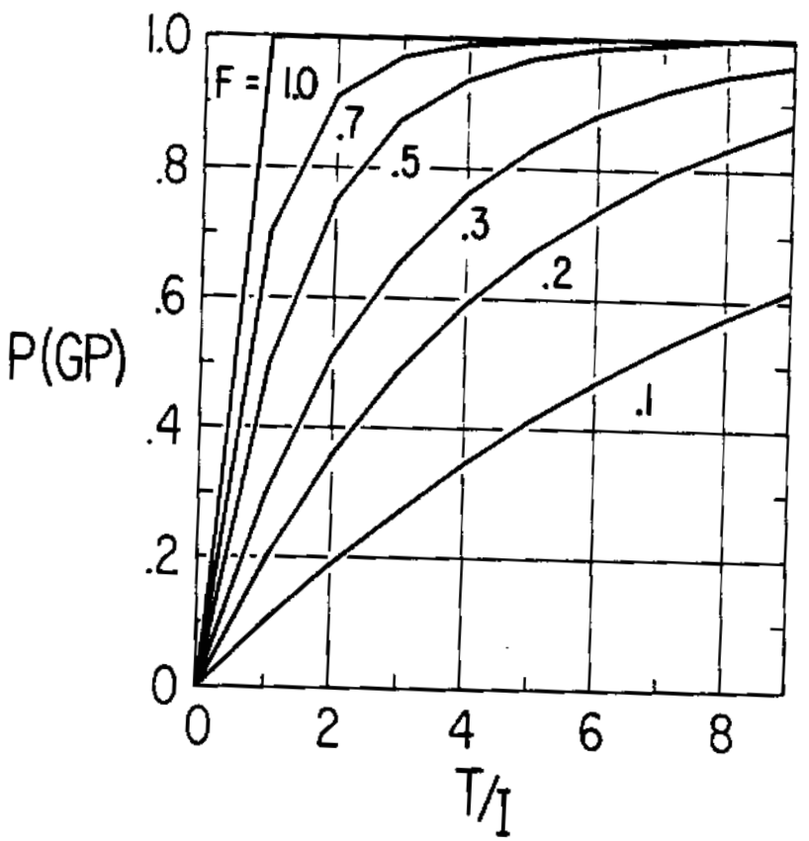

FIG. 2 THE PROBABILITY THAT AN ASSIMILATION WILL BE DETECTED IN A GROUP, P(GP), WHEN DIFFERENT FRACTIONS OF THE WORK GROUP, F, ARE SAMPLED, AND DIFFERENT INTERVALS BETWEEN SAMPLING, I, ARE USED

$$P(IN) = \sum_{n=1}^{\infty} P(L)_n \cdot P(M)_n \qquad \text{(iv)}$$

The development of expressions for $P(L)_n$ are illustrated in Figure 3. Here all possibilities of an individual being sampled during the four previous sampling periods are represented by vertical steps along a horizontal time axis. If personnel in a work group are randomly sampled at specific time intervals of length I, the probability of an individual selected for urinalysis having been selected with those in the previous sample, and thus having gone one interval between urinalyses is the ratio, F, of the number selected to the total number in the group

$$P(L)_1 = F = \frac{\text{Number selected}}{\text{Total in work group}}$$

The probability of him not having been selected in the previous sample but having been selected the time before and thus having gone two intervals between urinalyses is

$$P(L)_2 = (1-F)F,$$

and the probability that he will have been missed on the last two selections is

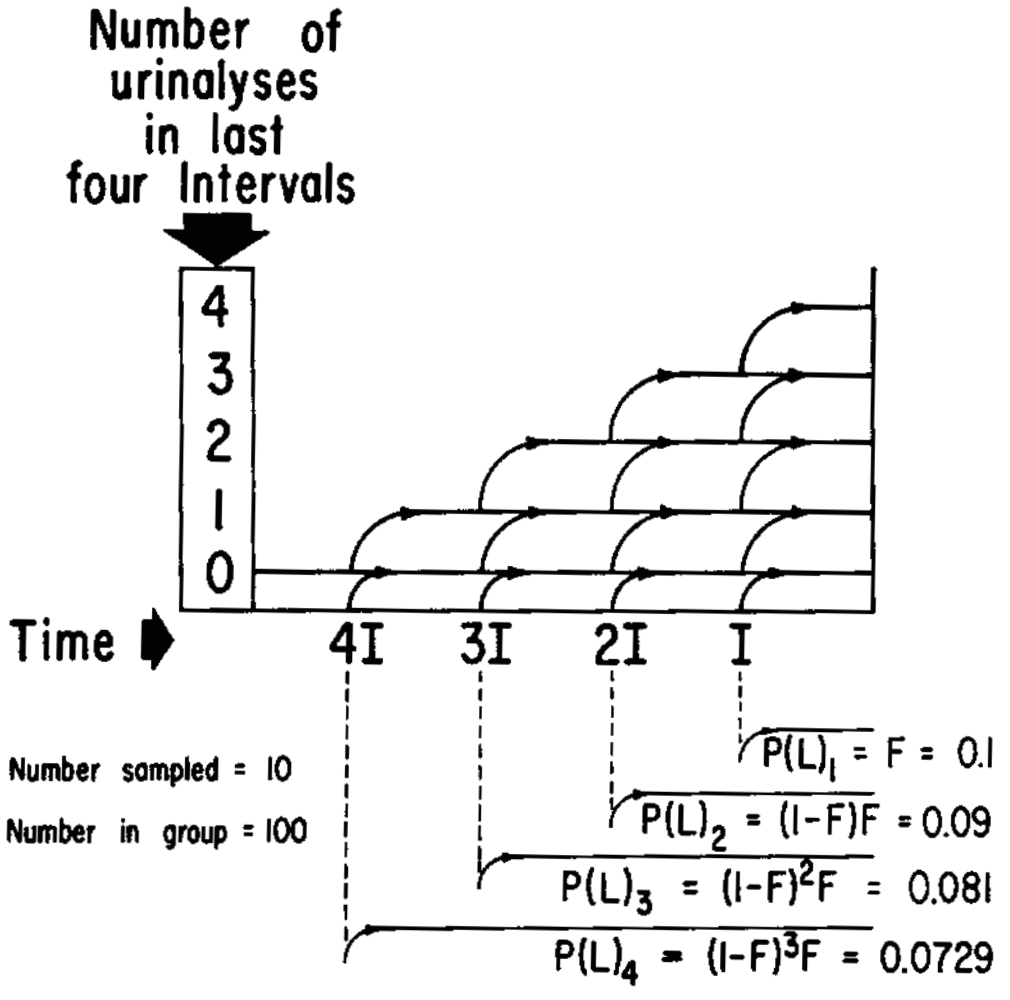

FIG. 3 THE PROBABILITY OF AN INTERVAL OF A CERTAIN LENGTH OCCURRING BETWEEN TWO CONSECUTIVE URINALYSES

$$P(L)_3 = (1-F)^2F.$$

Thus the probability of going n intervals between urinalyses is

$$P(L)_n = (1-F)^{n-1}F. \qquad (v)$$

Figure 4 illustrates the probability of detecting a single assimilation occurring during the interval between consecutive urinalyses. Assuming that the probability of an assimilation occurring at a particular time between urinalyses is the same as for any other time during the period, then the probability of an assimilation being detected by urinalyses is the ratio of the length of time, T, during which the rate of excretion is above the limit of detection, to the length of time between urinalyses. If I is the interval at which members of the work group are selected for urinalyses and n is the number of such

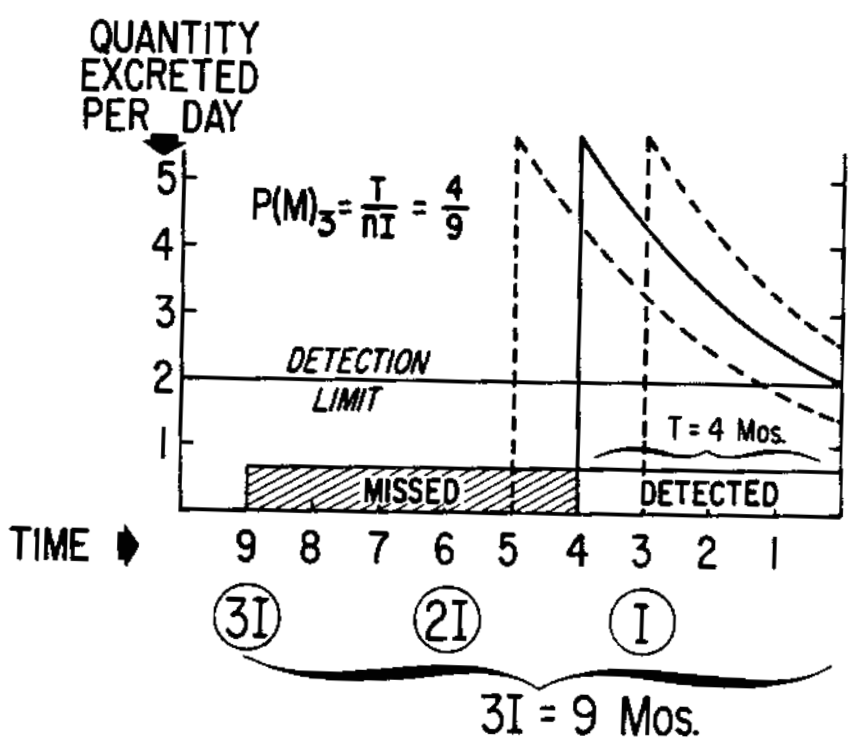

FIG. 4 THE PROBABILITY OF DETECTING A SINGLE ASSIMILATION OCCURRING DURING THE INTERVAL BETWEEN CONSECUTIVE URINALYSES

intervals between an individual's urinalyses, then the probability of detection after n intervals is

$$P(M)_n = \frac{T}{nI} \text{ or } 1, \qquad \text{(vi)}$$

whichever is smaller.

Thus, the probability of an acute assimilation being detected in an individual is found by substitution in equation (iv).

$$P(IN) = F\frac{T}{I} + (1-F)F\frac{T}{2I} + (1-F)^2F\frac{T}{3I} + \ldots$$

or

$$P(IN) = F\frac{T}{I}\sum_{n=1}^{\infty}\frac{(1-F)^{n-1}}{n}$$

or

$$P(IN) = \frac{T}{I}\left(\frac{F}{1-F}\right)\ln\left(\frac{1}{F}\right) \qquad \left(\frac{T}{I} \leqslant 1\right), \quad (F < 1). \quad \text{(vii(a))}$$

When $\frac{T}{I} > 1$, an additional expression must be added to the above equation since P(IN) cannot exceed 1.

$$P(IN) = F\frac{T}{I}\left[\left(\frac{1}{1-F}\right)\ln\left(\frac{1}{F}\right) - \sum_{n=1}^{m}\left(\frac{T}{nI} - 1\right)(1-F)^{n-1}\right]$$

$$\left(\frac{T}{I} \geqslant 1\right), \quad (F < 1) \qquad \text{(vii(b))}$$

where m = [T/I] as previously defined.

When F = 1,

$$P(IN) = \frac{T}{I} \qquad \left(\frac{T}{I} \leqslant 1\right) \qquad \text{(vii(c))}$$

or

$$P(IN) = 1 \qquad (\frac{T}{I} \geqslant 1) \qquad \text{(vii(d))}$$

Thus, if an individual has assimilated a certain quantity of radioactive material since his last urinalysis, the probability of detecting it in a given sample of his urine can be calculated.

Values of P(IN) for various values of T/I and F are plotted in Figure 5.

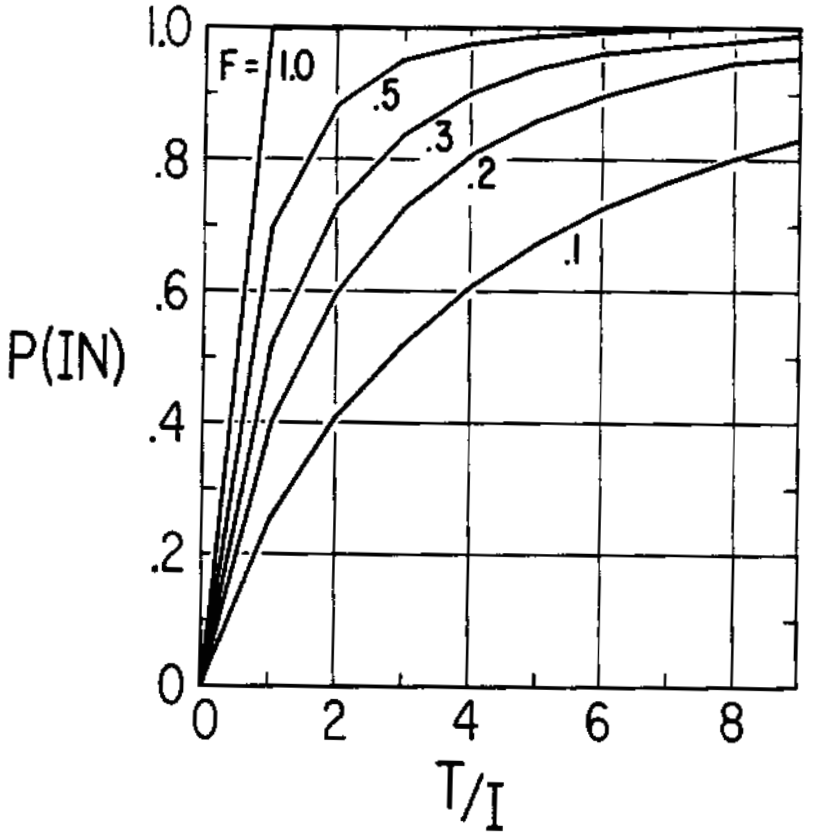

FIG. 5 THE PROBABILITY THAT AN INDIVIDUAL'S ASSIMILATION WILL BE DETECTED BY ANALYZING A SAMPLE OF HIS URINE, P(IN), WHEN DIFFERENT FRACTIONS OF THE WORK GROUP, F, ARE SAMPLED AND DIFFERENT INTERVALS BETWEEN SAMPLINGS, I, ARE USED

APPLICATION

To apply the above derivations to a hypothetical plutonium bioassay program, the questions asked are: 1) How good is the present sampling program? and 2) How can it be improved?

First, one of the above methods should be selected. For our example the group consideration is used, since detecting an assimilation by anyone in a group of employees is more meaningful than detecting an assimilation by a single urinalysis. Thus P(GP) is used rather than P(IN).

Next, values of T have to be calculated. For plutonium this can be done using the following equation reported by Langham[2]:

$$E = 0.0023\ DT^{-0.77}$$

where E, the quantity of plutonium excreted per day T days after assimilation, and D, the quantity of plutonium assimilated are in the same units. If E is expressed in d/m/day and D as the percent of the maximum permissible body burden (MPBB) of 0.04 μCi, then the equation becomes

$$E = 2.0424\ DT^{-0.77}.$$

Solving this for T gives

$$T = \left(\frac{2.0424\ D}{E}\right)^{1.3}$$

If T is the number of days before the excretion rate, E, falls below the bioassay reporting limit of 0.1 d/m/day, the above equation becomes

$$T = (20.424\ D)^{1.3}. \qquad \text{(viii)}$$

The coverage of an existing program can now be expressed in terms of the probability, P(GP), of detecting an assimilation of D % MPBB of plutonium in a group of employees.

For our hypothetical program, let us assume that the employees are divided into five groups according to the interval, I_o, at which they are sampled. Every member of a group is sampled at the end of the appropriate interval, thus the fraction of the group

sampled, F_o, is 1. The size of an acute assimilation, expressed as percent of the MPBB, which can be detected with a 50, 95, and 100% probability are calculated by obtaining a value of T from equation vii and substituting it in equation viii. These are given in Table I for the five groups - quarterly, Q; semi-annual, SA; annual, A; three-year, 3 yr; and five-year, 5 yr.

TABLE I

% of the MPBB which can be detected with a 50, 95, and 100% probability using the hypothetical sampling program.

Group	I_o (days)	D(% MPBB) P(GP) = .50	P(GP) = .95	P(GP) = 1.00
Q	91	0.93	1.52	>1.58
SA	182	1.58	2.59	>2.69
A	365	2.70	4.42	>4.60
3 yr	1095	6.29	10.31	>10.72
5 yr	1826	9.32	15.28	>15.89

The values in Table I answer the question of how good is the present sampling program. If these coverages are acceptable, our study will be complete. However, advantage should be taken of the ability of this method to indicate where improvements in the sampling program can be made.

A question frequently asked is, could the collection interval, I, be increased without changing the coverage. This would mean reducing the value of T/I while holding T and P(GP) constant. Looking at Figure 2, we see that this is usually possible if an appropriate increase is made in the fraction of the group sampled, F. In this example, however, F is assumed to be 1, so this is not possible.

The fraction of the group sampled might be reduced and compensated for by reducing the interval between sample collections to maintain the coverage. This raises the question of what effect this will have on the work load of the bioassay laboratory.

To compare one program with another having different values of F and I, the following expression for the comparative bioassay work load, W, is developed.

$$W = \frac{FI_o}{F_o I} \quad 100 \qquad \text{(ix)}$$

where I_o and F_o are the sampling interval and fraction of the group sampled under the basic program. Since here $F_o = 1$, this reduces to

$$W = \frac{I_o}{I} \quad F \; 100.$$

This may be carried one step further by substituting

$$\frac{1}{I} = \frac{1}{FT}\left[1 - \frac{1-P(GP)}{(1-F)^m}\right] + \frac{m}{T}$$

from equation (iii) in the above equation giving

$$W = \frac{I_o}{T}\left[1 - \frac{1-P(GP)}{(1-F)^m} + F_m\right] 100. \qquad \text{(x)}$$

It may be noted that when $m = 0$, this equation reduces to

$$W = \frac{I_o}{T} \quad P(GP).$$

Thus for a given P(GP), values of F and I have no effect on the laboratory work load when $\frac{T}{I} < 1$.

Let us now compare a sampling program which would provide a 50% probability of detecting the assimilation of 1% of the MPBB with the above program for the quarterly group. To do this, T/I is calculated from equation (iii) for various values of F. Next T is obtained from equation (viii) and I from the ratio of T to T/I. These results are given in Table II.

TABLE II

The % of the present urinalyses made quarterly required for a 50% probability of detecting the assimilation of 1% of the MPBB when different fractions of the group are sampled randomly.

F	T/I	I(days)	W (%)
1.0	.500	100	91
.9	.556	90	91
.8	.625	80	91
.7	.714	70	91
.6	.833	60	91
.5	1.000	50	91
.4	1.417	35	103
.3	1.952	26	107
.2	3.117	16	113
.1	6.592	8	120

A similar comparison is also made between the program for the annual group and one which would provide a 95% probability of detecting the assimilation of 5% of a MPBB. This is given in Table III.

TABLE III

The % of the present urinalyses made annually required for a 95% probability of detecting the assimilation of 5% of the MPBB when different fractions of the group are sampled randomly.

F	T/I	I(days)	W (%)
1.0	.950	431	85
.9	1.556	263	125
.8	1.938	211	138
.7	2.635	155	165
.6	3.365	122	180
.5	4.400	93	196
.4	5.892	69	212
.3	8.441	48	228

Table II shows that the fraction of the group sampled each time can be cut in half if the interval between sampling is also reduced from 100 days to 50 days with no increase in the bioassay laboratory work load. (While there is no increase in the work load, there is also no reduction caused by decreasing F. Therefore consideration based on psychological and administrative reasons should be given to sampling all members of a group after each interval.) A similar plateau is not seen in the level of Table III. Thus, all employees in this group should be sampled every 431 days to reduce the work load. Both tables illustrate that the work load of a bioassay laboratory can be reduced by judiciously redefining the desired coverage.

SUMMARY

The above derivations and examples provide methods for expressing the coverage afforded by any bioassay sample collection program. The probabilistic method is not restricted to plutonium, but has general applicability to all sampling procedures. Changes in the interval between urinalyses or the fraction of the group sampled can be related to the work load of the laboratory and, with some knowledge of the metabolism of the radionuclide, to the probability of detecting an assimilation. Sample collection programs can now be compared, appraised, or tailor-made to meet desired specification of economy of operation, probability of detection, and level of assimilation.

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AN AGE-DEPENDENT MODEL

FOR THE BODILY RETENTION OF CESIUM*

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Abstract

After an intake of cesium, this element is eliminated over a period of time. It has been found by Richmond et al. that a one-or two-exponential retention function is usually sufficient to fit the observed data. This retention model is valid for adults and children, but the elimination rates are different in each case. In this report a mathematical compartment model is proposed which allows compartment size or growth to be included naturally. This model is applied to the retention of cesium-137 by humans from birth through adult life. The biological half-times predicted with this model are compared to experimental values with favorable results although there is still much variation of the observed half-times within an age group. The implications of this model in regard to dose from single and continuous intakes are examined.

The retention of radioelements by humans was initially determined for the adult since the protection of radiation workers was a problem of paramount importance. Data from accident cases as well as from planned experiments had also accumulated for the adult more than for individuals of other ages. However, as data accumulated, it was apparent that the retention pattern of a radioelement might vary greatly with age. This appears to be the case for cesium. It is the purpose of this paper to present one theoretical, age-dependent, compartmental model and apply it to the retention of cesium.

Richmond et al.[1] used a two-exponential retention function to fit the observed retention of cesium-137 by normal adult males for a period of 550 days after a single oral intake. Except for the first 10 days after intake, the second exponential is dominant, contributing more than 99% to the total area under the retention function. Therefore, for purposes of dose estimation, or equilibrium level estimation in the adult, the retention of cesium may be considered to be given by a single exponential.

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It is well known that a single compartment with an elimination rate that is proportional to its contents is described by Eq. 1:

$$\frac{d}{dt} A(t) = -\lambda A(t) \qquad (1)$$

where $A(t)$ is the amount of material in the compartment and λ is the decay constant. This equation has a single exponential as its solution. The retention of cesium by the adult apparently may be considered to be retained in a single homogeneous compartment and eliminated in the manner just described.

To introduce the age dependence into the retention function, consider a single compartment with a definite size or volume. Let the size of this compartment vary with time, however. In order to write a differential equation governing the kinetics of this compartment, it is necessary to make one assumption. Let us assume that the rate of change of a quantity of material introduced into the compartment is proportional to the concentration of the material in the compartment. The kinetic equation is then

$$\frac{d}{dt} A(t) = -m \frac{A(t)}{W(t)} \qquad (2)$$

where $A(t)$ is the amount of material in the compartment, $W(t)$ is the volume of the compartment, and m is the constant of proportionality.

There is now the practical problem of determining what should be used as a measure of compartment size. Many different measures might be proposed; examples of some of these might be weight, muscle mass, body water, or potassium content. Since cesium is rather uniformly distributed throughout the body, let us take body mass to be a measure of compartment size for cesium. This is not to say that mass has physiological significance in cesium retention. What should be inferred is that the true compartmental volume for cesium is assumed to be proportional to body mass.

Although Eq. (2) may be applied directly, there is a simplification that can be made for ^{137}Cs retention. If at time t, the change in the compartmental half-life with time is small compared to this half-life, the compartment may be considered to have a constant half-life for material introduced into the compartment at time t. Therefore,

$$T_{1/2} = \frac{W(t) \ln 2}{m} \qquad (3)$$

After this simplification, it follows that for a single intake at any time, the elimination is exponential with a half-life determinable from the volume of the compartment at that time.

If $W(t)$ is a known function, then after determining the proportionality constant, m, the time dependence of the compartmental half-life will be determined. The constant, m,

is determined by using the experimentally determined biological half-life for cesium in the adult male and his body mass.

The adult values for body weight and half-life of cesium are used since they have been the topic of many more experiments and are known more precisely. The mass of the adult male is taken to be 70 kg. Although there is a wide range of biological half-times reported in the literature for cesium in adult males, a representative value of 100 days has been chosen. Having determined m from Eq. 2, the relationship between biological half-life for cesium and body mass is given by

$$T_{1/2}\ (t) = 1.43\ W(t). \qquad (4)$$

This equation was not derived by considering individuals but was determined for the average of populations of various body masses. The equation should only be used to determine the average biological half-life of a group of grossly normal individuals. Such parameters as percent body fat, environmental temperature, or work activity may greatly influence the biological half-life. However, a group of people of the same age chosen randomly should have an average biological half-life for cesium given by Eq. (4).

The growth curve for body mass from infancy to adulthood is given in Fig. 1. The curve for males is that given by Mitchell;[2] the one for females is taken from reference 3. Using these curves, the biological half-life for cesium was determined.

In Fig. 2 is a comparison of the biological half-life of cesium predicted by the model with some experimental results. The model predicts a cesium biological half-life for the newborn of about 5 days. From this value it increases to the assumed value of 100 days for the adult. Boni[4] has determined the cesium biological half-life of humans from 5 years of age through adulthood. His method is one in which the body burden of fallout cesium-137 as well as the urinary excretion is determined. From the single exponential model and assuming equilibrium conditions, the biological half-life may be determined. For the adult values determined in this way, the range of values about the mean is ± 50%. The model given here predicts a half-life about twice as large as Boni's results in the 5-to-10-year-age group. However, McGraw[5] has surveyed the literature and given a representative curve for the average half-life. His curve is quite close to the model in the 5-to-10-year-age group. It should be pointed out that the variation of the experimental values about McGraw's curve is quite large.

By applying Eq. (4) and using the body weight for females, the half-life of cesium in females was determined and is given in Fig. 3. Boni also has measured the biological half-life of cesium in females. As shown, the model predicts a half-life for females of about twice that observed by Boni.

Using measurements of stable cesium in tissue, the daily intake of cesium, and the single exponential model under equilibrium conditions, Snyder and Cook have produced

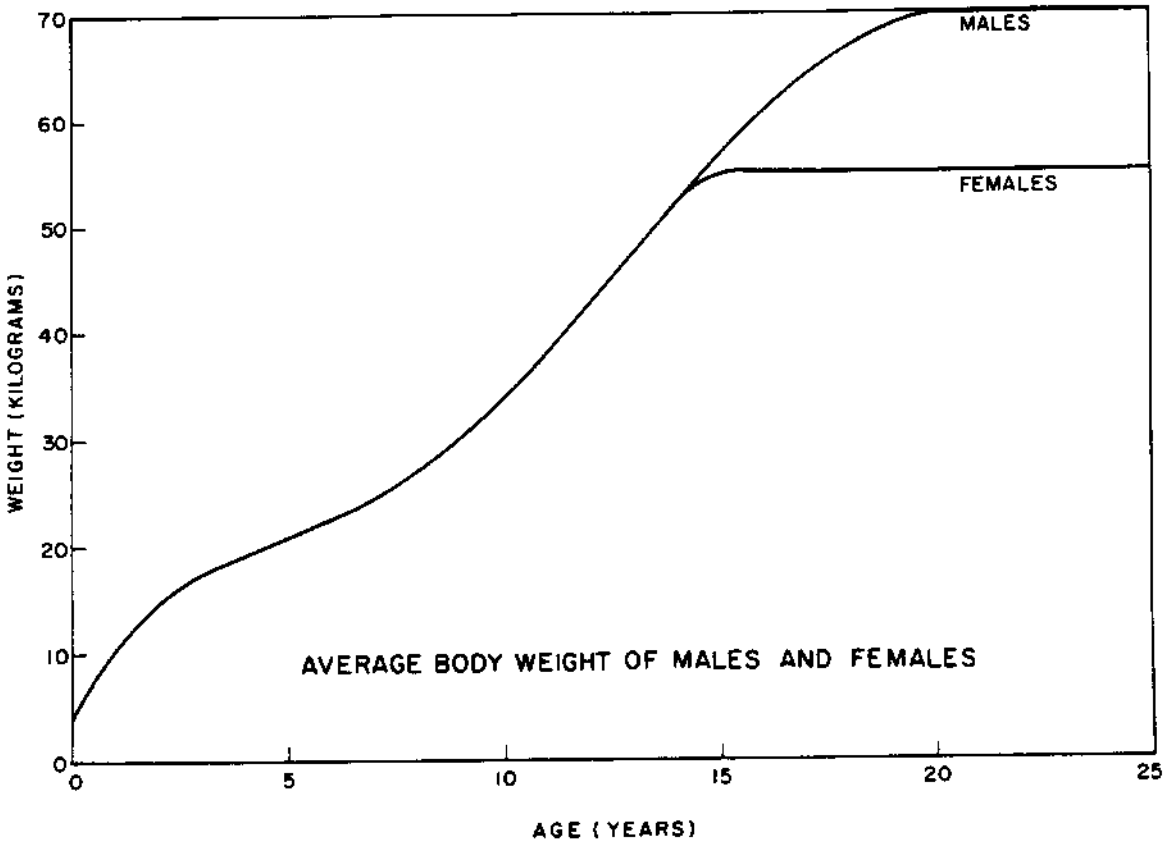


Figure 1.

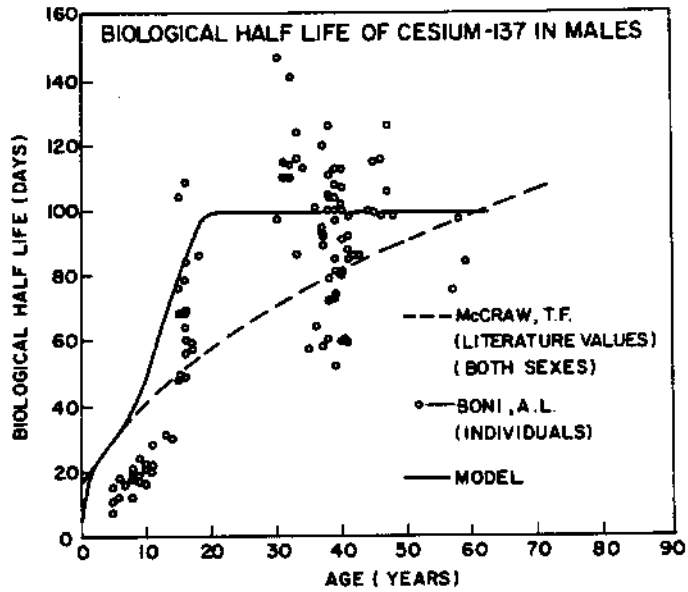


Figure 2.

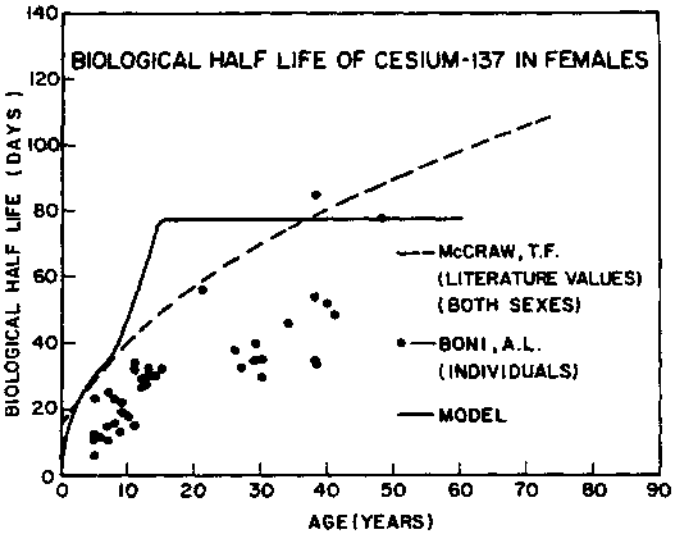


Figure 3.

estimates of the biological half-life with age which are given in Fig. 4. During the first 5 years, the agreement of the model with their values is good. There is agreement for the adult values also; however, the model gives somewhat higher values during the adolescent period.

In this paper we have examined a conceptually, very simple, age-dependent, compartmental model. Application of the model to cesium retention has not been any more successful nor less successful than prior models. It has not explained variation of the biological half-life within an age group. Other parameters besides age are evidently important. However, the model has been derived theoretically with few assumptions, and there is only one arbitrary constant to be determined. The model is capable of accounting for a large part of the variation in half-lives between the various age groups.

If individuals of various ages take in 1 μCi of cesium-137, the total dose delivered to the body of each has been calculated and is given in Table 1. The total dose is directly proportional to half-life and inversely proportional to body mass. By the model, half-life and mass are proportional. Therefore, total dose is independent of half-life or body mass. This is true when 100% of the emitted energy is absorbed. Beta dose is an example. The fraction of the gamma energy absorbed by the infant is slightly less than half that of the adult as will be shown later. Therefore, we see the model predicts that for identical single intakes of cesium-137, the infant will receive a beta-plus-gamma total dose of about 75% that of the adult.

The dose delivered from an internal body burden of cesium-137 will now be considered. Given a unit source of cesium-137 in the body of man, what is the dose rate at various positions in his body? Since it is relatively easy to determine the beta dose rate, let us dispose of this part before we examine the gamma-dose-rate problem. In Fig. 5 is shown the radiological decay scheme of cesium-137. The ranges of both the emitted beta

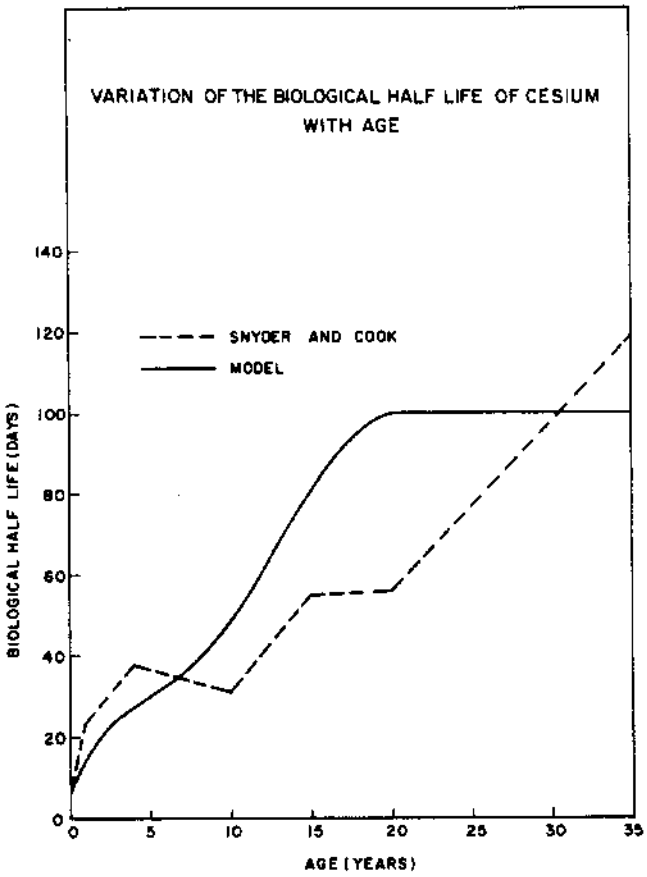


Figure 4.

particles and the electron are less than 0.6 cm in tissue. Since this range is small compared to the dimensions of the body, we will assume, as is usually done, that the entire kinetic energy of these particles is absorbed locally. The surface skin is an exception however.

TOTAL DOSE DELIVERED TO THE BODY FROM A SINGLE INTAKE OF ^{137}Cs

Age (yr)	Beta Dose (μrad/μCi)	Gamma Dose (μrad/μCi)	Beta Plus Gamma Dose (μrad/μCi)
0	2680	1040	3720
1	2680	1450	4130
5	2680	1650	4330
10	2680	1900	4580
15	2680	2140	4820
20	2680	2390	5070

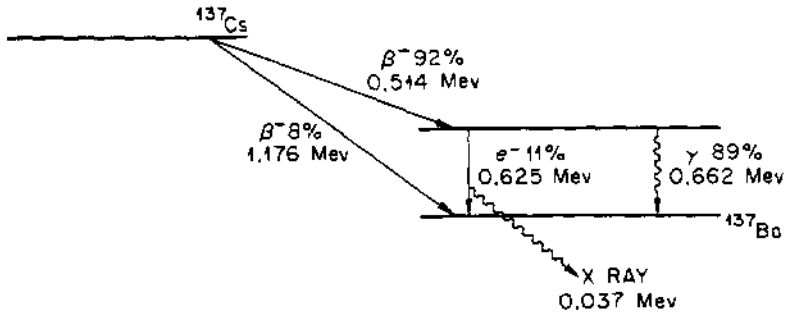
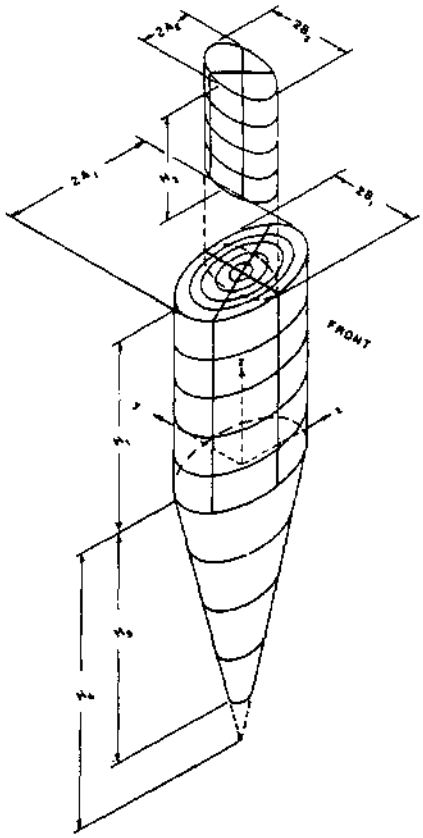


Figure 5.

Using an effective energy of 0.26 Mev/dis for the betas and the electron, a dose rate of 550 μrads/hr results from a ^{137}Cs concentration in the body of 1 μCi/kg. If a uniform distribution of cesium-137 in the body is assumed, every part of the body except the surface will be receiving a beta dose rate of 550 μrads/hr for each μCi/kg concentration of cesium-137. The surface will receive about one-half of the dose rate. By way of comparison, the total-body gamma dose rate for the adult is about 580 μrads/hr per μCi/kg as we shall see later.

The problem of determining the gamma dose rate delivered to the body is not as easily resolved, because the mean range in tissue of the 0.662-Mev gamma photon is 12 cm. This value is not small compared to the dimensions of the body, so we have the problem of determining the amount of energy that escapes from the body or, conversely, the amount that is absorbed. The theory of gamma photon interaction with matter has been known for some time. However, to apply this theory to other than thin slabs and simple geometrical shapes involves elaborate mathematical calculations. Understandably, previous attempts at estimating the gamma dose rate usually have not relied on this well-developed theory but have instead employed simplifying assumptions for the purpose of performing the calculations. One such method uses the effective radius concept of the ICRP.[6] The body or organ is assumed to be a sphere of tissue of a given radius with the entire organ burden located at its center. A first-collision calculation of dose to this sphere of tissue is then effected. This method conservatively estimates the gamma dose to the body from cesium-137 to be about twice as high as has been found in this report.

Through the use of the high-speed digital computer, it has become practical to apply the well-developed theory of gamma photon interaction with matter and dispense with many simplifying assumptions. However, we still need to specify the shape of the human body. In Fig. 6 is shown the type of phantom and coordinate system we have chosen. The head and neck are represented by the upper elliptical cylinder; the trunk and arms compose the elliptical cylinder of the center section; and the legs below the buttocks form the elliptical cone of the phantom. This form of the phantom is the same for all ages. Only the heights and axes of the elliptical cylinders and elliptical cone are varied to provide a phantom approximating the body size of grossly normal individuals ranging in age from infancy to adulthood. For this problem, six phantoms representing body sizes of human males of ages 0, 1, 5, 10, 15 and 20 years were constructed. The weights and dimensions completely



PHANTOM DIMENSIONS AND DOSE REGIONS

Age (yr)	Weight (kg)	H_1 (cm)	H_2 (cm)	H_3 (cm)	H_4 (cm)	A_1 (cm)	B_1 (cm)	A_2 (cm)	B_2 (cm)
0	3.473	23	13	15	20	5.5	5	4.5	5
1	10.171	33	16	27	36	8	7	6.5	7
5	19.654	45	20	46	57.5	11	7.5	6.5	7.5
10	31.902	54	22	64	80	14	8	6.5	8
15	54.041	65	23	78	97.5	18	9	7	9
20	70.037	70	24	80	100	20	10	7	10

Figure 6.

specifying the phantoms are given in Fig. 6. These dimensions were chosen after considering data on body weight, length, breadth, and circumference of body parts obtained from the Biological Handbook by Altman.[7] Reference material also was obtained from the phantom constructed by Hayes and Brucer.[8] Data on the relative volume of body parts were obtained from "Growth of Man" in Tabulae Biologicae by Krogman.[9]

As shown in Fig. 6 the phantom was divided into over a hundred subregions in which the dose rate was determined. There are four layers in the legs in which the dose rate was calculated. There were usually five layers in the trunk section. However, in phantoms for ages 0, 1, and 5 years, the trunk was divided into three, three, and four layers, respectively, in order to obtain a reasonably accurate estimate of dose rate in each. Inside the trunk the layers are further subdivided into five concentric bands. These bands are further cut by vertical cross planes to give the final and smallest volume elements in which dose rate was determined. The head section was sectioned into either two or four layers, depending on head size. With this subdivision of the phantom, the vertical variation of dose rate could be determined as well as the side-to-side and front-to-back variations.

A Monte-Carlo-type method of calculating the dose rate was used. This code is similar to the one used by Ellett, Callahan, and Brownell,[10] but the phantom used here

is different. The gamma-ray-attenuation coefficients for the medium were taken from Grodstein.[11] This method requires that the flight of a photon is mathematically followed between interaction sites. Through probabilistic rules, the energy deposition of the photon at an interaction site is recorded. After a large number of such simulated photon histories have been calculated, the average energy deposition per photon in a region is then estimated, and the dose per photon may be calculated. Photons of initial energy 0.662 Mev were randomly generated uniformly in the phantoms as follows: 80,000 in the phantoms for ages of 15 and 20 years; 100,000 in the phantoms for ages 1, 5, and 10 years; and 160,000 in the phantom for the newborn. For each photon the direction of flight was selected randomly. The flight distance to the first interaction site was determined randomly using the cross section of the medium at the energy of the photon. After selecting a new flight direction emanating from this interaction site probabilistically from the Klein-Nishina distribution, the energy deposition at this site can be determined. The process of photon flight is now repeated but with a decreased energy. Let $n - 1$, n, and $n + 1$ be consecutive interaction sites for a photon. The mathematical photon is characterized by eight independent quantities—x, y, and z, the coordinates of the present interaction site; a and b, the direction cosines specifying the direction of flight to the next interaction site; L, the length of the photon's flight path to the next interaction site; E, the energy of the photon during its flight; and W, the weight of the photon during its flight. The weight of a mathematical photon is the probability the photon exists and takes on all values from zero to 1. It is set equal to 1 for a photon just started from the source. However, a real photon has a weight of either zero or 1 at all times. Suppose a photon,

$$P_{n-1} = P(x_{n-1}, y_{n-1}, z_{n-1}, a_{n-1}, b_{n-1}, L_{n-1}, E_{n-1}, W_{n-1}),$$

is in flight between points $n - 1$ and n. We wish to know the energy deposition at point n and the location of the point $n + 1$, which may be found if we find P_n and use it in conjunction with P_{n-1}. The coordinates x_n, y_n, and z_n may be found by applying algebraic geometry using

$$x_{n-1}, y_{n-1}, z_{n-1}, a_{n-1}, b_{n-1}, \text{ and } L_{n-1}.$$

The new direction of flight, a_n and b_n, is determined by using E_{n-1} and the Klein-Nishina gamma photon scattering distribution. The new energy E_n is calculated from the angle of scatter, which involves a_{n-1}, b_{n-1}, a_n, and b_n. Length L_n is calculated as follows:

$$L_n = \frac{-1}{\sigma(E_n)} \ln N,$$

where $\sigma(E_n)$ is the attenuation cross section of the medium and N is a random number chosen uniformly on $0 \leqq N \leqq 1$. The weight W_n is given by

$$W_n = W_{n-1} \frac{\sigma_c(E_n)}{\sigma(E_n)} ,$$

where $\sigma_c(E_n)$ is the cross section for the Compton process. The energy deposition at point n is

$$E\Delta = W_{n-1}\left[\frac{\sigma_p(E_n - 1)}{\sigma(E_{n-1})} E_{n-1}\right.$$

$$\left. + \frac{\sigma_c(E_n - 1)}{\sigma(E_{n-1})} (E_{n-1} - E_n) + \frac{\sigma_{pp}(E_n - 1)}{\sigma(E_{n-1})} (E_{n-1} - 2e)\right],$$

where $\sigma_p(E_n)$, $\sigma_c(E_n)$, and $\sigma_{pp}(E_n)$ are the cross sections for the photoelectric, Compton, and pair production processes, respectively, and e is the rest mass of an electron in energy units. The total flight history of a photon may end in one of three ways. It may end by escaping from the phantom, or when its energy falls below 2 kev, or when its weight falls below 10^{-5}.

Let us look briefly at the restrictions of this method as we are using it. Other than the obvious inaccuracies that the shape of the phantoms only roughly approximates the shape of the human body and that the phantom remains in a fixed standing position and is in free space from which no backscatter occurs, there is one restriction that should be emphasized. This phantom is homogeneous throughout. There is no low density and low cross-sectional area for the lungs, nor is there a high density and modified cross-sectional area for bone. To take these into account would involve a rewriting of the entire code. Although the results obtained with the constant-density phantom will need to be refined in the future, the results presented here are an improvement over past ones.

In Fig. 7 is a graph of the total-body gamma dose rate vs. age from a ^{137}Cs source uniformly distributed in the phantoms. The units of the ordinate are in dose rate (μrads/hr) per unit activity concentration in the body (μCi/kg). Dose rates for the different phantoms are given per unit concentration of activity in the phantoms, but one may convert the values given to other bases of comparison. Throughout this paper we will use the units just described. From this graph we see that the total-body dose rate for the infant is slightly less than one-half that for the adult. This is due to the fact that the 0.662-Mev gamma rays have a higher probability of escaping from the infant phantom than from the adult phantom which is 20 times larger in the total mass. The total-body dose rate for the adult as determined by this Monte Carlo calculation is about one-half that obtained by an ICRP effective radius calculation. At this point let us refer to the gamma-plus-beta dose rate. The total dose rate from cesium-137 may be obtained by adding 550 to the values given on this graph or on any succeeding dose rate graph for a uniformly distributed source presented in this report. This is true for all of the phantoms.

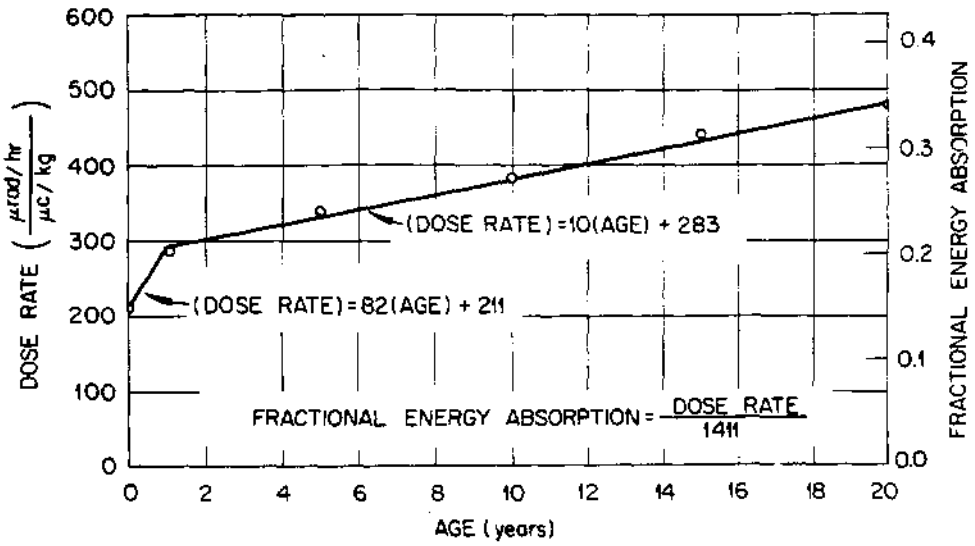


Figure 7.

Since a Monte Carlo computation is an involved and time-consuming procedure, it is more efficient to store the results of the calculation for application to other problems. The results have been stored in three modes—graphically, in tables, and in approximating formulas. As seen in the graph, the gamma dose rate vs. age has been approximated by two linear functions. There is no theoretical significance to these approximating functions. They are used as a convenient means of storing the data simply and for retrieving them within a certain range of error.

To show the variation of dose within the phantoms, we have chosen the results for the infant and adult phantoms only. Results for the other phantoms are similar to these two. We shall examine results from the adult phantom first. In Fig. 8 is a graph of the average dose rate in horizontal layers from head to foot of the phantom. The error bars on the Monte Carlo points are one standard deviation due to the statistical variability involved in Monte Carlo calculations. We note particularly that the average dose rate along the trunk is nearly constant and is about 15% greater than the average dose rate for the total body. The top of the head and bottom of the feet receive the lowest dose rate, being about a factor of 3 below the trunk average. The Monte Carlo points above those for the layer average are the dose rates along the vertical axis of the trunk. At this location, in the interior, are found the highest dose rates in the body. These are higher than the layer average by about 30%. Let us examine the approximate gonadal gamma dose rates. The ovaries, which would be located near the vertical axis of the trunk, receive this central dose rate. The testes receive a dose rate that is approximately that of the trunk average. As a point of perspective, the vertical distribution of gamma dose rate in the infant has been plotted on this same graph.

The variation of dose rate from the center of the trunk to its surface for the adult phantom is given in Fig. 9. Because little variation in dose rate exists among the layers of the trunk, we may average the values from all layers to obtain better statistics. This

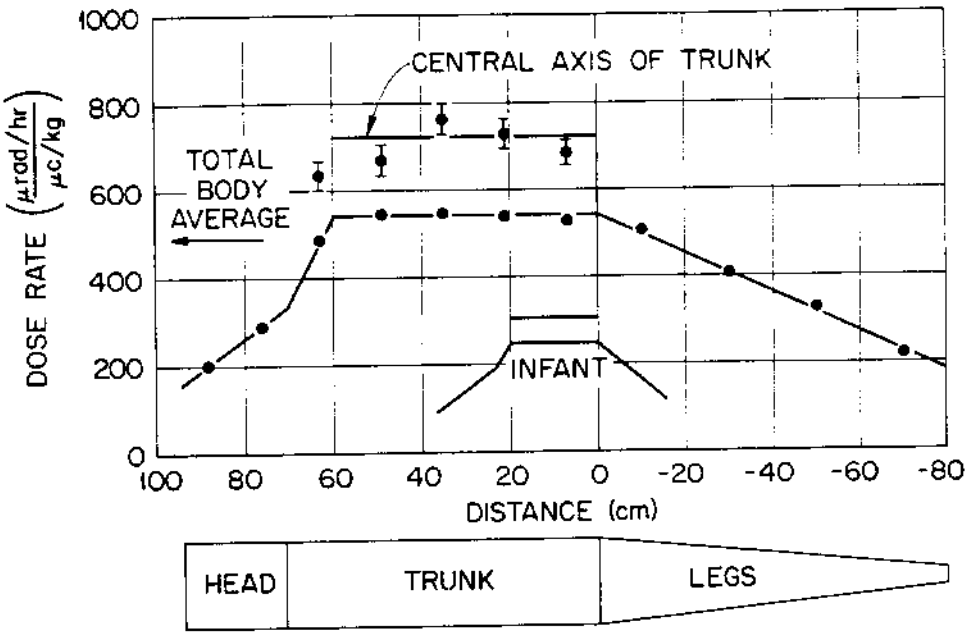


Figure 8.

was done, and the two curves seen here are the dose rates from the center to the front surface and from the center to the side surface. Of course, the dose rate from center to back is identical with the center to front dose rate and has been included. Similar remarks apply

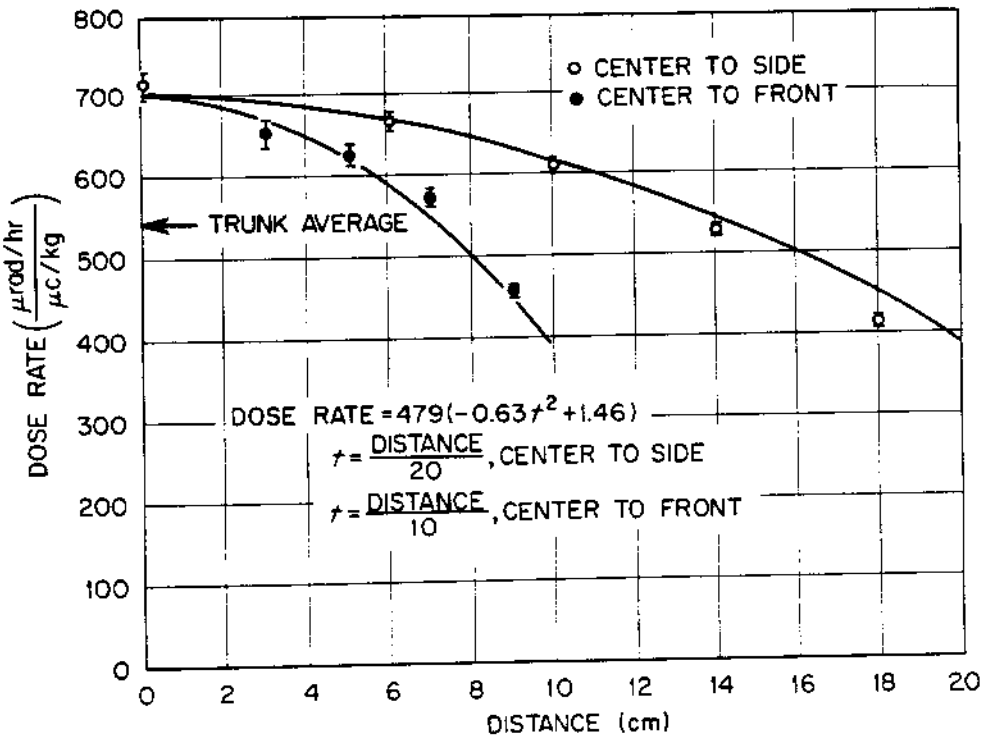


Figure 9.

to the variation of dose from left to right. From the Monte Carlo estimates, it was noted that the dose rate at the front surface was not very different from that at the side surface. Considering that the trunk is elliptical and twice as wide as it is thick, this result was a little surprising. The other phantoms are not as highly elliptical, and this result is valid for them also. The dose rate at the surface is about one-half the central dose rate.

In Fig. 10 is shown the vertical variation of dose rate in the infant phantom. It appears that the relative changes observed from head to foot are about the same as for the adult phantom. However, the entire graph is located at a lower dose rate than the one for the adult. The variation of dose rate from center to surface of the infant phantom is given in Fig. 11. Since the infant trunk is nearly cylindrical, being only 1 cm wider than it is thick, there is practically no difference in the center to front and center to side data. Again, the surface dose rate is about one-half the central dose rate.

Results from the other four phantoms are similar to the ones already shown. Results from all phantoms are shown in Fig. 12; also shown here is the normalized dose rate for each phantom. Zero on the abscissa is the center axis of the trunk, while the value 1 is the surface. To normalize the dose rate for a phantom, we divide by the total-body dose rate for that phantom. It may be observed that the variation of dose rates among the phantoms is about 10% after normalization in the manner described.

The equations approximating the data you have seen in the preceding graphs are tools that allow one to retrieve with sufficient accuracy the results found by the Monte Carlo method. All of these equations are given compactly in Table 2. The first function relates age to total-body gamma dose rate; the second function permits calculation of the average gamma dose rate from foot to head of the phantom; and the third function gives the gamma dose rate at any position inside the trunk. Functions 4 and 5 are derivable from 3, while function 6 is the beta dose rate.

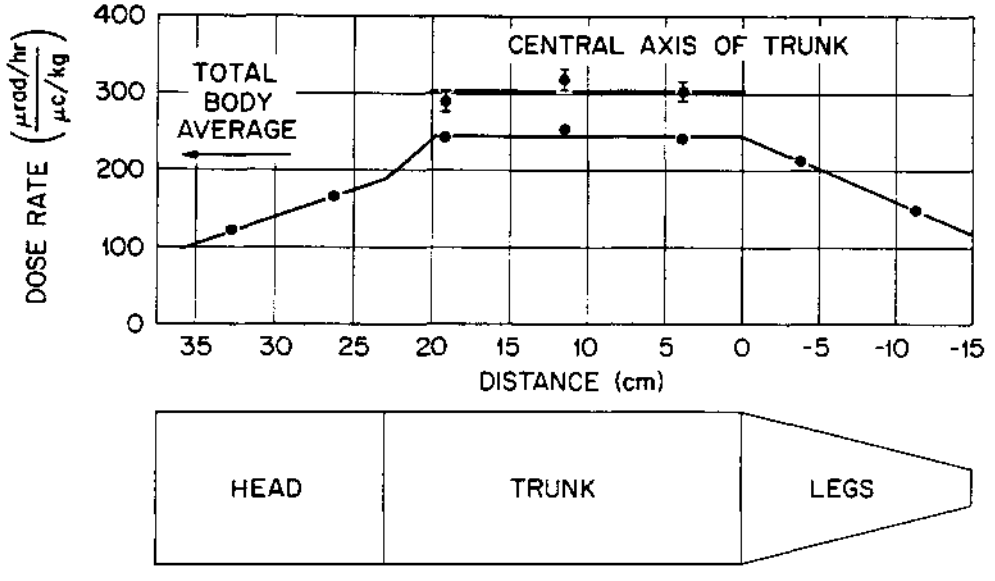


Figure 10.

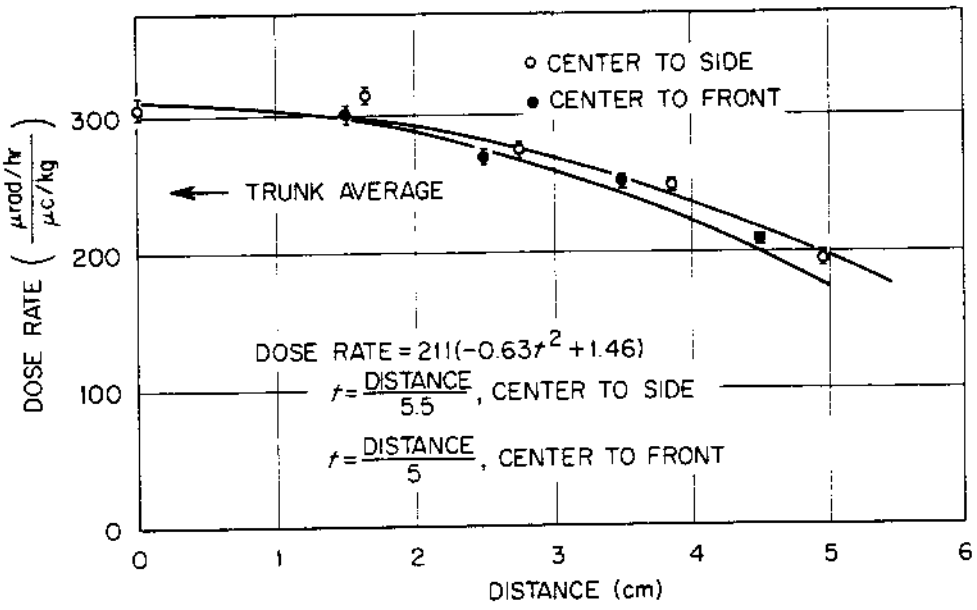


Figure 11.

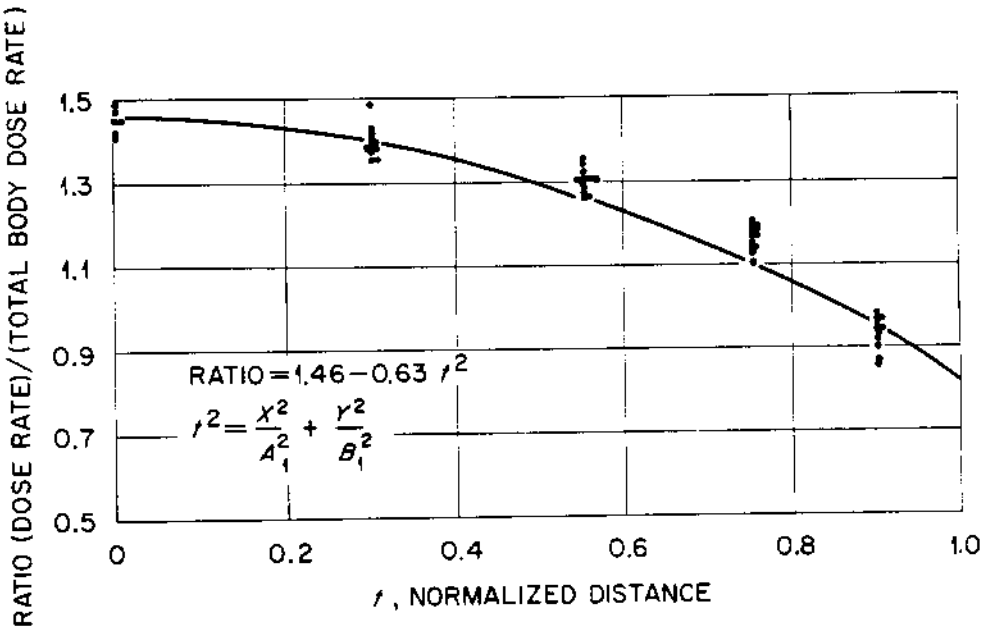


Figure 12.

Let us now consider a nonuniform distribution of cesium-137 in the phantom. It has been found by Yamagata(12) that the cesium concentration of muscle is about twice that of other soft tissues, the latter being fairly uniform. To simulate this distribution in the adult phantom, the volume of the leg section and about one-half of the trunk volume nearest the surface were taken to represent muscle. The equation separating these volumes is

DOSE RATE $\left(\frac{\mu rad/hr}{\mu c/kg}\right)$ IN PHANTOMS FROM A CESIUM-137 SOURCE UNIFORMLY DISTRIBUTED IN THE PHANTOMS

(1) $$D_{avtb} = \begin{cases} 82\ (Age, yr) + 211 \pm 5\%, & 0 \le Age \le 1 \\ 10\ (Age, yr) + 283 \pm 5\%, & 1 \le Age \le 20 \\ 483, & 20 \le Age \end{cases}$$

(2) $$D_{av}(Z) = \begin{cases} D_{avtb}\left[\frac{0.72}{H_3} Z + 1.15\right] \pm 25\%, & -H_3 \le Z \le 0 \\ D_{avtb}\left[1.15\right] \pm 5\%, & 0 \le Z \le \frac{6}{7} H_1 \\ D_{avtb}\left[-\frac{2.47}{H_1} Z + 3.25\right] \pm 20\% & \frac{6}{7} H_1 \le Z \le H_1 \\ D_{avtb}\left[-Z + H_1 + 2H_2\right] \frac{0.40}{H_2} \pm 20\%, & H_1 \le Z \le H_2 \end{cases}$$

(3) $$D(x,y) = D_{avtb}\left[-0.63\left(\frac{x^2}{A_1^2} + \frac{y^2}{B_1^2}\right) + 1.46\right] \pm 10\%, \quad 0 \le Z \le \frac{6}{7} H_1, \quad \frac{x^2}{A_1^2} + \frac{y^2}{B_1^2} \le 1$$

(4) $$D_{center} = 1.46\ D_{avtb} \pm 10\%$$

(5) $$D_{surface} = 0.83\ D_{avtb} \pm 10\%$$

(6) $$D_{\beta} = 550$$

where

D_{avtb} is the total body gamma dose rate

$D_{av}(Z)$ is the gamma dose rate in horizontal layers along the vertical axis Z

$D(x,y)$ is the gamma dose rate at the position (x,y) in the trunk

D_{center} is the gamma dose rate along the Z axis in the trunk

$D_{surface}$ is the gamma dose rate at the surface of the trunk

D_{β} is the beta dose rate everywhere in the phantom

$$\left(\frac{X}{14}\right)^2 + \left(\frac{Y + 1.5}{7}\right)^2 = 1.$$

In this muscle section the source concentration of cesium-137 was twice the remaining sections. Surprisingly, this distribution of the source did not produce any large change in the gamma dose rate anywhere in the body when compared with the uniform distribution of the same body burden. For example, the total-body dose rate for the nonuniform distribution was 2% less than that for the uniform case, while the dose rate along the central axis of the trunk for the nonuniform case was 90% of that in the uniform case. However, the beta dose rate would be twice as large in the muscle as in other soft tissue since all beta energy was assumed to be absorbed locally.

Acknowledgement

Appreciation for the coding and computer operations is expressed to Gordon G. Warner of the ORNL Mathematics Division.

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METABOLIC DATA ON INJECTED AND INGESTED ^{234}Th IN HUMAN BEINGS*

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Abstract

In the course of an experiment to determine the relative absorption of Ra and Th from the gastrointestinal tract of normal human beings, information on the metabolism of soluble ^{234}Th after intravenous injection, and on the metabolism of $^{234}Th(SO_4)_2$ after oral administration has been obtained.

Five elderly human subjects, 3 males and 2 females, were injected intravenously with carrier-free ^{234}Th in isotonic citrate. Bioassay techniques used in the metabolic studies include radioactivity measurements on blood, urine, and feces, as well as whole-body γ-ray measurements (chair and scan), and partial body (upper 20%, including head and arms) measurements using a new "skull and crossbones" (SXB) position, by means of which the gastrointestinal tract is shielded with Pb.

Whole body retention of Th is ~96% at 1 day, ~94% at 5 days, and ~90% at 2 months, the Th being excreted mainly in

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the urine. The cumulative urine-to-feces ratio at 5 days is ~12 for males and ~24 for females. The SXB measurements also indicate a sex difference, the amount of Th measured in the upper 20% of the body for the females being ~1.6 times greater than that for the males. Total blood retention of Th is ~10% at 1 day, ~1% at 5 days, and ~0.3% at 10 days.

A second group of elderly subjects, 3 males and 3 females, were administered orally gelatin capsules containing $^{234}Th(SO_4)_2$, $^{224}RaSO_4$, and $BaSO_4$ carrier, deposited on ZnS phosphor to simulate original Ra dial paints. The same bioassay techniques used in the metabolic studies after injection of ^{234}Th, which provided calibration data for the absorption studies, were used to determine the transport of ^{234}Th across the gut wall. The average value for fractional ^{234}Th transport is ≤ 0.0003, the most probable value being 0.0002. Individual values range from 0.0001 to 0.0006. Cumulative fecal excretion of ^{234}Th is >98% of the administered dose for 4 subjects, and >90% for the remaining 2 subjects, at 4 days. Whole body γ measurements show that cumulative excretion at 8 days is >99.8% for 5 subjects and ~98% for 1 subject.

The implications of these findings to the internal dosimetry and radiation protection guides for thorium in man are discussed.

Metabolic Data on Injected and Ingested ^{234}Th in Human Beings

INTRODUCTION

Information on the metabolism of thorium by human beings is essentially non-existent. What information is available had been obtained from studies on human subjects with long term burdens of Thorotrast. The metabolism of this colloidal material can be considerably different from thorium ion or thorium complex ion and can be inapplicable to the assessment of internal radiation dose for radiation protection purposes.

In carrying out an experiment on the relative absorption of radium and thorium on human subjects (1), it was necessary to obtain calibration information by injecting human subjects with thorium. Some of these results are directly applicable to the metabolism of thorium in human beings. These results, along with the results of an experiment on the absorption of

thorium, are presented here in a form useful for bioassay needs, and are the first, to our knowledge, relating to the metabolism of thorium in man.

For studies in human subjects ^{234}Th is the best choice since other thorium isotopes have either half-periods which are too short or have longer half-periods and hence produce a larger internal radiation dose. An isotope with a half-period longer than that of ^{234}Th would be desirable for longer term studies, but this is not possible and there is little choice in the matter.

MATERIALS AND METHODS

Carrier-free ^{234}Th is prepared by solvent extraction and ion-exchange techniques from ^{238}U slag (enriched in ^{234}Th) obtained from melts in graphite crucibles. For injection purposes the Th is converted to citrate at pH 3.5 and prepared in a way to yield a sterile and pyrogen-free product. For oral administration, a mock radium dial paint containing both ^{234}Th and ^{224}Ra is prepared by an adaptation of a method developed by Stover (2). The adaptation is concerned with the preparation of a single dose at one time, and the result is $Th(SO_4)_2$ and $RaSO_4$ carried on $BaSO_4$ intimately mixed in ZnS phosphor. The dry mock paint is contained in a gelatin capsule for administration.

Standardization of the ^{234}Th activity is carried out against spectroscopically pure U_3O_8 by comparing the gamma spectrum from a ^{234}Th citrate solution and that of a solution of U_3O_8 dissolved in HNO_3. The activity of the ^{238}U is calculated from its half-period of 4.51×10^9y and its abundance of 99.3% (3). Standardization of ^{234}Th in the mock radium dial paint is made by first stripping the spectrum of mock paint containing only ^{224}Ra from the mock paint containing both nuclides. The half-period of ^{234}Th determined during the experiment is consistent with the value of 24.1 days (3).

Figure 1 shows a gamma spectrum of ^{234}Th. The 1.00 MeV gamma ray gives a better signal to noise ratio than does the combination of 0.77-1.00 MeV and is used for standardization purposes and for several other measurements. The lower energy gamma rays (64 and 93 keV) are useful because of their 10-fold greater abundance even though greater self-absorption requires more careful experimental control.

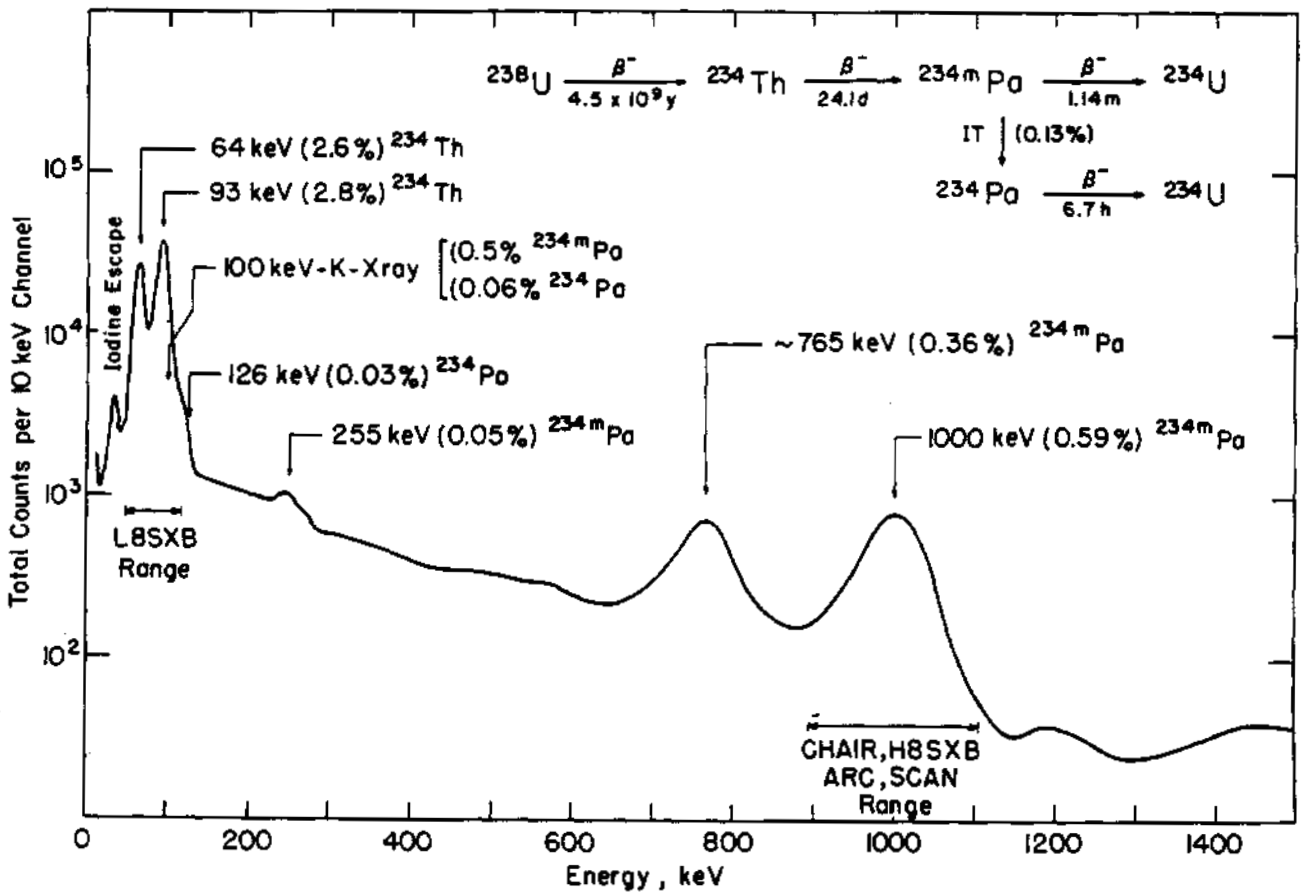

Figure 1. Simplified Decay Scheme and Gamma Spectrum of ^{234}Th.

This spectrum was obtained with an 8" x 4" NaI(Tl) crystal (resolution = 8.5% for ^{137}Cs). The curve shown is a composite spectrum with the portion below 200 keV made at a gain 10 times higher than the remainder and appropriately replotted to show all the details on one figure. Abundances and energies of the gamma rays are taken from Bjørnholm and Nielsen (4). The two ranges shown are used for body and sample measurements.

Body γ counting is carried out in the controlled background facility or whole body counter described in the IAEA Directory (5) under U.S.6.1. Standard chair measurements are made using a tilting metal chair. Whole body measurements are also made with the arc method developed by Evans (6), using an arc of 1.25 meters. The reproducibility of these two whole-body counting methods is ~2-3%.

Since whole body γ counting of subjects after oral administration of ^{234}Th would include the contents of the gastrointestinal tract, and since the absorption of ^{234}Th was anticipated

to be very low, a new partial body counting position was devised. The "skull and crossbones" (SXB) method is a body counting technique by which measurements of body burden are made from the unshielded upper (~20-25%) part of the body, while the G.I. tract and the lower part of the body are shielded from the detector. Thus, the effects of variable distribution of ^{234}Th in the body are minimized by measuring as much of the body as possible while adequately excluding the G.I. tract.

Figure 2 illustrates the subject-detector configuration in the SXB position. The subject sits on an adjustable chair and is pushed forward so that the chest is against the Pb shield, which consists of a 12" × 12" × 12" stack of bricks, an additional layer of two bricks (8" × 8" × 2") and second layer of one brick. The subject's arms embrace the 8" × 8" layer, with the chin resting on the top brick. A positioning guide (block of styrofoam 2.5 in. thick) attached to the crystal serves to maintain a fixed distance from the crystal face to the nasion.

The sensitivity and reproducibility of the method were checked using human subjects (Ra dial painters, Radithor drinkers, etc.) whose Ra and Th body burdens were measured with the chair and/or arc method. The results indicate that the effects of repositioning are sufficiently small to be considered insignificant, and that the efficiency for determination of body burden is comparable to that of the standard chair position.

Phantom studies indicated that a residual 1 μCi ^{234}Th in the G.I. tract would not be interpreted as a significant body burden, and also indicated that the measurement of an expected transport of 10^{-4} across the gut wall would require the oral administration of at least 100 μCi ^{234}Th. SXB measurements using the 64 and 93 keV ^{234}Th γ rays (49-116 keV) are denoted by the code "L8SXB", while those using the 1.0 MeV ^{234m}Pa γ ray (0.9-1.1 MeV) are denoted by the code "H8SXB".

Scan measurements are made with the subject lying supine or prone on a table 30 cm. below the face of the crystal. The crystal is tracked at a constant rate over a distance of 75 in. along the midline of the subject's body. Since the counting rates are low live-time control of the scan is not necessary and the counting rate is determined from the total counts divided by the counting period.

Twenty-four hour urine and feces samples are collected in individual 2 liter polyethylene bottles, preserved with HNO_3,

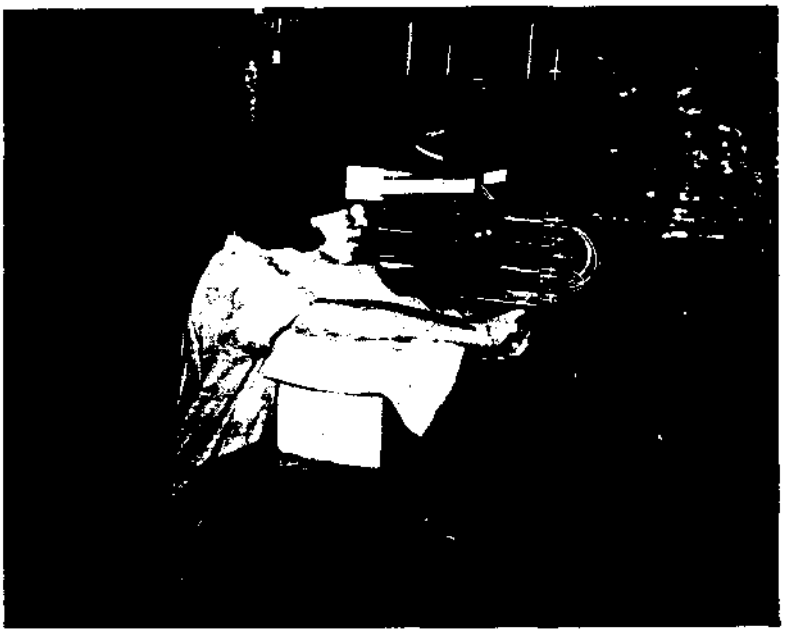

Figure 2. Illustration of a Subject in the "Skull and Crossbones" (SXB) Position.

The photograph shows a subject seated at the SXB assembly within the whole-body counter. The lead shield is supported on an angle-iron dolly which permits the whole structure to be moved in and out of the room. The 8" × 4" crystal is mounted on a crystal tracking assembly which allows the positioning of this crystal anywhere within the room. The whole body counter room is lined with lead. The ceiling, in addition, is lined with copper and tin. The shield behind the chair consists of copper and tin and this, in addition to the copper and tin which is mounted on the top surfaces of the lead shield, constitutes the shield for reducing the lead fluorescent x-ray contribution to the crystal without having to line the whole room with these two elements. The subject sits on a chair, used by draftsmen, which is adjustable in height and has a foam seat and backrest. The subject is pushed forward so that the chest is up against the lead shield, the subject's chin resting on the top lead brick and the arms surrounding the shield. The distance between the subject's head and the crystal is controlled by a block of styrofoam 2.5 in. thick placed between them.

and made to volume. The gamma activity of these samples is compared to that of standard solutions of the same volume.

Blood samples are drawn in heparinized plastic disposable syringes. Aliquots are dried in porcelain crucibles and ashed, the Fe in blood acting as a carrier for the ^{234}Th. The ash is taken up in HNO_3, transferred to planchets and counted in a low background proportional flow counter.

Control samples were obtained from each subject and control measurements were made on the subjects prior to the start of the experiment.

Healthy male and female subjects, ranging in age from 63 to 83 years, volunteered for the experiment. All underwent a complete history and physical examination, and were required to be free from any renal or G.I. disease, any endocrine or metabolic disease, any serious recent illness, any skeletal disorders, or unusual dietary or bowel habits. Clinical laboratory studies were conducted and x-rays of the long bones and skull were taken. The subjects participated either in the injection or ingestion studies, but no individual was used in both. During the experiment the subjects were housed for the collection of excretion samples and a trained nurse was in attendance to insure that no inadvertent contamination occurred during the collection of excretion samples.

Injection of ^{234}Th citrate is made in an antecubital vein. The activity administered is determined by measurements on the syringe contents before and after administration. Oral administration of ^{234}Th and ^{224}Ra mock radium dial paint is made by swallowing the gelatin capsule, using water in several steps, to insure that the capsule enters the stomach. The entry is verified with a survey meter.

Table I shows some of the physical characteristics and the dose schedule for each subject.

RESULTS

The calibration factors (net cpm/μCi retained) for the chair, H8SXB, and L8SXB positions are shown in Fig. 3. The retained body burden is calculated from excretion data.

The chair calibration shows a decrease of ~20% over the first two days then remains constant at (80 ± 3%) cpm/μCi retained over the 24 day observation period, with no significant difference between males and females. In contrast to the chair results, the calibration for the H8SXB position shows a 10-30% increase during the first day. The calibration factors for the H8SXB and L8SXB positions show a difference between the sexes, with the females having the higher values. For the H8SXB position, the average value for the females is (80 ± 3%) cpm/μCi, and for the males (50 ± 4%) cpm/μCi. The respective values for the L8SXB position

Table I. Dose Schedule and Physical Characteristics of Human Subjects

Subject	^{234}Th Administered (μCi)	Age (yrs.)	Ht. (cm)	Wt. (kg)
TIVM2	2.52	72	182	93.1
TIVM3	2.57	70	176	64.9
TIVM5	2.80	81	180	78.1
TIVF2	3.10	79	164	69.0
TIVF3	3.01	72	149	56.8
TRPOM1	89.6	83	168	65.4
TRPOM2	141	63	175	79.9
TRPOM3	123	75	159	68.8
TRPOF1	247	72	163	76.5
TRPOF2	173	81	146	58.3
TRPOF4	203	77	149	51.3

Subject Code: TIV = ^{234}Th intravenous; TRPO = $^{224}Ra + ^{234}Th$ oral; M = Male; F = Female.

are (1150 ± 3%) and (720 ± 5%) cpm/μCi. However, since the ratio L8SXB/H8SXB is ~15 for both males and females after t = 1 day, it is concluded that ^{234}Th and ^{234}Pa are present in the same ratio in both males and females, at least in the upper 20-25% of the body.

No reason is known for the apparent difference in distribution of ^{234}Th between males and females, a difference which might be expected to manifest itself in the chair measurements, but which does not. Arc measurements made with Pb bricks shielding the body from just above the sternum to the hips, and conducted to determine whether a significant excess of ^{234}Th was present in the liver, indicate no excess in this region (average counting rate with shield is 75% of counting rate without shield) with no significant difference between males and females.

The excretion data are given in Table II. The total excretion of 5-6% in 5 days indicates that the excretion of ^{234}Th is low. The excretion is predominantly by the urinary route as shown by the high cumulative urine to feces ratio of ~12 for males and ~24 for females. The two values in this ratio become a second point of difference between the sexes but it is not known whether this difference is related to the sex difference observed in the SXB calibration. The daily urinary excretion of ^{234}Th is not proportional to the amount of ^{234}Th in the blood, as shown in Fig. 5. The curves appear to meet at the end of the experimental

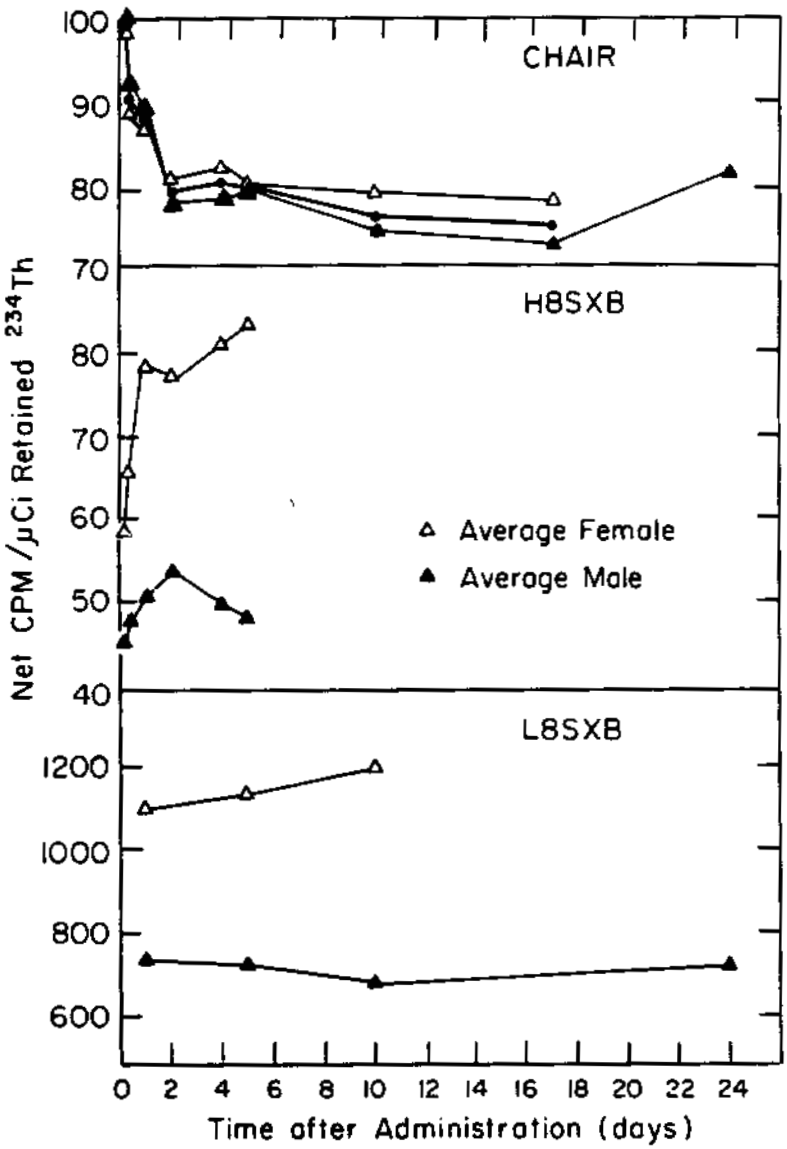

Figure 3. Calibration for Chair and "Skull and Crossbones" (SXB) Positions Following Intravenous Administration of ^{234}Th

The calibration measurements were carried out over a 24-day period until the excretion measurements were stopped. The retained Th is calculated as the difference between the amount administered and that cumulatively excreted up to the particular time indicated. After the first 5 days only urine was collected periodically since the excretion in the feces was negligible. The sex differences for the SXB measurements are discussed in the text.

Table II. Excretion of ^{234}Th Following Intravenous Injection

Subject	Time After Injection (Days)	Cumulative Excretion (% of Inj. Dose)	Cum. Urine / Cum. Feces
TIVM2	4	5.03	11.6
	5	5.30	12.2
TIVM3	4	6.18	12.1
	5	6.43	12.7
TIVM5	4	4.52	13.1
	5	4.81	12.4
TIVF2	4	5.60	27.0
	5	5.89	23.5
TIVF3	4	5.99	36.4
	5	6.38	25.6

period, but whether they continue parallel to each other or cross is unknown at this time. Whether the reason for this non-proportionality is due to an increase in the Th plasma clearance with time or to an exchange of Th between plasma and red cells or to other factors is also unknown at this time.

The retention results are given in Fig. 4. The results are a composite of excretion measurements and of measurements made with the chair and L8SXB positions. The retention drops to ~93% at 20 d and then changes very slowly through the 100-day observation period. Efforts to calculate the long-term disappearance rate are shown in Table III as sums of exponential terms

Table III. Parameters for Th Retention after I.V. Administration

A $\quad R_t = a_1 e^{-\lambda_1 t} + a_2 e^{-\lambda_2 t} + a_3 e^{-\lambda_3 t}$

	$a_1 \pm \sigma$	$\lambda_1 \pm \sigma$	$a_2 \pm \sigma$	$\lambda_2 \pm \sigma$	$a_3 \pm \sigma$	$\lambda_3 \pm \sigma$	Constraints on Least Squares Computer Fit	Long-Term Half Period (yrs.)
1a	0.061 ±0.005	0.630 ±0.120	0.939 ±0.005	2.07×10^{-4} $\pm 1.65 \times 10^{-4}$	-	-	4-parameter model $a_2 = 1 - a_1$	9.2 ± 7.3
1b	0.059 ±0.005	0.628 ±0.127	0.941 ±0.005	4.51×10^{-4} $\pm 1.80 \times 10^{-4}$	-	-	4-parameter model data for subject TIVF2 not used	4.2 ± 1.7
2a	0.026 ±0.009	3.0 ±4.0	0.047 ±0.008	0.213 ±0.081	0.927 ±0.005	5×10^{-5} $\pm 12 \times 10^{-5}$	6-parameter model $a_1 = (1-a_2-a_3)$ $\lambda_1 \leq 3.0$	38 ± 92
2b	0.0245 ±0.0067	3.0 ±3.1	0.0465 ±0.0064	0.232 ±0.055	0.929 ±0.002	0	5-parameter model $a_1 = (1-a_2-a_3)$ $\lambda_1 \leq 3.0$ $\lambda_3 = 0$	∞
B	$R_t = 0.96\ t^{-0.015}$ $(t \geq 1$ d.)						Graphical Analysis	$R_t = 0.83$ at 40 yrs.

A1 data calculated with P.N. Dean at Los Alamos Scientific Laboratory.

A2 data calculated by D. A. Gardiner, W. J. Blot, and S. R. Bernard at Oak Ridge National Laboratory.

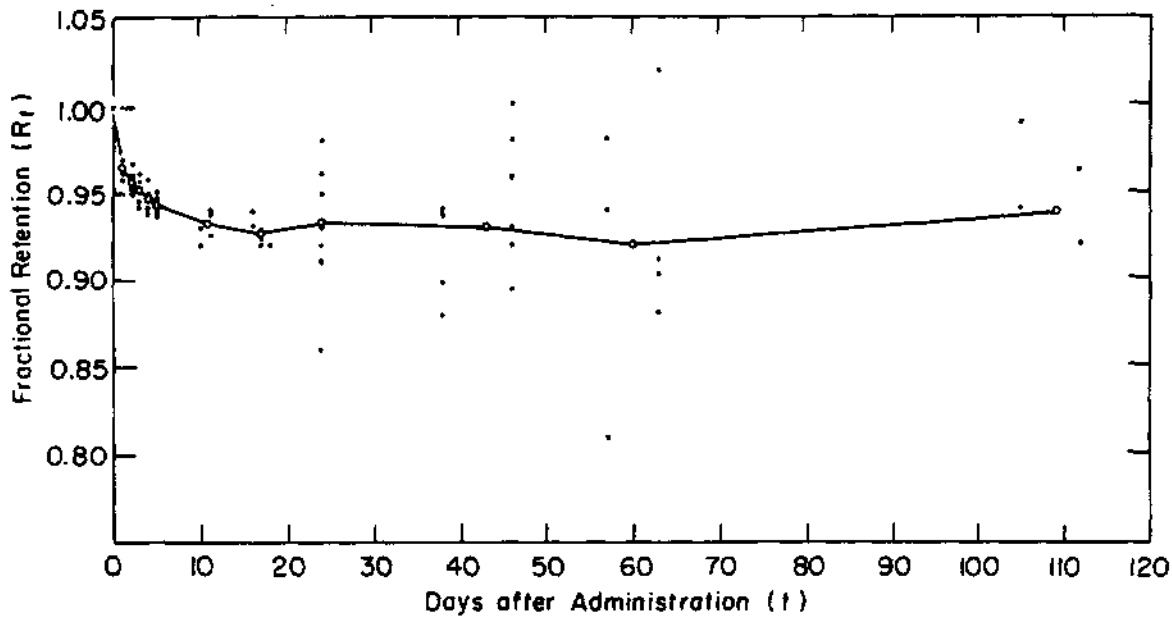

Figure 4. Retention of Intravenously Administered ^{234}Th.

The points indicate individual values without subject designation. The line represents a weighted average of measurements around selected days. Results up to t = ~20 d are based on excretion, from t = ~20-60 d on chair and L8SXB measurements; the remaining values are based solely on L8SXB measurements. All subjects do not necessarily appear at a particular time and occasionally two values (chair and L8SXB) appear for the same subject. The calculations for Table III take these factors into proper account. The variations in the data are consistent with the standard deviations of each measurement.

and as a power function. While it is difficult to determine accurately a long half-period from a short-term experiment, the best indication from the present results is that the half-period is probably > 5 years.

Figure 5 shows the results on the blood measurements expressed as a percentage of the administered dose in the estimated whole blood volume, there being no convenient way to express a thorium specific activity. The blood activity is ~10% at 1 day and ~0.3% at 10 days. For comparative purposes, the shape of the ^{234}Th blood curve is similar to the ^{224}Ra blood curve in human beings (1), but the absolute levels of ^{234}Th in blood are about 10 times higher.

The scan data, plotted as net cpm/μCi retained 10 days after administration against the subject's weight (kg) to height (cm) ratio, are shown in Fig. 6. The results indicate that the activity of the prone scan is ~15% greater than that of the

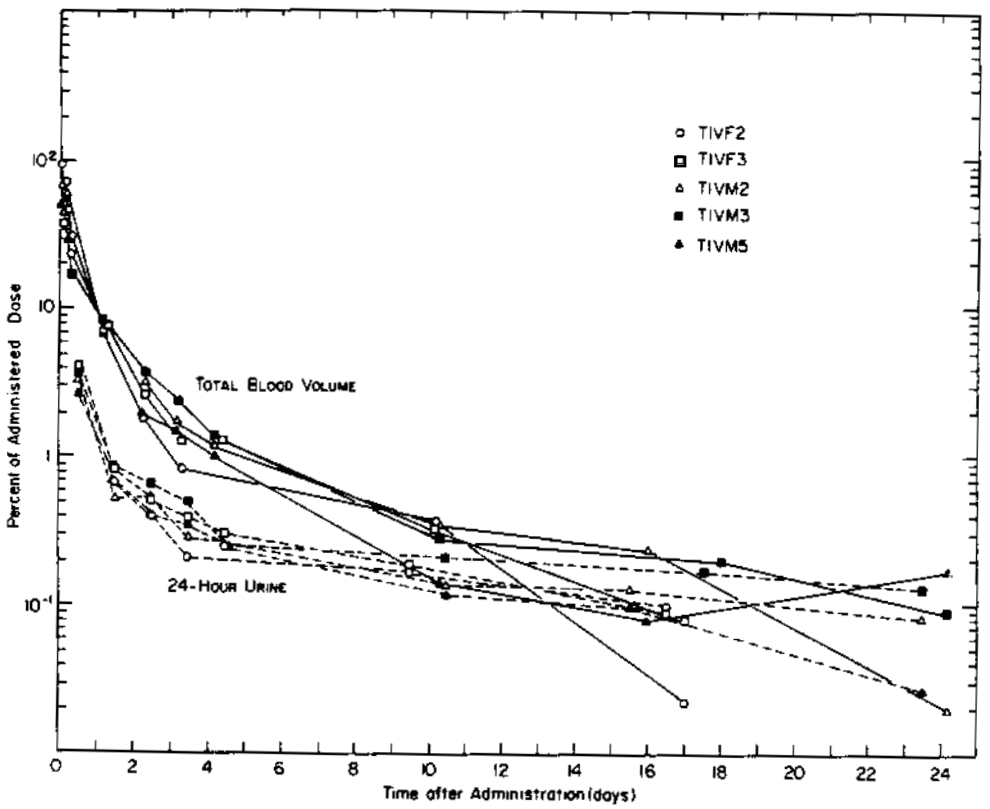

Figure 5. ^{234}Th in Estimated Total Blood Volume Following Intravenous Administration.

Errors in the blood values are ±30–40% at t = 10 d and increase to > ±100% at t = 24 d. The daily urine excretion results are included in the figure for comparison to the blood results. Errors for the urine data are consistent with the variations between subjects.

supine, perhaps due to ^{234}Th deposition in the skeleton. Both scan measurements are somewhat less sensitive than the chair measurements, but, in contrast to the chair results, both are essentially independent of the subject's thickness.

The 1.25-meter arc measurements were made on the subjects at t = 6h, 2d, and 4d. The ratio of body burden determined by the arc measurement to that determined from excretion results shows an unexplained trend with time, averaging 0.87 ± 0.05 at 6h, 1.08 ± 0.05 at 2d, and 1.16 ± 0.06 at 4d. Redistribution of the ^{234}Th in the body with time is not a likely explanation since the arc method is quite accurate even for a highly non-uniform distribution such as ^{224}Ra activity contained in a subject's stomach (1). The grand average of the above results is

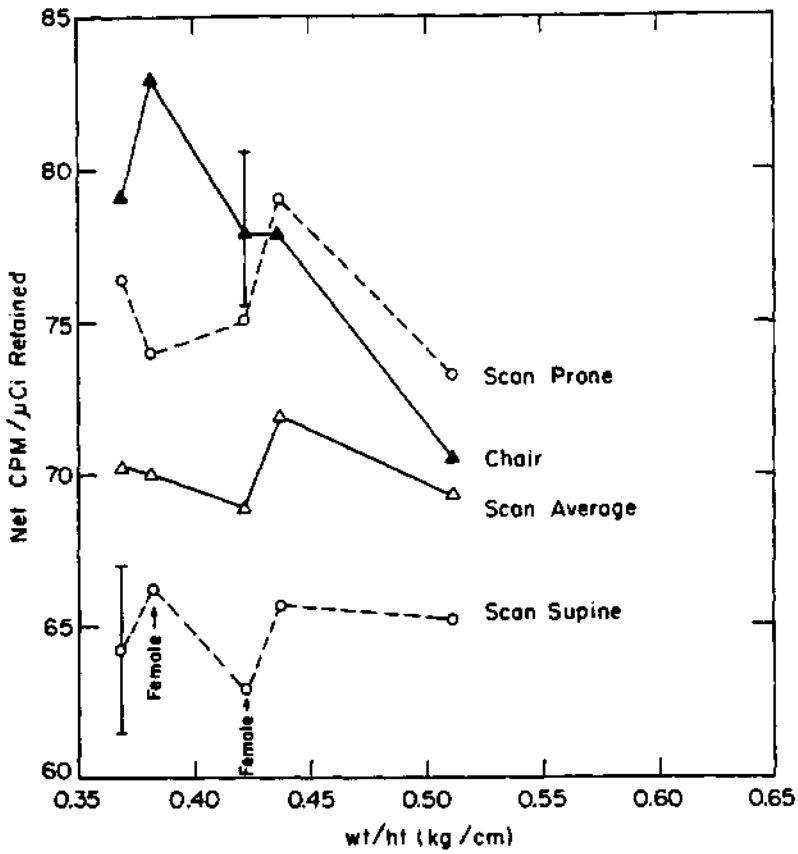

Figure 6. ^{234}Th Body Scan and Chair Measurements at 10 Days After Intravenous Administration.

1.04 ± 0.05 and the arc method can be used to measure absolute burdens of Th within ±15%.

The results on whole body retention and excretion, following oral administration of ^{234}Th in mock radium paint, are shown in Table IV. Essentially all the ^{234}Th is accounted for in the feces at 4d after administration. Very little activity is observed in

Table IV. Excretion and Whole Body Retention of ^{234}Th at 4 Days after Oral Administration

Subject	Cumulative Feces (% of Oral Dose)	Cumulative Urine (% of Oral Dose)	Whole Body Retention (% of Oral Dose)
TRPOM1	98.4	≤0.003	0.18
TRPOM2	99.4	0.005	1.6
TRPOM3	98.3	0.001	≤0.10
TRPOF1	98.2	0.001	8.6
TRPOF2	99.8	0.002	0.17
TRPOF4	99.3	0.004	5.3

the urine indicating that only a small amount of ^{234}Th has crossed the gut wall. The whole body retention is somewhat variable because the intravenous chair calibration is used to measure ^{234}Th activity moving along the G.I. tract, where most of the retained ^{234}Th is located, and because of counting statistics. Considering these conditions, the radioactive balance is good.

The ^{234}Th which has crossed the gut wall or rather the fraction transported (using the word transport to imply no particular mechanism) is shown in Table V. Since the amount transported is so low, three different parameters are used to determine the transport and to show that inadvertent radioactive contamination has not taken place. Transport is calculated by comparing the parameter activity following oral administration to that obtained after IV administration. Blood, urine and partial body (SXB) curves from oral experiments will be essentially parallel in time to those from IV experiments long after the transport process is completed. The urine and SXB results in Table V are determined long enough after the oral administration to be reliable. The blood samples were taken soon after the administration in order to get sufficient activity for counting statistics and these results would be expected to underestimate the transport, as the data tend to show. Taking all factors into account the most probable value for the transport of ^{234}Th is 0.0002.

Table V. Fractional Transport Across the Human Gut of ^{234}Th in Simulated Dial Paint

	Parameters		
Subject	Body γ Meas. L&SXB	Urine	Blood
TRPOM1	≤ 0.0003	≤ 0.0006	≤ 0.0001
TRPOM2	0.0006	0.0009	0.0003
TRPOM3	≤ 0.0003	0.0003	≤ 0.0001
TRPOF1	0.0002	0.0002	0.0003
TRPOF2	≤ 0.0001	0.0003	0.0001
TRPOF4	0.0002	0.0008	0.0001
Averages	≤ 0.0003	0.0005	0.0002

Most Probable Value: 0.0002

DISCUSSION

A convenient summary of the results useful for practical bioassay purposes is shown in Table VI. The gut transport of 10^{-2}% is low. Since the transport of ^{224}Ra in these subjects was ~20%, this would indicate that the ZnS of the mock paint was dissolved in the HCl of the stomach and the "insoluble" $RaSO_4$, even in the presence of $BaSO_4$, became ionized sufficiently to allow 20% to be transported. Since $Th(SO_4)_2$ is much more soluble than $RaSO_4$, it may be presumed that the value of 10^{-2}% for the transport of ^{234}Th applies equally to soluble Th as well as to the supposed "insoluble" $Th(SO_4)_2$ starting material. It would appear than that the transport of Th would be low (10^{-2}%) under most conditions.

Table VI. ^{234}Th Bioassay Parameters for Human Beings

Gut transport low (~10^{-2}%)

I.V. retention high (~100%)

Biological $T_{1/2}$ probably > 5 y

Whole blood/whole body = ~1/300 (2-20 d)

Urine/feces = ~10(♂) to 20 (♀)

Body meas. { Whole, SXB, Scan }

When Th ion gets into the blood stream, the retention of Th is high (~100%) as indicated by the data obtained from the intravenous administration of ^{234}Th. The retained Th has a long half-period but the best numerical result from these data is that the half-period has a probable value > 5 y. The half-period is long enough that, for practical purposes, only the physical half-period of ^{228}Th need be considered in toxicity studies involving this nuclide.

The whole blood to whole body ratio in the first 20 days is "constant" at ~1/300 within a factor of 3, after the first day or two. Measurement of the activity in whole blood can result in a convenient estimate of body burden when other measurements may not be possible during an emergency. Excretion of Th from the body is mainly by the urinary route, making fecal analyses unnecessary.

Body burdens can be measured using a whole body count. A partial body (SXB) measurement can result in a determination of absorbed Th at a sensitivity equal to that of the chair. If the activity is non-uniformly distributed in the body, such as being partially or all in the G.I. tract, then a scan measurement can give data which are nearly independent of the distribution and body size and shape and again with a sensitivity almost the same as the chair. Finally, the arc measurement can be used for absolute burden measurements, especially for purposes of calibrating whole body counters when the burdens are large enough for good statistical measurement.

There appears to be a general similarity in the handling of thorium by human beings and by other animals such as dogs (7), rats, rabbits and guinea pigs (8,9), the closest similarity occurring with dogs. On the other hand, there are enough differences between these species so that no simple extrapolation can be made to man.

The present data provide information on the metabolism of thorium by man but it is clear that more extensive data are desirable, particularly in establishing the long-term retention of thorium and the sex-related metabolic differences. From a practical standpoint, the gross metabolism of thorium by human beings currently assumed for the deduction of radiation protection guides (10) is similar to that indicated by this study.

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Ethical Considerations in Human Experimentation*

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During the past three or four years scientific journals and popular magazines have contained an increased number of articles about the ethics of human experimentation. Most of the writers "point with alarm" expressing concern that investigators, in their zeal, are being careless of the rights of the patient who serves as an experimental subject. This concern has been precipitated by publicity given to certain research activities. The Congressional investigators of the drug industry revealed some serious abuses. When the experimental injection of cancer cells into aged patients in a New York charity hospital received widespread condemnation in print, organized medicine felt the need to go on record as disapproving the method in which the study was carried out.[1,2] The attention given to this problem has been greatly accentuated by Dr. Henry K. Beecher, of Harvard Medical School, who has written extensively about it.[3,4] In my opinion, Dr. Beecher, like most men aroused in an intensely emotion-laden mission, has on occasion made misleading and exaggerated statements.[5]

Although there is recent emphasis on this problem, it is quite erroneous to suggest, as some lay science writers have, that it was largely neglected in the past and that until recently investigators have given little thought to the ethical aspects of human experimentation. Furthermore, it is incorrect to assume that, because a publication of scientific data makes no reference to consent from experimental subjects, such consent was not obtained.

Nevertheless, it is widely recognized that a serious problem does now exist and we may well seek the reasons for it. One is, obviously, the great increase in research of all types that is now being done and the corresponding increase in possible abuses. With this has come the growth of institutions and, in some projects staffed by a large group of physicians, a reduction in personal contacts between the individual physician-investigator and the patient. With the progress of medicine away from simple trials of therapy toward a search for basic knowledge, we find that a larger share of the investigations are concerned with studies not directly related to a practical trial of therapy; thus the subject may have little to gain directly. There is, or is believed to be, a growing intensity of competition among investigators, a desire for recognition, and a desire for academic posts that are filled on the basis of research achievement. Thus we have the opportunity for the investigator to let selfish interests

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predominate over his concern for the experimental subject. Whether or not such a trend exists, there is no doubt that the public has decreasing faith in the nobility of motives of physicians, and that patients are showing an increasing tendency to sue their physicians for malpractice, real or alleged. (Incidentally, except in connection with the trials of new drugs, there have been few if any lawsuits against physicians on the basis of acts performed in the course of clinical experimentation.) Quite different from the unduly ambitious investigator is the one who with completely unselfish motives becomes so fervid in his desire to help mankind that he uses poor judgement in relation to the risk to the individual patient-subject.

Whatever the reasons and explanations may be, there is no doubt that some experiments not ethically justifiable have been performed in recent years. Yet, an unresolved question is, How extensive is this problem? It is a truism that in all large fields of human endeavor one could, with careful search, find some examples of unsavory conduct. There is always the danger that a worthwhile activity will be discredited or destroyed because some publicity seeker dramatizes the exceptional, evil cases and gives the impression that the practices represented are typical. A balanced assessment of the whole field - "...on the one hand this is good, while on the other hand the weaknesses are..." - never attracts the attention that the muckraking approach can yield.

No one really knows how much of experimental medicine is open to challenge on ethical grounds; certainly this cannot be clearly evaluated without more intimate knowledge of what goes on than can be obtained from the published scientific literature. Furthermore, to put the findings in perspective one might need to compare them with some other activities; for example, the ethics of behavior toward patients of physicians not engaged in research. Lacking the hope of any such informed appraisal we must rely upon opinions. My own is that we are not facing an appalling situation but that we have a clear need for improvement.

In considering codes of ethics for investigators we need to be conscious of the various relationships that may exist between the investigator and the person who is the subject of the experiment. Subjects of experiments may fall in the following categories (and possibly others):

1. Independent normal volunteer (paid or donating service),
2. "Volunteer" who is in employ of laboratory, in military service, or in prison,
3. Self-experimenter,
4. Patient volunteers -
   a) Research directed toward diagnosis or therapy needed by subject,
   b) Research directed toward advances in diagnostic or therapeutic methods in general, or toward basic scientific advancement, unlikely to be helpful to the volunteer,
   c) Subjects serving as controls,
5. Healthy person taking new preventive material (i.e., vaccine) that may be potentially useful to him,
6. Tissue donor; research directed toward direct benefit to another person, related or unrelated.

This list clearly shows that ethical aspects of research vary greatly from experiment to experiment. No simple set of rules can deal specifically with all possible situations, but some rather general codes have been presented that give

useful guidelines. For background, the ancient Hippocratic Oath, and the interesting writings of Claude Bernard, in the middle of the last century, may prove useful. Relatively recent, carefully elaborated statements include the Nuremberg Code (1947),[1] the Declaration of Helsinki (World Health Organization) 1964,[7] and the statement by the British Medical Research Council, 1964.[8] Of these, the last seems to me the most useful because it attempts to cope in some detail with the subtleties involved. Beecher[4] has also stated general principles.

Among the considerations that are important in these codes and in our thinking about the subject are the following:

Informed Consent - Great emphasis is placed on the effort to have the subject truly understand the meaning of the experimental procedure in which he is to participate. Those who have dealt with this problem in practice realize that it is an ideal to be aimed at rather than an objective that can be achieved. Even a relatively simple experiment may be quite beyond the ability of the average patient to evaluate. Risks are never known with great accuracy, and the patient often decides on the basis of some intentional or unintentional signal from the physician he trusts, even if the experiment is being done by another physician.

Nevertheless, consent can be clearly given or refused, and it is important to have it documented. Whether it will often be really informed consent is another matter.

The Quality and Competence of the Research - The more hazardous the procedure, the more important it is that adequate preliminary work (i.e., animal experiments) be done, that relevant previous publications are known and considered, and that suitable precautions are taken. The potential value of the research must be thoroughly evaluated. Often the participation of a group of investigators is needed, as is the evaluation by independent physicians having no direct interest in the research and enlisted specifically as the protectors of the patient's welfare.

In our culture the supremacy of the rights of the individual is much stressed. Thus we are reminded that we must not take the responsibility of sacrificing, even to a small extent, one person's rights for the sake of helping many people even to a great extent. I am in agreement with this principle; I do not always find it easy to interpret in relation to specific research situations.

While performing a valuable service, those who have sounded the alarm about improper research practices need to be on guard against making unfair judgements and impairing research progress. They should remember that hindsight is a dangerous thing. For example, five years ago one could say, with a good deal of experimental data in support, that when cancer cells were taken from one person and injected into another, genetically different person, they would never survive and produce clinical malignancy in the recipient. Now there are reports of rare but definite exceptions to this rule. This new information may tempt us to change our evaluation of the ethical soundness of some previous research. It has been quite rightly pointed out, however, that research is either ethical or not at its inception.

Those who establish controls on any human activity often assert repeatedly that they do not wish or intend to restrict productivity. It should be clear, however, that denial of intent to restrict research accomplishments does not indeed prevent the

impairment in productivity that may result when the fears engendered in administrators lead to new regulations. One might concede that some restriction on achievement is a fair price to pay for increased protection to experimental subjects; if so we should pay it knowingly.

I have not attempted to even suggest the positive benefits that may accrue to the person who volunteers as an experimental subject. This is a topic that deserves much more attention than it has received in recent publications.

It is worthwhile that we have had our attention directed to the ethics of human experimentation. The main responsibility for dealing with it should be in the hands of the investigators, and future standards will depend largely on their integrity and conscientiousness. Scientific journals can perform a useful service by requiring that manuscripts indicate the nature of consent obtained from experimental subjects. It is to be hoped that if scientific administrators feel impelled to react to recent criticism with increased restrictions, the new rules will be carefully planned so as not to unduly inhibit good, desirable, ethical research.

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SOME GUIDELINES FOR STUDIES INVOLVING INTERNAL ADMINISTRATION OF RADIOACTIVE MATERIALS TO HUMAN VOLUNTEERS

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The Health and Safety Laboratory of the U. S. Atomic Energy Commission's Idaho Operations Office provides a routine invivo whole body counting program for the protection of the nearly 6,000 employees at the National Reactor Testing Station in southeastern Idaho. During the five-year period from 1961 through 1965, 7,134 invivo determinations were made. Foreign activity has been detected 4,625 times on 2,278 individuals including follow-up measurements made on the same individuals when significant exposure has occurred. In all, a total of 41 different radionuclides have been detected in humans, in addition to the naturally-occurring potassium-40 and cesium-137. Virtually all of the exposures have been received inadvertently during the routine performance of their duties. The exposures have generally occurred from inhalation of particulate matter of unknown particle-size distribution under uncertain circumstances.

Of the 4,625 times that foreign radionuclides have been observed in humans, not more than a half dozen have involved activities greater than about 1 uc. In perhaps 95% of the cases, the activity present was less than 0.1 uc., most of which was eliminated within a very few days. Since the maximum permissible body burden of most beta-gamma emitters is several microcuries or greater for continuous exposure, such levels are of very little physiological significance to the host. As a matter of fact, to save the time and expense of reducing the complex gamma spectra either manually or by a computer program, body burdens lower than about 0.1 uc. are merely recorded qualitatively as being present and are not even quantified. Yet, in almost every case, because of the extreme sensitivity of modern instrumentation, we have been able to determine the mode of excretion from the body, the effective half-life of the specific nuclide involved, and other valuable information from such minute and physiologically insignificant quantities of radioactive materials. This information is of particular importance because it has been obtained on actual human beings under practical conditions and consequently is much more informative and realistic than other data of this kind which is usually obtained by extrapolation from animal data. For example, one of the most important pieces of information derived to date from our routine whole body counting program has been the general philosophy that urinalysis is grossly inadequate as a routine monitoring technique for internal contamination in humans where inhalation of insoluble particulates is concerned. Since our experience has also indicated that inhalation of insoluble particulates is the most likely source of contamination to be encountered around operating reactors, routine urinalysis has been abandoned in our laboratory as a monitoring technique except for determination of the organ dose from systemically deposited nuclides or detection of certain specific scluble

nuclides which are known to be absorbed by the body and excreted in the urine. I wonder how much longer we would have continued using a technique for detection and assessment of internal contamination in humans that does not give the protection we had thought if instruments and techniques for direct measurement of gamma-emitting nuclides on humans had not been developed.

In view of the significant accumulation of very valuable information concerning the metabolic characteristics of a large number of radionuclides that has been obtained from the minute quantities of materials received inadvertently, deliberate exposure of human volunteers to similar minute quantities of radioactive materials under controlled conditions would permit a marked increase in the rate of accumulation of such fundamentally important biological data. Almost every dose calculation that I have ever made, or have heard others describe, has contained an apology or a hedge that the validity of the answer depended on whether or not certain assumptions used in the calculations were correct. In many cases, those assumptions were guesses at best, or were derived by extrapolation from animal data and their validity is certainly open to question when applied to humans. Most of the actual human data presently available was obtained from evaluation of human accidents involving intake of radioisotopes. In view of the extremely minute quantities of materials required and the very high sensitivity of modern instrumentation for their detection, why do we continue to penalize ourselves with half truths and calculations that at times border on the ridiculous when far better data is available for the taking from direct human studies without significant harm to the individual volunteer? Others have also pointed out this need for research programs involving humans to provide better data than is presently available for assessment of the dose received from internally deposited radionuclides (1). I would like to suggest a "Principle of Comparability" that it is both logical and prudent that we should be willing to place at least as much at risk to understand the fundamental effects of internal radiation on humans as we do routinely in developing a nuclear technology. In other words, exposures that are acceptable for day-to-day operation of a reactor should also be acceptable for studies to determine the effect of internal emitters in man.

The use of human subjects in scientific experimentation has generated much controversy concerning the ethics involved, particularly in the medical profession. Throughout much of recorded history, men of medicine have set down principles of good conduct to guide them in their relations with their patients. Many of these precepts apply directly to human studies involving radioactivity. Though by no means the oldest of pagan medical oaths, the oath of Hippocrates is the best known and the most enduring. Traditional and modernized versions continue to be used as a profession pledge of ethical behavior. When the American Medical Association was founded in 1847, it adopted the oath of Hippocrates in its pagan form. At the same time, it adopted a code of medical ethics published in 1803 by the English physician, Thomas Percival. In 1947, the first General Assembly of the World Medical Association appointed a committee to draft an updated wording of the Hippocratic oath. After minor changes, this was adopted in 1948 at Geneva by the second General Assembly as the "Declaration of Geneva." After World War II, the Nuremberg Code of Ethics in Medical Research was framed by a task group of the American Medical Association to guide the allied military tribunal in the prosecution of 23 nazi physicians accused of brutal experiments on political prisoners. This code is perhaps the one most frequently quoted where

human experimentation is concerned. Most recently, another code of ethics on which work was started following World War II was adopted by the Eighteenth World Medical Assembly in June of 1964 in Helsinki, Finland, as the Declaration of Helsinki. According to Dr. Harry S. Gear, Secretary General of the World Medical Association, recommendations in the Declaration of Helsinki "are offered to all medical men and their colleagues in other disciplines, who undertake scientific and clinical investigations involving human beings." The House of Delegates of the American Medical Association has since endorsed the Declaration of Helsinki as an ethical guide to clinical medical investigation. Representatives of the American Medical Association are currently meeting with members of the American Federation for Clinical Research and the American Society for Clinical Investigation in an effort to prepare a modern code of ethics for human experimentation.

The Helsinki Declaration outlines very strict rules for nontherapeutic clinical research and seems to be particularly pertinent to the type of studies being proposed. The nature, purpose, and risks must be explained to the subject, the subject must be fully informed and must give his free consent, and the patient must be in such mental, physical and legal state as to be able to exercise fully his power of choice. Consent should be obtained in writing and be witnessed. The investigator must respect the right of each individual to safeguard his own personal integrity and, at any time during the course of clinical research, the subject or his guardian should be free to withdraw permission for research to be continued. The investigator or the investigating teams should discontinue the research if in his judgment, it may, if continued, be harmful to the individual. The concept of valid informed consent is a particularly fundamental and important one, yet often requires a level of knowledge and freedom from constraint that is impossible to achieve with people that are ill, children, or those mentally incapable of comprehending the meaning and consequences of the scientific and technical principles involved. Inability to convey the necessary information and understanding does not in any way lessen the requirement for valid informed consent.

Several items from the Nuremberg Code would seem to be particularly pertinent to our proposed studies. The first item says "The voluntary consent of the human subject is absolutely essential." Item 6 points out a nearly self-evident point of logic that "The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment." Item 10 says in part "During the course of the experiment, the scientist in charge must be prepared to terminate the experiment at any stage, ..."

The official position of the United Kingdom has been greatly clarified recently by a statement of their Medical Research Council in their annual report for 1962 and 1963. The statement deals primarily with medical investigations in general but is directly applicable to work with radiation and radioactive materials. The council emphasizes the importance of proper safeguards both in procedures contributing to the benefit of the individual and, more specially, in procedures in which the individual concerned does not benefit directly from the investigation. Again, particular importance is attached to obtaining the individual's true consent, by which is meant "consent freely

given with proper understanding of the nature and consequences of what is proposed." Provided that these safeguards are ensured, the council clearly endorsed the concept of investigations involving volunteers, and concludes that "After adequate explanation, the consent of an adult of sound mind and understanding can be relied upon to be true consent." They further emphasize the responsibility on the professions, on the heads of investigating departments, and on individual investigators, to ensure that the conduct of all these investigations is irreproachable. The more obvious requirements that the experiment should be conducted only by technically qualified persons exercising the highest degree of skill and care throughout all stages of the experiment, and that no experiment should be conducted where there is any reason to believe that serious injury or death would occur are implicit in all of the codes of ethical conduct.

One of the greatest retarding influences on the accumulation of human data has been the feeling, particularly prevalent in some of the earlier codes, that experimentation must not be carried out on human subjects unless the subject himself expects to benefit. For example, the doctor can combine clinical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that clinical research is justified by its therapeutic value for the patient. Not only is this contrary to the spirit of sacrifice for the good of ones' fellow man so prevalent in many parts of the world but is totally unrealistic and undesirable when governed by sound ethical and moral principles. The proposed guide lines acknowledge and accept the spirit of both the Nuremberg Code and the Declaration of Helsinki but we submit that it is entirely appropriate for human subjects to accept small risks to themselves to help develop information that will be of value to others. Specifically, when the subject himself does not stand to benefit by the experiment being performed, the internal dose permitted shall not exceed the occupational exposure permitted workers in the atomic energy industry, as specified in Title 10 Part 20 of the Code of Federal Regulations for licensees and in AEC Manual Chapter 0524 for AEC and Contractor personnel.

The pertinent values are 3 rem per quarter or 5 rem per year for the whole body or 10 rem per quarter and 30 rem per year for the thyroid. For the sake of simplicity and to eliminate the need for factual information concerning which organ is critical, which may itself be the principle reason for the experiment, the higher levels permitted for single organs other than the thyroid are not permitted at present and the dose received is considered to be to the whole body. Although the 3 rem per quarter for whole body may be averaged over 13 weeks, the basic unit proposed for a single exposure is 0.3 rem for the first week, a value only slightly larger than the average value of 0.23 rem permitted for each of 13 consecutive weeks. An extensive table of activities required to produce a dose of 0.3 rem per week to the critical organ from a single exposure has been published (2) and is most helpful and convenient in determining the maximum permissible dose to be used as well as for administrative checking. Another significant point in this connection is that these values and the equations from which they were calculated have been prepared by a well known authority in the field of internal dosimetry, have been published in the open literature and are easily available to others. Another similar and more recent paper entitled "Radiation Doses from Administered Radio Nuclides" is also very

useful (3). However, published information tends to become outdated and all final calculations of dose must reflect the most recent methods and information recommended by the Federal Radiation Council and the International Commission on Radiological Protection.

One of the significant differences between doses administered from external or internal sources is the inability to terminate the latter on demand by removal of the source. Both common prudence and most of the medical codes suggest that the long-term dose commitment should be restricted to permit either the experimenter or the volunteer to reconsider his decision to continue the test. Consequently, limitations are imposed on the effective half lives that can be employed at a given level of activity so that more than one opportunity is presented to stop the experiment before even a 1-year's maximum permissible dose will have been committed irrevocably.

A summary of the maximum permissible intake for a single exposure as a function of half life and dose received is given in Table I. Obviously, when the half life is less than that shown in the table, the dose received will also be less than that shown. Specific guide lines are as follows:

1. The quantity of radioactive nuclides to be taken in a single day shall not exceed that required to deliver a dose to the critical organ of 0.3 rem for the first week after exposure as given in columns 5 and 8 of the published table (2), for ingestion and inhalation, respectively. These values have been chosen to permit integration of the dose received over a time period of one week. Where necessary, the values must be updated to reflect the latest information available.

Table I. Radiation Guides for Human Studies Involving a Single Exposure

Effective Half-life	Fraction of Columns 5 or 8[a]	Tests per Year	Maximum Dose Received, rem.				
			First Week	First Year		Total	
				1 Test	Max.	1 Test	Max.
18 days	1	4	0.3	1.29	5.16	1.29	5.16
13 weeks	1/4.3	4	0.069	1.25	5.00	1.33	5.32
1 year	1/10	1	0.03	1.15	1.15	2.3	2.3

[a]Table in Ref. 2

2. The maximum level of 0.3 rem in the first week may be used only with radionuclides having an effective half life in the critical organ shorter than 18 days so that the dose will not exceed the second limitation of 1.25 rem in the first quarter. The dose of 5 rem per year permitted by AEC Manual Chapter 0524 is permitted but only for four separate tests so that the dose can be terminated within a reasonable length of time (one quarter) if either the subject or experimenter should so decide. This limitation also ensures that the total integrated dose will not exceed approximately 5 rem for a maximum of four tests per year.

3. Nuclides with effective half lives longer than 18 days can be used provided the quantities are reduced to limit the long-term commitment. Nuclides with effective half lives in excess of one year are not employed in any case. With nuclides having half lives from 18 days up to 13 weeks, the values given in the published table (2) are reduced by the factor 4.3 so that the dose per year will not exceed 1.25 rem. Again, four tests per year are permitted to restrict the yearly dose to 5 rem and the total integrated infinity dose to only slightly more. For nuclides with half lives of 13 weeks up to one year, only one-tenth the quantity mentioned in the table is permitted per test and only one test is permitted per year to keep the dose for the first year down to about 1 rem and the total infinity dose down to about 2 rem. Use of nuclides with half lives in excess of one year is not likely to be necessary and is undesirable because of inability to terminate the exposure within a reasonable length of time.

4. Nuclides for which the thyroid is the critical organ can be used in quantities three times that specified in the table as permitted by AEC Manual Chapter 0524. Corresponding increases permitted by Manual Chapter for "other organs" can be utilized if the critical organ is known with some assurance. Otherwise, the dose should be limited to that permitted for the whole body.

5. If the source is encapsulated in polyethylene tubing or other impervious material that will not be released in the body and will be eliminated in about 24 hours, the maximum activity used and the number of experiments performed can be adjusted such that the dose received does not exceed 0.3 rem per week or 5 rem per year to that part of the gastrointestinal (G.I.) tract deemed to be the critical organ. As pointed out in the footnote to the table in reference 2, the values given in columns 4 and 7 for a dose rate of 0.043 rem per day may be considered as maximum permissible values for continuous exposure when the G.I. tract is the critical tissue. Consequently, either a single experiment at 7 times this value or 7 experiments at this value could be performed each week. If the source strength is sufficiently high or the nuclides sufficiently long lived to constitute any significant hazard to others if the capsule should be opened, the source will be recovered and properly disposed of after termination of the study.

6. Chemical toxicity is to be considered specifically in each case, and will become a limiting factor when the threshold limit is reached. For example, a solution of methyl iodide containing radioactive iodine tracer could be more toxic chemically than radiochemically if the specific activity were sufficiently low. Both the chemical and radiochemical purity of the activity being administered must be established beyond question.

Since many volunteers will inevitably be obtained from our own subordinates, we must be particularly careful to avoid any suggestion of coercion or mandatory participation as a condition of employment. Consent forms may not even be distributed for signature until the potential volunteer has been

contacted, the experiment to be undertaken thoroughly explained and his consent freely given. Similarly, to avoid any adverse public reaction, the general philosophy of human studies being carried out in a given laboratory must have been discussed openly with and concurred in by the local medical authorities without the slightest suggestion of attempted subterfuge. Each specific experiment must be approved by at least two reputable scientists with administrative responsibilities and authority in the organization, one of whom must be a medical officer, and must be carried out openly by the experimenters acting as a group rather than any single individual going it alone. In our laboratory, the Chief of the Medical Branch approves the medical qualifications of the volunteer and assures that all necessary medical aspects of the proposal have been reviewed adequately. The Chief of the Analytical Chemistry Branch approves the project from the standpoint of chemical and radiological toxicities. After the study has been completed the radiation exposure data is entered on the consent form and filed in the individuals medical record.

The above guide lines reflect the maximum quantity of radioactive materials that can be used only with good and sufficient justification and are thought to be relatively conservative. Even so, as a general philosophy, the actual quantity to be used in any given experiment shall not exceed the smallest quantity necessary to achieve the intended results.

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TISSUE SAMPLING FOR PLUTONIUM THROUGH AN AUTOPSY PROGRAM[a]

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There are three generally recognized methods available for the assessment of organ or whole body doses due to the intake and deposition of radionuclides:

a) measurement of the environment;
b) measurement of the excreta;
c) direct measurement of the exposed worker.

Environmental programs provide useful data for assessing dose to workers in a gross manner, but because the quantity of radioactivity taken into the body is not accurately known, they do not lend themselves to precise interpretations. Nevertheless, environmental data such as aerosol concentrations, particle size distributions, duration of exposure and chemical form of the contaminant are of prime importance as supportive information for other modes of dose assessment.

(a) This paper is based on work performed under United States Atomic Energy Commission Contract AT(45-1)-1830.

Measurement of radioactivity in excreta is another method of indirect assessment. Here again, the results may be imprecise because of biological variability, inadequate sampling techniques and lack of models responsive to the exposure conditions experienced by the worker.

Direct measurements of the exposed worker, of which the autopsy program can become a component part, provide the best available method for assessing organ retention and dose. "In vivo" measurements, however, have two serious limitations. They are restricted to external counting techniques and the assessment of individual organ doses can be masked or impossible to determine as in the case of trying to determine separately the contributions from the lungs and the pulmonary lymph nodes. Information obtained from autopsy samples can help considerably in future assessments made of the retention characteristics and doses to specific organs by the "in vivo" external measurement techniques.

When in the early 1940's, employees at the Hanford Atomic Energy Plant in Richland, Washington began to work with plutonium isotopes in various chemical forms, surveillance programs were initiated to determine the air concentration of plutonium, detect and control environmental contamination and estimate the internal deposition in the plant employees. The chief mechanism used to estimate the body burden of plutonium was the evaluation of bioassay data. It was recognized that the sole mathematical model developed for this type of evaluation was predicated on the results obtained from the administration of only one chemical form and by one method of administration.[1] Necessarily the extrapolation of the interpretations for application to various other chemical forms or to other methods of administration would be of questionable validity.

Through the cooperation of the local pathologist and personnel of the medical department, a modest autopsy program was started in 1949 to obtain various tissue samples from both former employees and residents. By analyzing the samples and segregating the results between those who formerly worked with plutonium and those who did not, we had a mechanism for determining the extent of deposition attributable to occupational exposures and relating this to the theoretical models that had been used earlier to estimate the depositions.

Considering the length of time that the program has been established, the total number of 286 cases seems somewhat small. This is still a rather large number, however, considering the sensitive nature of the program and the informal arrangements necessarily used to keep the program supported. Of the total, 242 represent non-occupationally exposed personnel and 44 represent personnel potentially occupationally exposed to plutonium at Hanford.

The types of samples collected have varied according to particular interests prevalent at the time the samples were taken, but in all cases lung, liver and bone samples were obtained although occasionally some of these results were lost. The routine collection of pulmonary lymph nodes was initiated in 1960 when studies commenced to assess the extent of plutonium depositions in these samples, especially following chronic occupational exposure to low activity aerosols. Also collected, but on an intermittent basis, and analyzed for Pu were blood, pancreas, prostate and seminal vesicle samples. The specific location for tissue sampling was not specified

to the pathologist, and as a result, tissues were taken from the most convenient or randomly selected areas of the designated organ.

The sample weights varied considerably; for instance, the lung samples varied from 10-300 grams, the liver samples from 15-300 grams, and bone samples, which were taken from the rib, varied from 4-25 grams. The weights of the lymph nodes, although referred to in some of the data, have little meaning inasmuch as the nodes were not stripped clean of associated tissue.

The chemical procedures used in analyzing the tissue were the standard procedures used for the separation of Pu in excreta, and the detection of the residual Pu was by counting tracks in NTA film exposed to the deposition of Pu on stainless steel discs. In recent years, sensitivity of about 0.05 dpm was obtained using this procedure. However, only average or expected yields from the chemical procedures could be used because the film detection technique is unsatisfactory for the discrimination of various isotopes of plutonium.

The pathologist when submitting tissue samples avoided, where possible, samples evidencing gross abnormalities although it was not always possible to do so. In each case the coroner's statement of death was obtained and included with the data so that these irregularities may be considered. For instance, resulting data on lung depositions may not be considered normal in the case of pulmonary emphysema or carcinoma.

The radiochemical analyses of tissues from former Hanford plutonium workers, presented in Table I, show that for a number of the former long-term Hanford workers, small but measurable internal depositions of plutonium were found. For these individuals some 523 urine samples were analyzed for plutonium during the course of their work with this material. A positive bioassay result, i.e. samples with activity greater than 0.05 dpm, was obtained for only one employee where three positive urine samples appeared following the accidental inhalation of plutonium oxide dust. The results were evaluated as having indicated no significant deposition; less than 1% of the maximum permissible body burden of 0.04 μCi with bone as a reference, had occurred. The data presented in Table I are interesting in that they demonstrate the presence of small body depositions of plutonium in plutonium workers whose depositions are below detection with present bioassay surveillance techniques. The data are, however, disappointing in that the sensitivity was insufficient to obtain statistically good results for bone and the lymph nodes. Another disappointing feature is the absence of more positive urinalysis data with which some of the current ideas of retention versus excretion could be tested.

A review of the data shows that the largest deposition of 130 x 10^{-3}d/m/g occurred in an employee who was not involved in any known accidents. Assuming standard man parameters, this concentration implies 0.1nCi in the liver. Since 15% of the plutonium in the blood reaches the liver, again using ICRP parameters, a blood content of 0.7nCi is indicated. Depending on the time of sampling after intake, such a deposition, if occurring all at once and if excreted according to the Langham model, would be detectable according to present practice for about 9 months after intake. The worker in question was sampled mostly on a quarterly basis but at no time did urinalysis yield positive

Table I
DATA FROM AUTOPSY

Case Number	Work Exposure in Plutonium Facility (years)	Date of Last Exposure	Dates of Known Incidents	Coroner's Statement of Death	Date of Death	AUTOPSY RESULTS							
						LUNG		LIVER		BONE		LYMPH NODES	
						Weight grams	Activity 10^{-3}d/m/g	Weight grams	Activity 10^{-3}d/m/g	Weight grams	Activity 10^{-3}d/m/g	Weight grams	Activity 10^{-3}d/m/g
1	2	1949	0	Calculus & Peritonitis	1949	13.3	<25	15.2	<22	7	<47	—	—
2	4	1950	0	Tuberculosis & Pericarditis	1950	24.8	<13	36.8	13	---	—	—	—
3	2	1951	0	Carcinoma Kidney	1952	---	< det.	---	< det.	---	< det.	—	—
10	10+	1955	9-11-52 4-14-53	Carcinoma Colon	1955	40	< 1.3	32.7	10	7.2	< 7	—	—
11	1.5	1955	0	Blast Injuries	1955	71.5	< 0.7	24.5	< 2	9	< 6	—	—
12	4.5	1955	0	Polyserositis	1955	33	< 1.5	21.5	< 2.5	8.5	< 6	—	—
13	7.5	1956	2-5-53	Pulmonary Emphasema	1956	48	24	27.5	76	12	< 4	—	—
14	1	1955	0	Bronchogenic Carcinoma	1956	30.8	< 1.6	25.8	< 2	8.4	< 6	—	—
4	4	1952	0	Coronary Arteriosclerosis	1952	---	< det.	---	< det.	---	< det.	—	—
5	1	1952	0	Peritonitis	1952	---	< det.	30	10	—	< det.	—	—
7	1.5	1953	0	Myocardial Infarct	1953	42	69	30	130	—	< det.	—	—
6	5	1953	0	Carcinoma Kidney	1953	42	7.1	30	7.0	—	< det.	—	—
8	1.5	1950	0	Malignant Melanoma	1953	---	< det.	—	< det.	---	< det.	—	—
9	5	1954	0	Ruptured Aneurysm of Aorta	1954	26	< 2	29	6.9	8	< 6	—	—

Table I (continued)

Case Number	Work Exposure in Plutonium Facility (years)	Date of Last Exposure	Dates of Known Incidents	Coroner's Statement of Death	Date of Death	AUTOPSY RESULTS							
						LUNG		LIVER		BONE		LYMPH NODES	
						Weight grams	Activity 10^{-3}d/m/g	Weight grams	Activity 10^{-3}d/m/g	Weight grams	Activity 10^{-3}d/m/g	Weight grams	Activity 10^{-3}d/m/g
15	9	1956	0	Subaracnoid Hemorrage	1956	50.8	1.3	27	9.5	5.5	< 9	---	---
16	1.5	1957	1-15-52	Rheumatic Heart	1957	34	0.9	24	2.2	6.5	3.7	---	---
17	8	1954	0	Carcinoma Rectum	1958	23	< 1.1	27	< 1	6.5	< 4	---	---
19	2	1953	0	Cerebral Hemorrage	1958	33	< 0.8	33	< 0.8	5	< 5	---	---
18	2	1958	4-29-55	Hodgkin's Disease	1958	43	1.4	27	2.6	---	---	---	---
20	2	1955	0	Laennec Cirrhosis-Liver	1958	35	< 0.7	26	1.2	12	8.1	---	---
21	8	1958	0	Laennec Cirrhosis-Liver	1958	30	< 0.9	23	< 1.1	6	< 4	---	---
23	1	1960	0	Subdural Hemorrage	1960	20	< 1.3	38	< 0.8	4	< 6	0.2	<130
24	2.5	1960	10-30-59	Bronchogenic Carcinoma	1960	41	< 0.8	20	4.4	6	< 4	0.6	< 40
25	10+	1960	0	Myocardial Infarct	1960	27	< 0.9	26	3.1	5	< 5	0.8	< 30
26	4	1961	0	Fibrosarcoma	1961	39	0.9	26	< 0.1	8	< 3	1.2	< 20
27	0.5	1961	0	Myocardial Infarct	1961	39	1.7	22	11	3.2	< 8	1.4	20
28	7	1953	0	Laennec Cirrhosis-Liver	1961	26	< 1	19	< 1.3	4.3	< 6	1.4	< 20
29	10+	1961	0	Cerebellar Hemorrage	1961	49	< 0.5	27	1.2	4.3	< 6	7.0	< 4
30	3	1962	0	Myocardial Infarct	1962	40	< 0.6	29	< 0.9	4	< 6	7	< 4
32	1.5	1962	0	Bronchogenic Carcinoma	1962	55	< 0.5	20	< 1.3	5	2.4	4	< 6

Table I (continued)

Case Number	Work Exposure in Plutonium Facility (years)	Date of Last Exposure	Dates of Known Incidents	Coroner's Statement of Death	Date of Death	AUTOPSY RESULTS							
						LUNG		LIVER		BONE		LYMPH NODES	
						Weight grams	Activity 10^{-3}d/m/g	Weight grams	Activity 10^{-3}d/m/g	Weight grams	Activity 10^{-3}d/m/g	Weight grams	Activity 10^{-3}d/m/g
31	10-	1962	10-14-57 12- 6-58	Skin Burns	1962	47	76	26	18	5	< 5	5	130
37	3.5	1956	0	Bronchogenic Carcinoma	1963	67	2.4	28	6	6.5	< 4	3.9	< 6
40	4	1962	0	Myocardial Infarct	1963	67	0.7	94	< 0.3	6.4	< 4	3.6	< 6
39	9	1963	0	Carcinoma Colon	1963	33	2.1	25	< 1	3.7	< 6	3.5	< 6
34	3	1963	0	Myocardial Infarct	1963	49	0.9	24	1.7	6.1	< 4	5.6	< 5
38	7	1963	0	Coronary Arteriosclerosis	1963	70	1.0	56	< 0.5	3.8	< 6	13	< 2
36	1	1963	0	Cerebral Hemorrage	1963	43	0.7	32	< 0.8	5	< 5	3	14
33	6	1962	1953 to 1961	Myocardial Infarct	1962	32	55	28	18	3.7	< 6	3.5	18
35	4	1962	0	Pulmonary Emphysema	1963	46	1.3	30	17	5	< 5	4	< 6
41	3	1963	0	Carcinoma Stomach	1963	90	0.9	35	1.0	8	< 3	4	< 6
22	13	1958	0	Myocardial Infarct	1958	54	20	27	17	6	< 4	---	---
42	8	1957	2-16-48	Ruptured Aortic Aneurysm	1964	280	0.8	277	0.6	7.2	< 4	6.5	< 4
43	3	1964	0	Emphysema	1964	271	0.4	120	7.5	23	< 1	8	< 3
44	1	1964	0	Carcinoma Lung	1964	148	1.6	87	0.7	12	< 2	---	---

results. Recent experiments with inhalation of plutonium oxides by dogs conducted by Drs. Bair and Park[2] at Battelle Northwest indicates that the excretion rate as a percentage of body burden may be considerably smaller than that given by the Langham model and depending on the state of the plutonium inhaled may preclude detection by urinalysis of the autopsy results reported here.

Bearing in mind the limitations of the program, particularly in extrapolating sample activity to the total activity for the organ concerned, the data indicate that the lung and the liver, for the majority of cases, are the favorite sites for deposition. There are 29 cases where either the lung or the liver is positive and in 19 of these 29 cases the liver contained a higher concentration of Pu than did the lung. The fact that the lymph nodes do not seem to contain high concentrations of Pu can be related to both the uncertainty of the sample size and to the uncertainty as to whether or not the lymph nodes that were obtained represented those having the highest concentration. It is of interest, however, that the bone depositions do not show the order of activity expected. The tabulations of the ICRP[3] suggest that when inhalation is the route of intake, one might expect five times the amount in bone as that in liver. However, the data of Bair, et al,[4] suggest for the acute cases, beagles sacrificed soon after intake, that about the same amount of plutonium oxide will be seen in the skeleton as in the liver. Park has reported about four times the amount of Pu oxide in the liver as that in the bone for dogs sacrificed at 900 days after intake. Langham[5] reports about the same in the skeleton as in the liver for a radiation worker exposed occupationally to both oxide and nitrate for 12 years prior to a radiation accident at Los Alamos. The autopsy results show that qualitatively, in 10 cases out of 23, the amount of Pu in the liver is at least three times that in the bone, assuming that Pu is uniformly distributed through the mass of the organ (standard man parameters).

Langham, et al[1] reported the results of measurements of plutonium concentration in tissues obtained at autopsy from nine chronically exposed workers at Los Alamos. Their measurements show qualitatively that the relative tissue concentrations are, in decreasing order, respiratory lymph nodes >lungs >liver >bone. In only one instance, that of case 31, does the present data clearly follow the suggested pattern.

For comparison, data from the literature regarding plutonium distribution in the human body and in dogs are presented in Table II. The frequency of cases as a function of amount of depositions and work experience are presented for the individuals listed in Table I together with non-occupational cases in Table III.

Qualitatively it can be concluded from the table that there is a greater likelihood of a larger deposition with increase in exposure time. Still unknown is whether this is caused by longer exposure to a chronic low-level concentration of plutonium or expresses the increasing likelihood of involvement with a minor or unnoticed accident with increasing time or association with the element.

As the program has evolved, both correctable and uncorrectable deficiencies have appeared and should be noted. The percent of yield of the chemical procedures needs to be known more precisely for each individual sample. Recent

TABLE II

PLUTONIUM DISTRIBUTION DATA OBTAINED AT AUTOPSY FOR HUMANS AND BEAGLE DOGS EXPRESSED AS PERCENTAGE OF THE BODY BURDEN AT DEATH OR AS PERCENTAGE OF THE INTAKE FOR THE DOGS[5]

	Langham's[a] Patient	Radiation[b] Worker	Beagle Dogs[c] Pu Citrate Injection	Beagle Dogs[c] PuO Inhalation
Reference	Langham et al[1]	Langham[5]	Stover et al[6]	Park et al[7]
Skeleton	66	36	58	0.4
Liver	23	49	11	1.7
Lungs		10		25.0
Respiratory Lymph Nodes		3		14.0
Spleen	0.4	0.3		

(a) Autopsy data obtained five months after injection of Plutonium Citrate.

(b) Occupationally exposed to plutonium for 12 years prior to a radiation accident at Los Alamos.

(c) Distribution data at death, 900 days after intake expressed as a percentage of initial intake.

TABLE III

DISTRIBUTION OF DEPOSITIONS BY WORK EXPERIENCE

Category	Number of Cases	Percentage of Cases					
		Lung			Liver		
		Units of $x\ 10^{-3}$ d/m/g			Units of $x\ 10^{-3}$ d/m/g		
		<1	1-5	>5	<1	1-5	>5
Work in Pu Facility	44	68	18	14	48	18	34
Non-Radiation Workers	77	83	17	0	82	17	1
Environmental Residents	165	85	15	0	90	10	0

The distinct break between the number of cases at a certain burden level for the plutonium worker and the non-plutonium worker and the environmental resident suggest that the latter two belong to the same class as having received plutonium predominantly as worldwide fallout from weapons testing.

The frequency of occurrence of measurable organ depositions as a function of time working with plutonium is presented in Table IV.

TABLE IV

DISTRIBUTION OF DEPOSITIONS AS A FUNCTION OF LENGTH OF EXPOSURE

Years of Exposure	Number of Cases	Percentage of Cases: Lung Units of $\times 10^{-2}$ d/m/g		Liver Units of $\times 10^{-2}$ d/m/g	
		≤ 1	> 1	≤ 1	> 1
< 5	30	97	3	83	17
> 5	14	72	28	65	35

animal data indicate variabilities as high as a factor of 3 between identical samples processed using NTA film analysis technique. It is now possible to tag the samples with Plutonium ^{236} and use alpha spectrometry instead of NTA film, thus the percent of yield for each sample will be known. The large variations in the total weight of the lung, particularly as associated with the cause of death, prevented extrapolation from a sample weight to an estimate of the activity in the total lung. To standardize the results, the entire left lung, including the hilar lymph node section, is now being used for analysis. The liver samples are now taken in sizes that weigh at least 200 grams. There has been much discussion concerning the selection of the bone sample. Various authorities indicate that the bone deposition for Pu seems highest in various locations such as the rib, sternum, vertebrae, femur, etc. Other factors additionally enter into the selection of this sample such as convenience for the coroner or the pathologist to obtain the desired samples either due to location or because of interference with further processing of the cadaver by the undertakers. After much deliberation, the sternum has been selected for future collection and analysis. The stripping of the tracheobronchial lymph nodes is not being routinely undertaken due to the difficulty of locating them. They will only be taken when clearly abnormal situations exist which make them readily observable or they appear to the pathologist to be of particular interest.

Autopsy programs, like other measurement programs, require precisely specified and controlled input from other sources in order to secure the maximum information. The most difficult and least precise information is the occupational exposure history on the employee. Typical of required data are: length and type of exposures, details on known radiation incidents, aerosol concentrations, particle size distributions and chemical forms and results of surveillance programs such as whole body counting and bioassay evaluation.

In conclusion, an autopsy program can become a useful adjunct to the three different measurement techniques used to assess organ doses due to internally deposited radionuclides. The importance of this program increases as the number of potential exposures to new and larger quantities of contaminants increases. Additionally, as the age of the nuclear industry increases, so does the age of the occupational worker who has perhaps already received prolonged low-level exposures. Difficulties and the sensitive nature that such programs can portray vary according to State law, company policies and perhaps the extent of personal association between the pathologist and the investigator. In spite of the problems associated with a program of this

type, it is a highly recommended source of information which can be developed into larger programs through the increased participation of hospital, other medical personnel, and other sites without adverse publicity. It certainly gives irrefutable information as to the concentrations and locations of the depositions of contaminates in man as a result of environmental pollution.

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