709902

M.I.T.-952-1

Annual Progress Report

Contract AT(30-1)-952

Radium and Mesothorium Poisoning and Dosimetry and Instrumentation Techniques in Applied Radioactivity

Robley D. Evans
Professor of Physics
Project Leader

10bb218

MAY 1964

DOE/HQ

A. Radium and Mesothorium Toxicity in Human Beings

1. Introduction

At the December 1963 meeting of the American Medical Association in Portland, Oregon, the M.I.T. group was awarded the Hull gold medal for its exhibit on "Radium and Mesothorium Poisoning in Human Beings: X-ray Abnormalities in 237 Cases".

Studies on 87 radium and/or mesothorium poisoning cases are reported this year. The following categories are represented: complete in-vivo study at M.I.T., breath radon samples taken in the field, exhumations, analysis of small bone or tooth samples, autopsies, and chromosome studies. Results on 10 complete exhumations are reported.

Detailed quantitative analysis of the data on over 300 M.I.T. cases has been completed. The results were presented at the I.A.E.A. Symposium on the "Assessment of Radioactive Body Burdens in Man" at Heidelburg, Germany, in May of this year.

The long-term effects of residence by 17 persons in a highly contaminated home have been investigated.

The study of the relative uptake by the gut of elements 88 and 90 is nearing completion. Details will be found in Section B of this report.

The new crystal suspension and tracking system has been installed and has been in operation since January 1964 (see Sec. E).

2. Calibration Data for Standard Chair Position in M.I.T. Cobafac

With the acquisition of a 400-channel RIDL analyzer, the calibration data for the standard chair position were reevaluated. Formerly, with the 256-channel RCL analyzer, the following calibration was used:

13.4 kev/channel; 0 kev = channel 4.4

For simplicity in channel-energy conversion the following calibration is now being used:

10.0 kev/channel; 0 kev = channel 0

Table 1 is a compilation of the old and new calibrations, along with other reference data, for the radioisotopes with which this laboratory is primarily concerned. The widths of the various energy bands under the new calibration do not conform exactly with the widths of the corresponding old ones but the error incurred is negligible. Thus, a smooth change-over has been made.

As an example of the convention used to calculate the energy band limits, consider the K^{40} data. The channel band summed runs from channels 103 to 123 inclusive. For a calibration of 10 kev/ch., 0 kev in channel 0, it is assumed that the mid-point of channels

1066219

DOE/HQ

132 and 159 have corresponding energies of 1320 kev and 1590 kev respectively and that the equivalent energy band has limits of 1315 kev and 1595 kev.

For convenient reference several other columns were added to the table. The values listed in column 11, "Net counting rate per unit activity," were determined as follows:

1. The K^{40} cpm/g K value is an estimate from chair measurements on 6 normal subjects (3 male and 3 female) whose average weight was 68 kg and whose average age was 38 yrs. The quantity of K in each subject was determined from the weight of the subject and the results of Dr. E. C. Anderson of Los Alamos on the K composition of human beings as a function of age and sex. The average quantity of K in these control subjects is assumed to be 118 g.

2. The Zr^{95} cpm/μc value is derived from the Cs^{137} calibration, correcting for differences in γ-ray abundance, and differences in crystal efficiency and photofraction as well as in self-attenuation due to different γ-ray energies. It is assumed that Nb^{95} is in transient equilibrium with Zr^{95} in the body, and that both are distributed in the body in a manner similar to Cs^{137}.

3. The I^{131} cpm/uc value for the whole body and for the thyroid are based on measurements carried out on 2 subjects after oral administration of I^{131} (1).

4. The Cs^{137} calibration was obtained from chair measurements carried out on 5 subjects after intravenous administration of Cs^{132} (2).

5. The Tl^{208} cpm/μc value for Ra-MsTh dial painters and Radithor cases has been calculated from the RaC 1.76 - Mev γ calibration. The Tl^{208} calibration for Thorotrast cases has been determined by chair measurements on 2 Thorotrast cases whose body burdens were first determined by the 1.25 meter-arc technique.

6. The RaB and RaC calibrations were obtained from chair measurements on several people (dial painters, etc.) whose body burdens had been determined by the 1.25 meter-arc technique.

7. The estimated calibration for MsTh in Thorotrast cases is based on measurements with ThB and Th^{232} sources in a sugar phantom, and is for $MsTh_{1,2}$ only. It does not include contribution from any daughters.

The contribution from K^{40} and Cs^{137} and the Cobafac background values were included for completeness. The percentage contributions from K^{40} were calculated from measurements on 2 subjects after intravenous administration of K^{42} (3). The percentage contributions from Cs^{137} were calculated from the calibration experiment referred to in item 4 above.

1. C. J. Maletskos and S. C. Littlefield, p. 44, NYO-9505 (1963).
2. C. J. Maletskos, et al., p. 39, TID-16349 (1962); p. 40, NYO-9505 (1963).
3. C. J. Maletskos, et al., p. 36, TID-16349 (1962).

1066220

DOE/HQ

^{224}Ra $T_{\frac{1}{2}}$ 3.66d

B. Differential Uptake of Elements 88 and 90 Following Oral Ingestion by Human Beings

^{234}Th $T_{\frac{1}{2}}$ 24.1d

1. Introduction

In the 1963 annual progress report of the Radioactivity Center[1], results of experiments with dogs to determine the relative uptake of Th and Ra isotopes through the gut were reported. A final dog experiment to determine Ra uptake was not ready for reporting at that time, and is presented in this section.

These dog studies were conducted to test experimental techniques to be used in absorption studies on humans, which are currently under way. This section describes experiments to determine the metabolism of Ra^{224} and Th^{234} following intravenous injection in humans of both sexes. These experiments, comprising the first phase of the human uptake study, were designed to calibrate various counting techniques to be used in the second phase, and have recently been completed. The second and final phase, actual measurement of the uptake of each isotope after oral administration in mock dial paint, has been initiated with pilot studies on two males, one receiving Th^{234} in mock paint, and the other Ra^{224} in like form.

This report presents in a preliminary fashion the results of this first phase, as well as results obtained from the pilot study for the oral experiments. A detailed presentation of all aspects of both intravenous and oral studies will appear in a future progress report.

2. Review

A brief review of the purpose of the gut uptake study (GUS), and an abstracted description of what has been accomplished prior to this report, follow.

Skeletal dose estimates for the Ra-MsTh patients currently being studied are complicated by the fact that some of the patients were exposed to mixtures of unknown proportions of Ra^{226}, MsTh (Ra^{228}), and RdTh (Th^{228}). Any burden of Ra^{226} or MsTh likely to produce effects in the body can now be measured with sufficient accuracy, but absorbed RdTh ($T_{1/2}$ = 1.9 yr.), in the intervening 30-40 yrs. since exposure, will have undergone considerable decay, to the extent that it will be masked by the RdTh grown in from the decay of MsTh in the body.

Dog experiments at Utah established that RdTh is roughly 10 times more toxic than Ra per unit dose. This fact, coupled with a much higher retention of RdTh over Ra, once in the blood, leads to the conclusion that the dosimetry on Radithor cases and on many dial

1. C. J. Maletskos et al., pp. 59-79, NYO-9505 (1963).

1066221

DOE/HQ

painters will have wide limits of uncertainty unless RdTh were taken up from the gut at less than, say, 1% of Ra.

The present study purports to determine the extent to which RdTh may have contributed to skeletal doses, based on its uptake from the human gut relative to that of Ra^{226} and Ra^{228}.

Ra^{224} ($T_{1/2}$ = 3.62 d) and Th^{234} ($T_{1/2}$ = 24.1 d) were chosen as the most favorable isotopes of elements 88 and 90, by virtue of their short half-periods and their optimum γ-ray spectra.

Carrier-free Ra^{224} was separated from Th^{228} by use of an anion exchange column. Carrier-free Th^{234} was separated from uranium ore (U_3O_8) and U^{238} slag, enriched 50-100 times in Th^{234}. Mock Ra paint for oral administration of the two isotopes was prepared, following the basic plan described by the Radiobiology Laboratory at the University of Utah[2].

A series of phantom studies were conducted to develop methods of measuring "true" body burdens of each nuclide in the presence of a significant amount of activity in the lumen of the gastrointestinal tract. Out of these studies came the skull and crossbones (SXB) method, which shields the gastrointestinal tract from the detector by means of several layers of Pb brick, and allows the detector to "see" only the head, shoulders, and arms of the subject.

The phantom studies gave an indication of the relative sensitivities for measuring the two nuclides, and several Ra-MsTh patients were counted in the SXB position to test its reproducibility, as well as the extent of physiological variations of the patients.

The SXB technique was calibrated for measurement of uptake in dogs. One dog was administered Th^{234} intravenously, and another was administered Ra^{224}. Subsequently, a mock dial paint, incorporating Th^{234} and encased in a gelatin capsule, was given to a dog, and results indicated that uptake was $\leq$ 2% of the ingested dose. Ra^{224} was likewise administered in a separate experiment, which is described below.

3. Uptake of Ra^{224} from Mock Dial Paint Administered Orally to Dog

A female mongrel dog (No. 1-GUS-4) was administered a capsule of dial paint containing 14.8 μc Ra^{224} with daughters in transient equilibrium (~ 17.1 μc of 10.6-hr Pb^{212}).

Gamma counts on the dog consisted of meter-arc measurements of the dog's ventral aspect only, to get a measure of retention, and of SXB measurements to determine uptake. It would have been more precise to have counted both aspects of the dog in the meter-arc position, since the pill was constantly in motion through the G.I. tract, and therefore geometry and γ attenuation in the dog would have been expected to be quite variable. This was

2. B. J. Stover, D. R. Atherton, and M. A. Van Dilla, AECU-3418, (1955).

1066222

DOE/HQ

demonstrated when a meter-arc count taken ~24 hrs after ingestion showed an increase of 7% over the initial meter-arc result shortly after ingestion of the "pill", despite a 3% loss of activity through the urine.

Figure 37 shows the counting rate of the dog in the meter-arc over the first 13 days after ingestion, as well as the counting rate in the SXB position. Observed counting rates were corrected for physical decay assuming a 3.62-day half-period.

A meter-arc measurement at 48 hrs after ingestion showed a decrease of ~30% from the initial meter-arc count, despite a loss of only ~5% of the pill activity through excretion. A remeasurement 2 hrs later gave the same result. This counting rate drop can be explained by hypothesizing a bolus in the rectum of the dog, containing the bulk of the total activity in the dog. Such a bolus would involve greater γ-attenuation, and a greater source-to-crystal distance than, say, the original pill in the stomach.

Indeed, at ~51 hrs after ingestion, the dog voided a feces sample which contained ~82% of the pill activity with daughters essentially in transient equilibrium. The dog was immediately counted again in the meter-arc position and the counting rate had dropped to ~16% of the counting rate of the previous hour.

The SXB position, where the dog's head and forelegs only are seen by the crystal (the major portion of its body being shielded by layers of Pb bricks), indicated a "true", or non-G.I. body burden of ~9% of the pill activity on the 5th day after ingestion, at which time the meter-arc measurement indicated a whole-body burden of approximately 10% of the pill activity.

Both the SXB and meter-arc positions had previously been calibrated by measurements on the same dog (No. 1-GUS-1) after intravenous administration of Ra^{224}, and it was these calibrations, on the 4th day after injection, that were used to obtain the above results for the 5th post-ingestion day.

The only SXB measurement done on the "intravenous" dog was that of the 4th post-injection day. The SXB results on the "oral" dog must be viewed with the consideration that the counting rate per unit whole-body activity could vary significantly with time after injection (or uptake). As it stands, the SXB results are remarkably constant from the 1st through the 13th post-ingestion day, and would tend to imply little or no biological depletion of the non-G.I. burden.

There was a rapid initial build-up of activity in the SXB position from 7 net cpm ~20 min after ingestion, to 277 net cpm (uncorrected for decay) 5-1/2 hrs later, to 766 net cpm (uncorrected) ~18 hrs later, following which the counting rate remained fairly constant after applying the 3.62-day half-period decay correction.

The SXB measurements in the first few hours after ingestion would largely reflect the uptake and distribution of Pb^{212} ($T_{1/2}$ = 10.6 hr) and/or Bi^{214} ($T_{1/2}$ = 60.5 min). Since the counting rate was increasing at a rate more rapid than build-up of Pb^{212} from the decay of Ra^{224} would warrant, one might speculate that uptake of Pb^{212} (and/or Bi^{214}) was taking place over an extended period of time (> 3 hrs), or that the Bi^{214} was not taken up significantly relative to Pb or Ra and was subsequently building up from Pb decay in the blood.

DOE/HQ

1066223

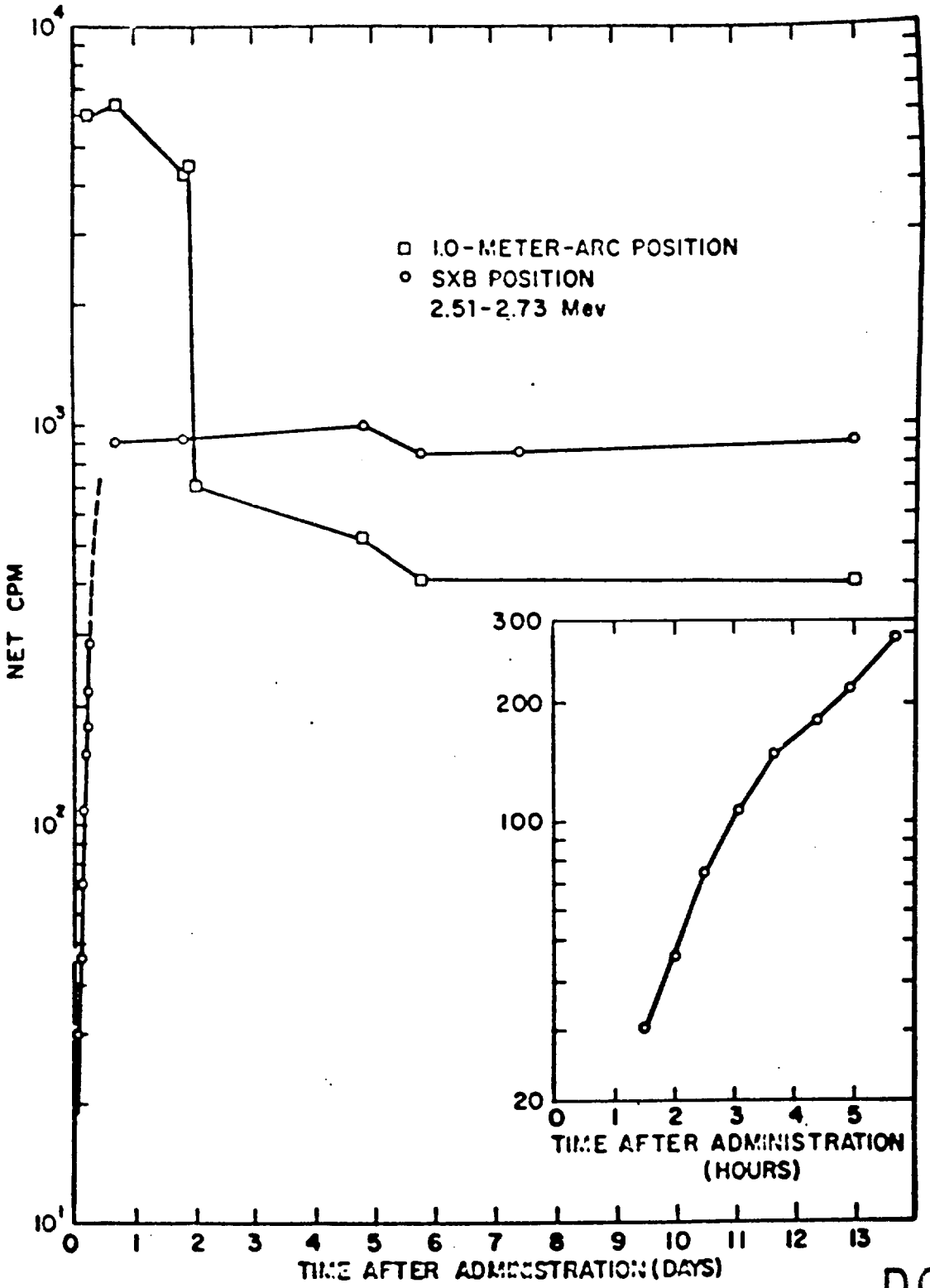


FIG. 37. DOG#1-GUS-4 NET COUNTING RATES AFTER ORAL ADMINISTRATION OF MOCK DIAL PAINT CONTAINING 14.8 μc Ra^{224} (WITH DAUGHTERS IN TRANSIENT EQUILIBRIUM).

DOE/HQ

1066224

Blood samples taken at ~1 hr, ~3 hrs, and ~4-1/2 hrs gave total blood Ra^{224} values of 0.02%, ~0.4% and 0.9%, of the ingested activity, respectively. Corresponding Pb^{212} values were 0.4%, ~1.4%, and ~1.6%. At ~18 hrs after administration, the Pb^{212} activity in the blood was ~7.0% of the ingested dose, while the Ra^{224} activity was ≤ 0.5%. The Pb^{212} value of ~7% assumes that the Pb in the blood was decaying with the half-period of the parent Ra. This is thus a minimum Pb value, and would require that essentially all the Tn (except the small fraction presumably exhaled) was decaying in the blood. Since the Ra^{224} intravenous study indicated a very rapid clearance of Ra from the blood, the Tn produced in tissue would require ready access to the blood. The likelihood is that some significant fraction of the Tn is decaying in the blood.

The complicating factors of possible differential uptake of Pb and Ra, and lack of precise knowledge of the time of uptake, make interpretation of the Pb blood values as an indicator of Ra uptake somewhat ambiguous.

However, the 4-1/2 hr Ra^{224} blood value of ~1% of the ingested dose, at a time when the Pb^{212} value was not yet at a maximum, indicates that Ra uptake based solely on blood data probably greatly exceeded 1%, when the rapid clearance of Ra is considered.

Figure 38 shows cumulative Ra^{224} excretion curves. The dog was harnessed and catheterized in the manner previously described and urine and feces samples were collected for 5 days after administration. In the intravenous study, dog No. 1 excreted in the urine a total of ~22% of the injected activity at 4 days after injection. The total of 7.6% of ingested dose excreted via the urine in the oral experiment at ~4 days after administration might, therefore, extrapolate to an uptake of 35% (7.6%/0.22) of ingested dose.

The "true" retention of ~9% indicated by the SXB result at 5 days after administration, plus the 7.6% measured in the urine, give a minimum uptake of ~17%, without considering the amount of endogenous Ra^{224} in the feces. Dog No. 1 had excreted ~37% of the total excreted activity in the intravenous study via the feces by the 4th day after injection. Thus, one might estimate that the total activity excreted in the oral experiment via endogenous fecal excretion plus urine excretion was 12% (7.6%/0.63), 4 days after administration of the pill. The uptake would then appear to be 21% (12% + 9%).

In the injection experiment, 35% of the injected activity was excreted in the first 4 post-injection days, whereas the above method of calculating uptake yields a 4-day excretion value of 57% (12%/21%). The retention 12 days after injection was ~40% in the intravenous study. An SXB measurement 13 days after ingestion in the oral study gave a value of 8% of the ingested dose, which would calculate to a 20% (8%/0.4) uptake.

Finally, uptake estimates can range from 14% (9% by SBX/0.65), based on a 4-day assumed total excretion of 35%, to 35% (7.6% in urine/0.22) based on a 4-day urine activity of 22%. A best estimate of ~20% seems indicated by the data.

1066225

DOE/HQ

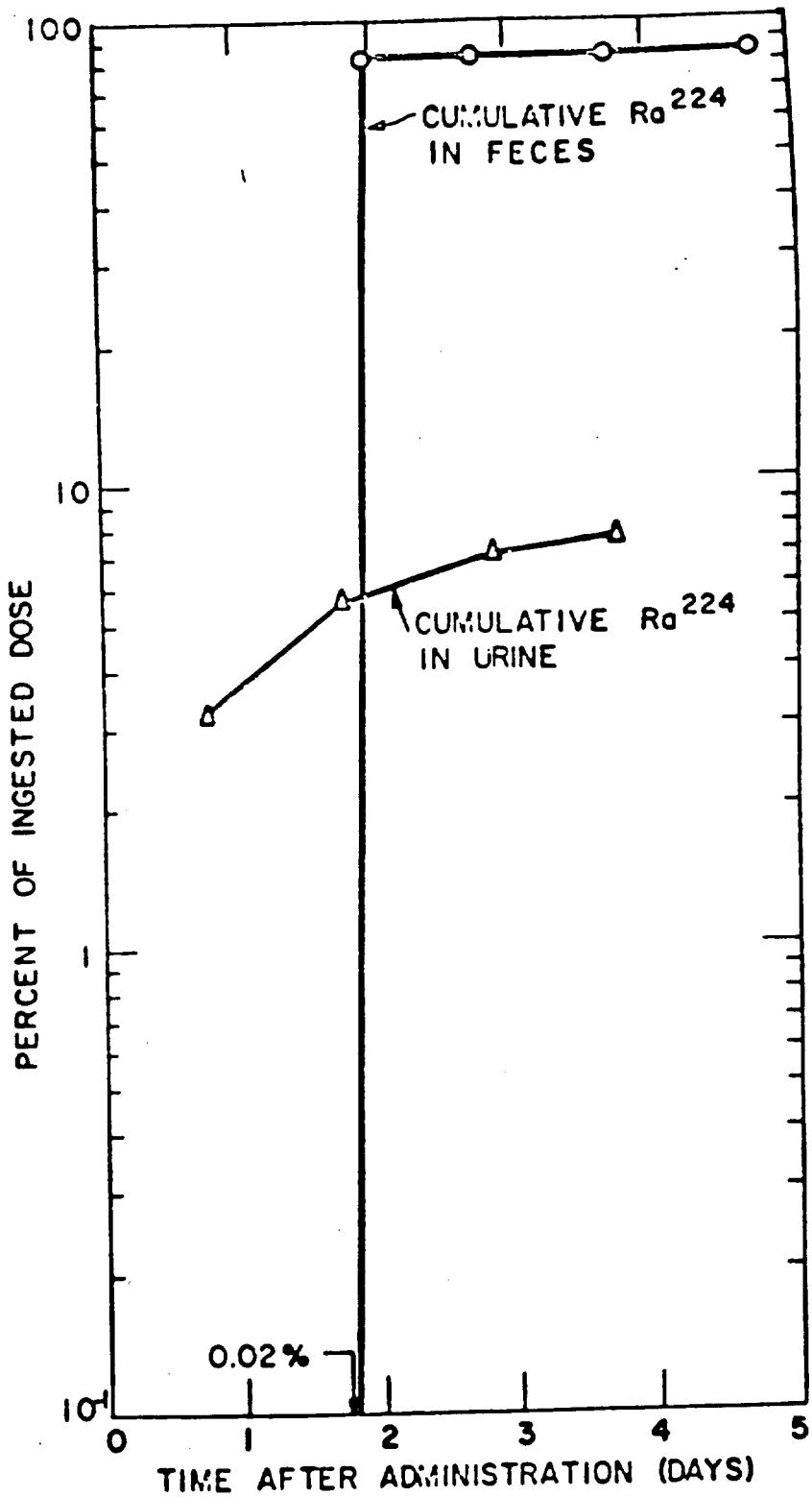


FIG. 38. DOG #1 -GUS-4
EXCRETION OF Ra^{224} AFTER ORAL ADMINSTRATION OF MOCK DIAL PAINT CONTAINING 14.8μc Ra^{224}

DOE/HQ

4. Materials and Methods for Human Intravenous Studies

a. Source and selection of subjects.

Most of the subjects used in these studies were obtained through The Age Center of New England, Boston, Mass., with the assistance of the Executive Director, Mr. Hugh Cabot. A few were retired M.I.T. employees.

Subjects were selected on the basis of their ability to meet the following criteria:

1. All must be ambulatory.
2. None must have had any operation within the preceding 6 mos.
3. None must have had any bone fracture within the preceding 2 yrs.
4. None must be taking any androgenic or estrogenic steroid substances (e.g., for symptoms of menopause, or prostate malignancy, cancer).
5. All should have normal values of
   - a. alkaline phosphatase
   - b. serum calcium
   - c. serum phosphate
   - d. BUN
   - e. urinalysis
   - f. hemogram
6. None must be taking unusual amounts of vitamins, in particular Vitamin D.
7. None must have any known disease of the parathyroid glands.
8. None must have any known rickets (renal or infantile).
9. None must have known:
   - a. chronic renal disease (including renal lithiasis)
   - b. idiopathic osteoporosis
   - c. malignancy with bony metastases
   - d. sarcoidosis
   - e. collagen disease
   - f. disease of any avitaminosis
   - g. endocrine disease
   - h. Paget's disease
   - i. gastro-intestinal disease of absorption (e.g., sprue or celiac disease)
   - j. osteomalacia
   - k. acromegaly
   - l. arthritis - with or without bony changes.
10. Acceptable bone x-rays within the past year.
11. All volunteers should have normal diet (i.e., have no unusual food fads).
12. All volunteers should be having normal bowel movements (i.e., 1 or 2 per day).
13. Volunteers should not require the constant use of laxatives or fecal softeners.

b. Examination of subjects.

Each subject had a complete physical examination. Clinical laboratory studies included a complete blood count, urinalysis, serum calcium, phosphorus, alkaline phosphatase, bilirubin, cephalin flocculation, serum electrophoresis, blood urea nitrogen, and a fasting blood sugar. In addition, all subjects had a set of screening x-rays which included the long bones, for the purpose of excluding any subject with bony abnormalities. Unless all the above criteria were within normal limits, the subjects were not accepted into the study.

1066227

DOE/HQ

c. Hospitalization and metabolic techniques.

The subjects were housed at the Sancta Maria Hospital, adjacent to M.I.T., during the metabolic phase of the experiments, or at the M.I.T. Infirmary. The diet consisted of the regular hospital or infirmary fare.

Subjects were injected at the M.I.T. Infirmary, then brought to the Radioactivity Center where they changed into pajamas for initial γ measurements.

The subjects were instructed in the technique of separating urine and feces during voiding. Individual feces samples were collected in a plastic bag which lined the receptacle of a portable commode kept in the Infirmary. The bag was transferred to a 2-liter polyethylene bottle, ~10 ml concentrated HNO_3 was added, and the bottle filled with water to a standard volume. The screw cap was then affixed and sealed with plasticene and friction tape to avoid leakage.

Twenty-four-hour urine collections were made by having the subject void directly into a 2-liter polyethylene bottle which he kept near him while at M.I.T. and which he took with him when he returned to the hospital. These were also filled with water to a standard volume.

Several 10-ml blood samples were taken from each subject on the day of injection, and one each day thereafter for several days, using plastic disposable syringes.

Preparation of injection materials.

Radiochemical separation and preparation of carrier-free Th^{234} from U^{238} slag highly enriched in Th^{234} was carried out essentially as described in the 1963 Progress Report[1]. A modification of the separation procedure therein described was necessary to obtain the high activities of Th^{234} necessary for the oral pilot study, and that modification is discussed in Sec. B-8. For the injection material, however, $Th^{234}Cl$, desorbed in the final step of the separation process from a small column of Dowex 1 x 8, 100-200 mesh, anion-exchange resin, was taken to dryness in a teflon beaker and diluted with a sterile isotonic citrate solution, pH 3.5. The radiochemical purity of the injection solution was checked by α and γ spectroscopy and by half-period measurements, and contamination by parent U^{238} and other Th or U isotopes was consistently $<10^{-4}$.

Separation of carrier-free Ra^{224} from Th^{228} was also carried out essentially as described in the 1963 Report. $Ra^{224}(NO_3)_2$, eluted from a column of Dowex 1 x 8, 100-200 mesh, anion exchange resin, as a final step in its separation process, was converted to $RaCl_2$ in a teflon beaker and diluted with sterile isotonic saline. The radiochemical purity of the injection solution was also checked, and contamination by parent Th^{228} was consistently $<10^{-4}$.

Both the Th and Ra solutions were filtered through a Millipore filter to remove bacteria and resin particles, autoclaved in a serum bottle, and tested for bacteria and pyrogens*.

These operations are carried out by Isoserve, Inc., Cambridge, Mass.

1066228

DOE/HQ

e. Standardization of injection syringes.

For both nuclides ~1-ml aliquots were injected. A pilot subject, done before the other Th subjects, received ~1 μc Th^{234}, while the other subjects received ~2.5 μc Th^{234}.

A pilot subject, done before the other Ra subjects, received ~0.25 μc Ra^{224}, while the remainder received ~1 μc Ra^{224}.

Radium syringes were standardized against an aged $Th(NO_3)_4$ standard while Th syringes were standardized against a known weight of pure U_3O_8 dissolved in acid to minimize effects on the Th^{234} γ spectrum at 0.77 and 1.01 Mev from the ~2.5 Mev β^- of Pa^{234m}. The standard so made had essentially the same spectral shape as a similar volume of acid containing pure Th^{234}.

The residual activity in each syringe was measured soon after injection, and sufficiently thereafter to insure that the equilibrium status of the injected material was well established. In the case of Ra^{224}, though its daughters were in transient equilibrium with it in the syringe before injection, a greater than equilibrium amount of Pb remained behind relative to the residual Ra. This phenomenon necessitated correcting early γ counts on the subjects for the non-equilibrium condition of the injected material.

f. Measurement techniques.

(1) Blood Specimens. Four blood samples were drawn on the day of injection and one sample was taken on each succeeding day. Of each 10-ml blood sample taken, 6 ml was transferred from the syringe to a 2-dram flip-top polyethylene vial for β^- counting in a well-type, thin plastic scintillator. The counting efficiency for 6 ml of blood was estimated as ~7% for the 2.5-Mev β^- of Pa^{234m}. The plastic scintillator was used to count Th^{234} blood samples until a more sensitive wide-β counter was located*. The wide β counter had an efficiency of ~30% for the Pa β^- and had a much lower background than the plastic scintillator (2 cpm vs. 30 cpm).

The first few Th blood samples were prepared for wide-β counting as follows: Each 6-ml sample was transferred from the flip-top vial to a 50-ml crucible and heated in a vacuum oven at 50°C for ~16 hrs, at 75°C for ~3 days, and finally at 100°C for ~8 hrs. Then it was ashed in a muffle furnace overnight**. The ashed contents of the crucible were washed into a 1 in dia. x 1/4 in. deep stainless-steel planchet with 0.1N HNO_3 and dried with an infrared lamp. The planchet was fastened into a holder for placement in the wide-β counter, and left to count overnight.

The majority of the Th^{234} samples were dried first with an infrared lamp and a hot plate, and then flamed, a 2-hr process as opposed to the lengthy vacuum-oven drying. Otherwise, the preparation of these samples was as described above.

---

* Wide-beta counting done with the cooperation of F. MacIntyre and R. Duce of the M.I.T. Department of Chemistry.

** Preparation of blood samples done with the assistance of J. Moor and N. Walsh of the M.I.T. Department of Nutrition.

1066229

DOE/HQ

Six-ml Ra^{224} blood samples were first counted in the thin plastic scintillator to determine Pb^{212} activity, then more sensitive Tn deemanation measurements for Ra^{224} activity were made.

For Tn deemanation, the following sample preparation was required. The 6-ml contents of the polyethylene vial were placed in a 50-ml crucible containing 1.0 ml (10 mg) Ba carrier. The crucible contents were partially dried by hot plate and infrared lamp, flamed, then muffled overnight in a 500°C oven. The resulting ash was dissolved, with the help of an infrared lamp, in 6N HCl. This solution was poured into a deemanation tube and brought to a 50 ml volume with crucible washings, using 6N HCl. The solution was deemanated by bubbling water-pumped N_2 through the tube at a rate of 1 liter per min. Thoron daughters were collected on a copper planchet (1 in. dia.) coated with silver-activated ZnS phosphor, with 3000 v applied. The planchet was then counted in an α-scintillation counter.

For the Ra and Th intravenous studies, control blood samples were obtained from laboratory personnel and prepared in the same manner as the "active" samples. Standards for each of the counting techniques were prepared by adding a known amount of Th or Ra to a normal blood sample, and then proceeding with the same method as heretofore described.

(2) Breath Thoron. Breath sampling was done on the Ra^{224} subjects by the usual method used in this laboratory. The subject breathes aged air through a face mask. Exhaled air passes through a chamber containing a copper planchet coated with ZnS phosphor (with a potential of 6000 v applied) on which Tn daughters are collected. The planchet is then counted in an α-scintillation counter.

Several samplings of each subject's breath were made on the day of injection, and one on each succeeding day on which whole-body γ measurements were done. Care was taken to detect and prevent leakage around the face mask. This was accomplished by comparing the flow rate from the tank of aged air with the flow rate entering the spirometer. When no leakage was indicated, the collector voltage was then applied.

Collection periods ranged from 5 min for the first-day measurements, to 60 min for the later measurements, when the Ra^{224} burden was quite low due to physical and biological decay.

A series of replications on two of the subjects over a short time interval indicated that measurements where the collection time was of the order of 5 or 10 min have an error of ± ~10%, even though counting errors are ±1%. The longer collection times perhaps remove the bulk of this error, but measurements requiring longer collection times have counting errors of the order of ±10%, so that an error of ±10% for all breath Tn results is indicated.

(3) Urine and Feces. Urine and feces samples in the 2-liter polyethylene bottles were counted with a 4 in. x 4 in. NaI(Tl) crystal in the "cave", a small enclosure with 6 in. thick steel walls. The 63- and 91-kev γ's of Th^{234} as well as the 1.01-Mev γ of Pa^{234m} were used in the calculation of Th^{234} activity, while the 240-kev γ of ThB and the 2.62-Mev γ of ThC" were used in the Ra^{224} analysis.

1066230

DOE/HQ

Many of the samples were found to be leaking when received from the hospital, which created problems of contamination of the counting apparatus. In addition, there was an apparent differential "plating out" of Pb and Ra onto the walls of the polyethylene bottles, as was indicated by the failure of two Ra^{224} excretion standards to give a consistent activity ratio when measured sequentially. Shaking of the standards seemed to affect this ratio markedly. Results on the Ra^{224} feces samples indicated that, besides the possible "plating" effect, the fecal material was evidently not distributing its Ra (and Pb) uniformly throughout the solution, to conform to the distribution in the standards. Repeat measurements over a several-day period gave poor reproducibility in many cases, and so the Ra^{224} values of the feces necessarily have large errors. Plans to recount these Ra^{224} feces samples under improved counting conditions were aborted when the feces samples were inadvertently discarded during the course of a vigorous housecleaning. Similar difficulties no doubt occurred with the Th^{234} samples. However, the total activity excreted in feces was ~1% of the injected dose, and therefore the Th^{234} measurements do not present a problem.

Radium urine samples did not seem to have an extreme problem of reproducibility, but they contained only a small fraction of the total excreted activity.

(4) Cobafac Counting. Standard 1.25-meter-arc γ measurements were done on all subjects shortly after injection. These were repeated at ~48 hrs and at ~96 hrs after injection, the primary purpose being an evaluation of the meter-arc technique by comparison of meter-arc results with retention as determined from excretion measurements.

Four other γ measurement methods were employed to follow retention: (a) the standard chair position, (b) the L8SXB position (SXB position with 8 in. x 4 in. crystal and with analyzer calibrated for ~1 kev/channel), (c) the H8SXB position (SXB position with 8 in. x 4 in. crystal and with analyzer calibrated for 10 kev/channel) and, (d) the TSXB position (SXB position with 4 in. x 1/4 in. crystal and with analyzer calibrated for ~1 kev/channel).

Measurement of the subjects after I. V. injection in the various SXB positions calibrated these positions for use in the oral phase of the gut uptake study. The standard chair position and the 1.25-meter-arc method are techniques for determining whole-body burden, whereas the SXB position is designed to measure retention after introduction of Ra or Th into the blood (e.g., after uptake from the G.I. tract).

Table 27 indicates the energy bands which were used to determine counting rates.

Table 27. Energy Bands for Various Counting Methods

Position	Ra^{224}	Th^{234}
Standard chair	2.515 - 2.725 Mev	0.895 - 1.105 Mev
1.25 meter arc	2.515 - 2.725 Mev	0.895 - 1.105 Mev
H8SXB	2.515 - 2.725 Mev	0.895 - 1.105 Mev
L8SXB	219 - 260 kev	50 - 116 kev
TSXB	175 - 200 kev	44 - 108 kev

Integral scanning, using the new power system described in Sec. E 7, was also done on on all subjects, and evaluation of these data is in process.

1066231

DOE/HQ

Figures 39 and 40 show the SXB position. The Pb bricks were covered with a layer of 1/16 in. tin and 10-mil copper to absorb Pb x-rays. A curved shield placed behind the subject, consisting of a layer of tin and copper, can also be seen in the pictures. This was designed to cut down Pb x-rays produced in the Pb lining of the wall by a large amount of activity in the gut after oral administration.

5. Results on Ra^{224} Injection Studies

Table 28 gives some characteristics and the radionuclide dose schedules for subjects receiving either Ra^{224} or Th^{234}, and the route of administration. The coding system for the subjects is described below the table.

The RIV subjects were followed by the methods described. Because of the limitations of each of the techniques employed, as well as the restrictions resulting from limitation of time, not all measurements could be done as often as might be wished. Figs. 41 through 45 give the net counting rates for each RIV subject, obtained in the various counting configurations, and demonstrate the relative counting efficiencies for each.

Because of the unreliable feces measurements, the feces excretion data have not been used in this report. However, they are sufficiently useful to allow an estimate of the feces/urine activity ratio of Ra^{224}. This value appears to be > 10. The excretion data are given in Table 29.

Figure 46 gives the net counting rate in the chair configuration per μc of retained Ra^{224}. The latter is based on meter-arc results. Meter-arc measurements done within hours after injection of Ra^{224} gave values which confirm directly (within a few percent) the amounts of Ra^{224} actually injected into each subject. On the basis of certain of the measurements, it was determined that subsequent meter-arc measurements probably reflect the same attenuation coefficient, and therefore the true body retention, even though the distribution of the radionuclides might be significantly changed from the 1st day. For each individual the last observation serves as the calibration by which radionuclide retention is determined using the chair position.

The lower half of Fig. 46 shows the average net counting rates per μc in men and women for the post-injection days on which meter-arc measurements were done. It is recognized that, at the end of the first post-injection week, the chair-to-meter-arc counting rates were still changing, probably reflecting redistribution of the radionuclide. However, the calibration obtained at this time represents the best available calibration factor since, after the 1st week, meter-arc measurements are too insensitive to be useful for determining retained activity.

Figure 47 gives the net counting rate for the HBSXB configuration per μc of retained Ra^{224} for each of the 5 subjects for the 3 days on which meter-arcs were done. Average counting rates for men and women (and their average) are shown in the lower half of the figure. During the 1st week redistribution is taking place, and is again reflected by the changing values shown on the graph. It is probably worth noting the apparently aberrant results given by RIV F_2. This particular subject seemed to be unable to maintain a constant position during the course of her measurements, which may have been a factor.

1066232

DOE/HQ

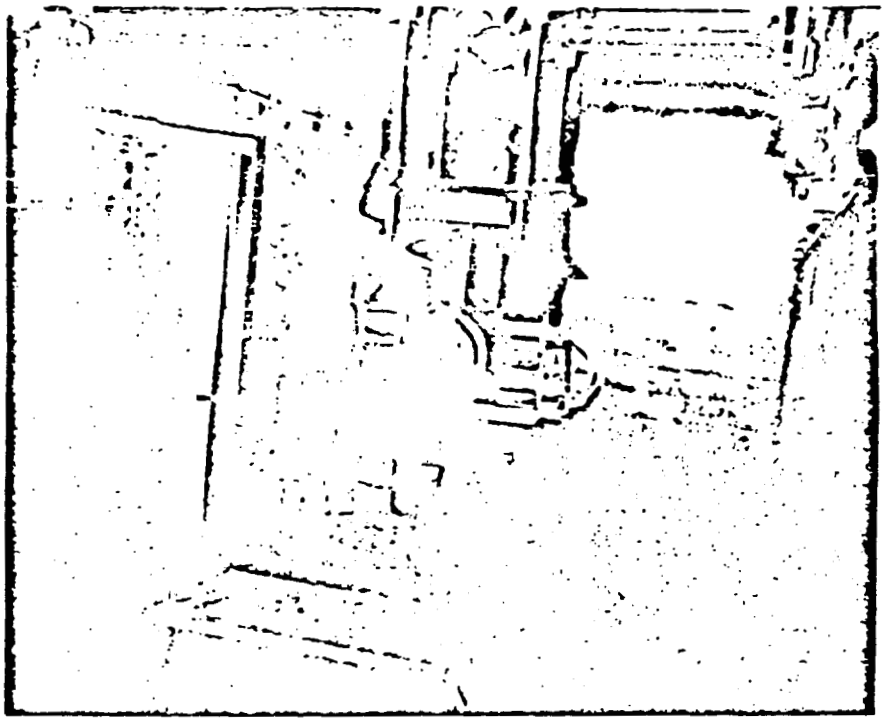


FIG. 39. Pb SHIELD - CRYSTAL CONFIGURATION FOR S X B MEASUREMENTS

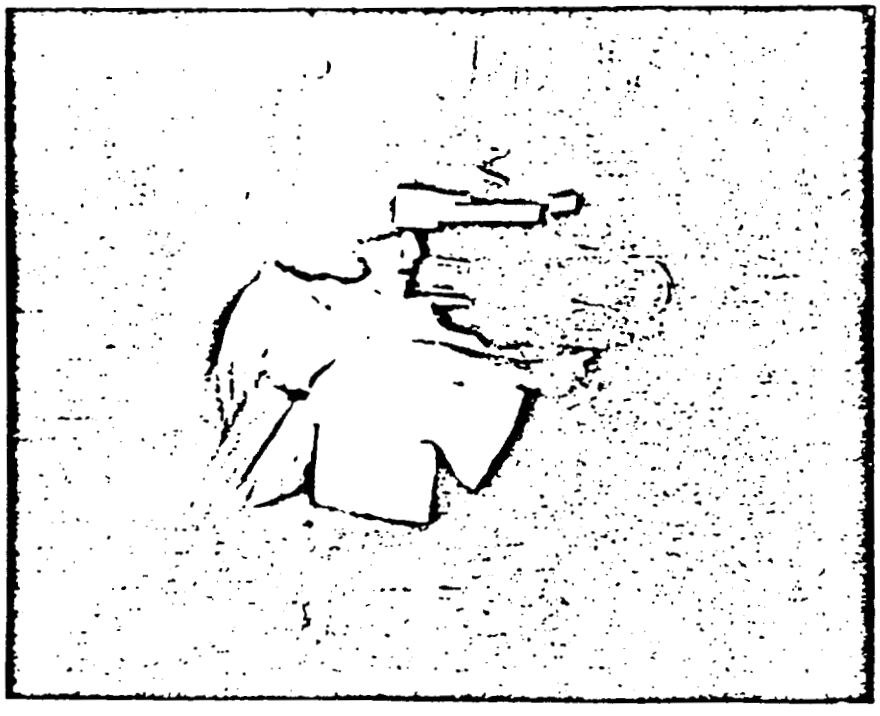


FIG. 40. SUBJECT IN S X B POSITION

Table 28. Characteristics and Dose Schedules for GUS Subjects*

Subject	Age	Weight (kg)	Height (in)	Amount of radionuclide administered (μc)		
				Pb^{212}	Ra^{224}	Th^{234}
RIVM1	82	58.9	65.0	0.223	0.236	
RIVM2	71	65.8	61.5	1.01	0.93	
RIVM3	76	67.2	63.0	0.95	0.88	
RIVM5	63	72.6	66.0	1.03	0.95	
RIVF1	71	66.6	61.0	1.01	0.92	
RIVF2	75	80.4	64.0	1.00	0.91	
RPOM1	72	85.6	69.0	2.82	2.45	
TIVM1	79	63.3	66.5			1.2
TIVM2	72	93.1	71.5			2.52
TIVM3	70	64.9	69.5			2.57
TIVM5	81	78.1	71.0			2.80
TIVF2	79	69.0	64.5			3.10
TIVF3	72	56.8	58.5			3.01
TPOM1	77	86.0	67.0			120.0

* Key for Coding of Subjects and Samples. In order to simplify the identification of subjects and specimens studied in these experiments a coding system was devised.

Subjects participating in radium or thorium studies were identified in Ra or Th subjects. Route of administration of the nuclide was denoted by IV or PO (namely, intravenous or by mouth). Sex was denoted by M or F. Type of excretion sample or blood sample was designated by U, F or B, followed by a digit to indicate which of a series of samples each specimen represented.

Thus, RIVM2 is the code for the second male in the group that received Ra^{224}. intravenously. Likewise, TPOF3 would be the code for the third female in the group receiving an oral dose of Th^{234} incorporated in mock dial paint.

NOTE: All observed counting rates in the RIV studies were routinely corrected to time of injection for the 3.62-day half-period physical decay of Ra^{224}.

All observed counting rates in the TIV studies were routinely corrected to time of injection for the 24.1-day half-period of Th^{234}.

The net counting rates appearing in the figures on the following pages are the net counting rates after the appropriate

1066234

DOE/HQ

Table 29. Excretion of Ra^{224} Following Intravenous Injection

	Time after injection (days)	Daily urine excretion (μc)	Daily feces* excretion (μc)	Cumulative total (μc)
RIVM2	1	0.010	0.13	0.14
	2	0.003	0.12	0.26
	3	0.002	0.29	0.55
	4	0.001	0.05	0.60
	5	0.001	0.12	0.72
RIVM3	1	0.034	0.03	0.06
	2	0.004	0.33	0.39
	3	0.002	0.11	0.50
	4	0.001	0.01	0.51
	5	0.001	0.01	0.52
RIVM5	1	0.024	0.01	0.03
	2	0.014	0.00	0.04
	3	0.001	0.01	0.05
	4	0.001	--	0.05
	5	0.001	0.02	0.07
RIVF1	1	0.011	--	0.01
	2	0.004	0.43	0.44
	3	0.002	--	0.44
	4	0.002	--	0.44
	5	0.001	0.19	0.63
RIVF2	1	0.007	--	0.01
	2	0.002	0.15	0.16
	3	0.001	0.18	0.34
	4	0.001	0.12	0.46
	5	0.001	0.05	0.51

* Feces values are unreliable but are presented here to give an indication of the relative excretion via feces and urine.

The percent retention of Ra^{224} is shown in Fig. 48. The first three retention values are based on meter-arc counts. Subsequent measurements were made using the chair configuration and applying the calibration factors derived from the last chair/meter-arc measurements given in Fig. 46. As shown, the subjects were followed for 21 days at which time the percent of retained Ra^{224} was ~20% of the injected dose.

Figures 49 and 50 show the fractional Tn exhalation based on the injected Ra^{224} activity and the retained Ra^{224} activity. Figure 49 is of interest in that it reflects both direct loss of Ra^{224} from the body and redistribution of the retained Ra^{224} as it moves

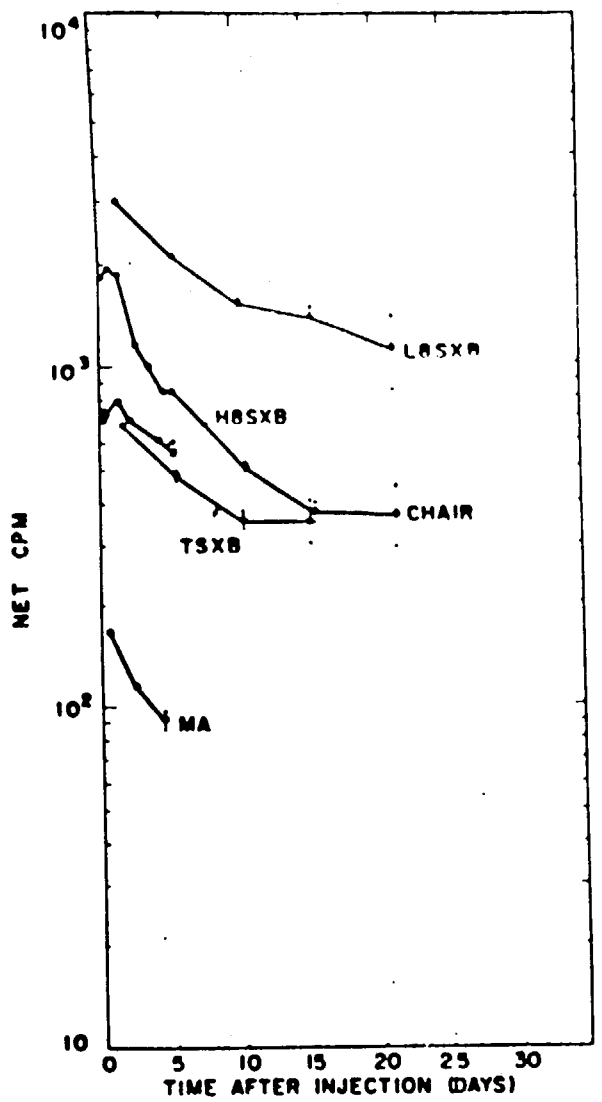


FIG. 41. COMPARATIVE NET COUNTING RATES AFTER INTRAVENOUS ADMINISTRATION OF Ra^{224} FOR VARIOUS COBAFAC COUNTING METHODS. SUBJECT RIVF1

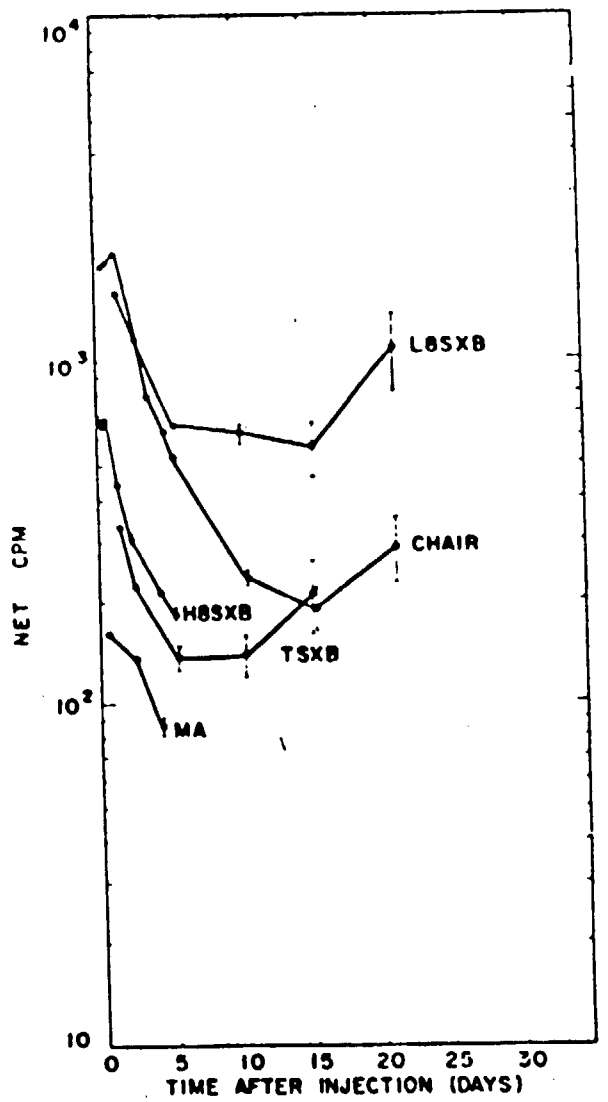


FIG. 42. COMPARATIVE NET COUNTING RATES AFTER INTRAVENOUS ADMINISTRATION OF Ra^{224} FOR VARIOUS COBAFAC COUNTING METHODS, SUBJECT RIVF2

1066236

DOE/HQ

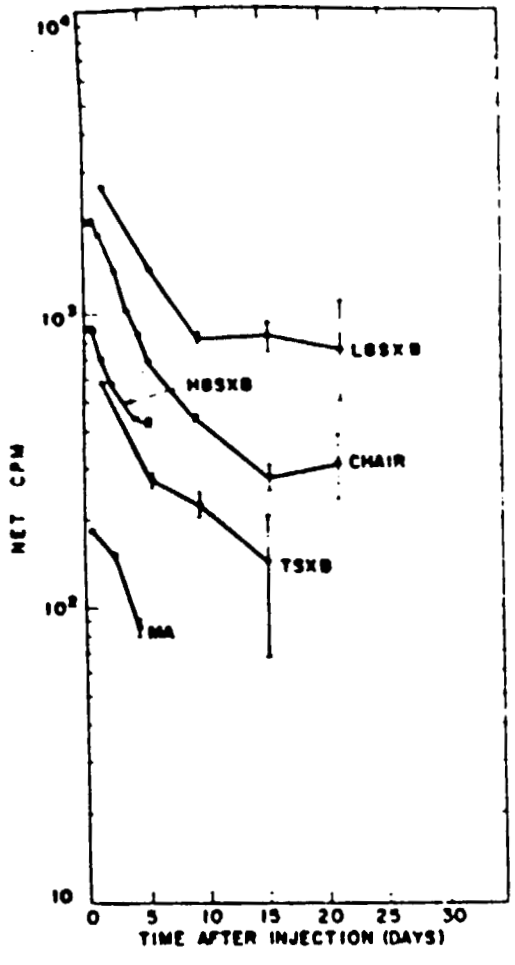


FIG 43. COMPARATIVE NET COUNTING RATES AFTER INTRAVENOUS ADMINISTRATION OF Ra^{224} FOR VARIOUS COBAFAC COUNTING METHODS, SUBJECT RIVM2

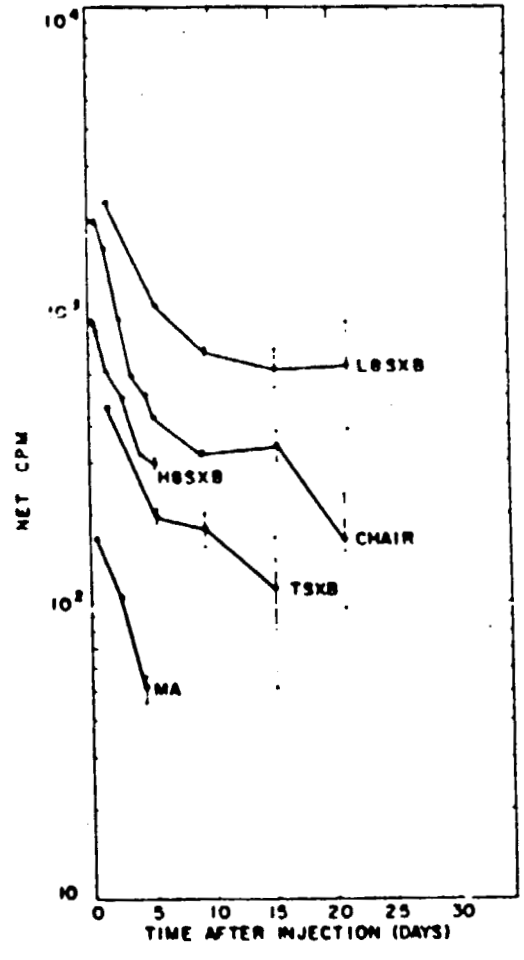


FIG 44 COMPARATIVE NET COUNTING RATES AFTER INTRAVENOUS ADMINISTRATION OF Ra^{224} FOR VARIOUS COBAFAC COUNTING METHODS, SUBJECT RIVM3

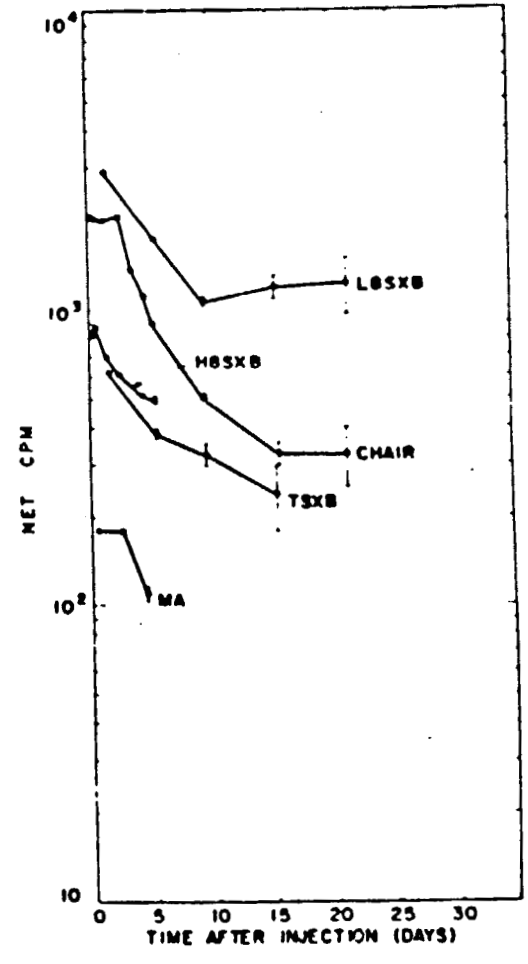


FIG 45 COMPARATIVE NET COUNTING RATES AFTER INTRAVENOUS ADMINISTRATION OF Ra^{224} FOR VARIOUS COBAFAC COUNTING METHODS, SUBJECT RIVM5

1066237

DOE/HQ

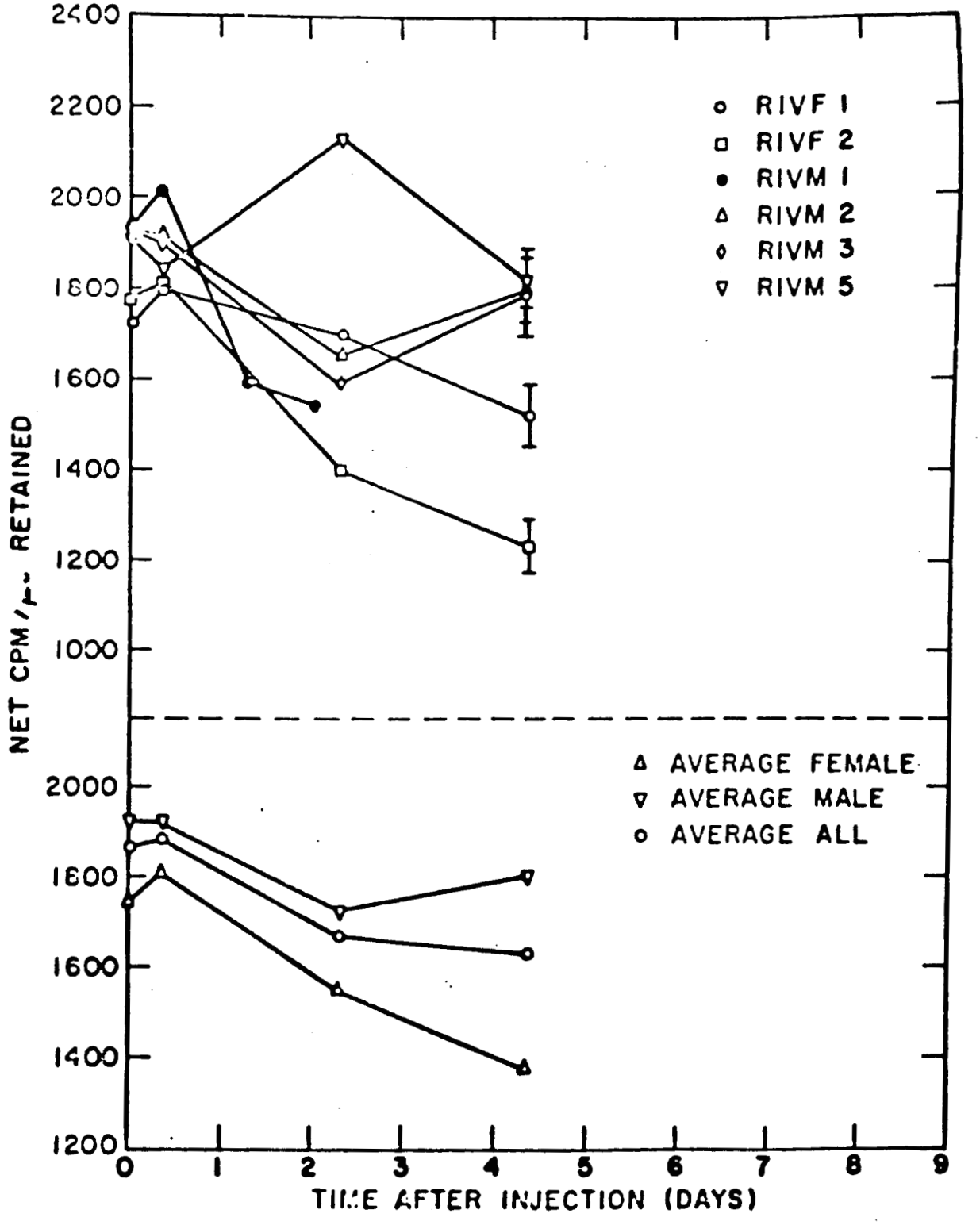


FIG 46. NET CPM/μc RETAINED FOR STANDARD CHAIR POSITION FOLLOWING INTRAVENOUS ADMINISTRATION OF Ra^{224}

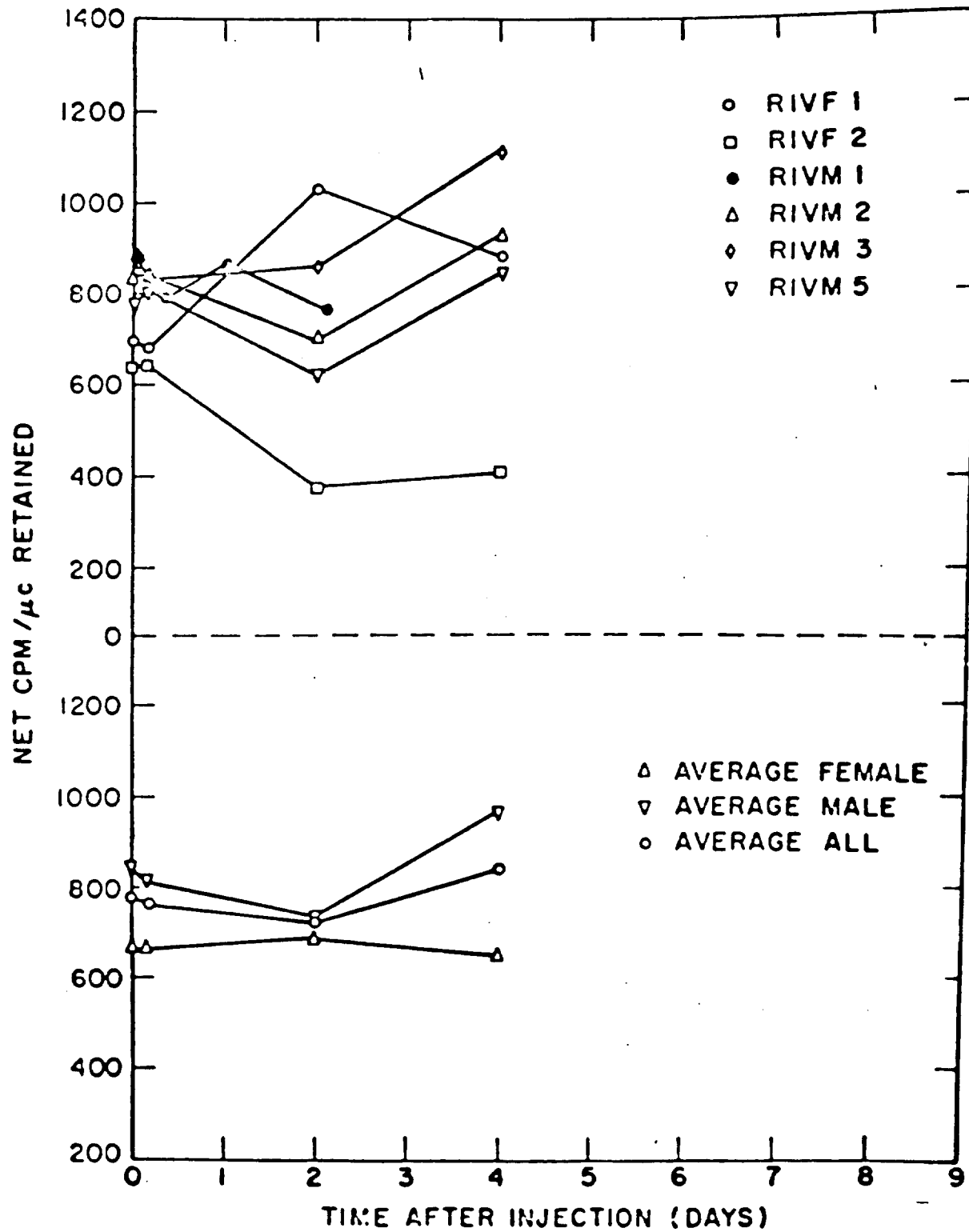


FIG. 47. NET CPM/μc RETAINED FOR H8SXB POSITION FOLLOWING INTRAVENOUS ADMINISTRATION OF Ra^{224}

1066239

DOE/HQ

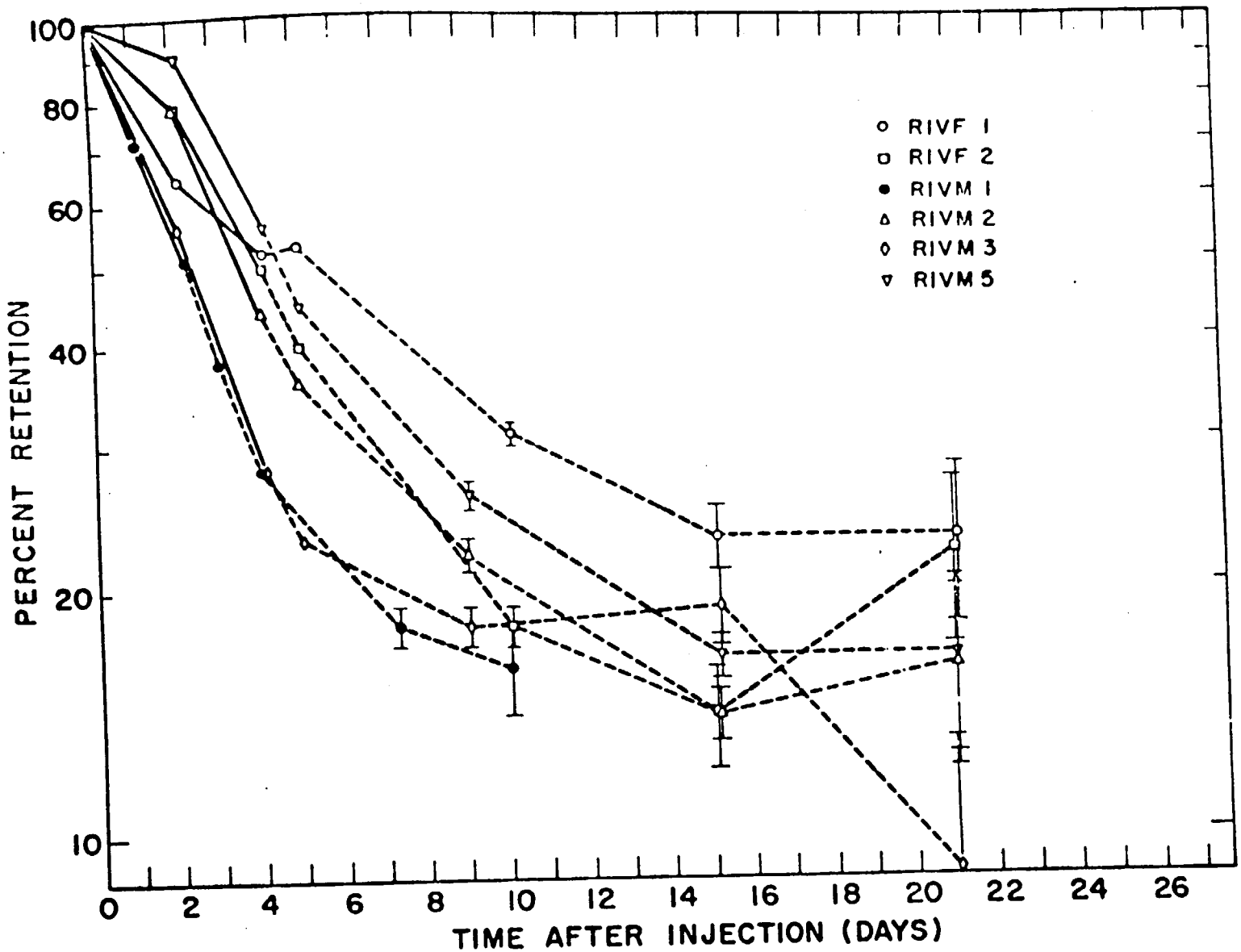


FIG. 48. RETENTION OF Ra^{226} ADMINISTERED INTRAVENOUSLY

1066240

DOE/HQ

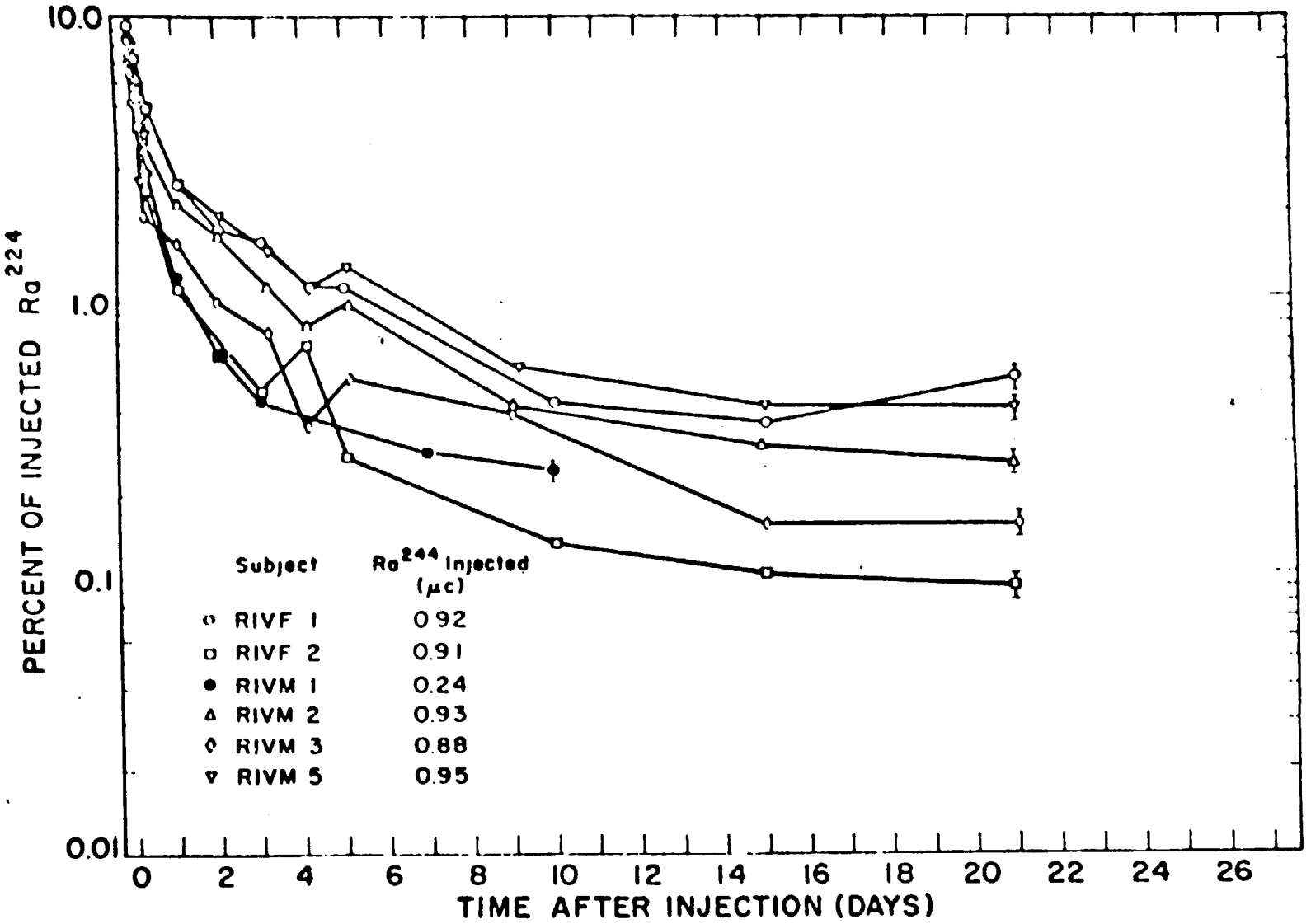


FIG. 49. Tn ACTIVITY EXTERNAL TO BODY AS PERCENT OF INJECTED Ra^{224} ACTIVITY

1066241

DOE/HQ

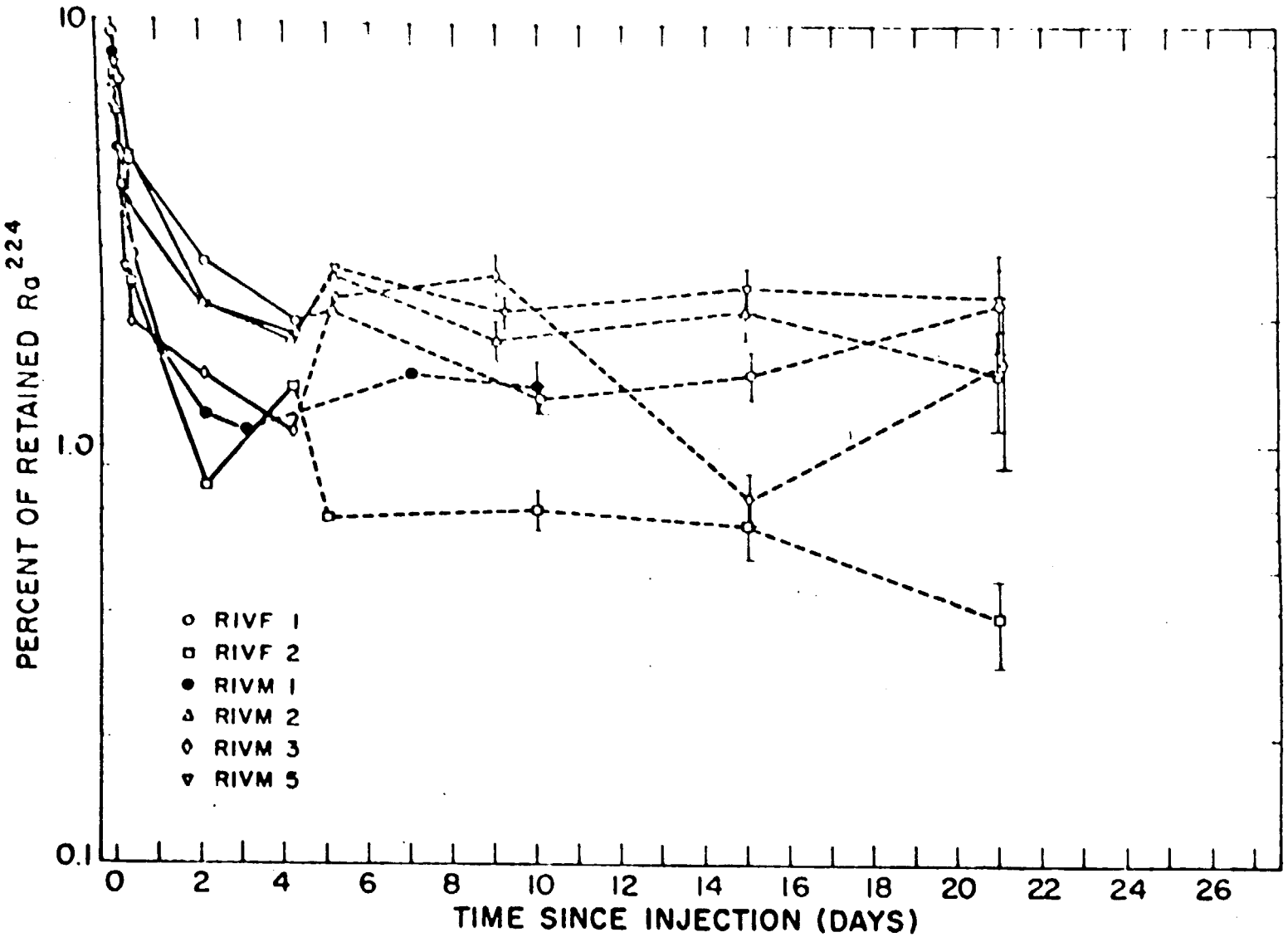


FIG. 50. Tn ACTIVITY EXTERNAL TO BODY AS PERCENT OF RETAINED Ra^{224}

1066242

DOE/HQ

deeper into bone. Figure 50, on the other hand, reflects more directly the probability that the retained Ra^{224} has become buried in bone, since the fractional Tn being exhaled has started to level off by the 4th post-injection day.

The percent of the injected Ra^{224} remaining in the total circulating blood is shown in Fig. 51. The total blood volume of each subject was estimated by assuming that it represents 8% of the total body weight. Clearance from the blood stream was rapid, there remaining < 10% within 1 hr. after injection. Analysis for Pb^{212} was also done, but complete data are not yet available. Preliminary calculations indicate that about 70% of the Pb^{212} injected was present in the total circulating blood volume 1/2 hr after injection. Parenthetically, it is of interest that these values closely parallel those obtained on a similar experiment on a dog previously reported[1].

6. Results on Th^{234} Injection Studies

Figures 52 through 56 give the net counting rates of each of 5 subjects for the various Cobafac configurations following intravenous administration of Th^{234}.

Excretion results are given in Table 30. They indicate that the predominant route of excretion is via the urine. It is interesting that the women appear to excrete less Th^{234} via feces than do the men, with a resultant urine/feces activity ratio approximately twice that of the men.

The percent retention of the Th^{234} is given in Fig. 57 and is based on excretion data. Twenty-four-hour urine samples were collected periodically throughout the study period, and were used to interpolate retention values after the 1st week.

Figure 58 shows the net counting rates in the chair configuration per μc of retained Th^{234}. A fairly pronounced redistribution in the first 2 or 3 days is indicated by the change in these values, which then remain essentially constant for the rest of the experimental period.

Figure 59 gives the counting rates per μc of retained Th^{234} in the H8SXB counting configuration. Of extreme interest is the fact that the 2 women gave a counting rate considerably higher than that of the men. The reason for this apparent sex difference is not obvious at the moment, but may be related to the relative sizes of the men and women and perhaps to the relative excretion via the feces. The same statement applies to Fig. 60, which gives the counting rates per μc of retained Th^{234} for the L8SXB position.

Figure 61 gives the percent of injected Th^{234} present in the estimated total blood volume. It is apparent that clearance of Th^{234} from blood is not as rapid as that for Ra^{224}.

1066243

DOE/HQ

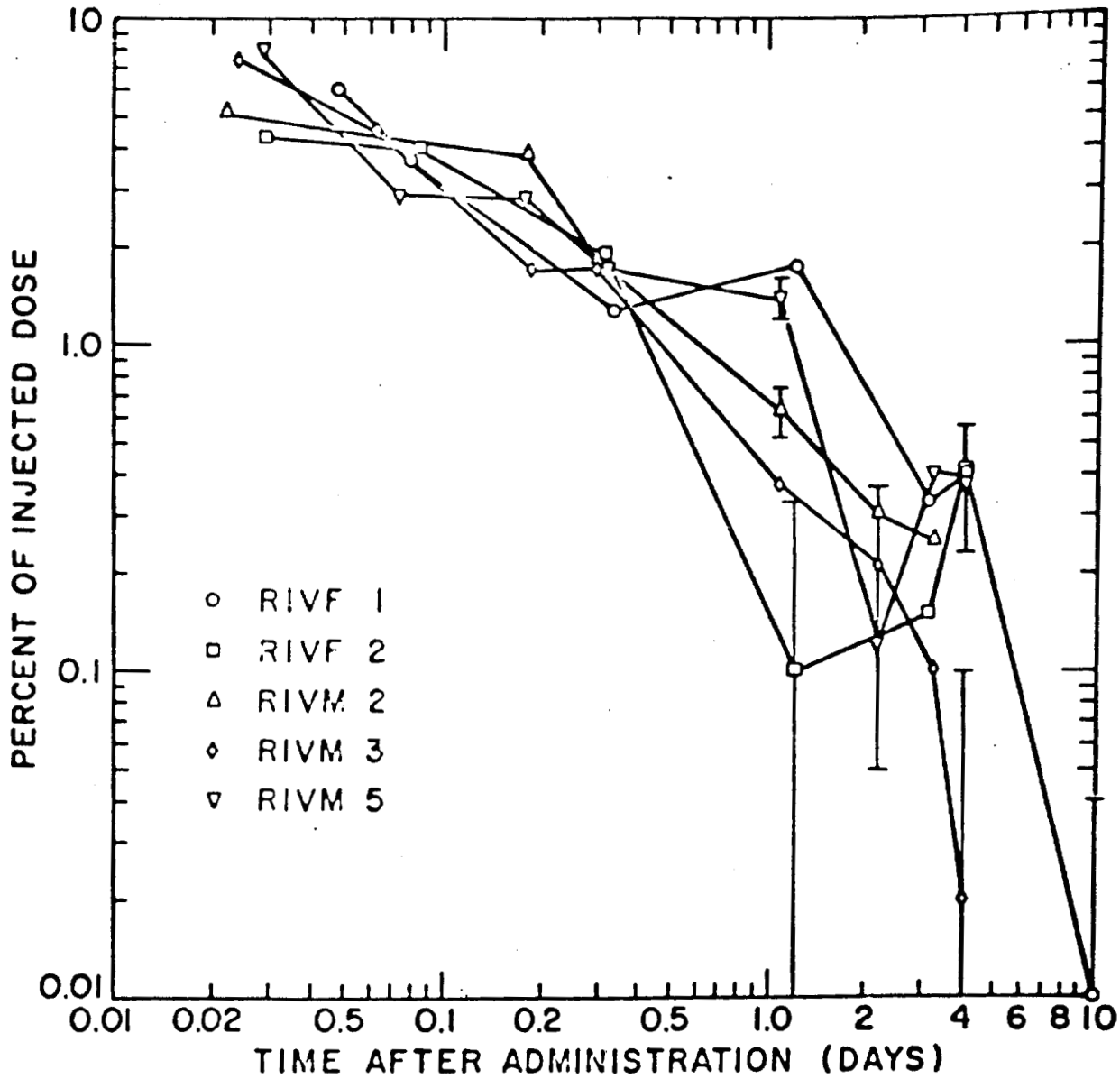


FIG. 51. Ra^{224} IN ESTIMATED TOTAL BLOOD VOLUME FOLLOWING INTRAVENOUS ADMINISTRATION

1066244

DOE/HQ

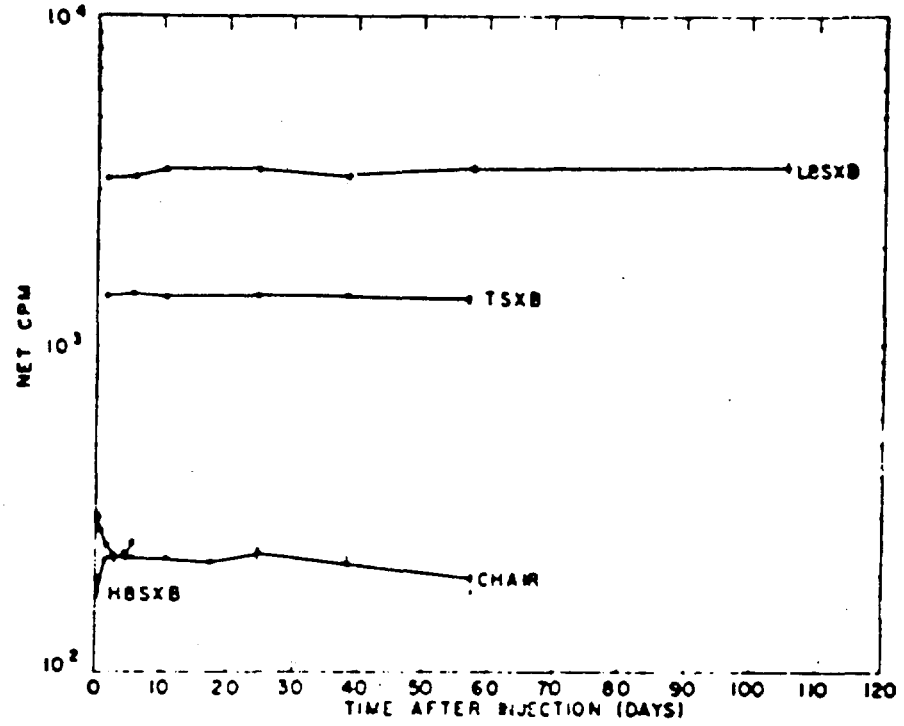
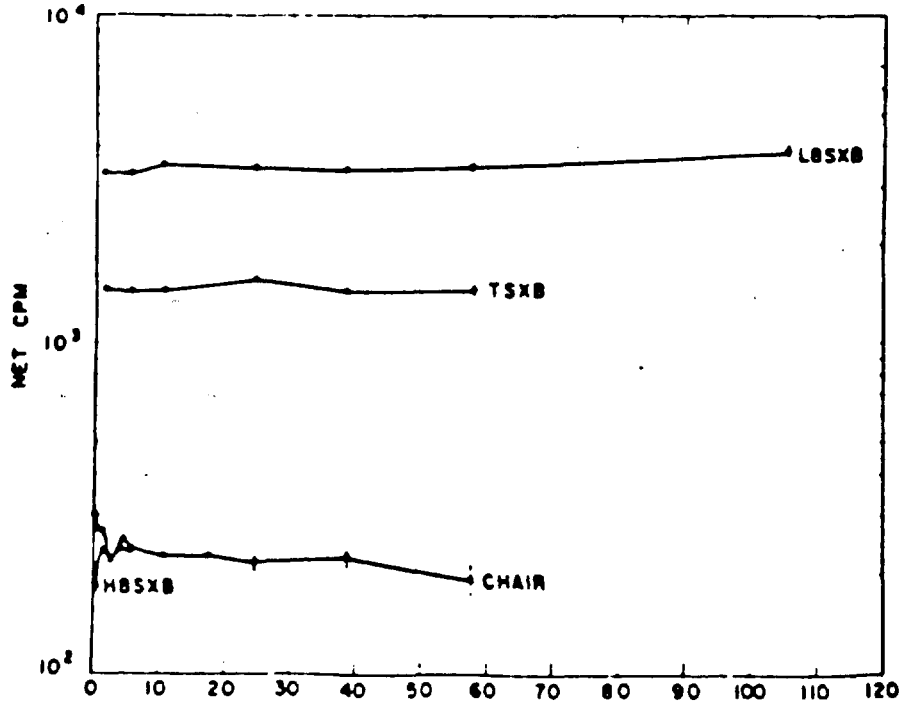


FIG 52 COMPARATIVE NET COUNTING RATES AFTER INTRAVENOUS ADMINISTRATION OF Th^{234} FOR VARIOUS COBAFAC COUNTING METHODS, SUBJECT TIVF2



1066245

DOE/HQ

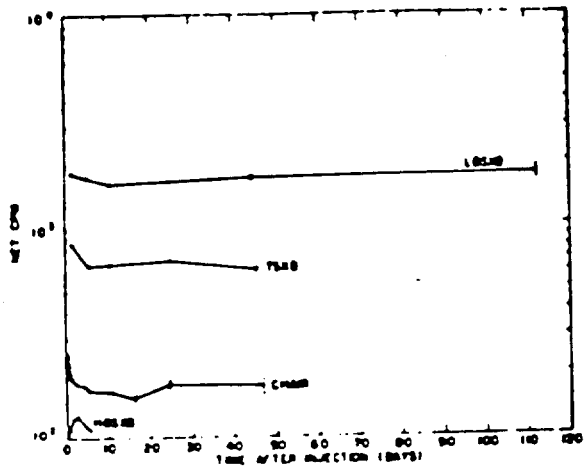


FIG 54 COMPARATIVE NET COUNTING RATES AFTER INTRAVENOUS ADMINISTRATION OF Tc^{234} FOR VARIOUS COBAFAC COUNTING METHODS
SUBJECT TYPE2

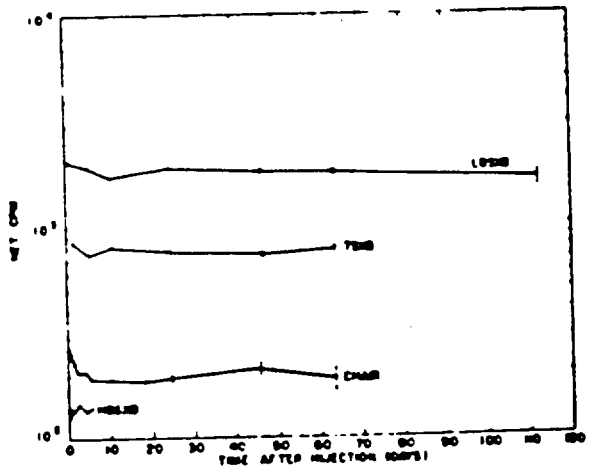
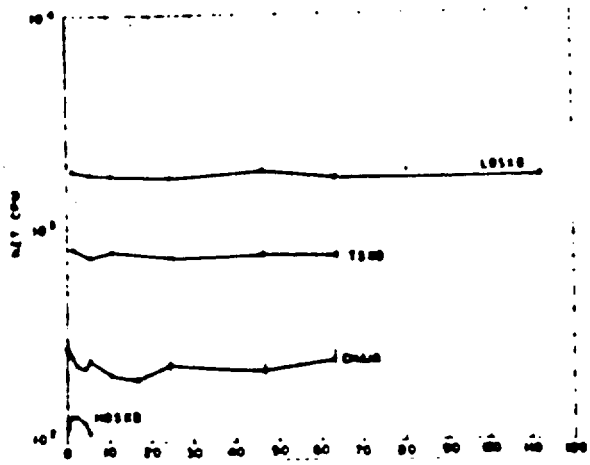


FIG 55 COMPARATIVE NET COUNTING RATES AFTER INTRAVENOUS ADMINISTRATION OF Tc^{234} FOR VARIOUS COBAFAC COUNTING METHODS.
SUBJECT TYPE3



DOE/HQ

Table 30. Excretion of Th^{234} as Percent of Injected Dose

Subject	Time after administration (days)	Cumulative urine (%)	Cumulative feces (%)	Cumulative total (%)	Ratio urine/feces
TIVM2	1	3.2	-	3.2	-
	2	3.7	-	3.7	-
	3	4.2	-	4.2	-
	4	4.5	0.38	4.9	11.8
	5	4.8	0.38	5.2	12.6
TIVM3	1	3.7	0.02	3.7	185
	2	4.6	0.24	4.8	19.1
	3	5.2	0.34	5.6	15.3
	4	5.7	0.47	6.2	12.1
	5	6.0	0.47	6.4	12.8
TIVM5	1	2.7	-	2.7	-
	2	3.4	0.10	3.5	34.0
	3	3.8	0.26	4.1	14.6
	4	4.2	0.36	4.6	11.7
	5	4.5	0.41	4.9	11.0
TIVF2	1	4.1	0.03	4.1	137
	2	4.8	0.06	4.9	80
	3	5.2	0.11	5.3	47
	4	5.4	0.20	5.6	27
	5	5.7	0.24	5.9	24
TIVF3	1	4.1	0.02	4.1	205
	2	4.9	0.10	5.0	49
	3	5.4	0.16	5.6	34
	4	5.8	0.16	6.0	36
	5	6.1	0.24	6.4	25

1066247

DOE/HQ

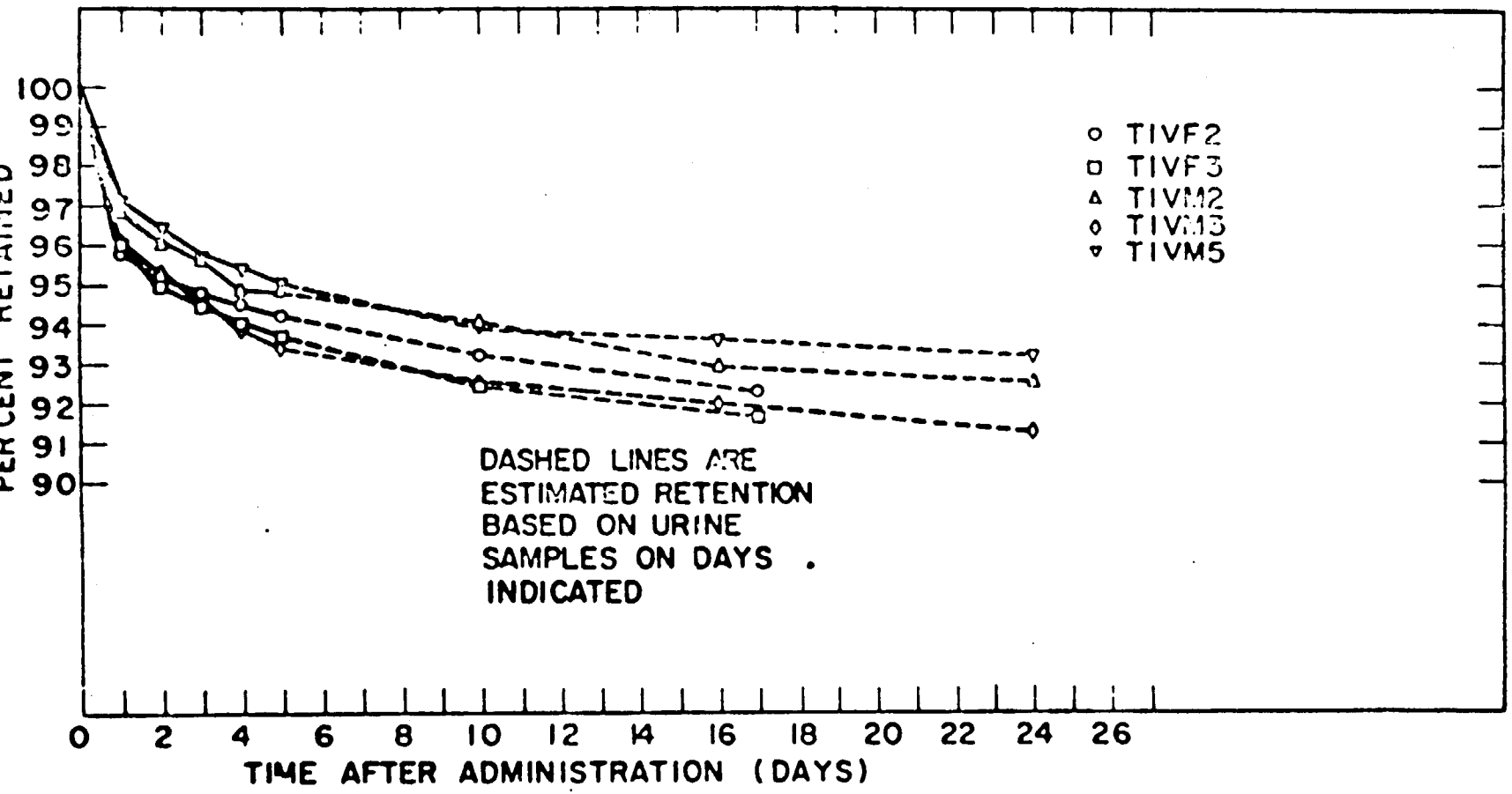


FIG. 57. RETENTION OF INTRAVENOUSLY ADMINISTERED Th^{234}

1066248

DOE/HQ

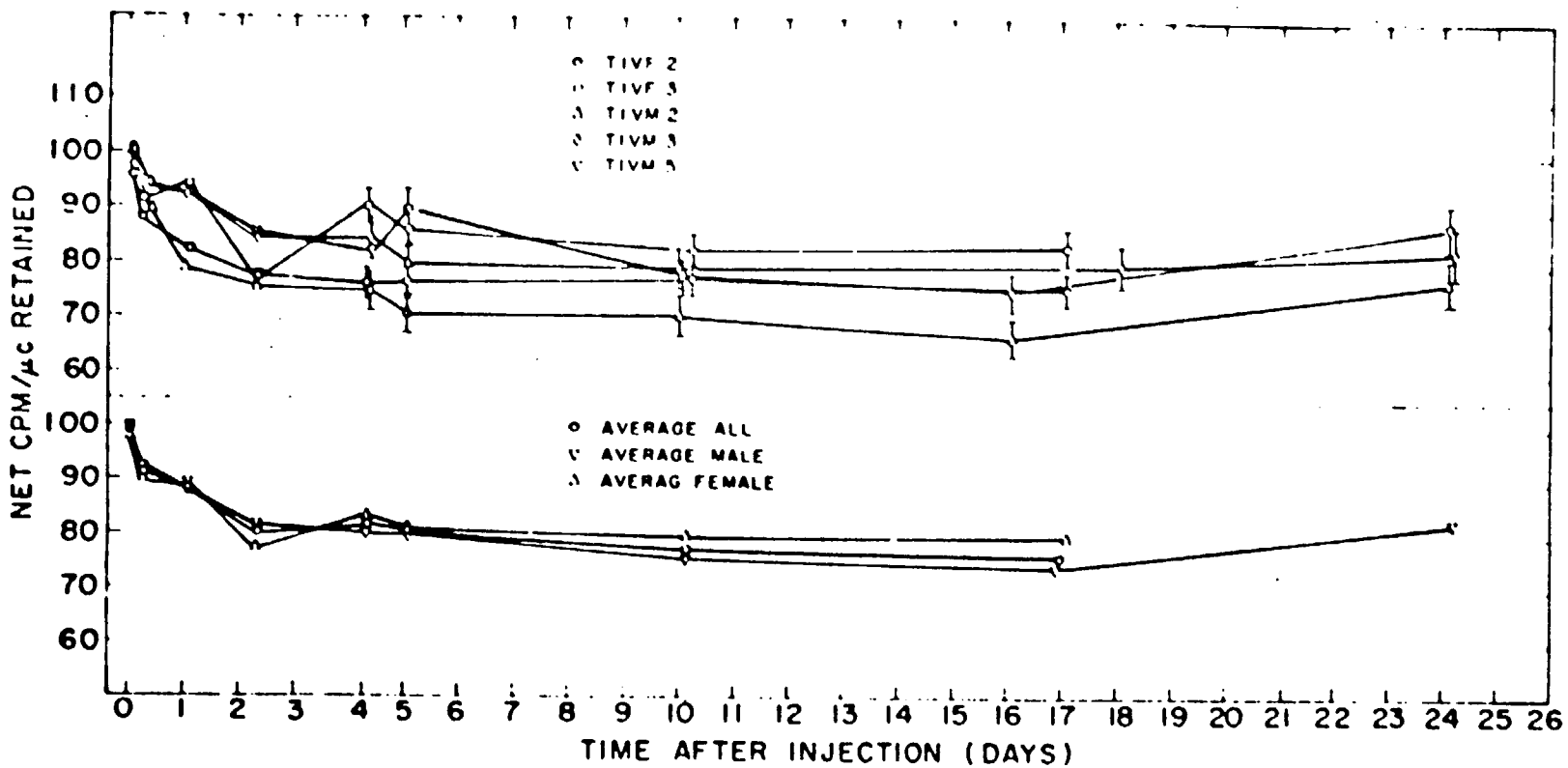


FIG. 58. NET CPM/μc RETAINED FOR STANDARD CHAIR POSITION FOLLOWING INTRAVENOUS ADMINISTRATION OF Th^{234}

1066249

DOE/HQ

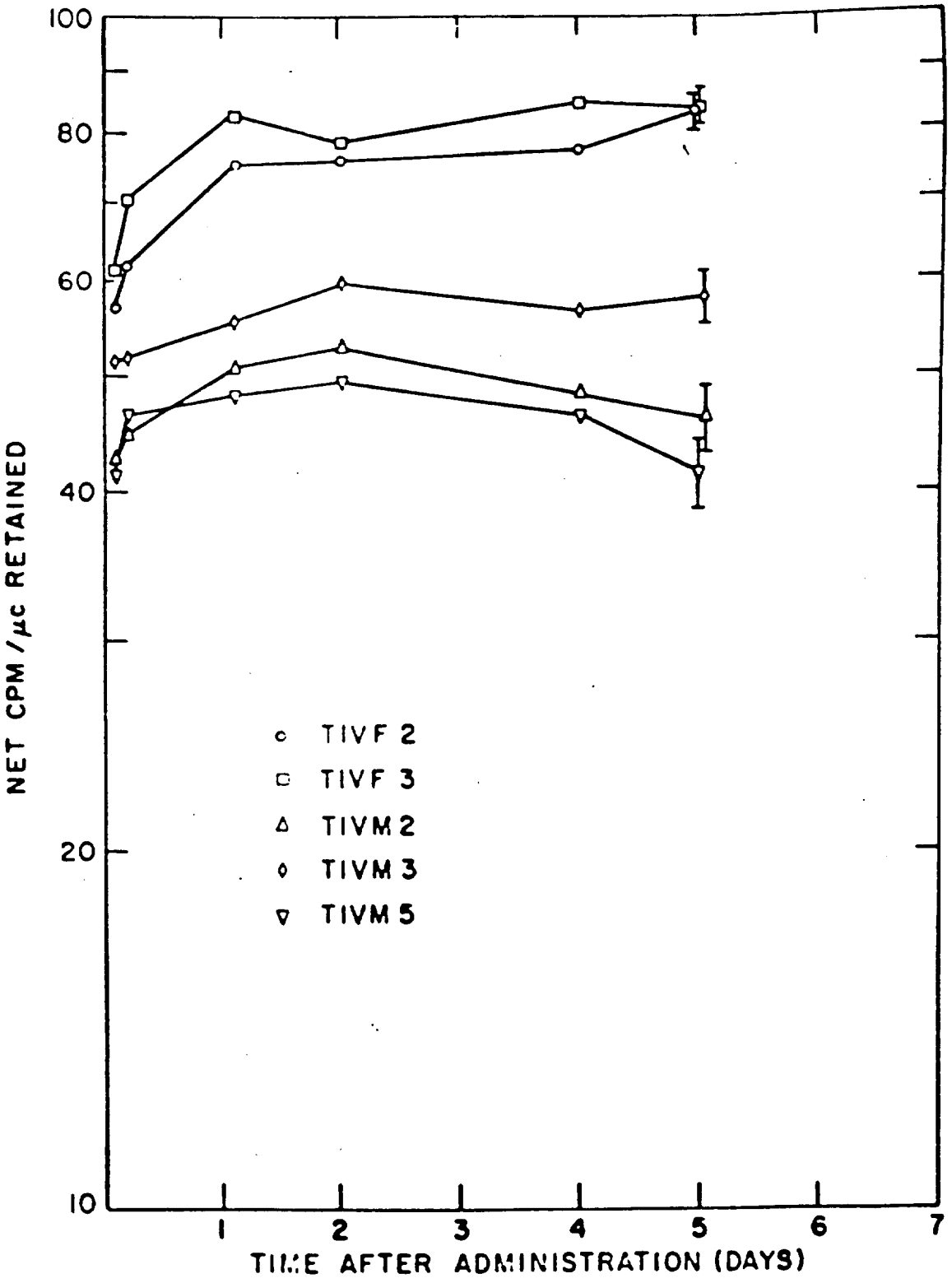
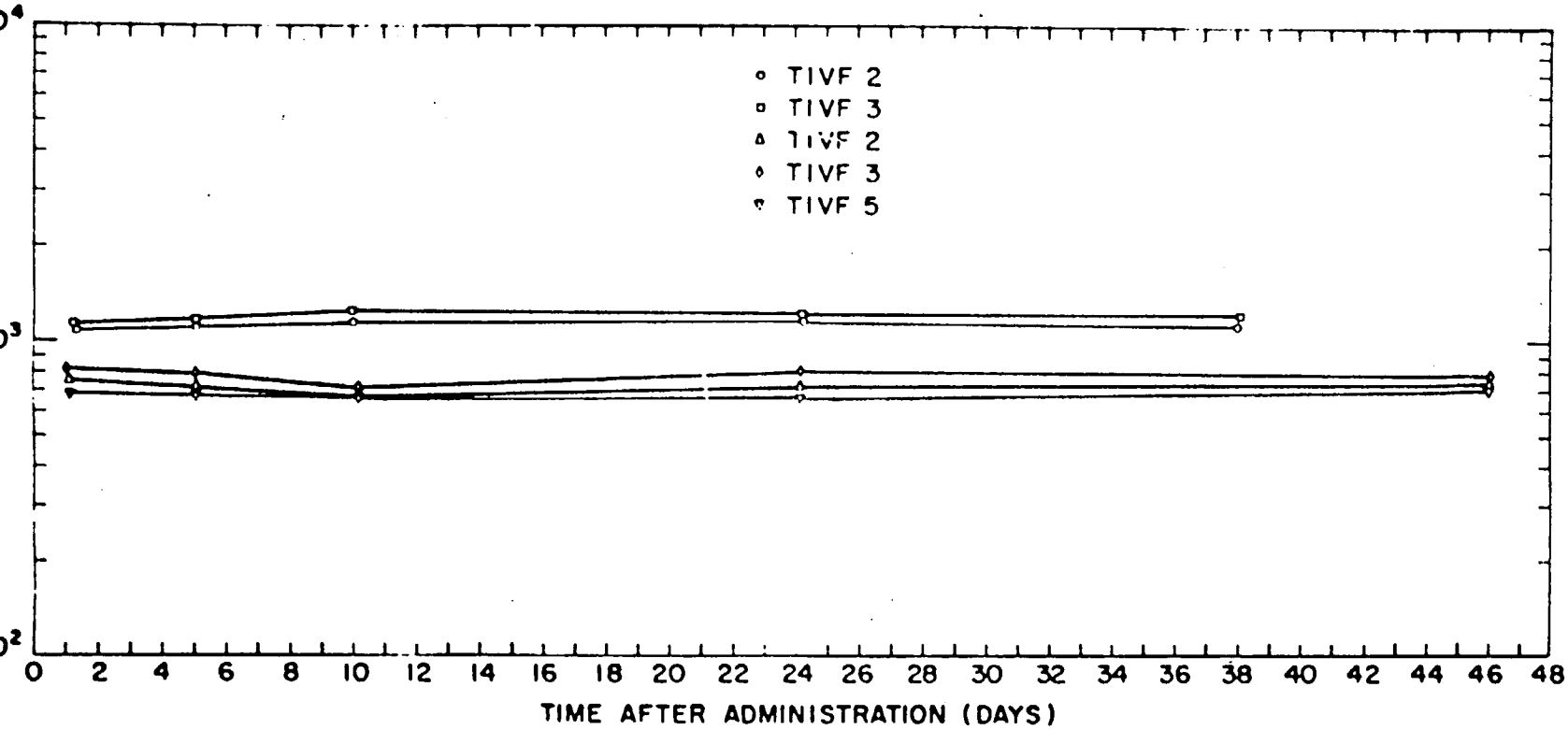


FIG. 59. NET CPM/μc RETAINED FOR H8SXB POSITION FOLLOWING INTRAVENOUS ADMINISTRATION OF Th^{234}

1066250

DOE/HQ



0. NET CPM/μc RETAINED FOR L8SX8 POSITION FOLLOWING INTRAVENOUS ADMINISTRATION OF Th^{234}

1066251

DOE/HQ

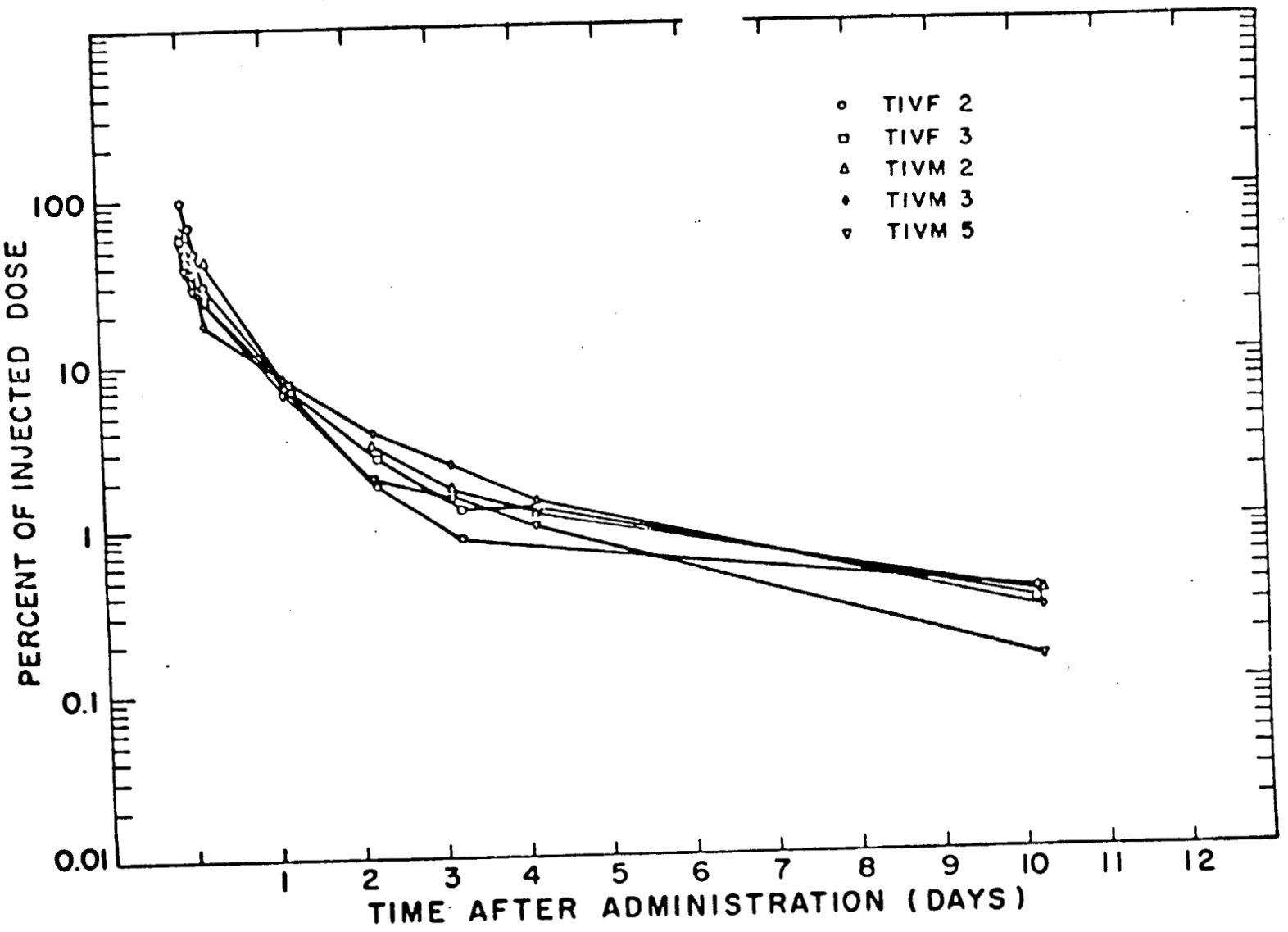


FIG. 61. Th^{234} IN ESTIMATED TOTAL BLOOD VOLUME FOLLOWING INTRAVENOUS ADMINISTRATION

10b-b-252

DOE/HQ

7. Uptake of Ra^{224} from Mock Dial Paint Administered Orally. Preliminary Results

Subject RPOM1 was given a capsule of dial paint containing ~2.45 μc of Ra^{224} with daughters in transient equilibrium. The capsule of paint was prepared essentially as described in the 1963 Progress Report.

Uptake of Ra^{224} from the gastro-intestinal tract was tentatively estimated at 12% of the administered dose, based on the calibration data obtained from the Ra^{224} injection studies.

On the 4th day after ingestion both chair and H8SXB measurements gave values of 5% for the retained body burden, indicating little, if any, residual activity remaining in the gut. Total urine activity for the first 4 days was ~0.3% of the administered dose, while total fecal excretion amounted to ~99% of the dose given. Therefore, retained activity (as measured by chair and H8SXB) and excreted activity gave a sum of ~104% of the dose administered.

Figure 62 shows the net counting rates in the various Cobafac configurations for RPOM1. Figure 63 shows the activity in the estimated total blood volume, and Fig. 64 shows the thoron activity external to the body as calculated from breath sampling measurements. Further evaluation of these uptake parameters is in process.

8. Uptake of Th^{234} from Mock Dial Paint Administered Orally. Preliminary Results.

Subject TPOM1 was given a capsule of dial paint containing 120 μc of Th^{234}. Preparation of the capsule required a modification in the separation of Th^{224} from U^{238} slag, because the amount of activity that could be obtained using the procedure described in the 1963 Progress Report was limited by the capacity of the anion-exchange resin column. A rapid and convenient solvent extraction method was developed for separating Th^{234} from large amounts of slag. In this method, the slag is dissolved in concentrated HNO_3. This solution is centrifuged to remove undissolved material and extracted several times with diethyl ether. The organic phase, containing most of the U^{238}, is back-washed with 4 M HNO_3 to recover any Th^{234} that extracted. The Th^{234}, contained in the aqueous phase with a small amount of U^{238}, is further purified using the anion-exchange resin procedure.

Uptake of Th^{234} from the gastro-intestinal tract is estimated at $\leq$ 0.03% of the administered dose, based on the calibration data obtained from the Th^{234} injection studies. Initial γ measurements in the SXB configuration showed the expected effects of scattering and absorption of γ rays from the activity in the gastro-intestinal tract. These measurements were not useful indicators of uptake while there remained significant activity in the G.I. tract. At 13 days after administration, however, when the chair measurements indicated $\leq$ 0.2 % of the ingested dose was present in the whole body, the L8SXB counting rate

1066253

DOE/HQ

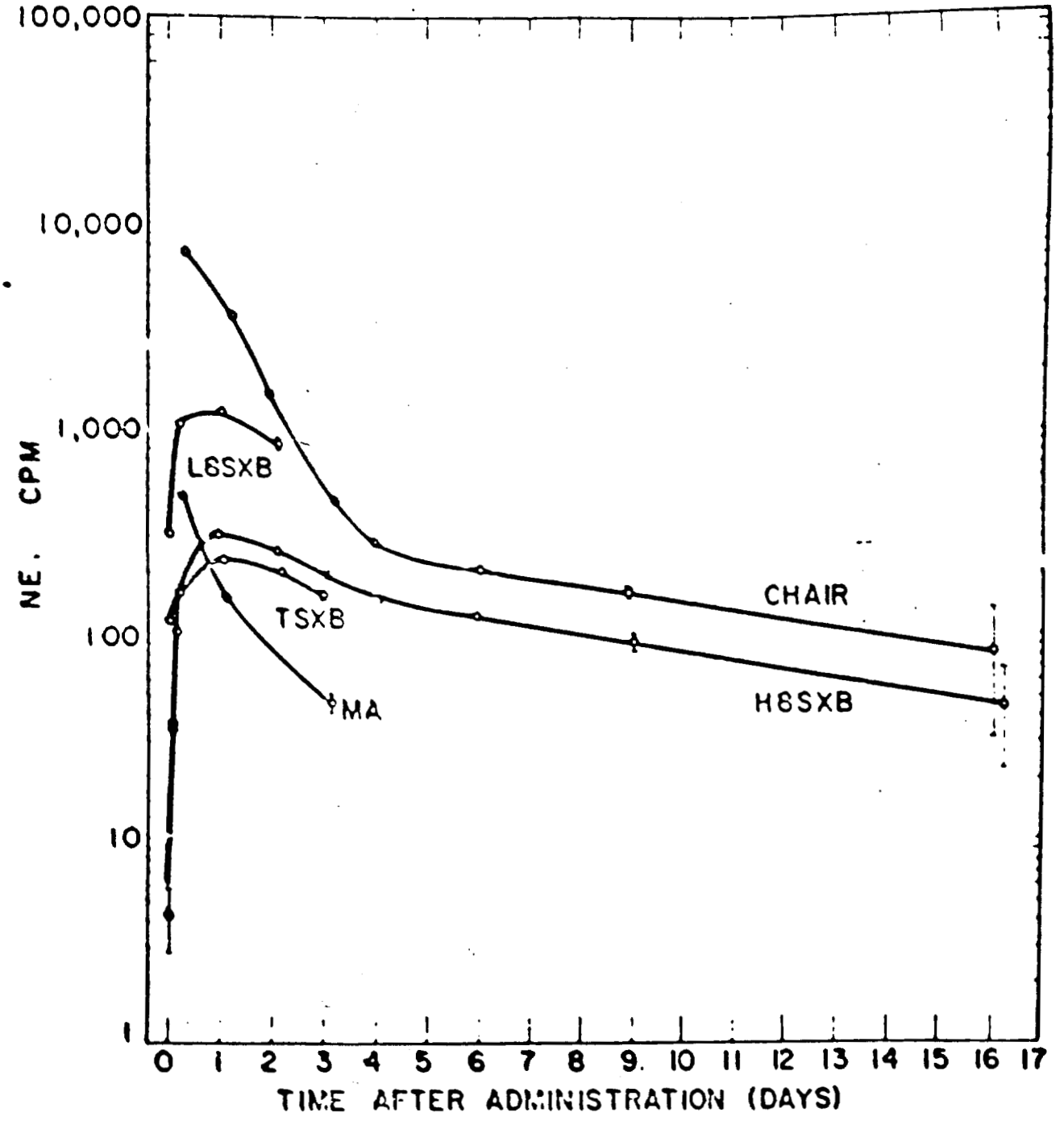


FIG. 62. COMPARATIVE NET COUNTING RATES AFTER ORAL ADMINISTRATION OF Ra^{224} FOR VARIOUS COBAFAC COUNTING METHODS, SUBJECT RPOM I

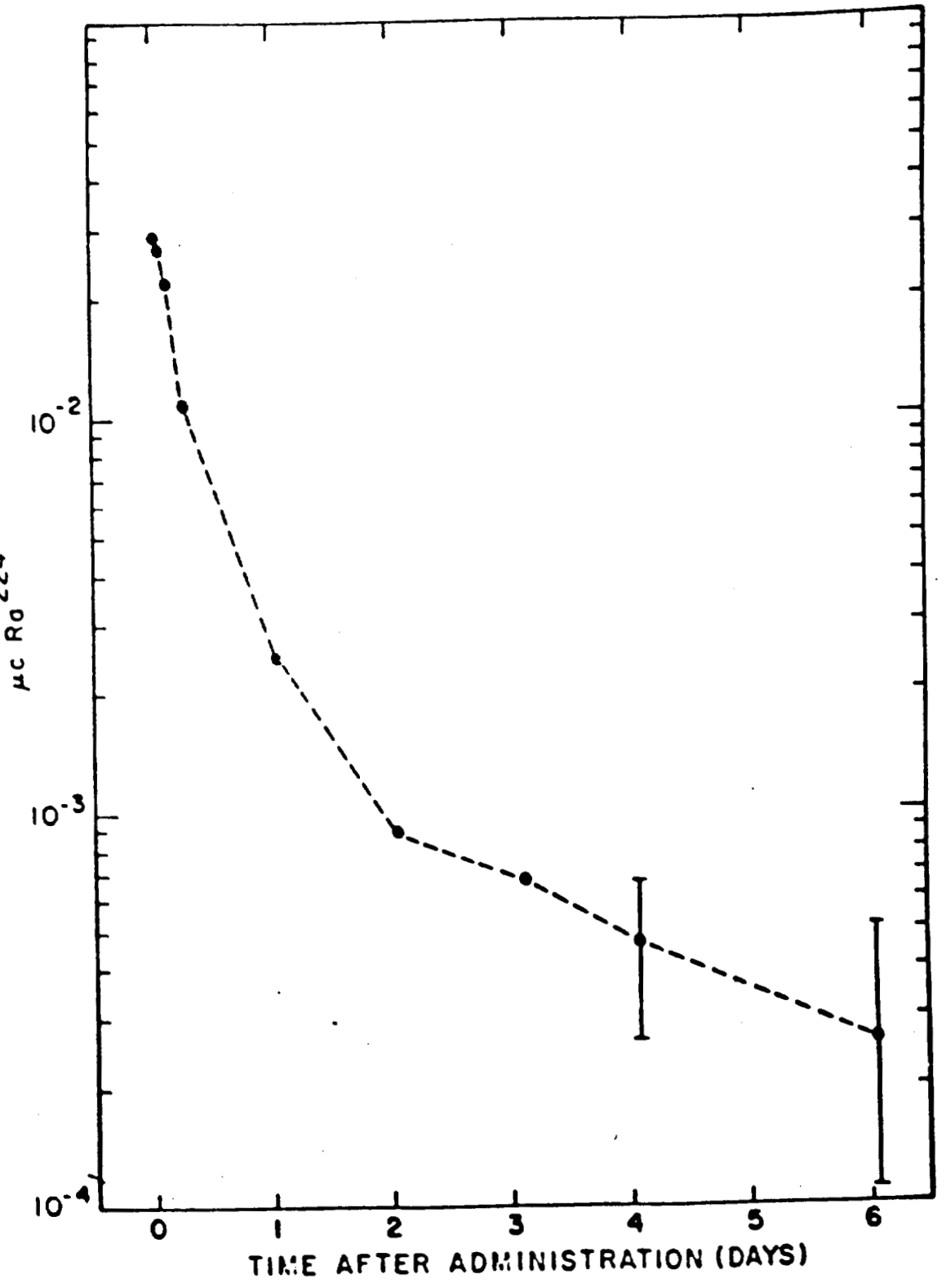


FIG. 63. Ra^{224} IN ESTIMATED TOTAL BLOOD VOLUME FOLLOWING

1066255

DOE/HQ

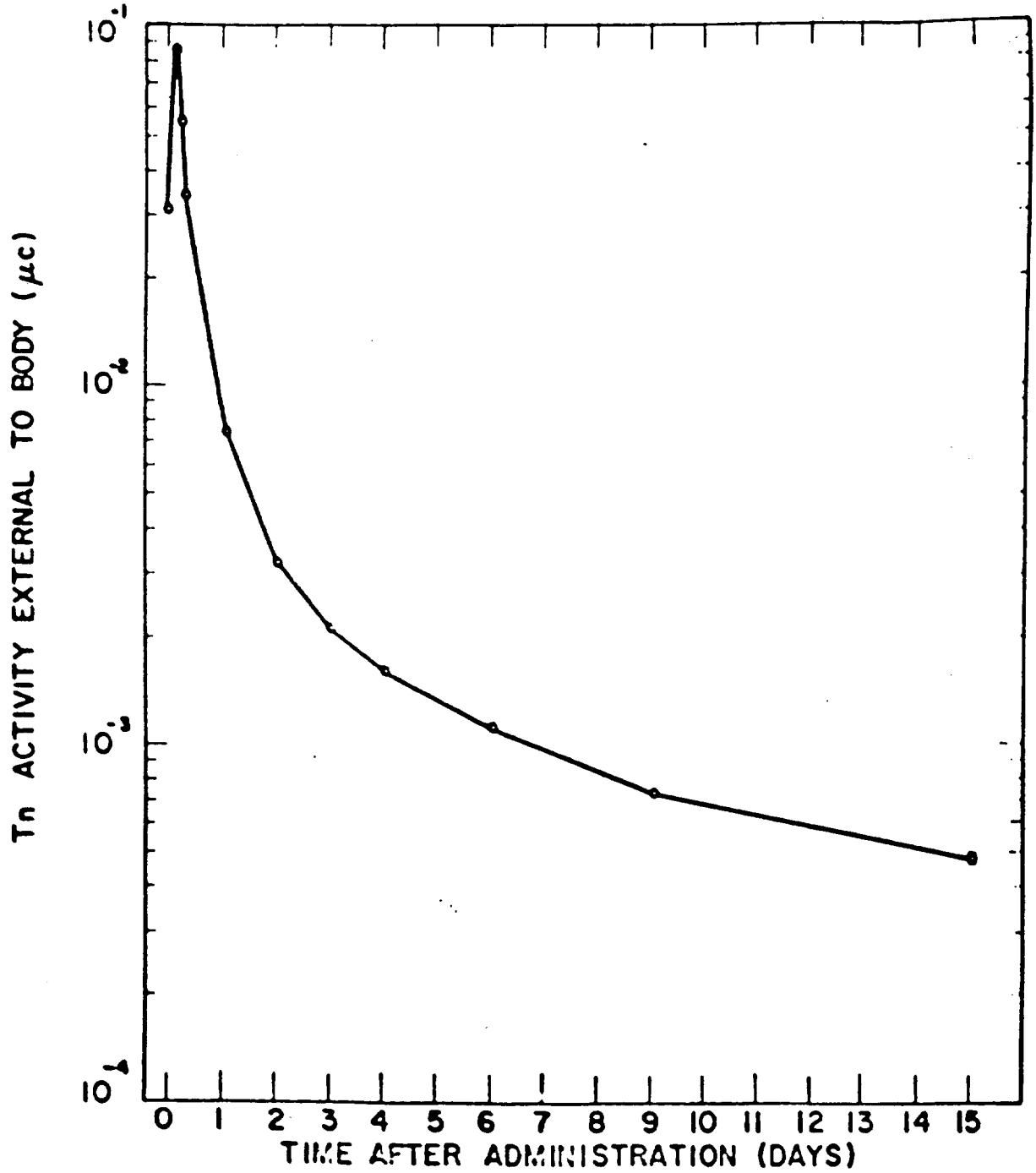


FIG 64. Tn ACTIVITY EXTERNAL TO BODY AFTER ORAL ADMINISTRATION OF Ra^{224}, SUBJECT RPOMI

106625b

DOE/HQ

of subject TPOM1 was not significantly different from his counting rate prior to administration of the dial paint.

Approximately 99% of the ingested activity was excreted in the feces by the 6th day after administration. No activity was found in urine or blood samples within the errors of measurement.

The Th/Ra uptake ratio based on the pilot studies is tentatively estimated at $\leq 2.5 \times 10^{-3}$. Plans to complete the second phase of the gut uptake study are underway. It is intended to administer a mock dial paint capsule incorporating both Ra^{224} and Th^{234} to 3 males and 3 females.

(C. J. Maletskos, H. P. Anderson, A. G. Braun, J. F. Byrum, S. D. Clark, M. M. Costello, E. D. Dillon, J. A. Foley, J. E. Gary, A. T. Keane, J. A. Kelley, M. Lubin, H. F. Osborn, M. M. Shanahan, N. C. Telles)

1066257

DOE/HQ