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DISTRIBUTION AND EXCRETION OF TECHNETIUM IN HUMANS*

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Abstract—Widespread use of ^{99m}Tc as a tracer in medicine and large scale separation of ^{99}Tc from fission product waste require that adequate knowledge of the metabolic properties of technetium be known so that realistic exposure limits can be imposed for the isotopes of interest. The present paper discusses a metabolic experiment using ^{95m}Tc (60 day $T_{1/2}$) and ^{96}Tc (4.3 day $T_{1/2}$) in which long-term excretion, retention and localization of these isotopes were measured using whole-body counting techniques. Following intravenous and oral administration both urinary and fecal excretion rates were measured and mathematical models were derived for technetium elimination. The latter should be helpful in estimating body burdens of the weak beta-emitting ^{99}Tc following inadvertent exposure.

1. INTRODUCTION

THE USE of technetium isotopes in both medicine and metallurgy has recently stimulated interest in the metabolic behavior of this element following intake into the body. ^{99m}Tc which decays by isomeric transition (gamma-ray emission) and has a half-life of 6 hr has found widespread use in biology and medicine both as a tracer and as a diagnostic tool in nuclear medicine. ^{99}Tc which decays by beta emission and has a half-life of 2×10^5 yr is produced in relatively high yield in the fission of uranium-235 and plutonium-239. It is present, therefore, in rather high concentrations in the fission product waste solutions which result from the chemical processing of reactor fuels. ^{99}Tc is currently being separated in kilogram quantities from such wastes at the atomic works near Richland, Washington.

In the event of an inadvertent exposure of plant personnel to ^{99}Tc, measurement of excreta would provide the best means of estimating body deposition, since its decay is not accompanied by gamma-ray emission and therefore cannot be detected by whole-body counting techniques. Technetium metabolism experiments have been performed with humans using the 6.0-hr ^{99m}Tc,[1] but due to the short half-life of this isotope, the duration of the experiments have been 3 days or less. In such a short time period one cannot accurately predict the long-term localization or retention of technetium in any particular organ of the body with any degree of certainty. This information is required to assign exposure limits for personnel who are engaged in the handling of technetium isotopes.

Accidental exposure can lead to deposition of the radioisotope in the body by both inhalation and ingestion. It is therefore of interest to determine the differences, if any, which result in the localization and subsequent metabolic behavior of technetium following oral and intravenous administration. Intravenous administration would simulate the behavior of that portion of the technetium which is rapidly solubilized in the lung and enters the blood stream a short time following exposure. Clearly, neither oral or intravenous administration can simulate the

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metabolic behavior of technetium in the lung which is only slightly solubilized.

The present study was undertaken to measure the long-term retention and localization of technetium in humans following both oral and intravenous administration, and to derive mathematical models for the elimination of technetium in the excreta.

II. METHODS

The technetium isotopes used in this experiment were ^{95m}Tc ($T_{1/2} = 60$ days) and ^{96}Tc ($T_{1/2} = 4.3$ days). Each isotope decays by electron capture and subsequent gamma-ray emission. The isotopes were prepared by Oak Ridge National Laboratory using high-energy proton irradiation of 95 per cent enriched ^{96}Mo metal. The technetium was separated from the irradiated molybdenum at the Volk Radiochemical Co., Chicago, Illinois, using solvent extraction techniques and was ultimately prepared as sodium pertechnetate in sterile water.

Pertechnetate was chosen as the chemical form in administering the technetium in that this is the most common chemical form of the element currently being used in medical and biological applications, and is the final chemical form in which technetium appears following its purification from fission product wastes. It seemed probable, therefore, that in the event of an accidental release of technetium, its chemical form would be as pertechnetate.

Localization and distribution of the technetium within the body was followed using a shadow shield whole-body counter.[2] Briefly, the counter consists of 400 lead bricks arranged such that a gamma-ray resulting from background cannot directly enter the detector, but a person can be moved past the detector on a movable bed propelled by a ball-bearing screw and electric motor. A 4-in. thick by 9⅜-in. diameter NaI(Tl) crystal is used as the detector and the pulses from this crystal are analyzed by a 512-channel multichannel analyzer

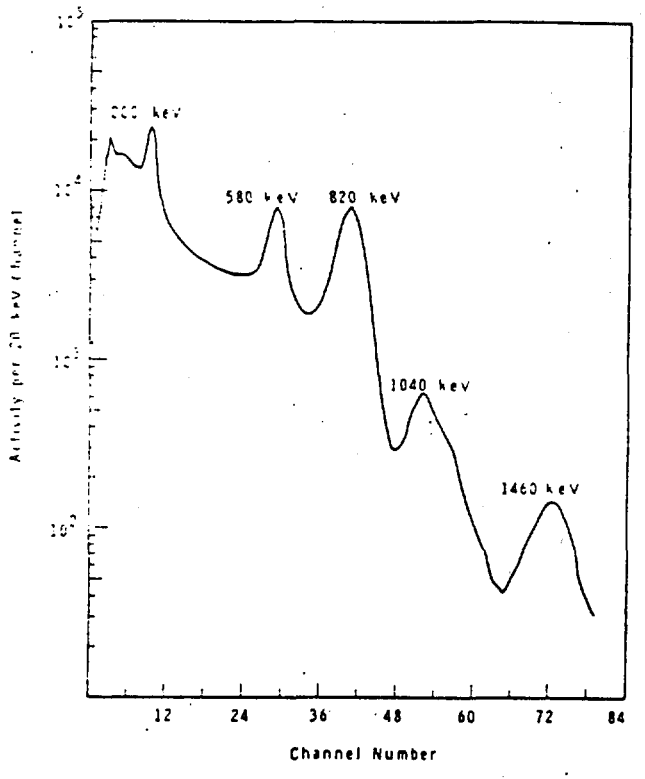

Fig. 1. Gamma-ray spectrum of subject following administration of $^{96}Tc + {}^{95m}Tc$.

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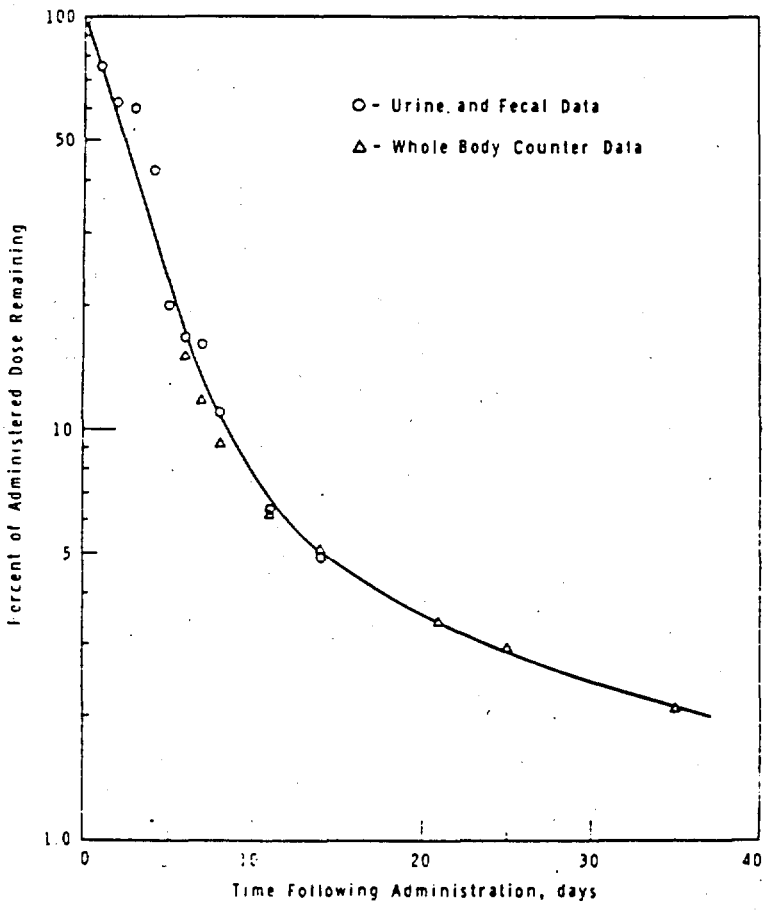

Fig. 2. Per cent original dose of ^{95m}Tc remaining following intravenous administration.

A slit system was employed which covered the majority of the large crystal with 2 in. of lead except for a 1-in. wide slit. This permitted differential scanning of the subject as he traveled under the crystal.

Figure 1 shows a representative gamma-ray spectrum of a subject following administration of the technetium isotopes. The characteristic gamma-ray photons of ^{95m}Tc occur at 0.201, 0.570 and 0.810 MeV while those of ^{96}Tc occur at 0.771, 0.842 and 0.806 MeV. The sum peak at 1.040 MeV is the result of gamma–gamma cascades in the decay of ^{95m}Tc, while the peak at 1.460 MeV arises from the ^{40}K present in all human beings.

Following administration of the technetium, total urine and feces were collected from each subject for a period of 8–10 days. During the first 3 days the distribution and translocation of the technetium was such that the whole-body counter could not be directly calibrated to give technetium retention. Instead, excretion analysis was used to determine body retention during this time by subtracting the measured technetium in the excreta from that in the originally administered dose. Between 3 and 8 days following administration, the whole-body counter results were normalyzed to the retention determined by excretion analysis and after 8 days the whole-body counter was used to measure the retention. Figure 2 shows the good agreement between technetium retention as determined by whole-body counting and subsequent excretion analysis.

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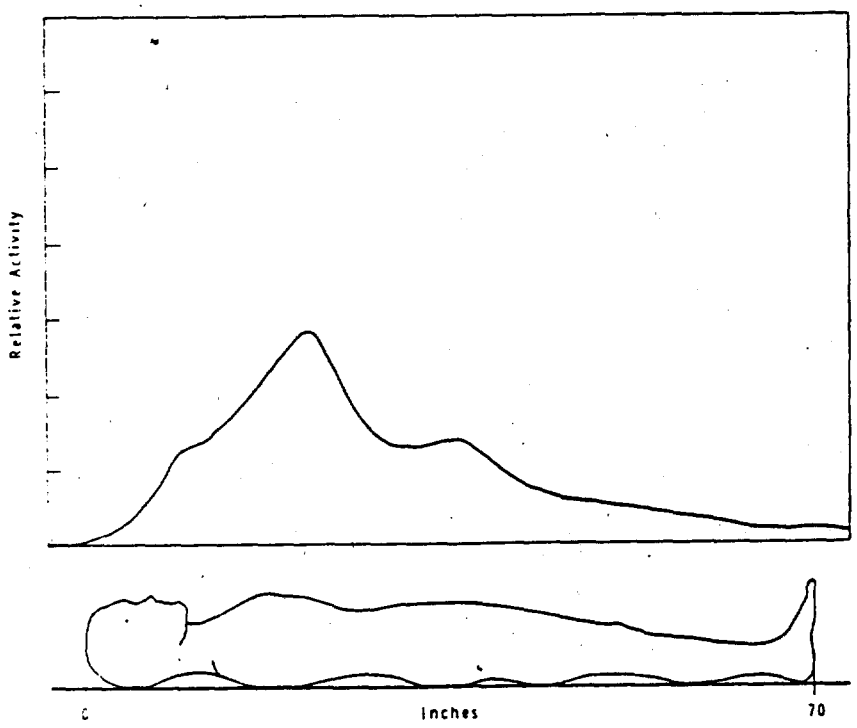

Fig. 3. Subject 10 min post intravenous injection.

The excreta samples collected from each of the subjects were counted beneath the large NaI (Tl) crystal in a fixed geometry and the per cent of the administered dose excreted was determined by comparing the counting rate of a standard counted in an identical fashion. In each instance the standard error of counting never exceeded 5 per cent and usually was less than 3 per cent. Blood and saliva samples were counted in a NaI (Tl) well-type scintillation counter and the per cent of the administered dose present was again determined by comparing the counting rates of the sample and a standard.

III. SUBJECTS

The isotopes were administered as the pertechnetate ion to eight normal human volunteers, ages 22–43 yr. Initially, 20 μc of ^{95m}Tc and 60 μc of ^{96}Tc were administered to the patients. Four subjects received an oral dose after an overnight fast, while the remaining four subjects received the dose intravenously. For the first week, subjects were hospitalized at the Clinical Research Center of the University of Washington Hospital. Samples of plasma, sweat, tears and intestinal mucosa were collected. After the first week, subjects were allowed to collect specimens at home. Observations were made for a period of 60 days on some subjects. Whole-body counts of the subjects prior to administration of the technetium isotopes showed only the presence of ^{137}Cs and ^{40}K, and none of the people had any history of contact with radioactive isotopes prior to the experiment.

IV. RESULTS AND DISCUSSIONS

4.1. *Localization and distribution of technetium*

Figures 3–6 show the distribution of technetium in humans with time following both oral and intravenous administration. In the case of intravenous administration, the technetium has already begun to localize in the area of the bladder as soon as 10 min after injection. Two hours following administration a distribution which was to become characteristic for all of the subjects regardless of administration route had occurred. The technetium had localized in

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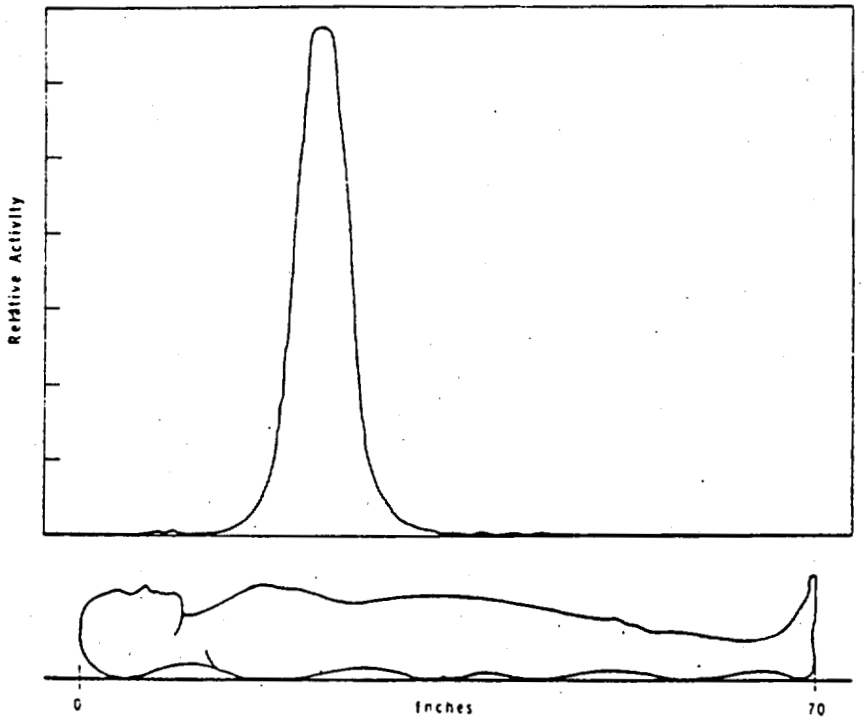

Fig. 4. Subject 10 min post oral administration.

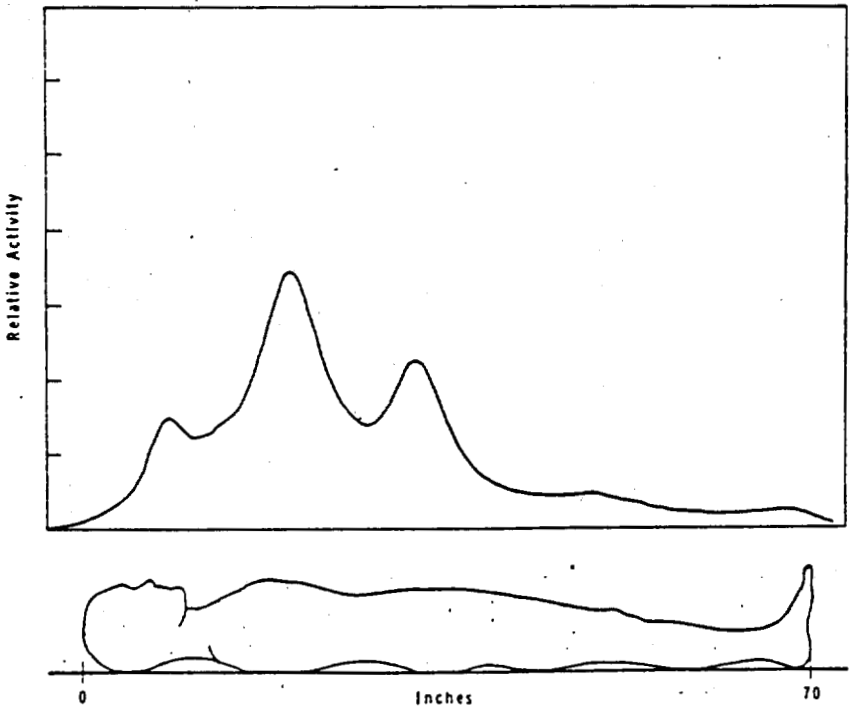

Fig. 5. Subject 2 hr post intravenous injection.

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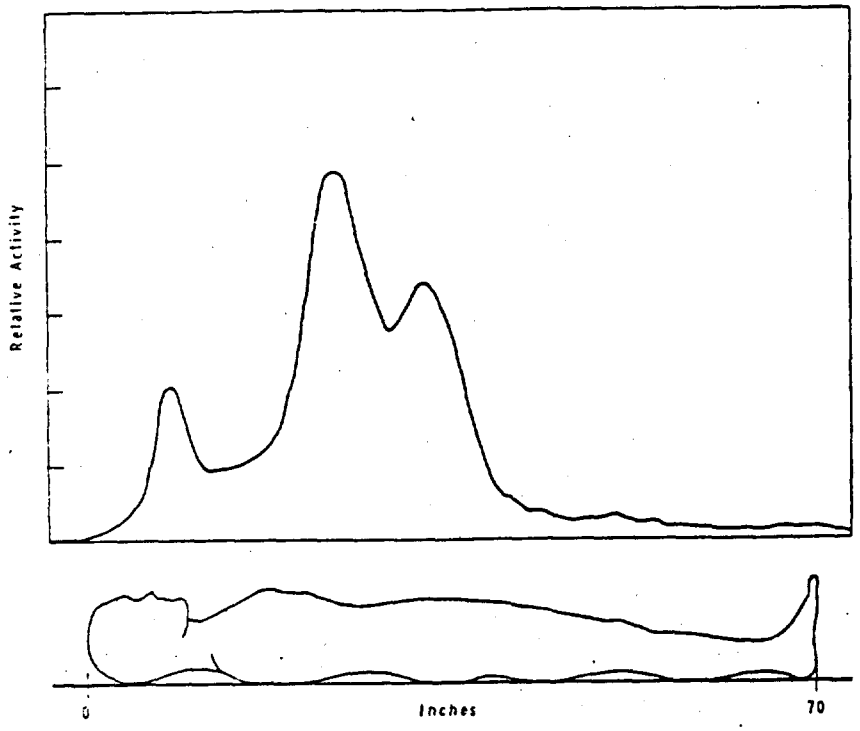

Fig. 6. Subject 2 hr post oral administration.

relatively large concentrations in the region of the salivary-thyroid glands, stomach, liver and bladder. The specific activity of the saliva itself was exceptionally high, approaching 95 per cent of the administered dose per liter of saliva some 2–3 hr following administration. After oral or intravenous doses, the saliva contained 10 to 30 times the concentration of technetium in the plasma. This concentration gradient was maintained for many days, although the total amount in the salivary glands was small after the first day. It was not possible to accurately measure the thyroid concentration of pertechnetate in this experiment due to the counting arrangement employed. The proximity of the thyroid and salivary glands gave rise to the activity peak in the area of the head as seen in Figs. 5–6. The rapid turnover of technetium in the salivary glands was monitored by measuring saliva and showed components of 2–4 hr and 1–2 days. The half-life of the activity in the area of the head was approximately 12–24 hr, indicating some early uptake of technetium into the thyroid, but its removal from this organ is probably quite rapid. When considering the immediate treatment of inadvertent exposure to ^{99}Tc it would appear worthwhile to stimulate salivation, since this could be a very effective means of decreasing the systemic burden of the isotope.

Technetium was not concentrated in the lacrimal or sweat glands; however, the specific activity of the nasal secretions was very large. In this connection it is interesting to point out that in the case of exposure to pertechnetate, nasal and oral swabbing cannot be used as an indication of exposure route due to the high concentrations of technetium which rapidly gets to the saliva and nasal mucosa.

To further define the localization of the technetium as excretion occurred, subjects were studied by photoscanning, localized surface counting with a shielded probe detector and by intestinal biopsy. Figure 7 shows a photoscan of a subject 3 days following oral administration when approximately 30 per cent of the administered dose remained. The photoscan illustrates localization of the technetium predominantly in the bowel and in its contents.

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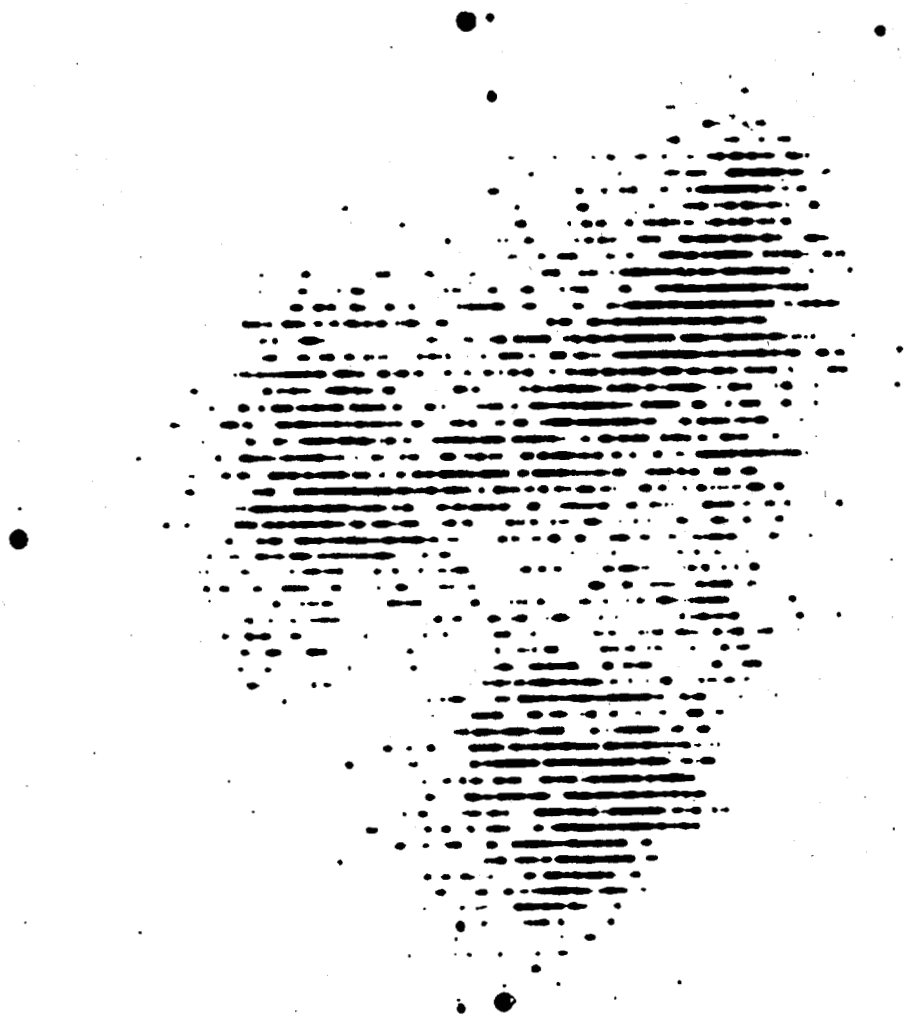

Fig. 7. Photoscan of subject 3 days following oral administration. Abdominal area showing distribution of Tc in transverse and descending colon.

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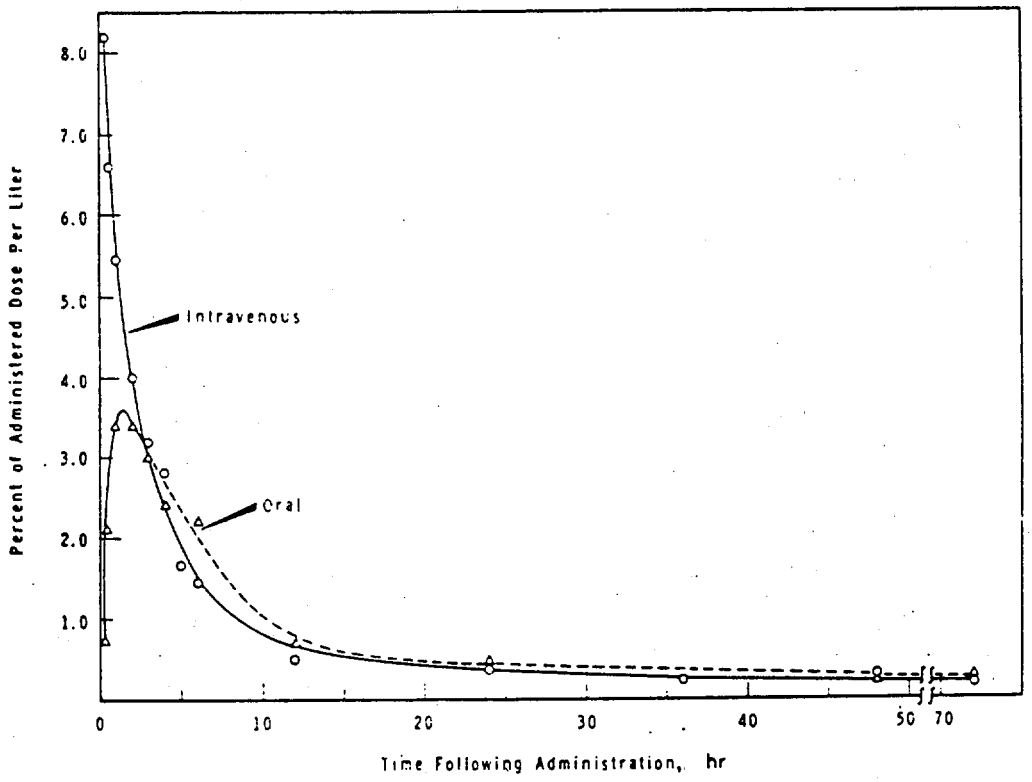

Fig. 8. Variation of blood concentrations of Tc following oral and intravenous administration.

Subsequent photoscans and localized surface counts showed a more diffuse pattern of radioactivity in the total bowel area. There was no evidence of localization of the isotope in either the liver or the kidney.

In three subjects, biopsies of the stomach, duodenum and rectal mucosa were performed at 2, 7 and 19 days following administration. Table 1 contains the results of these measurements and shows the general distribution of the technetium throughout the GI tract. No appreciable activity was observed in rectal mucosa, while stomach and duodenum mucosa had technetium concentrations of some 40–100 times that found in the plasma at comparable times.

Figure 8 shows the blood concentrations of technetium with time and indicates a rapid increase in the blood level of technetium following oral administration. Since no appreciable difference in excretion occurred for the two groups of subjects during this time period, one can estimate the fraction of the orally administered dose absorbed by comparing the areas beneath the plasma concentration curve of the

Table 1. Results of biopsy specimens

Subject	Method of administration	Time following administration (days)	Per cent of administered dose per kilogram of tissue		
			Stomach	Duodenum	Rectum
1	Oral	2	22.4	23.2	0.91
2	Oral	7	8.2	6.3	0.54
3	I.V.	19	1.2	0.45	—

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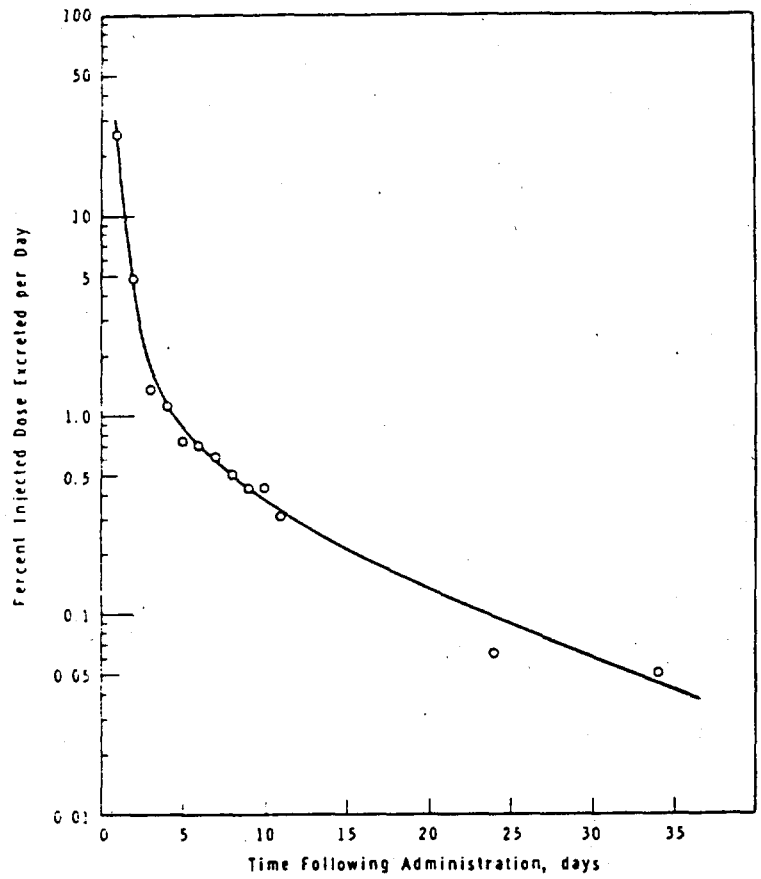

Fig. 9. Daily urinary excertion of intravenously administered ^{99m}Tc.

group to that of the intravenous group. Such a comparison suggests that some 96 per cent of the technetium which was administered orally was absorbed from the gut within the first 2 days. (This comparison was made assuming that the total blood volumes for the respective groups were similar.)

4.2 *Excretion of technetium*

Technetium is excreted very rapidly in the urine following both oral and intravenous administration. In this particular experiment it was not uncommon for a subject to excrete between 8 and 12 per cent of the administered dose in the first 6 hr following intake. By the third day, however, technetium elimination via the urine had decreased to about 1 per cent of the administered dose excreted per day (Table 2).

Fecal excretion, by contrast, reached its maximum value 3–4 days following administratio and thereafter decreased. Figures 9 and 1 show the characteristic excretion patterns ol tained from one subject following intravenou administration, while Fig. 11 shows the averag cumulative excretion of technetium with tim for all subjects investigated.

No difference was detectable between the I.V and oral groups in relation to the rate, and rou of excretion, or to the amount subsequent retained.

The experimental data have been fitted to three-term exponential expression showing th characteristic initial rapid decrease of the tecl netium in the urine during the first 3 day followed by longer half-lived components of 2. and 10.0 days respectively. At 28 days followin exposure, approximately 0.06 per cent of th dose is excreted per day via the urine.

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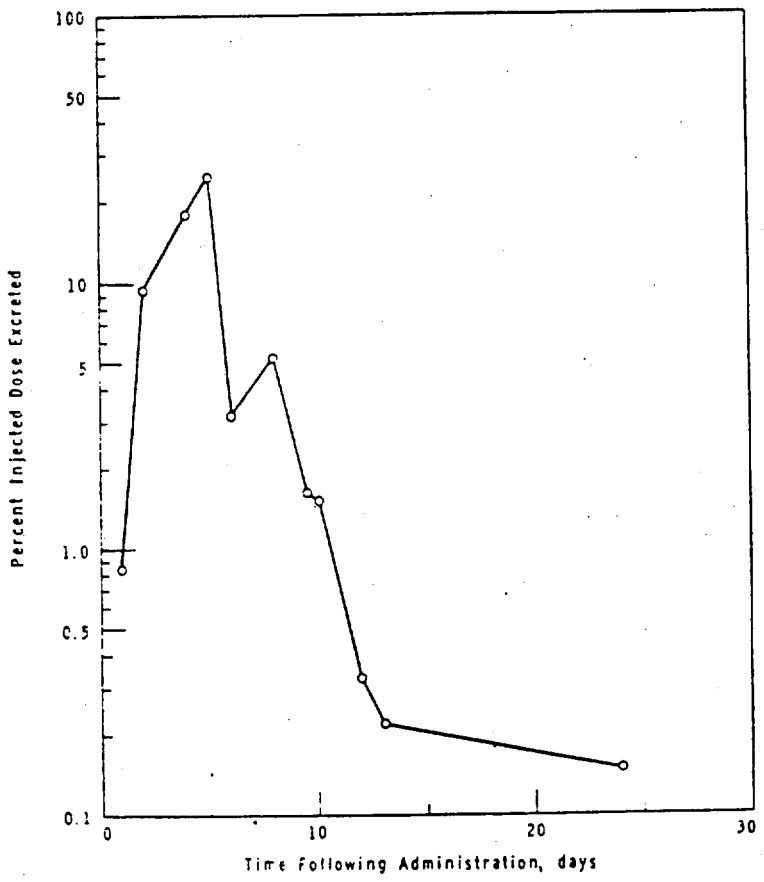

Fig. 10. Fecal excretion of intravenously administerd ^{99m}Tc.

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Table 2. Urinary excretion of technetium following oral and intravenous administration as pertechnetate

Days following administration	Average urinary excretion (% administered dose excreted/day)
1	27.76 ± 8.5*
2	2.44 ± 1.55
3	1.17 ± 0.18
4	0.84 ± 0.28
5	0.63 ± 0.20
6	0.52 ± 0.15
7	0.41 ± 0.16
8	0.35 ± 0.10
9	0.37 ± 0.18
10	0.25 ± 0.13
11	0.23 ± 0.08
14	0.16 ± 0.04
16	0.13 ± 0.05
18	0.11 ± 0.04
20	0.09 ± 0.03
22	0.07 ± 0.03
25	0.06 ± 0.02

* Standard error of the mean.

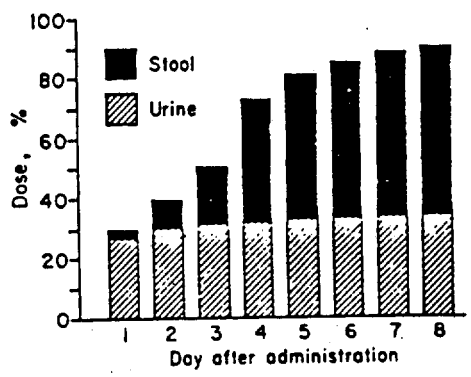

Fig. 11. Cumulative excretion of technetium.

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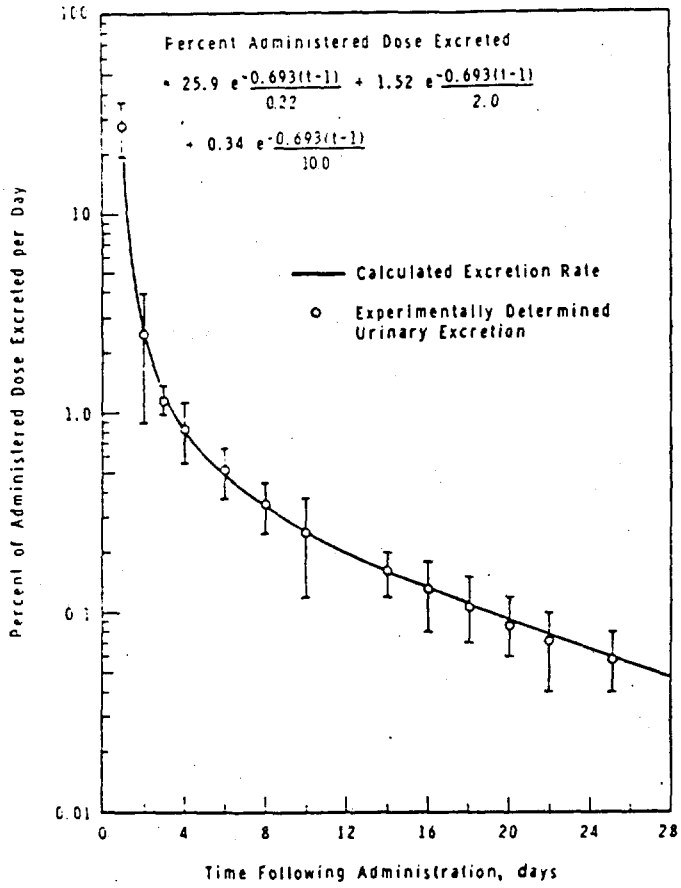

Fig. 12. Variation of the daily urinary excretion of technetium with time. Oral and intravenous.

Figure 12 can be used to estimate an initial exposure to technetium if one knows the time of exposure and the amount of technetium excreted by way of the urine in a 24-hr period following exposure. As an example, if one had measured 0.001 μc in a 24-hr urine specimen obtained from an individual exposed some 28 days prior to the urine sampling, his estimated intake of pertechnetate would have been 1.5 μc.

4.3. *Retention of technetium*

The retention of technetium with time for all eight subjects in this experiment has been averaged and is shown in Fig. 13. Once again the retention has been fitted to a three-term exponential expression. Solution of this equation for the time of 50 per cent retention (and therefore 50 per cent excretion) gives $t = 2$ or a biological $T_{1/2} \doteq 2$ days. The last term in the mathematical expression shows a half-life of 22 days and as previously mentioned is dependent upon the turnover of technetium in the G.I. tract.

SUMMARY

It is of interest to compare the results of the present investigation with the biological parameters published in the ICRP Committee Report II.[3] Table 3 shows such a comparison and indicates, at least in the instance where technetium isotopes are present as pertechnetate, the need for re-evaluating the maximum permissible body burdens, and air and water concentrations to which individuals may be exposed.

There seems to be little, if any, localization of

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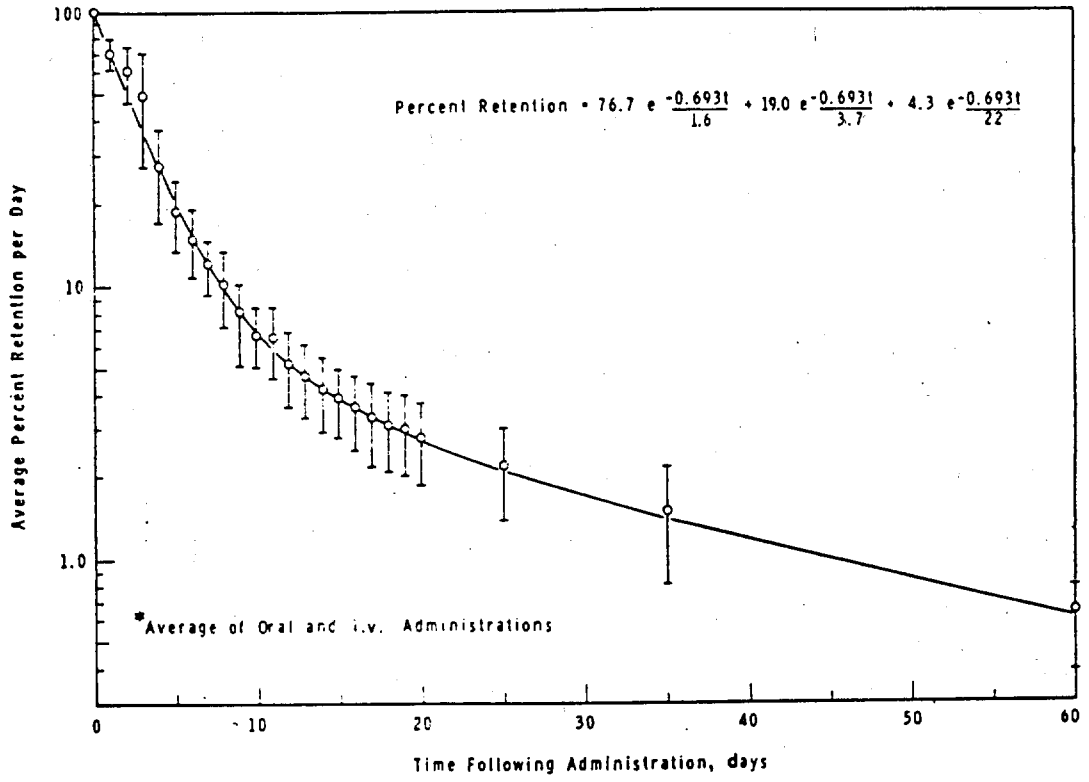

Fig. 13. Retention* of technetium with time.

Table 3. Comparison of biological parameters obtained in present research with ICRP *recommendations*

	ICRP	Present research
Effective half-life in body	1 day	2 days
fraction absorbed on ingestion	0.5	~0.95
organs where technetium localizes	G.I. (LLI)	G.I. (LLI), G.I. (S)
	Kidney	—
	Liver	—

technetium in the kidney or liver, but intsead it seems to concentrate mainly in the GI tract and stomach. Finally, urinalysis coupled with blood analysis at early times provides the best method of assessing body depositions of technetium as pertechnetate following accidental exposure.

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