JOURNAL OF NUCLEAR MEDICINE 8:50-59, 1967

Fate of Sodium Pertechnetate-Technetium-99m

Dr. Muhammad Abdel Razzak, M.D.,[1] Dr. Mahmoud Naguib, Ph.D.,[2] and Dr. Mohamed El-Garhy, Ph.D.[3]

Cairo, Egypt

Technetium-99m is a low-energy, short half-life iostope that has been recently introduced into clinical use. It is available as the daughter of ^{99}Mo which is recovered as a fission product or produced by neutron bombardement of molybdenum-98.

The aim of the present work is to study the fate of sodium pertechnetate-^{99m}Tc and to find out any difference in its distribution that might be caused by variation in the method of preparation of the parent nuclide, molybdenum-99.

MATERIALS & METHODS

The distribution of radioactive sodium pertechnetate milked from ^{99}Mo that was obtained as a fission product (supplied by Isocommerz, D.D.R.) was studied in 36 white mice, weighing between 150 and 250 gm each. Normal isotonic saline was used for elution of the pertechnetate from the radionuclide generator. The experimental animals were divided into four equal groups depending on the route of administration of the radioactive material, whether intraperitoneal, intramuscular, subcutaneous or oral. Every group was further subdivided into three equal subgroups, in order to study the effect of time on the distribution of the pertechnetate. Thus, the duration between administration of the radio-pharmaceutical and sacrificing the animals was fixed at 30, 60 and 120 minutes for the three subgroups respectively. Then the animals were dissected and the different organs taken out. Radioactivity in an accurately weighed specimen from each organ was estimated in a scintillation well detector equipped with one-inch sodium iodide thallium activated crystal. This was compared with activity in an accurately measured sample from the administered pertechnetate to permit calculation of percentage of administered dose per gram of each organ.

The whole procedure was repeated on another group of nine mice, after pre-

[1]Medical Unit and Division of Nuclear Medicine, Faculty of Medicine, Cairo University.
[2]Department of Pharmacology, Faculty of Veterinary Medicine, Cairo University.
[3]Nuclear Chemistry Department, A.E.E., U.A.R.

treatment with potassium perchlorate in the dosage of one mg orally. In this particular group, the sodium pertechnetate-^{99m}Tc was injected intramuscularly.

The disappearance of labelled pertechnetate from the circulation was studied in six dogs. For this purpose, the animals were put under intravenous nembutal anesthesia before the administration of the radioactive material through the femoral vein. Serial blood samples were collected at three-minute intervals for 15 minutes and then every quarter hour for 90 minutes. Radioactivity in an accurately-measured 2 ml from each blood sample was measured in the scintillation well detector. The same experiment was then repeated on another two dogs after the oral administration of 50 mg of potassium perchlorate.

Lastly, in order to investigate the effect of variation in the method of preparation of the parent ^{99}Mo on the distribution pattern of radioactive pertechnetate, the same procedure that has been described above was repeated on another batch of nine white mice, using ^{99m}Tc that was milked from ^{99}Mo prepared by neutron bombardment.[1] The radioactive material was administered intramuscularly.

[1]Produced by the Nuclear Chemistry Department, A.E.E., U.A.R.

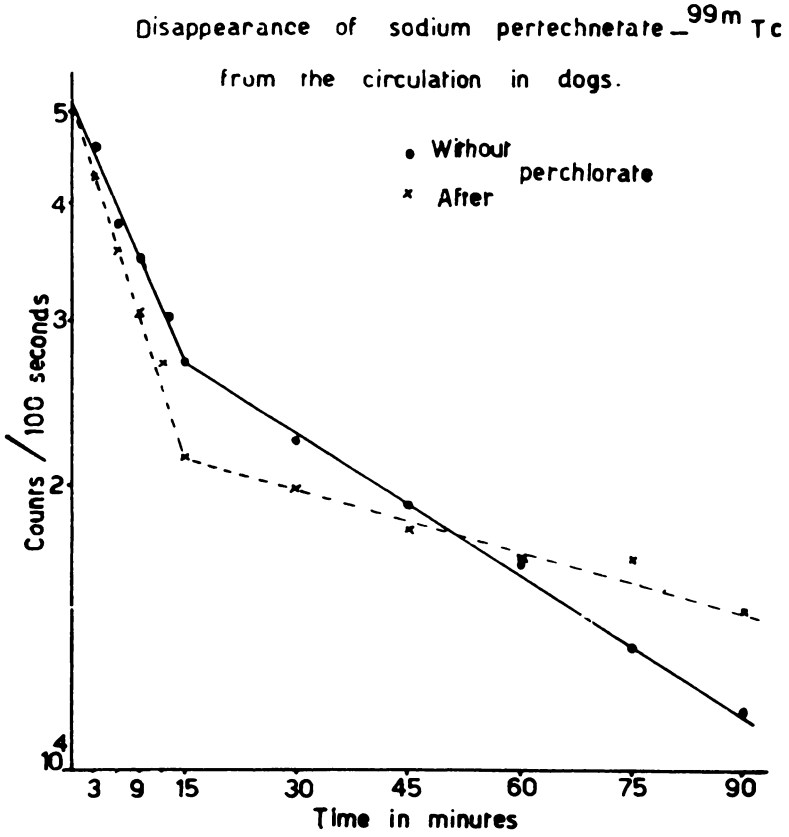

Fig. 1. Disappearance curve of labelled pertechnetate from the circulation of dogs without pretreatment with perchlorate and after the oral administration of 50 mg potassium perchlorate.

RESULTS

The tissue distribution of sodium pertechnetate-^{99m}Tc expressed as per cent of dose per gram tissue is summarised in Table I. This table illustrates the differences in distribution that happened with time and/or with changing the route of administration of the radioactive material. In order to calculate the percentage

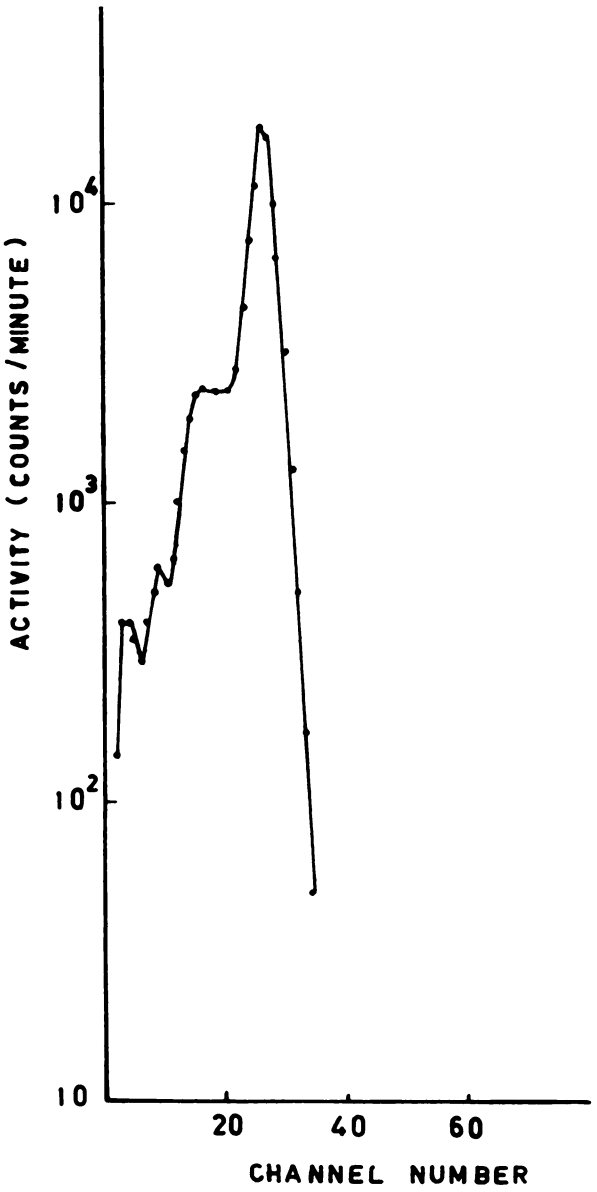

Fig. 2. Gamma ray spectrum of ^{99m}Tc milked from ^{99}Mo prepared by neutron bombardment of ^{98}Mo. Energy per channel is 5.5 keV.

of dose that accumulates in any organ at any specified time, it is necessary to multiply the per cent of dose per gram at that time by the weight of the particular organ. Table II shows the average weights of some organs expressed as percentage from the total body weight obtained in 10 white mice. By calculation, the amount of radioactivity that could be accounted for in the organs examined after 30 minutes from the parenteral administration of the labelled pertechnetate was 40 to 70% of the injected dose. From Table I, it can be seen that the highest concentration of radioactivity was in the stomach and kidneys, followed by the liver and lungs and then the other organs. Radioactivity per gram tissue was noticed to decrease with time, except in the case of the kidneys where it rose after going down.

After perchlorate (Table III), the concentration of radioactivity per gram in all the studied organs was lower than without this drug, particularly so with the kidneys and stomach. Furthermore, this effect was seen to decrease with time, except with the kidneys.

In the dog experiments, the disappearance of labelled sodium pertechnetate from the circulation followed a biphasic exponential pattern(Fig. I). The first part was rapid, with a mean disappearance half-time of 17 ± 4 minutes. (Mean ± 1 S.D.), and the range, was from 11 to 22 minutes. The second phase was rather slow, with a disappearance half-time that ranged between 41 and 75 minutes with a mean of 64 ± 15 minutes (Mean ± 1 S.D.). Meeting of these two seg-

Fig. 3. Gamma ray spectrum of ^{99m}Tc milked from ^{99}Mo that was obtained as a fission product. Energy per channel is 7 keV.

TABLE I

DISTRIBUTION PATTERN OF SODIUM PERTECHNETATE-^{99m}Tc MILKED FROM ^{99}Mo THAT WAS OBTAINED AS A FISSION PRODUCT AT VARIOUS TIME INTERVALS AND USING DIFFERENT ROUTES OF ADMINISTRATION INTO WHITE MICE. EACH METHOD OF ADMINISTRATION WAS TESTED ON NINE ANIMALS.

	Percent of administered ^{99m}Tc/gm tissue at different time intervals											
Route of administration	*Intraperitoneal*			*Intramuscular*			*Subcutaneous*			*Oral*		
Time after administration in minutes	30	60	120	30	60	120	30	60	120	30	60	120
Liver	1.68	1.17	0.38	2.03	0.93	0.65	2.62	1.76	0.39	0.18	3.09	0.30
Kidneys	10.69	4.75	5.57	8.92	3.45	9.33	9.21	18.67	14.23	0.20	0.60	0.50
Testes	1.60	0.67	0.25	0.89	0.56	0.28	1.89	1.05	0.31	0.06	0.12	0.10
Heart	0.88	0.56	0.13	1.13	0.46	0.25	1.53	0.80	0.25	0.08	0.16	0.13
Spleen	1.48	1.05	0.17	1.19	0.42	0.48	1.19	0.76	0.30	0.08	0.15	0.16
Salivary gland	0.83	0.35	0.16	1.16	0.47	0.17	1.42	1.18	0.23	0.09	0.18	0.16
Lungs	1.92	1.35	0.29	3.16	0.86	0.46	2.85	2.80	0.51	0.18	0.91	0.63
Stomach	8.47	6.70	4.06	15.06	9.26	4.36	6.67	9.42	4.60	5.13	10.05	5.57

ments occurred at 10 to 20 minutes from isotope injection and the mean was 15 ± 4 minutes (Mean ± 1 S.D.) After perchlorate, the only significant change noticed was in the second phase of pertechnetate disappearance curve. This segment became much slower than before and showed a disappearance half-time of 110 to 130 minutes.

The tissue distribution of sodium pertechnetate-^{99m}Tc milked from ^{99}Mo that was prepared by neutron bombardment was more or less the same as when the ^{99}Mo was recovered as a fission product, except for the concentration of radioactivity in the kidneys which was noticed to be much lower (Table IV). Furthermore, the decrease in the level of radioactivity in the various organs with time was much slower.

DISCUSSION

The 140 keV gamma emissions of ^{99m}Tc were first used clinically by Sorensen and Archambault in 1963 (1) for photoscanning of the liver through the administration and hepatic localization of the parent nuclide Molybdenum-99. In the same year, Harper *et at* (2) reported their results concerning the suitability of injected ^{99m}Tc for scanning of the liver, thyroid and, later, the brain. Since then, newer applications for this isotope are being introduced by various authors (3-8).

In the present work, it was noticed that the stomach contained the highest level of radioactivity irrespective of the route of administration of sodium pertechnetate—Technetium-99m (Table I). This finding agrees with the results of previous workers in this field (4, 9-12). However, with the oral route the concentration of radioactivity in all the investigated organs, with the exception of the stomach, was rather low. This condition might be explained by the technical difficulty encountered during the oral administration of the labelled pertechnetate to white mice and/or the defective or delayed absorption of the radioactive material. As regards the other routes of administration, that is, intraperitoneal intramuscular and subcutaneous, it was found that the tissue distribution and behav-

TABLE II

WEIGHT OF SOME ORGANS OF WHITE MICE EXPRESSED AS PER CENT FROM THE TOTAL BODY WEIGHT. MEAN OF 10 MICE.

Organ	*Weight of different organs in grams in an animal of 230 gms*	*Percentage from total body weight (Mean of 10 mice)*
Liver	9.480	4.25
Kidneys	1.730	0.72
Testes	4.400	1.36
Heart	0.910	0.40
Spleen	1.120	0.40
Salivary glands	1.150	0.50
Lungs	1.260	0.65
Stomach (Empty)	2.180	0.88

iour of radio-pertechnetate was more or less the same with minor differences that could be accounted for by the difference in the rates of absorption between the various routes of administration applied. Next to the stomach, the highest level of radioactivity was found in the kidneys, followed by the liver and lungs, and then the other organs (Table V). The thyroid gland was not included in this study since its uptake of ^{99m}Tc has been well investigated by previous workers (4, 9) who reported that about 2% of the labelled pertechnetate localized in the thyroid gland and that the count rate over the thyroid closely followed that of the parotid salivary gland (4). Radioactivity per gram from the various organs examined in the present series of experiments with the exception of the kidneys was noticed to decrease markedly with time. The calculated half-time for this decrease was about 34 minutes for the heart, lungs, testes and salivary glands, whereas for the liver and spleen $T_{\frac{1}{2}}$ amounted to 45 minutes. This finding, together with the rather high level of radioactivity in the liver, denotes a higher

TABLE III

EFFECT OF ORAL POTASSIUM PERCHLORATE ON THE DISTRIBUTION PATTERN OF INTRAMUSCULARLY INJECTED LABELLED PERTECHNETATE.

	Percent of dose/gm					
	Without pertreatment			*After perchlorate*		
Time after I.M. injection of ^{99m}Tc (minutes)	30	60	120	30	60	120
Liver	2.03	0.93	0.65	0.92	0.57	0.33
Kidneys	8.92	3.45	9.33	1.45	1.19	1.04
Testes	0.89	0.56	0.28	0.65	0.40	0.24
Heart	1.13	0.46	0.25	0.70	0.45	0.23
Spleen	1.19	0.42	0.48	0.63	0.40	0.27
Salivary gland	1.16	0.47	0.17	0.76	0.44	0.23
Lungs	3.16	0.86	0.46	1.03	0.66	0.31
Stomach	15.06	9.26	4.36	1.87	0.98	2.08

affinity of this organ for the sodium pertechnetate-^{99m}Tc. As regards the rate of disappearance of radioactivity from the stomach, it was noticed to be even slower, the effective half-time being 66 minutes. In contrast to these results, the concentration of radioactivity per gram kidney tissue did not show significant changes during the period of observation. This phenomenon might be caused by the fact that radioactivity leaving the other organs for elimination would go to the kidneys, which were shown to be the main route for excretion of the Technetium-99m. (4, 6, 10).

After pretreatment with potassium perchlorate, the concentration of radioactivity per gram in all the examined organs of white mice was lower than without this drug (Table III), denoting competition between the two agents or a blocking effect exerted by the perchlorate on the uptake of the various organs for sodium pertechnetate-technetium-99m. This condition would naturally lessen the role played by tissue uptake in lowering the ^{99m}Tc blood level. A support for this explanation was obtained in the dog experiments, where marked prolongation of the disappearance time of labeled pertechnetate from the circulation was observed after perchlorate (Fig. I).

When the tissue distribution of sodium pertechnetate-^{99m}Tc that was milked from neutron-activated molybdenum was examined, it was found to be very much similar to that of ^{99m}Tc obtained from the fission product, ^{99}Mo, with two main differences. One difference was the much lower level of radioactivity per gram kidney tissue, while the other was the slower disappearance of activity from the various organs over the period of observation. These findings could be logically attributed to the complete absence of radiocontaminants, such as ^{99}Mo, ^{103}Ru, ^{106}Ru, ^{132}I and ^{131}I that were shown to be present in the ^{99m}Tc milked from fission-produced ^{99}Mo (13), and that are eliminated through the kidneys. This concept can be supported by a comparison of the gamma ray spectra of two sam-

TABLE IV

TISSUE DISTRIBUTION OF ^{99m}Tc THAT WAS MILKED FROM ^{99}Mo PREPARED BY NEUTRON BOMBARDMENT. THE RADIOACTIVE MATERIAL WAS INJECTED VIA THE INTRAMUSCULAR ROUTE IN WHITE MICE.

Time after the I.M. injection of ^{99m}Tc	*Percent of dose/gm*							
	Liver	*Kidneys*	*Testes*	*Heart*	*Spleen*	*Salivary gland*	*Lungs*	*Stomach*
30 minutes	1.66	2.77	0.78	1.06	1.03	1.34	1.92	11.90
60 minutes	1.46	2.64	0.57	0.89	0.98	1.13	1.36	10.95
120 minutes	1.10	2.19	0.38	0.40	0.45	0.61	0.92	8.00

ples of sodium pertechnetate-^{99m}Tc milked from ^{99}Mo that was prepared on one occasion by neutron bombardment, whereas in the other instance it was obtained as a fission product (Figs. 2, 3). As regards the objection raised about the rather large size of generators needed to yield a sufficient activity of ^{99m}Tc from neutron-activated molybdenum, it has been recently shown that more than 100 mC of ^{99m}Tc could be supplied by a generator of reasonable dimension (14, 15). Since this difficulty has been overcome, we think that ^{99m}Tc obtained from ^{99}Mo prepared by neutron bombardment and which is free from radiocontaminants would be preferable.

SUMMARY

The tissue distribution of sodium pertechnetate-^{99m}Tc was studied in white mice. The highest levels of radioactivity were found in the stomach and kidneys, followed by the liver and lungs, and then the other organs. Furthermore, radioactivity per gram tissue of all the organs examined with the exception of the

TABLE V

TISSUE DISTRIBUTION AND DISAPPEARANCE HALF-TIME OF INJECTED PERTECHNETATE-^{99m}Tc FROM THE VARIOUS ORGANS. EACH COLUMN REPRESENTS THE MEAN OF NINE MICE.

Organs	*Percent of dose/gm at various time intervals from the injection of sodium pertechnetate-^{99m}Tc*			*Disappearance half-time of pertechnetate (minutes)*
	30 min.	*60 min.*	*120 min.*	
Liver	2.11	1.29	0.47	44
Kidneys	9.61	8.96	9.71	—
Testes	1.46	0.76	0.28	36
Heart	1.18	0.61	0.21	36
Spleen	1.29	0.74	0.32	45
Salivary gland	1.14	0.67	0.19	33
Lungs	2.64	1.67	0.42	32
Stomach	10.07	8.46	4.34	66

kidneys decreased markedly with time. The effective half-time for this disappearance of activity was shortest in the heart, lungs, testes and salivary glands, medium with the liver and spleen, and slowest for the stomach.

After pretreatment with potassium perchlorate, the disappearance of labelled pertechnetate from the circulation of dogs became slower and the tissue concentration of radioactivity in white mice was much lowered.

As regards the distribution of ^{99m}Tc obtained from ^{99}Mo prepared by neutron bombardment, it proved to be similar to that described above, except for the much lower level of radioactivity in the kidneys and the slower disappearance of activity from the organs.

Reasons were suggested for the explanation of these findings.

ACKNOWLEDGMENT

We would like to record our thanks to Dr. H. Badrawi, Mr. H. Osman and Mr. S. Hassaballa for their invaluable help.

REFERENCES

1. SORENSEN, L. B. AND ARCHAMBAULT, M.: Visualization of the liver by scanning with ^{99}Mo molybdate as tracer. *J. Lab. and Clin. Med.* **62**:330, 1963.

2. HARPER, P. V., LATHROP, K. A. AND MCCARDLE, R. J.: Improved liver scanning with ^{99m}Tc in fat emulsion. *J. Nuclear Med.* **4**:189, 1963.

3. HARPER, P. V., LATHROP, K. A. AND RICHARDS, P.: Technetium-99m as a radiocolloid. *J. Nuclear Med.* **5**:382, 1964.

4. MCAFEE, J. G., FUEGER, C. F., STERN, H. S., WAGNER, H. N. AND MIGITA, T.: Technetium-99m pertechnetate for brain scanning. *J. Nuclear Med.* **5**:811, 1964.

5. MCAFEE, J. G., STERN, H. S., FUEGER, G. F., BAGGISH, M. S., HOLZMAN, G. B. AND ZOLLE, I.: Technetium-99m labelled serum albumin for scintillation scanning of placenta. *J. Nuclear Med.* **5**:936, 1964.

6. DEGROSSI, O., GOTTA, H., OLIVARI, A., PICTORINI, V. AND CHWOJNIK, A.: Possibilities of using Technetium-99m in place of radioiodine in thyroid function studies. *Nuclear-Medizin.* **4**:383, 1965.

7. QUINN, J. L., HAUSER, W. AND CIRIC, I.: Analysis of 100 abnormal brain scans using Technetium-99m as pertechnetate. *J. Nuclear Med.* **6**:333, 1965.

8. WITCOFSKI, R., MAYNARD, D. AND MESCHAN, I.: The utilization of Technetium-99m in brain scanning. *J. Nuclear Med.* **6**:121, 1965.

9. HARPER, P. V., LATHROP, K. A., MCCARDLE, R. J. AND ANDROS, G.: The use of Technetium-99m as a clinical scanning agent for thyroid, liver and brain. Medical Radioisotope Scanning, I.A.E.A., Symposium, Athens, April 1964, **2**:33, 1964.

10. SMITH, E. M.: Properties, uses, radiochemical purity and calibration of Technetium-99m. *J. Nuclear Med.* **5**:871, 1964.

11. SMITH, E. M.: Internal dose calculation for Technetium-99m. *J. Nuclear Med.* **6**:231, 1965.

12. MATTHEWS, C. M. E. AND MALLARD, J. R.: Distribution of Technetium-99m and tumour/brain concentrations in rats. *J. Nuclear Med.* **6**:404, 1965.

13. ALLEN, J. F.: An improved Technetium-99m generator for medical applications. *Internat. J. Appl. Rad. & Isotopes.* **16**:332, 1965.

14. MIKHEEV, N. B., EL-GARHY, M. AND MOUSTAFA, Z.: Generator for production of Technetium-99m from irradiated Molybdenum. *Atompraxis.* **10**:263, 1964.

15. EL-GARHY, M., MOUSTAFA, Z. AND MIKHEEV, N. B.: Separation of Technetium-99m from irradiated Molybdenum. *Atompraxis.* February, 1966.