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Technetium-99m Pertechnetate Uptake and Scanning in the Evaluation of Thyroid Function

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Technetium-99m as pertechnetate is accumulated by the thyroid but not appreciably organified. In this study, a method of determining thyroidal uptake from the scintiscan is described. The mean uptake in euthyroid individuals as measured by this method was 1.73 ± 0.85% with a normal range of 0.50–4.00%. Uptake was not affected by organic blocking agents. In a comparison of the overall accuracy of pertechnetate and 24-hr radioiodine uptakes, the pertechnetate uptake was slightly superior, with only 5.9% errors in 488 patients. Radioiodine uptakes were in error in 7.8% of 270 individuals. In hyperthyroid patients, the accuracy of the pertechnetate uptake was 89.6% while the radioiodine uptake had an accuracy of 75.0%. Both uptake determinations were highly inaccurate in hypothyroidism.

THE UTILIZATION of ^{131}I for diagnostic thyroid studies has been routine for more than two decades. Despite this, it is not a completely satisfactory agent for this purpose for a number of reasons. A relatively high radiation dose from the energetic beta emission is cause for concern in the light of the experience with the Marshallese exposed to fallout radiation, primarily radioiodines.[1] While no deleterious effects from diagnostic uses of iodine-131 have been demonstrated, they have not been specifically looked for.

Another reason for dissatisfaction with iodine-131 is its rather long half-life. While this factor may be useful for long-term turnover studies, it is detrimental when repeat studies such as triiodothyronine (T_3) suppression or TSH stimulation are to be performed shortly after a routine diagnostic examination. The long half-life also contributes to the radiation dose.

Other radioiodines which have been used for thyroid studies include ^{125}I and ^{123}I. The former has a very long half-life but the low gamma energy allows it to be discriminated against if repeat studies are performed with a radionuclide of higher energy. Uptake studies are difficult but can be performed.[2] The radiation dose from iodine-125 is still considerable although less than with iodine-131. Iodine-123 has ideal characteristics: absent beta emission, short half-life, and a low gamma energy which may be efficiently detected and collimated.[3] (Also see article by Wellman in this issue.) Unfortunately, at this time, it is not so readily available in sufficient purity or as inexpensive as the other radionuclides. The situation in the near future may be very different.

Technetium-99m has many excellent features. It is plentiful and inexpensive. Its gamma energy is close to that of iodine-123 and there is virtual absence of beta-like activity. The half-life is short so that repeat examination can be performed after a very short interval. Disadvantages are the relatively low thyroid

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uptake and the high background activity at the optimum time for examination. Despite these factors, we have found technetium-99m pertechnetate to be a useful nuclide for diagnostic evaluation of the thyroid and in some respects superior to iodine-131.

Biological Behavior

In 1949 Baumann and Metzger[4] predicted, on the basis of studies with other elements in periodic group VII, that technetium would be selectively extracted from blood by the thyroid. This was experimentally proved by Baumann et al. several years later using the long-lived technetium-99.[5] Apparently, the localization of technetium, as pertechnetate, in the thyroid is due to the configuration and size of the pertechnetate ion and its similarity to other ions such as perchlorate, perrhenate, and iodide. The uptake in the gland requires cellular integrity and metabolic energy.

There is some controversy concerning the fate of "trapped" pertechnetate. Socolow and Ingbar[6] demonstrated apparent binding of technetium activity on chromatographic analysis of thyroids in propylthiouracil-treated rats. There is also some indication of binding by increasing thyroid/blood ratios with time.[7] This may be part of the generalized tendency for intracellular distribution of technetium at late intervals following administration. Other investigators have failed to demonstrate any evidence of protein binding of technetium.[8,9] In any event, the degree to which this takes place at early intervals after administration is negligible and would not invalidate the evaluation of the thyroid "trapping" mechanism.

Methods of Determining Thyroidal Uptake of Technetium

The determination of per cent uptake of an administered dose of technetium-99m as pertechnetate is more complicated than in the case of iodine-131. This is true because of the high background activity present, the rather low level of uptake in hypo- and euthyroid individuals, and the presence of technetium in the nearby salivary glands in concentrations similar to that found in the thyroid. As a consequence, several methods have been developed to determine the concentration of technetium in the thyroid and the average normal values differ somewhat, depending on the method utilized.

A method similar to that used with iodine-131 was employed by DeGrossi et al. with some success.[10] Their euthyroid range was from about 2 to 11%. Cheguillaume et al.[11] also used this method at first and obtained average values of 4.2% in euthyroid individuals. They later modified their method[12] by placing a 2-mm lead filter on the neck over the region of the thyroid as determined by prior scintigraphy to obtain background readings. The results for both methods correlated rather well.

The perchlorate "washout" method has been used by a number of investigators.[13,14] With this method the neck activity is determined before and after a 1-g dose of perchlorate. The difference in the two determinations represents that activity which had been accumulated by the thyroid. This method has resulted in somewhat higher values than we have obtained with a scintigraphic technique. As used by Kuba et al.,[13] this method required two visits 24 hr apart. Their upper limit of normal was 4.5% and technetium uptakes proved to have an accuracy of 93% in assessing functional activity. However, Harden et al.[15] have demonstrated the washout of technetium from salivary glands as well as the thyroid. This could result in errors in uptake determinations in some cases.

The utilization of the scan was suggested by Andros et al.[14] Their method included the scan of a standard absorbed on filter paper and required corrections for estimated gland thickness and depth. A similar method was used by Shimmins et al.[16] They scanned the neck and counted dots in a circular area including the thyroid. Background was counted in a semicircular region just below the thyroid. A neck phantom containing a standard was scanned immediately following this. In a limited series, the mean 20-min uptake in euthyroid individuals was 3.7% with limits of 1.5–6.3% and in hyperthyroid patients the mean was 19.0% with a range of 7.5–33.0%. These authors also measured the intrathyroidal technetium space (euthyroids = 532 ± 130 ml, hyperthyroids 3205 ± 498 ml) and the unidirectional thyroid clearance (euthyroids = 36.8 ± 7.9 ml/min, hyperthyroids = 287 ± 62.8 ml/min).

Our own method[17] is similar to that of Shimmins et al. The thyroid region is scanned with relatively wide line spacing and high dot factor at 30 min after intravenous administration of 2.0–2.5 mCi of $^{99m}TcO_4$. Using the same factors, a standard containing 3% of the administered activity in 23 ml, inserted into an I.A.E.A. neck phantom, is scanned immediately afterward. Dots are counted over a blocked-off area containing the thyroid as well as adjacent background strips on either side. After correction for difference in area the background dots are subtracted from the thyroid region dots. The net thyroid counts are divided by the standard and multiplied by 3 to give per cent uptake in the thyroid.

If a computer or multichannel analyzer system is available the determination can be made more accurately and with less effort. However, the dot counting technique is simple, rapid, and can be done with the usually available equipment.

Results

We have now performed approximately 1000 examinations on over 650 different patients. In the evaluation of the accuracy of this method all patients who had a history of iodine administration were excluded. Subjects with clinical symptoms, signs, and data suggestive of acute or chronic thyroiditis were treated separately. Final diagnoses were made by evaluation of history, physical examination, and laboratory data utilizing an uptake and a measurement of bound iodine in the plasma, either protein-bound iodine (PBI) or thyroxine-bound iodine (T_4-I), by the Murphy-Pattee method. Where indicated, suppression tests were performed by administration of triiodothyronine, 25 µg three times a day for 8 days, and then repeating the examinations. Other determinations such as for free thyroxine, thyroid-autoantibodies, or thyroxine binding globulin were obtained when necessary.

A total of 488 different patients who have had technetium uptake determinations are available for analysis at this date. For a period of time we were not doing radioiodine uptake determinations so that only 270 of these patients had this determination performed at 24 hr after an oral dose of ^{131}I.

The mean values for uptake in the thyroid of ^{99m}Tc and ^{131}I for various functional states are listed in Table 1. Our values for ^{99m}Tc uptakes average approximately half the values found by Shimmins et al.[16] and 40% less than the values reported by Kuba.[13] The differences could be explained in large part by the dimensions of the standard used as well as the method of background subtraction.

Thyroid/plasma ratios and thyroidal technetium space were determined in a limited number of patients after estimating thyroid volume from scans. In 38 euthyroid individuals the mean thyroid/plasma ratio was 12.7 ± 7.2 and the technetium space was 241 ± 125 ml. The thyroid/ plasma ratio in nine hyperthyroid patients was 33.7 ± 12.9 and the technetium space 1250 ± 1301 ml. These values are approximately half those of Shimmins et al.[16] and are in accord with the lower uptake determinations in our series. They also are considerably less than the results of similar determinations performed with iodide by Berson and Yalow[18] on patients with blocked glands.

A more useful comparison of pertechnetate and iodide uptakes is a histogram (Figs. 1 and 2) showing distribution of values for the several functional states under consideration. The most striking difference is the marked overlapping of the euthyroid and hyperthyroid distributions with the 24-hr radioiodine uptake, this being much less with the pertechnetate uptakes. The separation of hypothyroid from euthyroid individuals was not very satisfactory with either

Table 1.—Thyroidal Uptake of Pertechnetate and Iodide

	$^{99m}TcO_4^-$ (% Uptake, 30 min)	$^{131}I^-$ (% Uptake, 24 hr)
Euthyroid		
Male	1.52 ± 0.79 (57)	24.9 ± 6.8 (27)
Female	1.76 ± 0.86 (323)	26.3 ± 8.4 (175)
Total	1.73 ± 0.85 (380)	26.1 ± 8.2 (202)
Females on oral contraceptives	2.05 ± 1.13 (31)	27.6 ± 8.4 (17)
Hyperthyroid		
Male	8.19 ± 6.24 (12)	60.1 ± 11.3 (10)
Female	9.76 ± 6.29 (32)	59.1 ± 21.9 (22)
Total	9.33 ± 6.24 (44)	59.4 ± 19.0 (32)
Hypothyroid		
Male	0.60 (1)	6.1 (1)
Female	0.52 ± 0.12 (10)	8.5 ± 2.9 (5)
Total	0.52 ± 0.37 (11)	8.1 ± 5.9 (6)
Previous Therapy for hyperthyroidism		
Euthyroid	1.44 ± 0.96 (13)	26.6 ± 13.9 (7)
Hyperthyroid	9.35 ± 6.85 (4)	43.2 ± 18.2 (4)
Hypothyroid	1.33 ± 0.80 (5)	20.4 ± 0.8 (2)

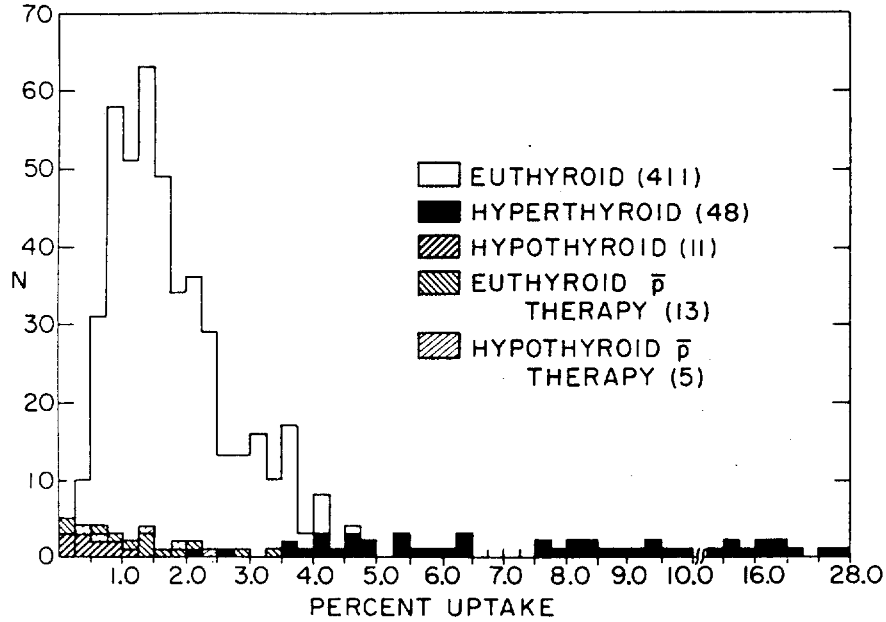

Fig. 1.—Histogram of distribution of ^{99m}Tc uptake values.

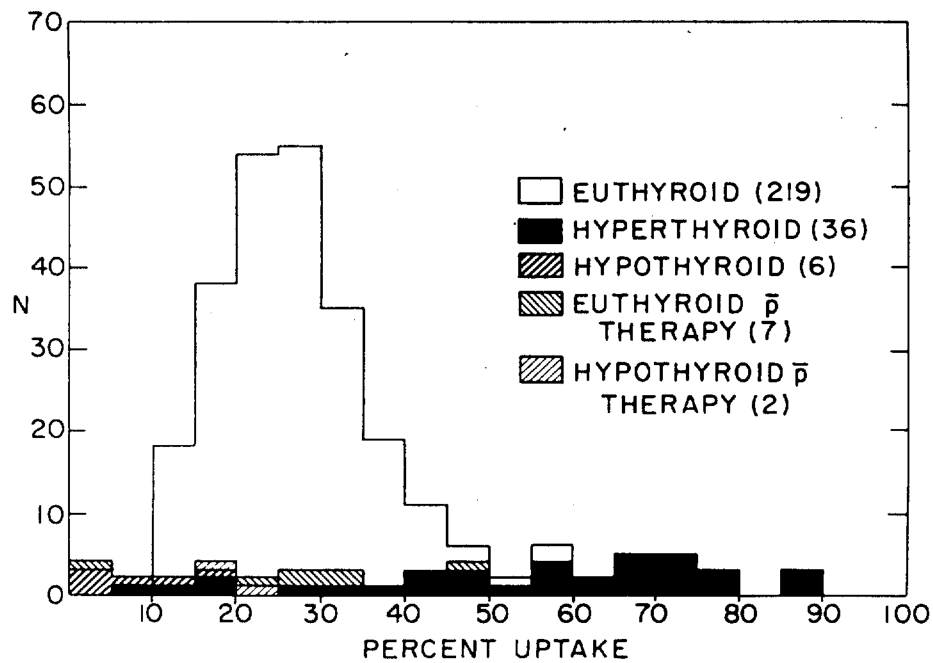

Fig. 2.—Histogram of distribution of ^{131}I uptake values (24 hr).

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type of uptake.

Analysis of errors (Table 2) indicates that the overall accuracy of the pertechnetate uptake is about the same as for the iodine uptake, 94.1% and 92.2% respectively. However, with hyperthyroid patients, the rate of errors with radioiodine was more than double that found with technetium. This failed to be statistically significant however, possibly due to the relatively small number of patients in this category. In hypothyroidism both uptakes were markedly inaccurate.

It is of interest to compare the accuracy of uptakes with the determination of bound iodine in the blood. The PBI determinations were performed in our laboratory and were accurate in 95.9% of cases. The T_4-I was accurate 86.4% of the time. These had been performed at an outside laboratory and showed a high incidence of error (40%) in hyperthyroid individuals. We have since begun to perform these determinations ourselves and they now are more reliable.

Response to TSH Stimulation and Suppression

The pertechnetate uptake by the thyroid responds in a manner very similar to the radioiodine uptake. A major advantage with ^{99m}Tc, of course, is the absence of residual activity at the time of the second uptake. The 8-day half-life of radioiodine necessitates making a background measurement and using it for correction of the second uptake.

Table 3 lists the patients with various conditions who have undergone T_3 suppression tests (as well as one patient suppressed with thyroid extract). It can be seen that suppression is perhaps more marked in its effect on the pertechnetate uptake than on the iodine uptake. However, the difference is not statistically significant.

The effect of TSH stimulation on thyroid uptake is more variable (Table 4). The first 12 patients on this list were Marshall Islanders, most with markedly abnormal glands due to radiation injury from fallout.[1] While response was rather remarkable in some instances the comparison between pertechnetate and iodine uptake was inconsistent.

Effect of Organification Blocking Agents

Another distinct advantage of using pertechnetate for function studies is that the uptake is unaffected by the administration of blocking agents. This makes it possible to evaluate the functional status of hyperthyroid patients while under treatment without the necessity of stopping medication. In most patients we have studied there has been insignificant change or none immediately following placement of the patient on chemotherapy.

Table 2.—Accuracy of $^{99m}TcO_4^-$ and $^{131}I^-$ Uptakes

	$^{99m}TcO_4^-$			$^{131}I^-$		
	Patients	Errors	% Error	Patients	Errors	% Error
Euthyroid	424	15	3.5	226	8	3.5
Hypothyroid	16	9	56.3	8	4	50.0
Hyperthyroid	48	5	10.4	36	9	25.0
Total	488	29	5.9	270	21	7.8

Thyroiditis

In several instances of acute thyroiditis, there has been complete, or nearly complete, suppression of both the pertechnetate and iodine uptakes. This is associated with elevated PBI and T_4-I. Several months later, without any therapy in the interim, repeat examinations have showed return to or toward normal values (Fig. 3).

A discrepancy in the effect on the pertechnetate and iodine uptakes has been noted in Hashimoto's thyroiditis. While the pattern is not consistent, often the pertechnetate uptake is elevated in the face of a normal or even low PBI or T_4-I (Table 3). Occasionally, the iodine uptake is also elevated, but less often in comparison with the pertechnetate uptake.

Thyroid Imaging with ^{99m}Tc

There are two major factors to consider in order to obtain an optimal representation of the distribution of radioactivity in the gland when using ^{99m}Tc. The first of these is proper collimation. Many physicians are still using collimation designed for use with iodine-131. This is very inefficient since collimation designed for the low, 140-keV gamma of technetium-99m will provide three to four times the count rate, thus improving the quality of the scan and reducing the time required for completion of the study.

A second factor relates to high background activity due to the relatively low thyroid-to-plasma ratios with ^{99m}Tc compared with ^{131}I. This background can be disturbing, particularly in cases of low uptake. We have found that this can be considerably reduced by using an overlapping technique and a moderately large light spot for photorecording.[19] At the present time, we use a 4.5- by 4.5-mm photorecording light spot and a line spacing of 0.75 mm. With this

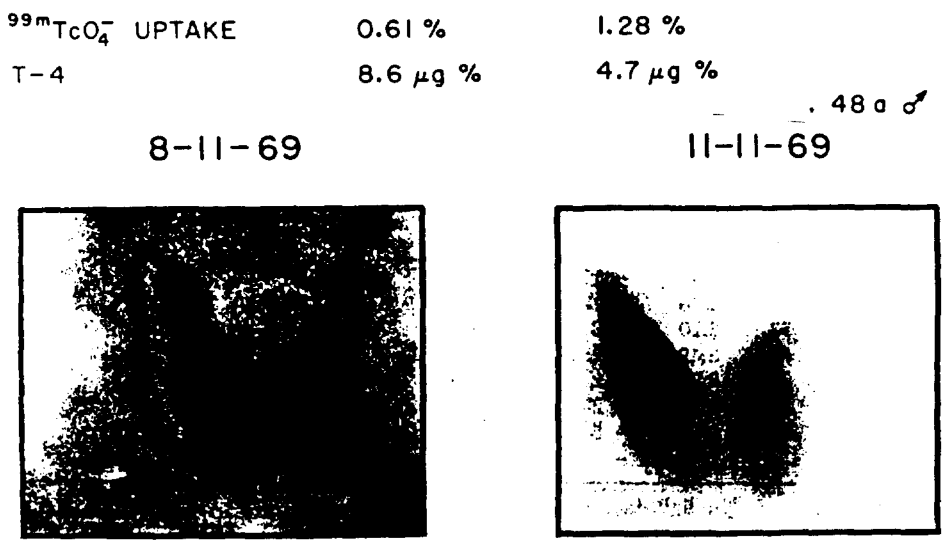

Fig. 3.—Scans and data on two examinations 3 mo apart in a man with acute thyroiditis. No treatment was given in the interim.

Advantages of Technetium-99m

There are a number of advantages to the use of technetium-99m, particularly for thyroid imaging but also for functional evaluation. The radiation dose is very low. For a 2.5 mCi administered patient dose the thyroid dose is 0.2–1.8 rad and the whole body dose 0.03 rad. With iodine-131 the thyroidal dose is 26–106 rad for a scanning dose and the whole body dose is 0.02 rad. However, with administered activity for uptake only, the iodine-131 dose is one tenth this or less. The low radiation dose allows one to do studies in children with less trepidation by far with ^{99m}Tc than with ^{131}I.

The short half-life of technetium allows repeated studies such as TSH stimulation or suppression without interference from the first study. Corrections for residual activity are unnecessary.

Information can be obtained in one patient visit. This is a convenience for the patient as well as for scheduling in the Department of Nuclear Medicine.

The amount of activity in the thyroid gland at the time of study is about 50 μCi on the average for technetium-99m and only about 10–15 μCi for a scanning dose of iodine-131. Add to this the fact that there are more usable photons at the peak for technetium and that collimation is more efficient and it is obvious that information can be obtained more accurately and readily than with iodine-131.

SPONTANEOUS REGRESSION OF HYPERTHYROIDISM

3-2-70 | 3-23-70 | 7-13-70

AFTER SUPPRESSION

	3-2-70	3-23-70	7-13-70
$^{99m}TcO_4^-$	2.68 %	3.42 %	0.81 %
$^{131}I^-$	41.5 %	55.5 %	19.1 %
T_4	5.7 mcg %	6.3 mcg %	4.8 mcg %
PBI		9.0 mcg %	5.4 mcg %

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Fig. 4.—Series of examinations in a patient who had mild hyperthyroidism. Far left is first examination before suppression. Middle picture is repeat examination following 8 days of suppressive therapy with 75 μg l-triiodothyonine per day. Note increase in uptake values. The examination on the right was performed 4 mo later without intervening treatment for hyperthyroidism.

system the line structure is lost and background is made an even density rather than discrete random densities since it requires several passes over any one region before the density can build up to a visible level. We find this preferable to using background subtraction.

Some examples of our results with this method are shown in Figs. 4 and 5.

It is our impression that functioning nodules are observed more often in scans performed with pertechnetate. Many of these functioning nodules have not been palpable. There have been isolated instances where others have found functioning nodules with pertechnetate scans which were not seen on ^{131}I scans.[20,21] These nodules may be localized regions of thyroiditis with intact trapping but deficient in binding. We have not performed a systematic comparison of scans done with technetium and with iodine but we have not noted any discrepancies in those instances where double nuclide scanning has been performed.

Table 3.—Results of TSH Suppression

	% $^{99m}TcO_4^-$ Uptake			% $^{131}I^-$ Uptake			T_4 or PBI (μg/100 ml)	
	Pre	Post	% Change	Pre	Post	% Change	Pre	Post
				Euthyroid Patients				
*†	8.80	2.66	− 70	—	16.7	−	3.3	5.1
	4.07	0.56	− 86	35.5	12.1	− 66	10.3	—
	2.25	0.69	− 69	27.1	—	−	7.7	—
.	3.50	0.79	− 77	31.8	2.4	− 92	6.8	[illegible].9
.‡	4.97	0.68	− 86	36.5	11.6	− 68	7.8	
Mean			− 78			− 75		
				Nontoxic Nodular Goiter				
	1.60	0.78	− 51	40.3	24.7	− 39	7.6	4.6
	2.27	1.45	− 36	16.3	16.8	+ 3	5.1	4.6
.	1.25	0.31	− 75	15.2	4.0	− 74	3.1	3.1
‡	3.71	1.52	− 59	41.0	27.4	− 33	8.5	—
.	5.61	0.83	− 85	43.3	0.1	− 100	5.7	4.5
.	2.25	0.69	− 69	27.1	—	−	7.7	—
§	1.15	1.26	+ 10	26.5	20.0	− 25	5.8	5.8
Mean			− 52			− 45		
				Hyperthyroid Patients				
	3.72	3.08	− 17	38.8	40.2	− 4	8.3	8.9
	7.90	8.30	+ 5	41.6	51.5	+ 24	11.1	11.4
	4.53	6.10	+ 35	66.2	72.0	+ 8	5.5	6.1
	2.68	3.42	+ 28	41.5	55.5	+ 34	5.7	6.3
	4.04	2.91	− 28	40.2	41.9	+ 4	8.1	6.6
	6.36	7.91	+ 24	56.6	50.4	+ 11	8.1	7.7
	2.17	0.99	− 54	49.9	31.7	− 36	8.2	4.9
Mean			− 1			+ 5.9		

Bold-face print is T_4; light-face print is PBI.
*Thyroiditis.
†Suppression with thyroid extract.
‡On oral contraceptive.
§Graves' disease without hyperthyroidism.

PRIVACY ACT MATERIAL REMOVED

Table 4.—Results of TSH Stimulation

	% $^{99m}TcO_4^-$ Uptake			% $^{131}I^-$ Uptake		
	Pre	Post	% Change	Pre	Post	% Change
	1.15	1.34	+ 17	13.1	28.9	+ 121
	2.56	3.35	+ 31	22.0	29.1	+ 32
	3.64	4.59	+ 26	17.9	25.7	+ 44
	1.70	6.78	+ 299	19.8	54.9	+ 177
	1.52	2.49	+ 64	31.2	40.0	+ 28
	2.90	2.76	− 5	21.0	25.4	+ 21
	0.65	1.14	+ 75	5.5	27.6	+ 402
	2.23	3.46	+ 55	19.5	24.2	+ 24
	2.56	4.40	+ 72	18.3	12.7	− 31
	1.97	4.76	+ 142	31.1	26.7	− 14
	1.36	3.00	+ 121	22.2	14.0	+ 37
	1.26	2.02	+ 60	29.0	22.9	− 21
	1.28	4.80	+ 275	24.4	41.0	+ 68
	0.15	0.33	+ 120	4.6	4.6	0
Mean			+ 97			+ 63

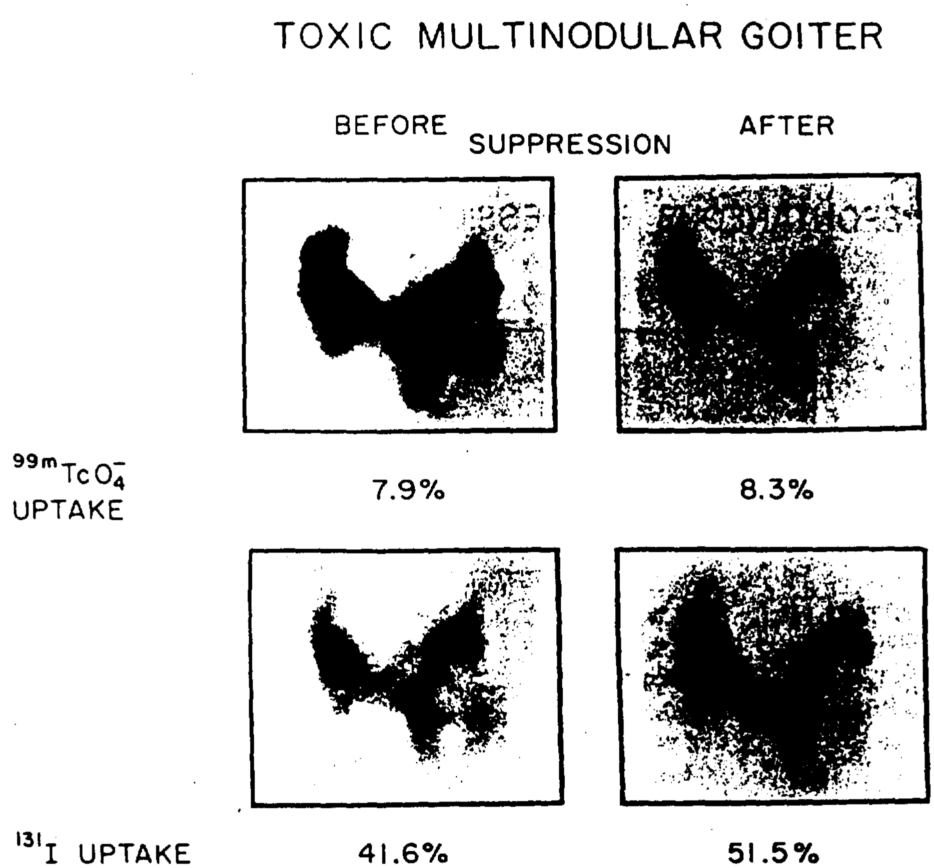

Fig. 5.—Series of scans before and after suppression with l-triiodothyronine utilizing ^{99m}Tc and ^{131}I in a patient with toxic nodular goiter.

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