JOURNAL OF NUCLEAR MEDICINE 5:489-499, 1964

# Evaluation of the Resin Uptake of $I^{131}$ Triiodothyronine as a Test of Thyroid Function[1]

**Edith H. Quimby and Elizabeth Hiza**

*New York City*

Sterling and Tabachnick in 1961 presented a test of thyroid function in which the radioactive iodine tracer is added to the patient's serum *in vitro* (1). The test has several advantages, of which possibly the most important is that previous medication with inorganic or organic iodine does not affect the validity of the results, as it does conventional $I^{131}$ uptake or protein-bound iodine determinations. Also, since the patient receives no radioactive material, the test may be used for children and pregnant women, and may be repeated as often as seems desirable.

The groups of patients in the Sterling and Tabachnick report were small, but the results were sufficiently striking to warrant an extensive test of the method. Over a two year period, 670 patients have had 937 tests in the Radioisotope Laboratory at the College of Physicians and Surgeons. The present paper offers an analysis of these findings.

## METHOD

The method used is essentially that published by Sterling, but with minor modifications. The necessary materials are $I^{131}$-labelled triiodothyronine[2] (T-3) and an amberlite resin.[3]

The triiodothyroinine is diluted to a final concentration of less than 0.12$\mu$g triiodothyronine per ml. For continuity, each dilution is checked against that of the previous week. All tracer material is kept refrigerated at 5° C.

The resin, which comes as a chloride, is converted to the formate form by washing with a 1 M solution of sodium formate adjusted to a pH of 5.0 ± 0.2. For this purpose, 50 gm of the resin are placed in a chromatography column and the sodium formate solution poured over it and allowed to drip through. The effluent is tested for chloride ion with a 0.1 N silver nitrate solution, and the washing continued until the effluent is chloride free. This requires approximately

[1]From the Department of Radiology, College of Physicians and Surgeons, New York City.

[2]Obtained as Triomet from Abbott Laboratories, 100 microcuries each week. To the shipment is added 0.2 ml of a 2.5 per cent solution of Red Cross human serum albumin, to help stabilize the material.

[3]Amberlite 1RA-400, a Rohm & Haas product, available from many laboratory supply agencies.

6 liters of sodium formate, somewhat more than Dr. Sterling (1) found necessary. Washing slowly does not reduce the amount of sodium formate required, so quick washing is employed. The washed resin is stored in the refrigerator under an equal volume of sodium formate.

The resin material can be obtained in various particle sizes which might exhibit different absorption properties. This had also been observed by Scholer (2). If not taken into account, this might invalidate the making of comparisons between results obtained with different particle sizes. For this reason a method of employing a control serum, as described below, was developed, eliminating the effect of differences in resin.

For testing the thyroid function of an individual, approximately 10 ml of blood are drawn into a Becton-Dickinson vacuum tube and allowed to clot. The tube is then spun at 2300 rpm for 10 minutes and the serum decanted. If it is not to be used immediately, it is stored in the freezing compartment of the refrigerator.

A large pool of sera from the medical chemistry laboratory is maintained for the control measurements. This is kept at about 800 ml, to make sure it is truly representative of normal blood. A sample of this is run with every batch of tests, to control day-to-day variations in T-3 stock, resin brands, and temperature. Repeated freezing and thawing of sera have little or no effect on the final result. This is evident from the fact that the control pool is repeatedly frozen and thawed, and day-to-day variations on a single pool gave an average of 1.6 per cent.

One control and five patient sera are usually run at one time. Four ml of each specimen are necessary if duplicate determinations are to be made. However, it is often difficult to get 4 ml of each patient serum. After a long series of duplicates had been run it was evident that a single determination should give a reliable result. Therefore a single 2 ml sample is now used.

*The steps in the procedure are as follows:*

1. For each patient specimen and the control serum a test tube is placed in an ice bath (2-6°C). Into each tube is put 2 ml of serum and 0.2 ml of the T-3 dilution. The tubes are tapped to insure mixing, and then allowed to equilibrate for 30 minutes, standing in the ice bath.

2. During this 30-minute period the resin tubes are prepared, also in an ice bath at 2-6°C, two for each tube in step 1. Exactly 1 ml of resin is pipetted into calibrated tubes for the well-type scintillation counter. This is best done by using an inverted pipette and inserting it under the sodium formate solution covering the resin. If more than 1 ml of the resin should be delivered into the counting tube, it can be suctioned off with an aspirator.

3. The resin in the counting tubes is washed 3 times with 5 ml of tap water from a wash bottle. The supernatant fluid is removed each time by aspiration, and the resin left slightly moist.

4. At the end of the 30-minute period, duplicate 1 ml samples of each serum-T-3 mixture are prepared, and added to the 1 ml of washed resin in the counting

tubes. The counting tubes are left uncorked, and positioned vertically in a test-tube rack on a horizontal shaker in a refrigerator at 2-6°C. Here the tubes are shaken at 203 cycles per minute, for one and one-half hours.

5. At the end of this period the tubes are again placed in an ice bath and kept there except during the 1 minute initial count in the well scintillation counter. After this count, they are returned to the ice bath until the serum is removed.

6. Following the initial count, the serum is washed from the resin by repeated applications of 5 ml of tap water from a wash bottle, the supernatant liquid being removed by suction. At the final (fourth) washing the water level is left at the 2 ml mark etched on the tube. A second count is now made in the well counter.

7. The calculation of resin uptake of the patient's serum relative to the control is obtained by the formula—

$$\frac{\dfrac{\text{count after washing of patient serum}}{\text{count before washing}}}{\dfrac{\text{count after washing of control serum}}{\text{count before washing}}} = \frac{x}{1}$$

By always considering the value for the control serum as 1.0, values for different patient's sera are related to a common base, and are therefore comparable.

Residual $I^{131}$ in the serum, either from treatment or a previous diagnostic test, is not a deterent to the T-3 resin uptake determination. All bloods received in the laboratory for this test are routinely checked for radioactivity. Active specimens necessitate an additional 2 cc of serum in order that a duplicate sample, without the added T-3 material, be run. The readings of the duplicate sample are subtracted from the test readings for the final results.

*Principle of the test.* Sterling and others have discussed the principle behind this test, and it is not necessary to go into this in detail. Briefly, it has been shown that circulating thyroxine is primarily bound to a specific blood protein fraction, the thyroxine-binding-globulin fraction. Triiodothyronine is similarly, but less firmly, bound to the same fraction. In the presence of increased thyroxine levels, as in hyperthyroidism, more of the specific thyroxine-binding sites are filled. When additional $I^{131}$-labelled triiodothyronine is added, it finds fewer binding sites available and therefore more of it remains unattached. Thus it is available to be bound by the anion exchange resin. The binding, or uptake by the resin, is therefore increased when the serum is that of a hyperthyroid individual, and conversely, decreased for the hypothyroid.

*The clinical material.* The clinical material consisted at first of patients on whom other tests for thyroid function were being performed. Later, as the resin test appeared to crystallize, some patients were sent to check a clinical evaluation. In addition, certain special groups were sought out, such as pregnant women, adolescents, patients on estrogens and other specific therapies, such as dilantin. In evaluating the test, the diagnosis used for each individual was that of the responsible physician. Many of the patients were also subjected to other tests, namely the 24-hour $I^{131}$ uptake, the protein-bound iodine, the basal metabolic rate, and the serum cholesterol. Correlations of findings in each of these with the resin uptakes will be presented below.

## RESULTS

The basic data for hyperthyroid, euthyroid, and hypothyroid sera, (Fig. 1) are plotted from values for patients unequivocally falling into these groups according to the clinical diagnosis. There were 239 euthyroid without medication of any sort, 36 hyperthyroid, either untreated or still toxic, and 43 hypothyroid, either primarily or as a result of medication. Those individuals who were euthyroid on medication or after treatment for hyperthyroidism are not included in this group.

The mean value for the basic euthyroid group was 0.98, with $\sigma = 0.135$. Seventy per cent of this group had values within 1 $\sigma$ of the mean, 94 per cent within 2 $\sigma$, that is, between 0.71 and 1.25. In the entire survey 383 cases were clinically euthyroid, including treated hyperthyroids and others on various medications. Of this entire group, 254, or 66 per cent were within 1 $\sigma$ of the mean; 360, or 94 per cent within 2 $\sigma$. Therefore a range of 0.70 to 1.30 should embrace all euthyroids.

For the basic hyperthyroids (36 cases), the mean was 1.89, with $\sigma = 0.42$. Thus a range of 1.05 to 2.73 should cover all of these.

In the basic hypothyroid group of 43 cases, the mean was 0.71, with $\sigma = 0.26$. Thus the range for such cases should be 0.45 – 0.97.

With ranges derived in this manner, there is considerable overlap. Closer scanning of the data makes some narrowing reasonable. For instance, in the basic euthyroid group, of those with values less than the mean only 7 (or 3%) were less than 0.80. On the other hand, for those greater than the mean, only 9 (or 3.8%)

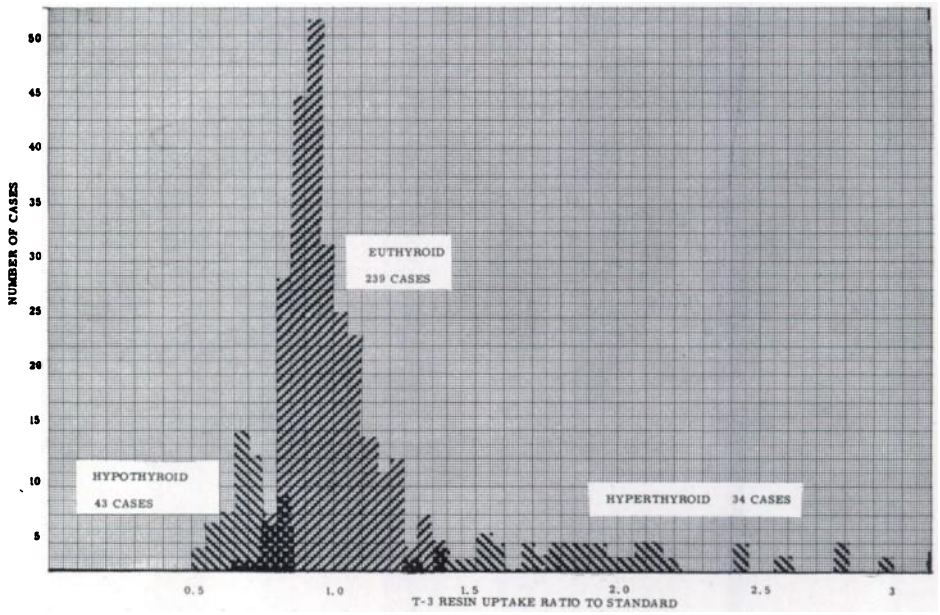


**Fig. 1. Basic data for hypothyroid, euthyroid, and hyperthyroid uptake ratios. Diagnoses for the 318 cases included were made by their physicians on the basis of clinical and laboratory findings.**

were over 1.30. An adjustment of the normal range, then, to set it at 0.80 to 1.30 seems reasonable. Readings above 1.30 will then be assumed to indicate hyperfunction of the gland, and those under 0.80 hypofunction.

With limits set in this manner on the basis of 318 cases, the larger group of 512 cases later available was evaluated. In this group two of the 57 hyperthyroids, or 4 per cent, gave readings in the euthyroid range. Of the 383 euthyroid, 13, or 3 per cent fell in the hyperthyroid region and 15, or 4 per cent in the hypothyroid, a total of 7 per cent misplaced. Ten clinically hypo-functioning patients of the 72, or 14 per cent, gave readings in the normal range. Overall, then, 40 of 518 patients, or 8 per cent gave resin readings not in accordance with clinical findings. These discrepancies were much more likely to occur in hypothyroid individuals than in others. These variations are less than those customarily accepted for the 24-hour $I^{131}$ uptake.

Of the first series of 239 uncomplicated euthyroids, 214 individuals also had one or more supplementary tests,—$I^{131}$ 24-hour uptake, protein-bound iodine (serum precipitable iodine) basal metabolic rate, serum cholesterol determination. There were also 34 frank hyperthyroids and 32 hypothyroids with one or more of these tests. Various comparisons may be made among these data.

It was not possible to demonstrate an upward trend in either $I^{131}$ uptake or PBI with increasing resin value, within the euthyroid group. If the normal resin range is taken as 0.80 to 1.30, of the PBI as 4.0 to 8.0, and of the $I^{131}$ uptake as 15 to 50, the following tabulation is informative:

| *Test* | *Accepted Range* | *No. of Comparable Cases* | *No. in Accepted Range* | *% Out of Normal* |
|---|---|---|---|---|
| | | *Euthyroid Group* | | |
| Resin | 0.80–1.30 | 132 | 122 | 7 |
| $I^{131}$ | 15–50 | 132 | 116 | 12 |
| Resin | 0.80–1.30 | 173 | 162 | 6 |
| PBI | 4.0 –8.0 | 173 | 158 | 9 |
| | | *Hyperthyroid Group* | | |
| Resin | Over 1.30 | 26 | 25 | 4 |
| $I^{131}$ | Over 50 | 26 | 22 | 15 |
| Resin | Over 1.30 | 22 | 21 | 4.5 |
| PBI | Over 8.0 | 22 | 20 | 9 |
| | | *Hypothyroid Group* | | |
| Resin | Less than 0.8 | 18 | 16 | 11 |
| $I^{131}$ | Less than 15 | 18 | 10 | 44 |
| Resin | Less than 0.8 | 29 | 25 | 14 |
| PBI | Less than 4.0 | 29 | 16 | 45 |

In the euthyroid and hyperthyroid groups the $I^{131}$ uptake shows the expected error of about 15 per cent; the PBI a lesser one, and the resin uptake least. However the hyperthyroid group is small for conclusions. In the hypothyroid group both $I^{131}$ and PBI show wide variations; the resin is apparently much better but this may be fortuitous for this small group.

No useful correlation was possible with either the serum cholesterol or the basal metabolic rate. It is commonly accepted that neither of these tests is as satisfactory an index of thyroid function as either the PBI or the $I^{131}$ uptake. Findings in this series serve only to support this opinion.

VARIOUS SPECIAL GROUPS WERE STUDIED:

1. *Treated hyperthyroids.* Thirty-eight hyperthyroids who had become euthyroid after $I^{131}$, surgery, propylthiouracil, or combined therapy, had resin uptakes between 0.69 and 1.34. Only 17 had had resin uptakes while they were hyperthyroid, of these 16 were above 1.35, and the 17th 1.26. Three of the final readings in the group as a whole were under 0.80, namely 0.69, 0.70, and 0.77 in the upper hypothyroid region. Certainly the final decision as to whether a hyperthyroid patient has been adequately treated is a clinical one, but a decided drop in resin uptake would be suggestive information.

2. *Adolescents.* Since the T-3 resin uptake is known to be affected by estrogens and androgens, it was felt that the adolescent population warranted special investigation. Fifty-four euthyroid individuals (males and females between 10 and 18) with a mean age of 14½ were studied. Thirty five of them had other tests for thyroid function in addition to a clinical diagnosis. The rest consisted of teenagers who were serving as hospital volunteers and had undergone routine physical examinations with no irregular findings. The mean resin uptake value for this entire group was 0.95, which is in the center of the adult euthyroid range. All but 9 (83%) of the adolescents had values within the normal adult range. It may accordingly be concluded that the normal range of the T-3 resin uptake is the same for adults and adolescents.

3. *Children Below 10 Years.* This group proved interesting because of consistently low resin uptake values. Only 15 children were studied: their ages ranged from 1½ to 9½ with an average of 6 years. Most of the cases were hospital patients with obstructional kidney disorders and unremarkable thyroid histories, who were presumably euthyroid. The mean resin uptake value for this group was 0.83. This is still within the normal adult range, but definitely on the low side. Six of these children had values in the hypothyroid range. Since these were not entirely normal children it is not certain that their sera would be typical of childhood euthyroidism. This may well be an area for further study.

4. *Ante-partum Patients.* After preliminary investigation on pregnant patients who were at, or close, to term, it was decided that the estrogen effect during pregnancy could best be evaluated by periodic determinations throughout the term. A total of 19 euthyroid patients were tested at their regular ante-partum clinic visits throughout pregnancy and up to delivery. The ante-partum period ranged from 37 ½ to 44 weeks or, 40 weeks on the average. This was divided into

trimesters of 1-12 weeks, 14-28 weeks (no patient was seen in the 13th week), and 29 weeks to delivery. The earliest case seen was 7 weeks pregnant.

Seventeen tests were done on patients in their first trimester. Resin uptakes were from 0.52 to 0.76 with a mean of 0.61; thus all were in the "hypothyroid" range. Since each patient was rarely seen more than once during this period, the overall numbers are small. Nevertheless, the resin uptake values at this time are already quite distinct from those of non-pregnant individuals as well as from those of the 2nd trimester.

During the 2nd trimester (14-28 weeks) 70 tests were done and the mean dropped to 0.47, range 0.37-0.61. This is definitely lower than the first trimester value.

The last trimester is represented by 112 tests with a mean value of 0.45, range 0.31-0.59. This is only slightly below the second trimester value; the difference is not significant.

A separate group of 36 patients, with resin uptakes done at the time of delivery *only*, presented a mean value of 0.47, range 0.31-0.68. This correlates well with the above series. In no case was the value lower than 0.31.

Resin uptake determinations were also made on thirteen additional pregnant women, who presented some question of thyroid disorder—gland diffusely enlarged, cold intolerance, etc. All gave values well within the mean for their respective periods and were subsequently judged euthyroid.

5. *Post-partum Cases.* Eleven of the original 19 pregnant patients consented to continue in the study during the post-partum course. Their resin uptakes grad-

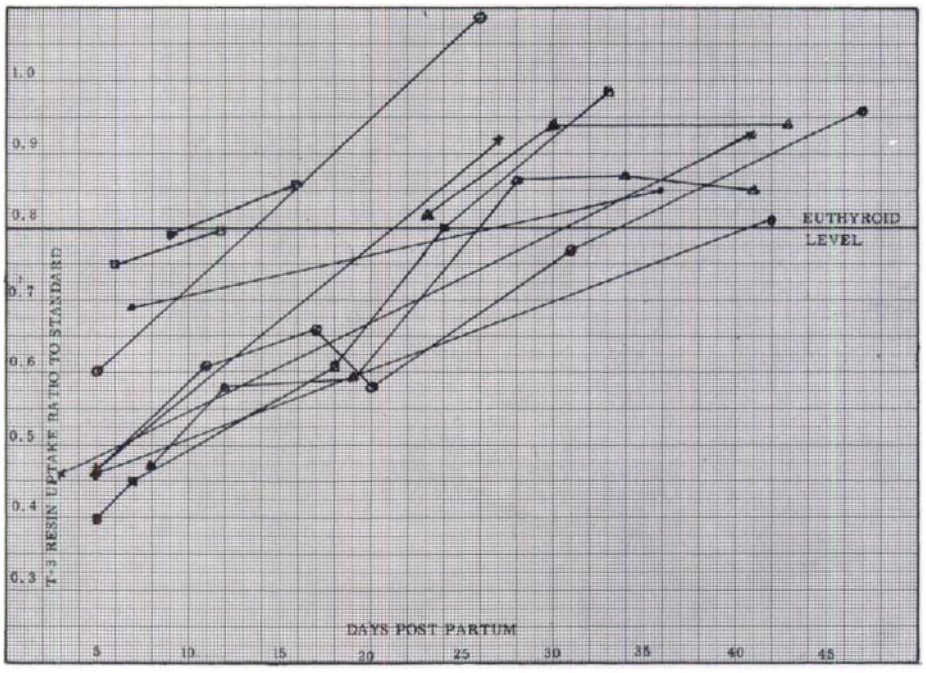


**Fig. 2. Pattern of return to normal resin values in eleven post-partum women.**

ually increased in a fairly consistent pattern (Fig. 2), and generally reached normal about the 25th post-partum day. One of the 11 showed a normal result at the 12th post-partum day, but then dropped slightly below normal and stayed there. The blood specimens were drawn at rather irregular intervals to cause the least inconvenience to the new mothers. However, the trend, even on so few cases, is obvious.

6. *Estrogen Effect in Non-Pregnant Women.* Nine female patients were taking estrogens of various types (Enovid, Premarin, Norlutin, etc.), a few were also on thyroid medication such as cytomel. All were considered euthyroid. In all cases the resin uptake was depressed and seemed to mimic the 1st trimester of pregnancy with a mean value of 0.59.

7. *Androgen effect.* The administration of androgens apparently causes a definite increase in the resin uptake. It was possible to study three male and one female patients before and after such therapy. Pretreatment values were 0.63, 0.66, 0.76, and 0.88. On treatment, these rose to 1.04, 0.95, 1.33, and 1.21. The first two were teen-age boys.

Early in the series, it seemed that males, in general, exhibited slightly higher uptakes than did females. However as the study progressed it was apparent that the differences were insignificant. In the basic group of 239 uncomplicated euthyroid cases, there were only 53 males. However their basic values (0.99) are in agreement with those of the females (0.98).

In view of the obvious estrogen/androgen effect, a study of post-menopausal females was to be desired. It was only possible to collect a small group, with only 32 over age 60 (mean age: 68). The average resin uptake for this group was 1.00, range 0.81 to 1.49.

Although a slight increase in mean value was observed, there seems to be little doubt that neither the endocrinologically normal male or the post-menopausal female gives values outside the basic norm.

Contrary to these findings is a recent preliminary report by DiGiulio *et al* (4) indicating that normal values for males and post-menopausal females are significantly different from those of pre-menopausal females. They felt that unrecognized differences could be attributed to techniques having poor discrimination between the groups.

*Dilantin.* It has been reported (3), that dilantin is capable of occupying the binding sites of TBG (thyroxine-binding-globulin) and would, therefore, be expected to increase the resin uptake. Cases before and after dilantin treatment were, unfortunately, very difficult to get and only one such study was made. The resin uptake increased from 0.78 to 0.90 after two weeks on 50 mg dilantin. Eight other patients, already on dilantin for varying periods, and diagnosed as euthyroid, showed a mean resin uptake of 1.02, range 0.81 to 1.27. This is not appreciably different from the normal range.

The in vitro effect of dilantin was also observed by adding it to the incubation mixtures of 12 serum samples (12.5 $\mu$g/ml serum). The initial uptake values of the serum samples, *i.e.* prior to dilantin, ranged from 0.63 to 1.07. With the addition of dilantin, each determination showed an increase ranging from 0.01 to 0.28. Therefore, the only uptakes that were significantly affected were those

in the borderline regions. From these data it can be concluded that the effect of dilantin on the resin uptake is minimal.

*Duplication of results.* An investigation of the early results on 485 duplicate 2 ml samples showed the average difference between such samples to be 1.6 per cent. Later, when it became necessary to use only 2 ml of serum for each patient determination, the average difference between two 1 ml samples was 1.2 per cent. This was based on 372 determinations. Accordingly the measurement of duplicate samples was discontinued.

It will be remembered that all the values given previously, are related to an assumed value of 1.0 for the pooled sera. However it may be worth while to include the original percentage uptakes for these sera. These values should be helpful to other groups who may wish to utilize the basic technique but be forced to change certain factors, such as resin brand or temperature to fit their particular working conditions. Use of these percentages would permit an approximate intercomparison.

The pooled sera, used as the basic control, gave an average value of 20.6 ± 2.4 per cent uptake of the $I^{131}$, with a range of 15.6 to 27.3. These values cover a 1½ year period, using 8 different pools, each having an initial volume of about 800 ml.

## DISCUSSION

This *in vitro* method of assaying thyroid function appears to be at least as accurate as the 24-hour $I^{131}$ uptake; according to the series here reported it is somewhat better, and is in fact not inferior to the PBI. It has several advantages over the usual *in vivo* tests:—1. Only one patient visit is necessary, instead of the usual two. 2. A rigid schedule of appointments for counting is not necessary. Blood can be drawn at any time, and serum stored for convenience. 3. Previous medication with organic or inorganic iodine or desiccated thyroid does not affect the validity of the results. 4. It is practicable to repeat the test as often as desired, and the procedure will not be complicated by iodine remaining from earlier tests. 5. Since the patient receives no radioactive material, the test may be used for children, pregnant women, or anyone else in whom the presence of radioactivity is contra-indicated—*e.g.* those about to undergo other tests with radioactive materials.

In a busy isotope laboratory, a disadvantage is the amount of time required to complete the test—considerably longer than the 24-hour uptake, although not so long as the chemical PBI. The need for special facilities for keeping everything refrigerated before and during the test may be a drawback. The fact that results obtained with different resin batches are not always strictly comparable is inconvenient, but the device of standardizing each batch relative to a large sample of pooled sera makes it simple to keep all values comparable within a single institution. However before values from different laboratories are considered comparable even on this basis, it would be desirable to obtain a series of cross-comparisons.

This has been done for one other laboratory in New York. Comparison studies on sera exchanged with Dr. Kenneth Sterling's laboratory, and with that of the Mt.

Sinai Hospital pointed out the group-to-group variations in normal uptakes when percent values were employed, and emphasized the usefulness of the ratio values. In a small group of 39 patient sera, exchanged with Mt. Sinai, only 3 showed significant disagreement between the 2 laboratories. Five others showed discrepancies of lesser degree and they were all in the borderline region (5).

It is not suggested that this test replace the 24-hour untake in a busy department. The extra time necessary would usually preclude this. But as a supplementary or substitute test in special cases, it appears to be very much worthwhile.

## SUMMARY

An *in vitro* test of thyroid function has been evaluated in a series of about 1000 measurements. The test consists in adding to the patient's serum a known amount of $I^{131}$ labelled triiodothyronine, mixing this with an ion-exchange resin, and measuring the amount of radioactive iodine absorbed by the resin. All uptake or absorption values are related to that obtained with a sample from a large pool of mixed sera (chemistry laboratory or blood bank) which is assumed to represent the normal individual. On the basis of the reading of this sample as 1.0, values from 0.80 to 1.30 indicate euthyroidism. Above 1.30 the indication is for hyperthyroidism and below 0.80, for hypothyroidism.

In a series of 383 individuals clinically euthyroid, 3 per cent gave unduly high readings and 4 per cent unduly low. This is better than would be expected of the 24-hour $I^{131}$ uptake test. Of 57 hyperthyroids, 4 per cent gave readings in the euthyroid range; of 72 clinically hypothyroids, 14 per cent gave readings in the euthyroid range; (this is comparable to the $I^{131}$ uptake).

Adolescents and children give readings in the adult euthyroid region. The very young children tend to be in the lower part of the range; the teen-agers fall in the center.

Very early in pregnancy the value for the euthyroid woman drops into the low hypothyroid range and remains there until a few weeks post-partum.

It is not suggested that this test replace the 24-hour uptake, or any other currently employed test. It is an addition to the battery of tests available. It does have the outstanding advantage of not being influenced by previous medication with iodine. It is somewhat more difficult and time consuming than the standard uptake test, but no more so than the PBI.

## ACKNOWLEDGEMENTS

The authors are greatly indebted to Dr. Kenneth Sterling for his assistance in setting up the test, and for his continued interest and encouragement. The entire medical staff of the Thyroid Service were most cooperative in furnishing patients and their diagnoses for the basic series. Members of Department of Obstetrics and Gynecology made possible the pregnancy study. All of the personnel of the isotope laboratory were involved in making the measurements; their help is gratefully acknowledged. Particular thanks are due to Miss Marcella Edwards, who went to the homes of many post-partum patients to obtain the

blood samples for completing the pregnancy study. The intercomparison with the Mt. Sinai Hospital study was made possible by the cooperation of Dr. Josi Mayer.

REFERENCES

1. STERLING, K., TABACHNICK, M.: Resin Uptake of $I^{131}$-Triiodothyronine as a Test of Thyroid Function. *J. Clinical Endoc. and Metab.* **21**:456, 1961.
2. SCHOLER, J. F.: A Simple Measure of Thyro-Binding by Plasma: A Test of Thyroid Function. *J. Nuclear Med.* 3:41, 1962.
3. OPPENHEIMER, J., FISHER, L. V., *et al.:* Depression of the Serum Protein-Bound Iodine Level by Diphenylhydantoin. *J. Clinical Endoc. and Metab.* **21**:252, 1961.
4. DIGIULIO, W., WEINHOLD, P., *et al.:* The Thyroxine-Protein Dissociation Index, A Modified T-3 Resin Uptake Procedure. *J. Nuclear Med.* **4**:359, 1963.
5. MEYER, J.: Mt. Sinai Hospital, New York City. *Personal Communication.*

## Announcement to Authors
## Preliminary Notes

Space will be reserved in each issue of THE JOURNAL OF NUCLEAR MEDICINE for the publication of one preliminary note concerning new original work that is an important contribution in Nuclear Medicine.

Selection of the preliminary note shall be on a competitive basis for each issue. One will be selected after careful screening and review by the Editors. Those not selected will be returned immediately to the authors without criticism. Authors may resubmit a rejected or revised preliminary note for consideration for publication in a later issue. The subject material of all rejected manuscripts will be considered confidential.

The text of the manuscript should not exceed 1200 words. Either two illustrations, two tables, or one illustration and one table will be permitted. An additional 400 words of text may be substituted if no tables or illustrations are required. Only the minimum number of references should be cited.

Manuscripts should be mailed to the Editor, Dr. George E. Thoma, St. Louis University Medical Center, 1402 South Grand Blvd., St. Louis, Missouri 63104. They must be received before the first day of the month preceding the publication month of the next issue, *e.g.*, preliminary notes to be considered for the September, 1964 issue must be in the hands of the Editor before August 1, 1964.