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Resin Sponge Modification of the I^{131} T3 Test[1]

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Measurements of the saturation of thyroid hormone-binding protein by indirect methods have been employed as clinical tests of thyroid function. The *in vitro* tests currently available include the erythrocyte uptake of I^{131} labeled triiodothyronine (T3), (1), the use of a granular resin as the competing medium instead of erythrocytes (2,3,4), and most recently, the incorporation of a resin within a standard sized plastic sponge (5). The simplicity of the resin sponge technique and its independence from hematocrit, hemolysis, and red cell anomalies seemed to offer an advantage over the erythrocyte uptake method. The present study was undertaken to evaluate the practical application of the resin sponge uptake method and to compare clinical usefulness with a previous three year experience with the erythrocyte uptake technique.

MATERIALS & METHODS

The resin sponge uptake of I^{131} T3 was performed by the method of Mitchell (5). Individual plastic syringes with the I^{131} T3, resin sponges, tubes and caps, plungers and aspirator tips were supplied as the "Triosorb T3 Diagnostic Kit" (Abbott Laboratories.) Each plastic syringe contained not more than 0.01 μc of I^{131} in 0.002 μg of T3 (Fig. 1).

PROCEDURE

Analyses were performed on the day of collection or on samples stored in the frozen state. One ml aliquots of serum were pipetted into the tubes provided. The entire contents of each syringe was added to the tubes without mixing. At one minute intervals the resin sponges were placed in the tubes and mixing was achieved by depressing the sponge with the plunger of the syringe several times. Care was taken to express all the air bubbles from the sponge.

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TABLE I

% T-3 RESIN SPONGE UPTAKE

#1 Pooled Normal Sera	*No. of Determinations*	*Mean*
Jan. 25, 1963—Oct. 10, 1962	144	30.4
Oct. 11, 1962—Dec. 31, 1962	61	35.3
April, 1963	25	35.1
#2 Pooled Normal Sera		
April, 1963	32	35.6

The initial total radioactivity of each sample was measured in the well counter during the incubation period. The tubes were left standing for exactly one hour at room temperature (25° C). Using the aspirator tip and suction, all liquid was aspirated from the tube by squeezing the sponge. After refilling the tube with water, this was repeated three times. The residual radioactivity in the washed sponge was then counted and the percent uptake by the incorporated resin calculated. Corrections were made for temperature (1% for each degree above or below 25° C). The value of a pooled normal serum standard performed in duplicate was determined and a correction factor for the day calculated and applied to the test results.

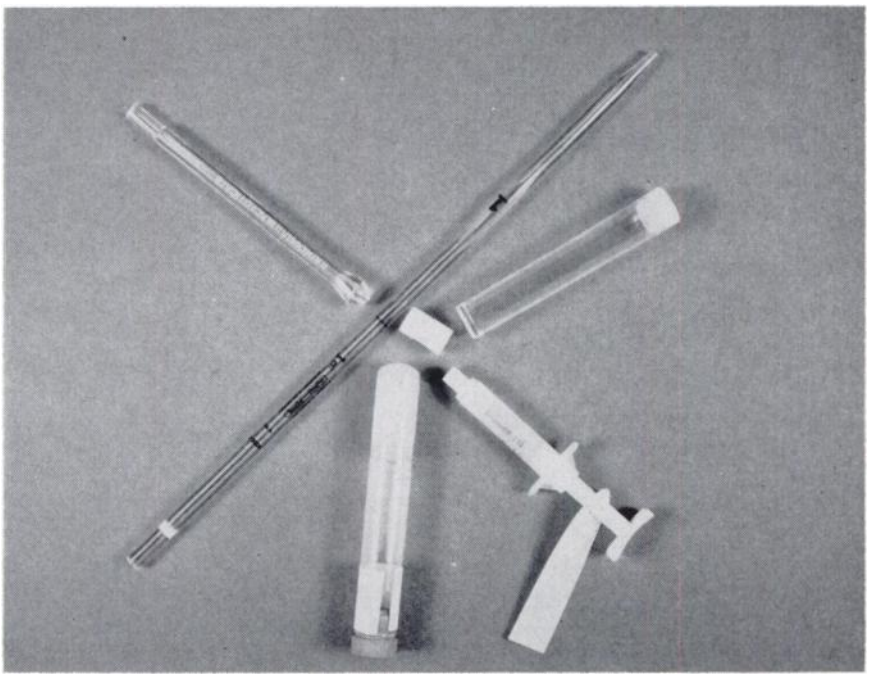

Fig. 1. Materials used in performance of the resin sponge I^{131} T3 test: Serum, incubation and counting tube and cap, I^{131} T3 capped syringe, resin sponge, 1 ml. pipette and aspirator tip.

TABLE II

Group	Erythrocyte—T3 No.	%	Accuracy	Resin Sponge—T3 No.	%	Accuracy
Non-pregnant Euthyroid	70	95%	(67/70)	75	91%	(68/75)
Hyperthyroid	21	62%	(13/21)	29	97%	(28/29)
Hypothyroid	31	16%	(5/31)	19	37%	(7/19)

RESULTS

The normal range for the resin sponge uptake was determined by analyses of the sera of 49 known euthyroid subjects. The mean difference between duplicate determinations was 0.95 per cent. One was greater than 2 per cent (2.1). The mean value for resin sponge uptake of the 49 sera was 29.86 per cent (S.D.± 2.48%). A normal range of 25-35 per cent was established (± 2 S.D.).

The necessity for a correction factor derived from duplicate daily analyses of a pooled serum standard became evident early in the study. Considerable daily variations in results occurred (Fig. 2); the mean value for the standard rose from 30.4 per cent to approximately 35 per cent where it remained during the study period. Presumably changes in details of production of the resin sponge were responsible for this shift (Table I).

CLINICAL RESULTS

A total of 274 patients were examined by one of the authors. The status of thyroid function was assessed clinically and by at least two of the following standard diagnostic procedures: serum protein-bound iodine; thyroidal uptake of I^{131}; basal metabolic rate; or achilles tendon half-relaxation time. Determinations of

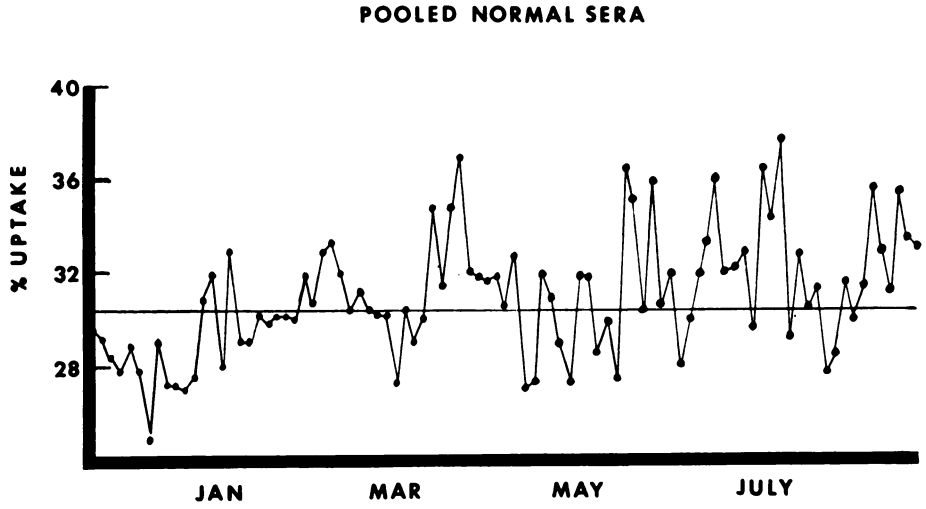

Fig. 2. Variations in the percent resin sponge T3 uptake of a pooled normal serum standard. The mean (30.4%) is represented by the horizontal line.

the erythrocyte incorporation of I^{131} labeled T3 were done on the blood of 122 non-pregnant subjects. Determinations of the resin sponge T3 uptake were done on the sera of 123 additional non-pregnant subjects and the two groups compared. The 29 pregnant subjects examined were not included in this comparison. The results are summarized in Table II and Figure 3.

The mean resin sponge uptake for 75 euthyroid non-pregnant patients with a variety of non-endocrine diseases was 30.9 per cent with a range of 25.5 – 37.5 per cent. All but 7 euthyroid subjects demonstrated values within the 95 per cent confidence limits for the normal range (25-35%). The percentage accuracy for the resin sponge method was slightly less than that for the erythrocyte T3 method. The ten euthyroid patients with simple goiter demonstrated values within the 95 per cent confidence limits of the normal range (mean 29.3%).

The mean resin sponge T3 uptake for 29 hyperthyroid subjects was 47.1 per cent with a range of 32.8 – 69.5 per cent. In comparison with the erythrocyte T3, the resin sponge method improved the diagnostic discrimination between euthyroid and hyperthyroid subjects. Only one hyperthyroid subject had a resin sponge uptake value within the established normal range.

Improvement in discrimination between hypothyroid and euthyroid patients was demonstrated with the resin sponge method but the percentage accuracy remained poor. Sixty three percent (12/19) resin sponge uptake values in hypothyroid subjects fell within the normal range. The mean value for 19 subjects was 26.6 per cent with a range of 22.7 – 36.0 per cent.

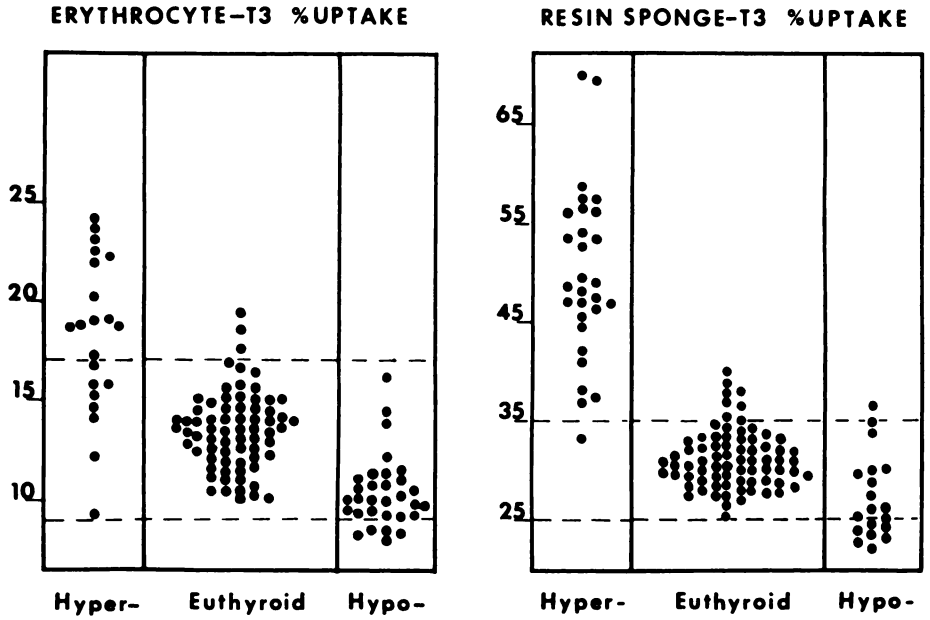

Fig. 3. Values obtained by erythrocyte T3 method in 122 non-pregnant subjects compared with resin sponge T3 values obtained in a similar group of 123 non-pregnant subjects.

Resin sponge T3 values were determined for 29 pregnant women during either the first or second trimester. In addition, values were determined in 27 of these women on the third postpartum day and in 21 of these at 6 weeks postpartum. The results are shown in Figure 4.

The mean value for 29 women during the first or second trimester of pregnancy was 21.4 per cent. Only one woman in the first trimester of pregnancy demonstrated a value within the 95 per cent confidence limits of the normal range (30.8% at 6 weeks). The mean value for 27 of these women on the third postpartum day was 21.5 per cent. Two subjects demonstrated values within the normal range (28.8, 29.5%). Twenty-one of the same women were available for re-examination 6 weeks after delivery. The mean resin sponge uptake value at this time was 31.2 per cent. One woman demonstrated a slightly elevated value of 35.6 per cent; the remaining 20 women all had values within the normal range.

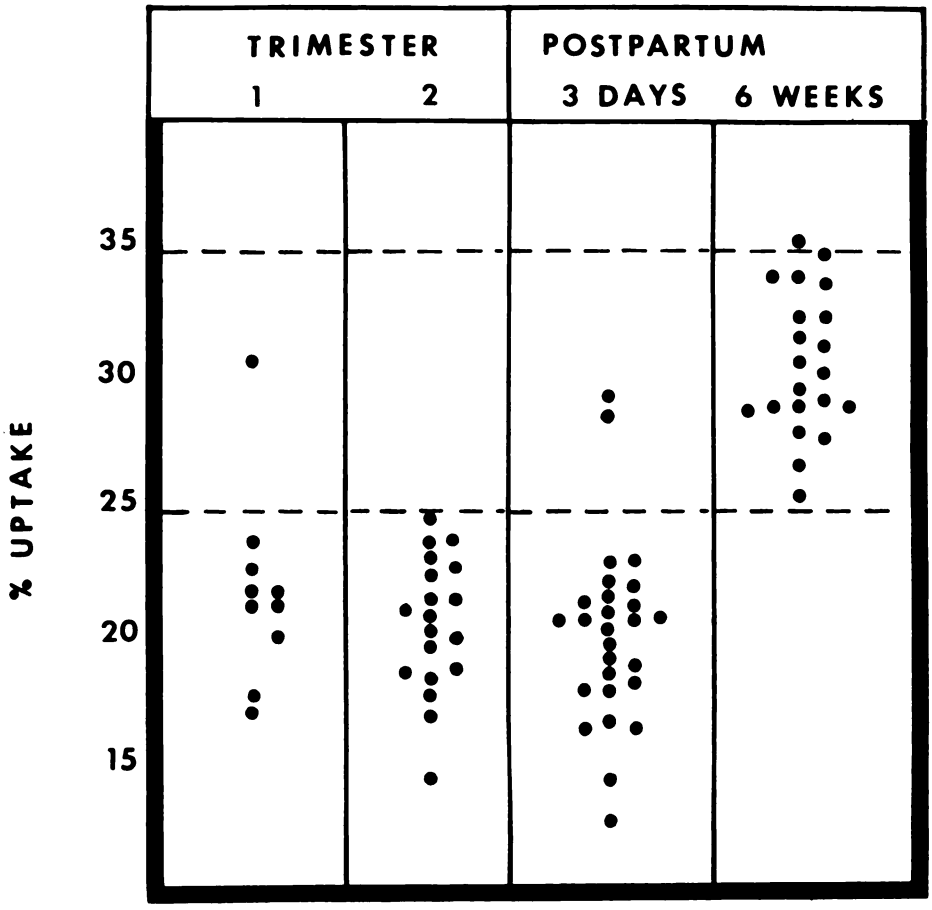

Fig. 4. Resin sponge T3 values obtained in a group of women during pregnancy, after delivery and 6 weeks postpartum.

DISCUSSION

The erythrocyte uptake of I^{131} triiodothyronine, introduced by Hamolsky et al in 1957 (1), has been employed as a laboratory test of thyroid function. The advantages and limitations of this technique as a clinical measure of thyroid status are well known. To overcome some of the inherent inaccuracies and technical difficulties of the erythrocyte T3 method, Mitchell (2,3) and Scholer (4), developed a simple, reliable method using a strongly basic ion exchange resin labeled with I^{131} T3 instead of erythrocytes as the competing medium for the added I^{131} T3. The technique consists of adding plasma (2 ml) to 0.1 gm aliquots of the filtered, washed, dried resin, agitating the mixture for 2 hours at 37° C, and measuring the supernatant plasma radioactivity after settling or centrifugation. Plasma radioactivity is related to total tube radioactivity (corrected for decay) and the "thyro-binding" index is calculated by comparing results with those of a standard pooled plasma determined at the same time.

Elimination of the errors and problems of hematocrit differences, cell hemolysis, storage of test samples and lack of satisfactory pool control was demonstrated by Scholer, using the loose resin technique (4).

In 1960, Mitchell in an effort to eliminate "sporadic fluctuations—, probably related to some of the intrinsic properties of the granular type resins" modified the loose resin procedure by making use of a commercially prepared mixture of polyurethane foam and a finely ground anion exchange resin, Amberlite IRA-400 (200-400 mesh) in the chloride cycle. The mixture was then produced as a plastic cylindrical sponge 1.7 cm x 1.0 cm with the resin held evenly distributed throughout (5). This modification eliminated the necessity for constant shaking during the incubation period as well as the transfer of radioactive supernatant serum by pipette. The uniformity of composition of the resin sponge permitted reproducibility of results.

The mean value and normal range for euthyroid subjects by the resin sponge method demonstrated in the present study were identical with those reported by Mitchell. The simplicity in performance and reproducibility of test values was also confirmed.

The clinical results of the present study demonstrated good diagnostic discrimination between hyperthyroid and euthyroid patients and between pregnant women and euthyroid patients. Although the resin sponge technique improved diagnostic discrimination in the hypothyroid patients when compared with erythrocyte T3 technique, over one-half of patients with hypothyroidism demonstrated values within the normal range. This troublesome overlap in hypothyroid patients was similar to the experience reported by Mitchell (5).

CONCLUSION

The resin sponge technique is superior to the erythrocyte method for performing the I^{131} T3 test in terms of simplicity, convenience and elimination of errors characteristic of the erythrocyte procedure. The use of a pooled serum standard is an additional advantage.

Separation of hyperthyroid patients and pregnant women from euthyroid

subjects is relatively clear cut with the resin sponge method. Resin sponge test separation of hypothyroid patients from euthyroid subjects, although better than that demonstrated with the erythrocyte method, remains unimpressive. A clear cut low uptake value has diagnostic significance in non-pregnant subjects but a normal value does not rule out hypothyroidism. The resin sponge I^{131} T3 uptake is not recommended as a screening test for hypothyroidism.

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REFERENCES

1. HAMOLSKY, M. W., STEIN, M. AND FREEDBERG, A. S.: The Thyroid Hormone-Plasma Protein Complex in Man. II. A New *in vitro* Method for Study of "Uptake" of Labeled Hormonal Components by Human Erythrocytes. *J. Clin. Endocrinol. & Metab.* **17**:33, 1957.
2. MITCHELL, M. L., WHITEHEAD, A. B., AND O'ROURKE, M. E.: Differential Absorption of Hormones from Serum. *(Abstract) J. Lab. & Clin. Med.* **52**:930, 1958.
3. MITCHELL, M. L.: Resin Uptake of Radiothyroxine in Sera from Non-Pregnant and Pregnant Women. *J. Clin. Endocrinol. & Metab.* **18**:1437, 1958.
4. SCHOLER, J. F.: A Simple Measure of Thyro-Binding by Plasma: A Test of Thyroid Function. *J. Nuclear Med.* **3**:41, 1962.
5. MITCHELL, M. L., HARDEN, A. B. AND O'ROURKE, M. E.: The in vitro Resin Sponge Uptake of Triiodothyronine—I^{131} from Serum in Thyroid Disease and in Pregnancy. *J. Clin. Endocrinol. & Metab.* **20**:1474, 1960.

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