Studies on the Metabolism of the Thyroid Hormone by the Double Tracing Method (II)

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In the previous report we demonstrated the method of synthesis of 3', 5'-131I-T4 by coupling DIT with DIHPPA Taurog's exchange labelling method of 3', 5'-125I-T4, and the technic of individual counting of 125I & 131I.

In the course of work, satisfactory results were not obtained with the method of Taurog, in which T4 sometimes decomposed and which was not so good yield.

The present report is referring to our improved labelling method of 3', 5'-125I-T4 and usefulness of 125I/131I ratio on the identification of partially deiodinated metabolites of T4.

1) Labelling method of 3', 5'-125I-T4.

In this procedure oxidated 125I2 in a small test tube by HCl and H2O2 is extracted with ethylether, which is then mixed with 50% ethanol solution of T4 (ph 5) and incubated for exchange reaction in room temperature.

Points of excellence of this method are follows. a) The fraction of radioactivity which is brought to the exchange reaction mixture is very large; in this method 90-95%, Taurog's method 30-35%. b) The decomposition of T4 does not occur. c) Very good yield; this method 70%, Taurog's method 25-30%. d) No particular apparatus is needed, etc.

2) Usage of 125I/131I ratio on the identification of T4 metabolites.

Papachromatography and paper electrophoresis are chiefly employed for the separation and identification of T4 metabolites. But in these experiments the identifications have been sometimes very difficult. The adoption of 125I/131I ratio made this much easier. This 125I/131I ratio made this much easier. This 125I/131I ratio is not the ratio of simple counts of 125I and 131I but the ratio which is corrected by calculation as the ratio of initial mixture of both T4 equal 1.0. Accordingly 125I/131I ratio means the ratio of numbers of iodine atoms of 3', 5'-positions per those of 3,5-positions, Namely T4: 1.0, T3: 2.0, so on...

This 125I/131I ratio was applied to the identification of T4 metabolites in bile of rats which were injected both T4 mixture. On two-dimensional paper chromatogram the ratio of T4 and T3 spots confirmed by standard compounds were 0.98 and 0.54 respectively. The ratio of T4 spot was 1.07. These values agreed with the theoretical values.

Revaluation of Triiodothyronine Suppression Test

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About 300 subjects with thyroid disorder have been examined T3 (triiodothyronine) suppression test in our clinic in these 6 years. 131I thyroidal uptake were not suppressed sufficiently after T3 100 ug per day for 6 days treatment or ot, so this report intended to ascertain of the period of T3 treatment when all euthyroid patients acquire the sufficient suppressibility.

Twenty-one nontoxic goitrous patients and 131I treated hyperthyroid patients were studied the change of the suppressibility in the
course of T₃ 100ug per day administration.

The suppressibility was determined on 3rd and 6th day in each 26 of these patients (16 nontoxic goitrous patients and 10 ¹³¹I treated hyperthyroid patients), and on 6th and 13th day in the other 9 patients (5 nontoxic goitrous patients and 4 ¹³¹I treated hyperthyroid patients) during T₃ 100ug per day treatment.

The following results were obtained:
1. In most all of nontoxic goitrous patients, the suppressibility increased gradually according as the prolongation of the period of T₃ administration.

The mean (±SE) of the suppressibility of 3rd day was 40.8 ±6.1% and that of 6th day was 67.7 ± 5.6%. Suppressibilities of all nontoxic goitrous patients on 13th day were more than 93.6%.

2. In treated hyperthyroid patients, the suppressibility was not changed by prolongation of T₃ treatment until 13 days.

From these results, it was suggested that the suppressibility after T₃ 100 ug per day for 13 days would be more beneficial to evaluate the thyroid function precisely than for 3 or 6 days.

¹³¹I Triiodothyronine Resin Sponge Uptake (R.S.U.) Test in Diagnosis of Thyroid Diseases (III)—Usefulness of R.S.U. test in Evaluation of Therapeutic Effect of ¹³¹I and Mercaptoimidazole

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1) Of the hyperthyroid patients made euthyroid by ¹³¹I treatment, 89% shows R.S.U. values within normal range, whereas only 55% of the same patients shows ¹³¹I thyroidal uptake rate within normal range. The comparison of these figures attests to the usefulness of R.S.U. test in the evaluation of the therapeutic effect of ¹³¹I.

2) The pattern of changes of R.S.U. after ¹³¹I treatment can be divided into 5 groups:
i) R.S.U. returns within normal range within 2 months after the treatment and remains normal thereafter. This pattern is seen most frequently. ii) R.S.U. becomes below normal for a short period of time 2 to 5 months after the treatment and then returns within normal range. iii) After once becoming normal, R.S.U. returns above the normal range several months later, with reappearance of symptoms of hyperthyroidism. iv) After 2 to 3 months following the treatment, R.S.U. remains at the border-line low levels without any sings of hypothyroidism and v) R.S.U. remains at border-line high levels without any sings of hyperthyroidism.

3) When R.S.U. remains high more than 3 months after ¹³¹I treatment, it is most likely that the dose of ¹³¹I is insufficient and the administration of the second dose is necessary.

4) Within 1 to 2 weeks after the administration of the therapeutic dose of ¹³¹I, the R.S.U. value is often higher than the pretreatment level. The R.S.U. value becomes lower than before the administration of ¹³¹I more than 4 weeks later in majority of cases.

5) R.S.U. is normal in the majority of cases of hyperthyroidism made euthyroid by Mercaptoimidazole treatment, whereas the thyroidal ¹³¹I uptake rate is normal only in about the half of these cases.