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'-^{131}I-T_4 by coupling DIT with DIHPPA Taurog's exchange labelling method of 3', 5'-^{125}I-T_4, and the technic of individual counting of ^{125}I & ^{131}I.

In the course of work, satisfactory results were not obtained with the method of Taurog, in which T_4 sometimes decomposed and which was not so good yield.

The present report is reffering to our improved labelling method of 3', 5'-^{125}I-T_4 and usefullness of ^{125}I/^{131}I ratio on the identification of partially deiodinated metabolites of T_4.

1) Labelling method of 3', 5'-^{125}I-T_4.

In this procedure oxidated $^{125}I_2$ in a small test tube by HCl and H_2O_2 is extracted with ethylether, which is then mixed with 50% ethanol solution of T_4 (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 T_4 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 ^{125}I/^{131}I ratio on the identification of T_4 metabolites.

Paperchromatography and paperelectrophoresis are chiefly employed for the separation and identification of T_4 metabolites. But in these experiments the identifications have been sometimes very difficult. The adoption of ^{125}I/^{131}I ratio made this much easier. This ^{125}I/^{131}I ratio made this much easier. This ^{125}I/^{131}I ratio is not the ratio of simple counts of ^{125}I and ^{131} I but the ratio which is corrected by calculation as the ratio of initial mixture of both T_4 equal 1.0. Accordingly ^{125}I/^{131}I ratio means the ratio of numbers of iodine atoms of 3', 5'-positions per those of 3,5-positions, Namely T_4: 1.0, T_3: 2.0, so on . . .

This ^{125}I/^{131}I ratio was applied to the identification of T_4 metabolites in bile of rats which were injected both T_4 mixture. On two-dimensional paperchromatogram the ratio of T_4 and T_3 spots confirmed by standard compounds were 0.98 and 0.54 respectively. The ratio of TA_4 spot was 1.07. These values agreed with the theoritical values.

Revaluation of Triiodothyronine Suppression Test

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About 300 subjects with tyhroid disorder have been examined T_3 (triiodothyronine)

There were some euthyroid patients whose suppression test in our clinic in these 6 years. ^{131}I thyroidal uptake were not suppressed sufficiently after T_3 100 ug per day treated for 6 days. It is reasonable to make sure whether all of euthyroid patients acquire sufficient suppressibility after T_3 100 ug per day for 6 days treatment or ot, so this report intended to ascertain of the period of T_3 treatment when all euthyroid patients acquire the sufficient suppressibility.

Twenty-one nontoxic goitrous patients and ^{131}I treated hyperthyroid patients were studied the change of the suppressibility in the

course of T_3 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 ^{131}I treated hyperthyroid patients), and on 6th and 13th day in the other 9 patients (5 nontoxic goitrous patients and 4 ^{131}I treated hyperthyroid patients) during T_3 100ug per day treatment.

The folowing results were obtained;

1. In most all of nontoxic goitrous patients, the suppressibility increased gradually according as the prolongation of the period of T_3 administration.

The mean ($\pm$SE) of the suppressibility of 3rd day was 40.8 $\pm$6.1% and that of 6th day was 67.7 $\pm$ 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 T_3 treatment until 13 days.

From these results, it was suggested that the suppressibility after T_3 100 ug per day for 13 days would be more beneficial to evaluate the thyroid function precisely than for 3 or 6 days.

^{131}I 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 ^{131}I and Mercaptoimidazole

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

2) The pattern of changes of R.S.U. after ^{131}I 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 ^{131}I treatment, it is most likely that the dose of ^{131}I is insufficient and the administration of the second dose is neccessary.

4) Within 1 to 2 weeks after the administration of the therapeutic dose of ^{131}I, the R.S.U. value is often higher than the pretreatment level. The R.S.U. value becomes lower than before the administration of ^{131}I more than 4 weks 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 ^{131}I uptake rate is normal only in about the half of these cases.