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Comparative Studies of Iodine-131- and Iodine-125-Labeled Triiodothyronine in Resin Uptake Studies

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ABSTRACT

This paper describes a six week comparison of ^{131}I- and ^{125}I-labelled triiodothyronine in the T3 resin uptake test on sera from 29 patients referred for thyroid investigation.

It is shown that after four weeks storage, the ^{131}I-T3 fails to distinguish the sera of hypo- and hyper-thyroid patients from the normal range, whereas the ^{125}I-labelled material succeeds, and shows only slight reduction in sensitivity even after six weeks storage.

The failure of the ^{131}I-T3 test is attributed to liberation of free ^{131}I and unlabelled iodotyrosines which occurs to a greater extent than with the ^{125}I-T3. The effect is attributed to loss of ^{131}I-label due to radioactive disintegration rather than to autoradiolysis.

INTRODUCTION

During the past few years, a number of workers have described resin uptake procedures using ^{131}I-triiodothyronine (T3), which give an index of levels of endogenous thyroid hormone in human serum (3-8). During the past two years, one of these techniques (3) has become a routine test procedure at this hospital.

Even though the specific activity of ^{131}I-T3 was still sufficiently high for accurate counting for periods greater than four weeks after production, it was found that erroneous resin uptake results were obtained. This was thought to be caused by loss of iodination on disintegration of ^{131}I, thereby changing the chemical constitution of the hormone. It was decided that it should be pos-

sible to reduce this defect considerably by using ^{125}I instead of ^{131}I-labelled material, the former having a longer half life (57.4 days) than ^{131}I (8.04 days).

This paper describes the results of a six-week comparison of the two materials in the T3 resin uptake test.

EXPERIMENTAL MATERIAL AND METHODS

The sera used in this investigation consisted of three pools; the euthyroid pool obtained from 20 normal subjects, the hyperthyroid pool (six mildly hyperthyroid patients) and the hypothyroid pool (three mildly hypothyroid patients). Only mildly abnormal pools were chosen as these lead to a more stringent comparison of the two labelled T3 materials. These sera were stored in 2.2 ml lots at $-10°C$.

The ^{131}I-T3 and ^{125}I-T3 preparations were obtained from the Radiochemical Centre, Amersham, the specific activities on arrival were 10 and 2 mC/mg, respectively. On arrival, the preparations were diluted to 10 ml with 0.85% sodium chloride solution (pH 7.4) to which was added 400 mg dried human serum albumin. The solution was stored in 1 ml lots at 10°C. For use each 1 ml lot was diluted to 0.1μg T3/ml.

The resin uptake method used in these experiments has been described previously (3). Briefly it consists of incubating 0.01 μg of labelled T3 with 2.2 ml serum and then shaking two 1-ml lots of the mixture with 40 mg Amberlite CG4B chloride cycle ion exchange resin (Rohm & Haas) and 4 ml 0.85% NaCI (pH 7.4) for 4 hours. The total radioactivity of the sample is assayed in a well-type scintillation counter (Count 1). The resin is then removed by centrifuging and 2 ml of the supernatant fluid counted (Count 2). All samples were counted to an accuracy of one per cent or better. The resin uptake is given by:

$$\text{Percentage Resin Uptake} = 100 - \frac{(\text{Count 2}) \times 250}{\text{Count 1}}$$

The mean of two duplicates is taken.

Because of the difference in energy of the radiation from ^{131}I (0.364, 0.638 MeV) and ^{125}I (0.028 MeV), the discriminator and high voltage settings of the scintillation counter were chosen for each isotope to yield the optimum source/background ratio consistent with stable counting conditions.

RESULTS

Although the specific activity of the ^{125}I-T3 on arrival at our laboratory was only 2 mC/mg compared with 10 mC/mg for ^{131}I-T3, by using optimum counting conditions for each isotope, the count rate of ^{131}I-T3 was less than that of an equal amount of ^{125}I-T3 at three weeks after arrival.

The resin uptake of each plasma pool was measured at weekly intervals for a period of six weeks. The results are shown in Figures 1, 2. In Figures 3, 4 the resin uptake values are expressed as a percentage of the euthyroid pool. The normal range was assessed from a study of 40 controls and 150 euthyroid pa-

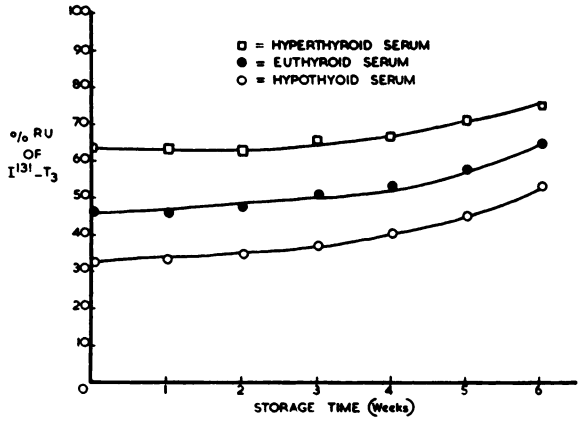

Fig. 1. Effect of ^{131}I-T3 storage time on resin uptake.

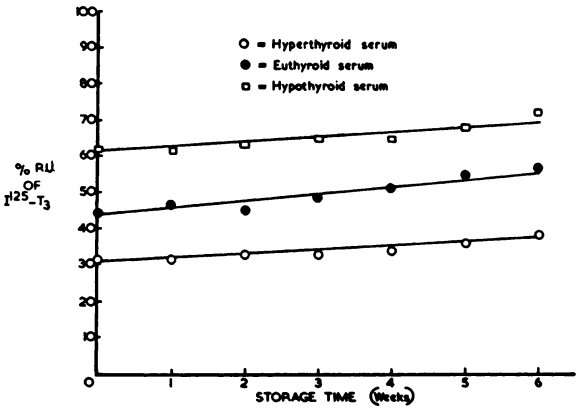

Fig. 2. Effect of ^{125}I-T3 storage time on resin uptake.

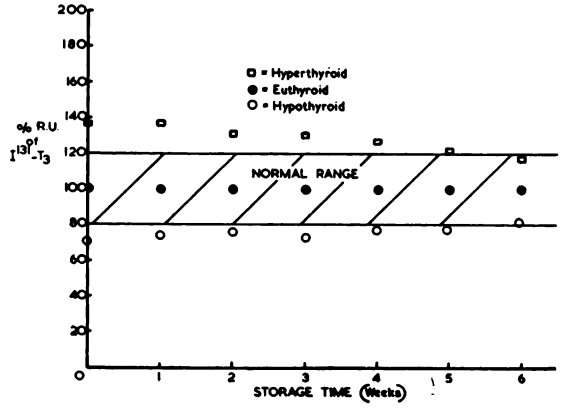

Fig. 3. Effect of ^{131}I-T3 storage time on resin uptake expressed as percentage of that for normal (euthyroid) pool.

tients. It is clear that after about four weeks, the ^{131}I-T3 resin uptake test fails to distinguish the hyperthyroid and hypothyroid pool from the normal range whereas, the use of ^{125}I-T3 does. Even if these experiments had been continued for a considerably longer period, it seems very probable that the ^{125}I-T3 resin uptake values would have remained significantly different from the normal range (Fig. 4).

During the six-week period the resin uptake curves of Fig. 1 rose more than those of Fig. 2, the mean rise for the three ^{131}I-T3 curves (Fig. 1) being 16% compared with only 8.3% for ^{125}I-T3 (Fig. 2). This results in the apparent convergence of the curves in Figure 3. There is also some convergence of the curves in Fig. 1, the difference between the resin uptake for the hyper- and hypothyroid pools being 30% at the beginning and only 22% at the end of the six-week period. In contrast, the convergence of the ^{125}I-T3 resin uptake curves (Fig. 2, 4) is negligible.

In a separate series of experiments, samples of ^{125}I-T3 and ^{131}I-T3 which had been stored for various periods, were separated as described by Galton and Pitt-Rivers (2) into free radioiodine and radioactively labelled T3, di- and mono-iodotyrosine and protein-bound iodine. Typical results are shown in Figure 5.

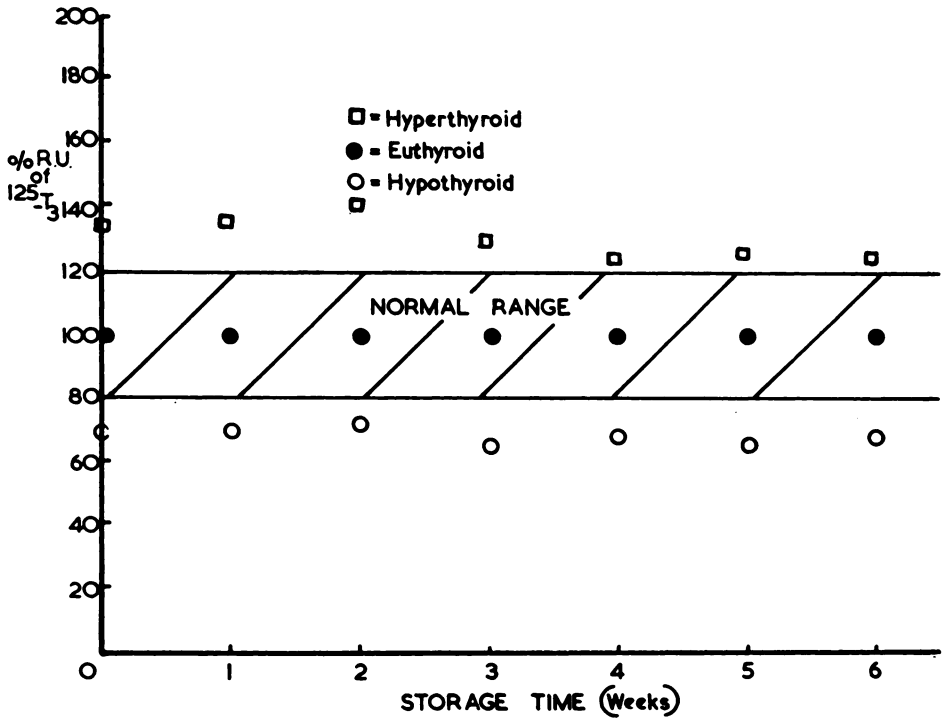

FIGURE 4.

Fig. 4. Effect of ^{125}I-T3 storage time on resin uptake expressed as percentage of that for normal (euthyroid) pool.

Although the percentage of free radioiodine is substantially the same in all cases, there are clearly more breakdown products of T3 from the ^{131}I labelled preparation after only two weeks storage and even more after eight weeks. Therefore, storage time increases the ratio of free ^{131}I and T3 breakdown products to ^{131}I-T3. The liberation of free ^{131}I accounts for the observed increase with storage time in resin uptake for all three serum pools. It may well be that the serum proteins do not have the same specificity for binding iodotyrosines as they have for T3. This would result in some convergence of the resin uptake curves as observed.

DISCUSSION

The results indicate that ^{131}I-T3 is less stable than ^{125}I-T3. It seems unlikely that antoradiolysis can account either for dissociation of radioactive iodine from T3 or for decomposition of the peptide part of the hormone molecules. For, over a period of six weeks storage as described in these experiments, the ^{131}I-T3 dose of radiation was calculated to be only 2200 r, and that of ^{125}I-T3, 250 r. However Bayly and Weigel (1) detected autoradiolysis of ^{14}C-labelled glucose with G(-M) values as high as 900 in the presence of only very small quantities of water.

Nevertheless, in a short series of experiments at this hospital, preparations of ^{125}I-T3 and ^{131}I-T3 were irradiated with doses of up to 3000 r from cobalt-60, and these doses had no effect on the resin uptake values measured subsequently.

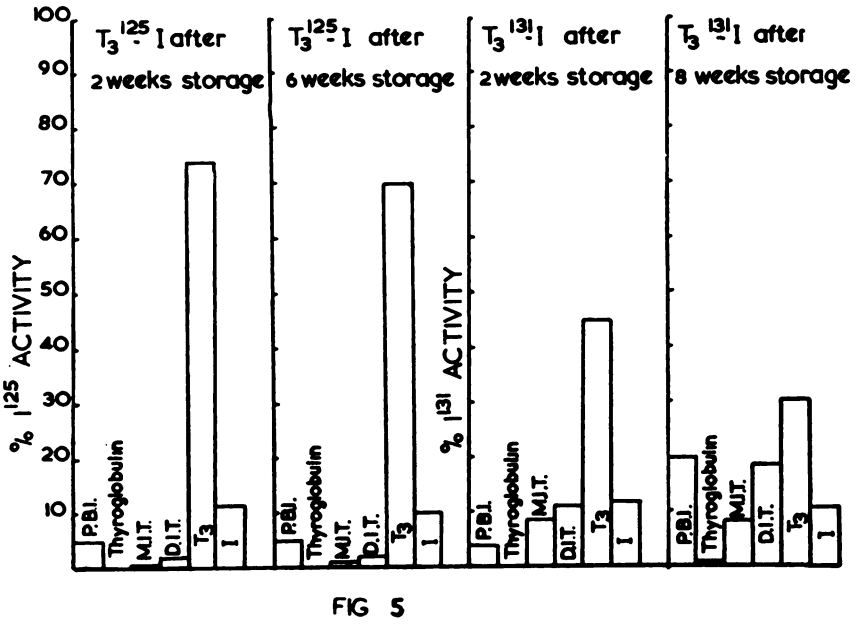

Fig. 5. Effect of storage time on ^{125}I-T3 and ^{131}I-T3: breakdown products.

The observed results would be explained if on loss of iodination by disintegration of an ^{131}I atom, the T3 molecule were weakened, resulting in the loss of a further one or two ^{131}I atoms, or alternatively, dissociation of the molecule into mono- and di-iodotyrosines.

Of course the possibility cannot be discounted that ^{131}I-T3 is less stable than ^{125}I-T3 because of the different methods of preparing ^{131}I and iodine-125. The difference could result in a greater degree of harmful impurities being introduced into the ^{131}I-T3 on labelling.

Although the specific activity of the particular sample of ^{125}I-T3 supplied for these experiments was only 20% of that of the normal ^{131}I-labelled samples on arrival at this hospital, the results indicate that the ^{125}I-labelled hormone is much more suitable for the resin uptake procedure unless frequent supplies of ^{131}I-T3 are available.

ACKNOWLEDGMENT

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