Accurate diagnosis followed by equally accurate physiotherapy is applicable to 17% of our patients. It should be obtainable on the spot, and at once. Any two or three doctors clubbing together could easily afford the services of a physiotherapist and thus benefit their patients. Any doctor who follows this suggested line of training would have the satisfaction of curing most of his sufferers from "rheumatism" and "fibrositis," and rejoice in the contrast with the unhappy time when he could merely prescribe an analgesic tablet or liniment. This type of treatment is most rewarding to the patient, and keeps him out of the clutches of the lay healer. I find this new sphere of work most exhilarating, and, as a general practitioner living in this antibiotic and bureaucratic age, enjoy increasing my diagnostic powers in a fresh field. This interesting work, coupled with the services of a physiotherapist grounded in accurate manual work, transforms my day and has limitless possibilities for every practitioner.

DIAGNOSIS OF THYROTOXICOSIS BY A SIMPLE OUT-PATIENT RADIOACTIVE IODINE TECHNIQUE

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The availability of radioactive iodine for use in clinical medicine has led to the development of various new diagnostic methods for assessing thyroid function. There are, however, relatively few centres at which isotope techniques can be used, and, furthermore, many of the tests are somewhat complex. They involve considerable co-operation from the patient, or they require the examination of the patient with complicated electronic apparatus. The value of the various radioactive iodine tests of thyroid function has been discussed by Myant (1952), and Goodwin, Macgregor, Miller, and Wayne (1951) have compared the relative merits of those most commonly used.

The avidity of the thyroid for iodine can be assessed either by direct measurement of the amount or rate of uptake of the isotope in the patient's neck or by measuring the amount excreted in the urine, the latter indicating the balance of the administered dose that is not utilized by the thyroid. The capacity of the gland to synthesize and discharge thyroid hormone can be measured by assaying the radioactivity present in the plasma (Ansell, Macgregor, Miller, and Wayne, 1953). This latter measurement probably represents most accurately the functional state of the gland, especially if there is a doubt regarding the presence of hyperthyroidism. Such a test has the advantage that the patient is

involved in no more inconvenience than is necessitated by a venepuncture, since the actual physical measurements do not require his presence.

For reasons discussed elsewhere (Goodwin *et al.*, 1951) we believe that the best and most comprehensive picture of a patient's thyroid status can be obtained only by a combination of several clinical and radioactive iodine tests. Nevertheless, so far as the diagnosis of thyrotoxicosis is concerned, the single measurement of the radioactivity present in the protein fraction of plasma 48 hours after a tracer dose gives information of considerable diagnostic value.

This paper briefly describes an attempt to assess the clinical usefulness of such a test when used without the supporting evidence supplied by simultaneously performed alternative tests, and when used at a hospital without full facilities for isotope work.

Method of Investigation

All patients studied were seen by two of us in Nottingham (W. S. W. and P. J. B.). An initial clinical diagnosis was made, and after the result of the radio-iodine test was known the patient was observed to determine his progress. A final clinical diagnosis was eventually reached in all cases, usually after a therapeutic test with methylthiouracil. The test has been used, therefore, in its proper context, as an additional diagnostic tool, and not as a final arbiter to supersede clinical judgment.

Measured doses of between 25 and 30 μ c. of radioactive iodine were dispensed in Sheffield and dispatched by train to Nottingham, where they were given to patients whose urine was tested by the method of Foote, Mackenzie, and MacLagan (1952) to detect the previous administration of iodine-containing compounds. Forty-eight hours after administration of the isotope 20-ml. samples of blood were withdrawn and returned to Sheffield for assay. The concentration of radioactivity in whole plasma and in the protein-bound iodine fraction was measured, the proteins being precipitated with trichloroacetic acid; this precipitate was then dissolved in caustic soda and measured as a solution (Goodwin *et al.*, 1951).

Interpretation.—On the basis of an extensive experience of the limitations and merits of this test, the results were interpreted as follows: levels of activity in excess of 0.4% per litre in the protein-bound fraction were considered to indicate definite thyrotoxicosis; values below 0.2% per litre were interpreted as excluding the presence of thyrotoxicosis. We realize that such an interpretation invariably leads to the presence of toxicity being missed in a very small number of cases, but, on the other hand, the presence of toxicity is never falsely suggested, since, in our experience, values of protein-bound plasma activity in excess of 0.4% per litre do not occur in the absence of thyrotoxicosis in the previously untreated patient. Intermediate values lying between 0.2% and 0.4% per litre were interpreted according to the proportion of the whole plasma activity that was protein-bound, proportions over 50% usually indicating thyrotoxicosis even if the absolute amount in the protein-bound fraction was below 0.4% per litre. The accuracy of measurements below this level of activity, is, however, not great.

Results

Here are given the results of the application of the test to the first 50 patients in whom subsequent progress has been followed and an eventual diagnosis decided upon.

Samples were sent from Nottingham after withdrawal from six definitely thyrotoxic patients, and in each case the interpretation of the result of the test suggested toxicity. All results for the 48-hour protein-bound plasma activity lay in the range of 0.7% to 2.8% per litre. Samples were also analysed from 22 control normal or definitely non-toxic cases, and in each case the correct interpretation

was put upon the test. Of the 22 cases, 21 had levels of protein-bound plasma activity at 48 hours of 0.1% per litre or less, in 13 cases no appreciable activity being detectable at all with the dose given. In one case a level of 0.2% per litre was observed.

Samples were taken from a further 22 cases in which there was a greater clinical doubt regarding the true diagnosis. In 15 of these (Group A, Table) the patients were thought

Results of Tests of 48-Hour Plasma Radioactivity

Case No.	48-hour Plasma Activity (% Dose per Litre)	48-hour Protein-bound Plasma Activity (% Dose per Litre)
<i>Group A</i>		
1	1.23	0.98
5	1.66	1.30
6	0.62	0.56
20	3.17	2.26
22	1.99	1.46
27	2.06	1.83
28	0.56	0.34
31	0.35	0.31
32	1.87	1.59
39	0.99	1.00
40	0.56	0.55
47	1.07	0.85
48	0.25	0.24
49	0.98	0.58
50	0.64	0.48
<i>Group B</i>		
3	0.68	0.59
8	0.79	—
14	1.46	1.36
33	0.34	0.38

See text for classification of Groups A and B.

initially to be clinically thyrotoxic, and in each case the radio-iodine test suggested toxicity, and the subsequent progress and disposal of the case confirmed this view. In four cases (Group B) in which the initial clinical impression was that the patients were probably not thyrotoxic the radio-iodine test suggested toxicity, and their subsequent progress showed the test to have been accurate. In these 19 cases, therefore, the test was of real clinical value inasmuch as it definitely proved a doubtful clinical diagnosis or corrected an erroneous one. In the three remaining cases the test was at variance with the final clinical opinion—in one instance thyrotoxicosis being suggested in a patient in whom it was neither initially nor subsequently thought to be present, and normal function being suggested in two cases in which the clinical diagnosis was thyrotoxicosis.

The two patients who were thought to be normal as a result of the test had 48-hour protein-bound plasma activity levels of 0.1% per litre or less, but the clinical picture and response to therapy was such as to leave no doubt in our minds that these patients were in fact thyrotoxic. In the one patient in whom the clinical diagnosis was normal thyroid function, but the result of the test indicated thyrotoxicosis, the level of protein-bound plasma activity was 0.57% per litre, the whole plasma activity being 0.62% per litre. This patient was a woman of 37 who had palpitations, loss of weight, and dyspnoea. She had no marked heat intolerance or sweating, was quiet when examined, and had no tachycardia. She had a diffuse enlargement of her thyroid gland and "staring" eyes. Treatment for two months with methylthiouracil had no effect on her symptomatology, and an emotional disturbance was diagnosed despite the presence of the high levels of activity in her plasma.

Discussion

These results would indicate, therefore, that the accuracy of our clinical assessment is of the same order as the accuracy of this particular radioactive iodine test of thyroid function. In addition, however, it must be noted that objective confirmation of a hesitant clinical diagnosis was obtained in numerous cases; if full reliance had been put upon the test with a view to the decision whether or not to institute treatment in a given case, a correct decision would have been reached in 47 out of the 50 cases, whereas

first clinical impressions were shown to be in error in four cases. Furthermore, the information obtained from the radio-iodine test was simply and conveniently obtained, whereas in many instances a careful and balanced clinical assessment was available only after prolonged observation and therapeutic trial, and the application of other ancillary diagnostic tests.

It must always be remembered that there must be a complete range of thyroid activity, and by the very nature of the disease it cannot be expected that there will be a sharp dividing line between patients who are not thyrotoxic and those who are. Myant (1952) says: "However we define normality, the limit we set between normal and pathological is an arbitrary one, and no test can tell us what this limit should be." What is important to the patient and to the physician is that some assistance be provided towards the decision whether or not specific treatment is required. Furthermore, it frequently is necessary to exclude thyrotoxicosis as a factor when other diseases are also present, and the diagnosis of so-called "thyrocardiacs" is often difficult. It is our belief that such decisions are assisted by the objective evidence provided by the use of radioactive iodine tests of thyroid function. If possible, studies of both the gland uptake of the isotope and the discharge of radio-thyroxine should be carried out.

The latter test is essentially simple to perform and does not require the patient's co-operation in the collection of urine samples, nor does it necessitate bringing the patient and the electronic apparatus together. Its only disadvantage is that a higher dose of the isotope is necessary for its performance compared with that required for urine studies (25–30 μ c. as against 10 μ c.) and the time involved in the processing and assaying of the samples is appreciably greater than that required to assay urine. We believe, however, that the greater diagnostic accuracy obtainable, and the greater convenience to the patient, render it a useful and valuable addition to the diagnostic armamentarium of the physician.

Summary

The radioactivity present in the protein-bound fraction of the plasma 48 hours after the administration of a tracer dose of 25–30 μ c. has been used as an aid to the diagnosis of thyrotoxicosis.

Fifty patients were studied in a hospital 40 miles from the centre containing the electronic apparatus, and doses of the isotope and samples of plasma were dispatched by train.

In 28 cases the results of the test and the clinical assessment were in full agreement, and in a further 19 patients a doubtful clinical diagnosis was confirmed or an erroneous one corrected. In three cases misleading information was provided by the test.

It is suggested that where it is not possible to perform simultaneous tests of gland uptake of radioactive iodine the measurement of protein-bound plasma radioactivity 48 hours after a tracer dose is of valuable diagnostic assistance. It can be carried out with minimal inconvenience to the patients, at a distance from a fully equipped centre, and in doubtful cases gives immediate information which would otherwise involve prolonged observation of the patient and of the effects of treatment.

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