THE EXCRETION OF RADIOACTIVE IODINE AFTER ORAL ADMINISTRATION OF SMALL DOSES

By

K. F. Stöa

When a certain test dose of $^{131}$I is to be followed in the organism, this can usually be done in four different ways. The simplest method undoubtedly is to measure the percentage of absorption in the thyroid of a certain radioactive dose by placing a measuring instrument on the gland region. Another method involves the use of the so called autoradiographic technique, i.e. the microscopic slices of thyroid are placed on a photographic film. Thus one is able to localize the absorbed iodine.

Thirdly the circulating radioactive substance in plasma, and possibly plasma fractions, can be measured. Finally the amount of $^{131}$I excreted in the urine can be determined.

For several reasons we chose the last mentioned method for diagnostic purposes. Measurement of the urinary excretion after oral administration causes little discomfort to the patient. Moreover with this method extremely small doses of radioactive substance are needed, and hence any risk to the test object from radiation can be disregarded. Furthermore, the risk run by the staff of the laboratory is reduced to a minimum.

The determinations of radioactivity in the urine test can be made with great accuracy by using a dipping counter. Finally, it is of great importance that the small doses of iodine given, can very reasonably be regarded to be of no significance as an addition to the patients' daily supply of iodine in the food (Arnott et al., 1949).

Measurement of $^{131}$I in the urine for diagnostic purposes were tried by Hertz & Roberts as early as 1942. Since then many investigators have been engaged in these problems (Keating et al., 1947; Mc Arthur et al., 1948; Skanse. 1949).
During the first few years of these experiments, relatively large doses of radioactive iodine were used, and the experimental technique varied greatly. In recent investigations especially in Britain (Mason & Olliver, 1949; Arnott et al., 1949), extremely small radioactive doses, — from 5 to 10 µc have been given. However, any generally accepted standard technique can not be said to exist as yet.

The investigations reported here, have aimed at finding a simple and practical routine method for diagnostic function tests of the thyroid.

METHODS

The radioactive iodine used for the experiments, was produced at the British Atomic Energy Research Establishment, Harwell, and was delivered as potassium iodide. The transmission took place via the Norwegian Institute for Atomic Energy, Oslo. In wintertime the isotope material was sent by train Oslo–Bergen. Usually it was conveyed by air.

The measuring equipment (Fig. 1) was constructed and built largely in accordance with the equipment worked out by Bergh (1950), and employed by Bergh & Eieland (1950), e.g. for measuring small amounts of radioactive copper and zinc in the urine of cattle.

We used as liquid counter a G 10 Pb tube delivered by E. K. Cole Ltd., London, mounted in a cylinder with a diameter of 5.4 cm. and height of 16.5 cm. The fluid volume applied was 200 ml. The cylinder made of glass, and equipped with a stop cock for outlet at the bottom, is surrounded by a 2.5 c., thick lead shield. As recording apparatus a scale of 64 was used with negative high voltage on the cathode of the counting tube.

The patients each receive about 8 µc I$^{131}$ as «a glass of water» about two hours after breakfast. To the solution is added as «carrier» 50 µg inactive sodium iodide. The urine is then collected as carefully as possible in accurately measured portions, and at fixed times. An aliquot part corresponding exactly to $\frac{1}{16}$ of the test dose, is set aside as a

![Fig. 1.](image)

Device for measurement of gamma radiation in urine.

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control, and measured together with the urine samples. To dilute the solutions that are to be measured, and to clean the equipment, a 1 per cent NaI solution is used. The »background value« of the apparatus is determined immediately before each measurement. A voltage of 1120 Volts has been used.

RESULTS

To examine the accuracy of the measuring method, countings were made in a series of solutions, the $I^{131}$ contents of which were known. The results of these measurements show that the relation between the concentration of $I^{131}$ and the counting rate is linear within rather wide limits (Fig. 2). The method is very sensitive (Fig. 2, Table 1) and exact (Table 1). Activities of 0.02 $\mu$C and less, can easily be determined.

Table 1.

Measurement of solutions with known concentration of $I^{131}$.

<table>
<thead>
<tr>
<th>Activity calculated, $\mu$C per 100 ml. (A)</th>
<th>Counts per minute. (C)</th>
<th>C/A</th>
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</table>

Average value ....................... 9695 ± 44¹

1. Mean error = 0.45 per cent of the mean value.
Calibration curve for measurement of $^{131}I$ in solution.

**Fig. 2.**

The urinary excretion of $^{131}I$ in euthyroid subjects after administration of about 8 $\mu$C radioactive KI.

**Fig. 3.**

Normal average excretion of radioactive substance during 24 hours after oral administration of small amounts of $^{131}I$. 20–30 years: 7 cases. 30–40 years: 11 cases. 40–50 years: 9 cases. 50–60 years: 8 cases. 60–70 years: 6 cases.

**Fig. 4.**

In 41 control subjects who, on the basis of clinical data, could be assumed to have a normal thyroid function, the excretion of radioactive substance in the urine was measured within a period of 24 hours after the administration of small doses of radioactive iodine. The average excretion in these 41 individuals
is found to be 51.6 per cent of the dose given, the variations ranging from 31.3 to 77.4 per cent (Fig. 3). 19 of the subjects examined were males, 22 females. The average values found for the two sexes lie very close to each other. In males per 24 hours an average excretion of 52.8 per cent and in females of 50.4 per cent is found. To a certain extent the excretion seems to be dependent on age, as the higher age groups show somewhat lower values (Fig. 4).

In 36 subjects experimented upon, 21 females and 15 males, fractional measurement has been made of excreted I\textsuperscript{131} during a period of 24 hours after administration as recommended by Mason & Oliver (1949). By these experiments the amounts of radioactive substance excreted have been measured in urine portions collected with the greatest possible accuracy, 2, 4, 6, 9, 12 and 24 hours respectively after the administration. The normal average curve determined in this way is shown in Fig. 5.

\begin{figure}
\centering
\includegraphics[width=\textwidth]{diagram.png}
\caption{Excretion of radioactive substance after oral administration of small doses of I\textsuperscript{131}. Normal range: values of 36 euthyroid subjects. Patients with Graves' disease: 22 cases. The black line in the normal area shows the average output.}
\end{figure}
With the same technique, the excretion of radioactive iodine has been investigated in 22 patients evidently suffering from Grave’s disease. All of them, with the exception of one, show a 24 hours’ excretion far below the lowest value in the normal material (Fig. 5). The reduction in the excretion proves to be especially marked during the last 18 hours of the 24 hour period. The curves therefore show a characteristic bend 6 hours after the administration, as after this time they rise only slightly. Measurement of the amount of $^{131}I$ excreted in the interval between 6 and 24 hours after the administration, therefore, show the greatest deviation (Fig. 6). In the material consisting of 22 patients suffering from Graves’ disease, all measurements showed excretion values below 10 per cent. The lowest value found in the 41 persons examined, all of them believed to have a normal thyroid function, was 13.2 per cent.

Of 5 patients, with a definite clinical diagnosis of myxedema, four showed values very close to the normal average in the 6–24 hours’ test (Fig. 6). One of the patients lay close to the upper limit of the normal. Thus the advantage of the technique of investigation employed in the diagnosis of thyroid hypofunction seems to be very doubtful.

**DISCUSSION**

These investigations were made to find a good routine method for the diagnostic examination of patients with thyroid abnormalities. There is much evidence that a direct measurement of the iodine absorption of the thyroid gland, if

![Fig. 6.](image)

Excretion of $^{131}I$ in the interval between 6 and 24 hours after oral administration of small doses radioactive KI. Black columns: 22 cases of Graves’ disease. White columns: 41 normal experimental persons. Shaded columns: 5 cases of myxedema.
possible in combination with determinations of radioactive iodine in plasma, will give a more accurate and representative picture of the thyroid function, than will the picture obtained by means of urine analyses only. On the other hand, a routine method should be simple and practical, and should be of the last possible discomfort and risk to the patient. The urine test, as done in our laboratory, undoubtedly fulfills these demands.

The results show that the measuring technique works satisfactorily. The method used is exact as well as sensitive, and hence very small amounts of radioactive isotope can be determined quantitatively in the urine.

Taking everything into account, the normal values presented here seem to agree well with the values given by other investigators. For instance Mason & Oliver (1949), during the first 24 hours after iodine administration, found excretions varying between 28 and 72 per cent, and Werner and his collaborators (1948) between 28 and 76 per cent. As already shown, the corresponding values in my material are between 31 and 77 per cent. In the interval between 6 and 24 hours, the excretion was found by Oliver & Mason to lie between 10 and 25 per cent. In the present material the values are considerably higher, viz. 13–35 per cent. In one case as much as 41 per cent was excreted (Fig. 6).

The best picture of the rate of excretion, and the best basis for judging it is undoubtedly attained by plotting in each case the excretion curve in relation to the normal diagram (Fig. 5).

The evident cases of Graves' disease examined, as seen in Figs. 5 and 6, all showed a marked deviation to reduced excretion, and thus to increased absorption of the radioactive iodine given. Five patients suffering from myxedema showed values that were within the limits of the normal range of variation (Fig. 6).

Treatment with certain therapeutic agents may completely disturb the result of an isotope examination. In several patients treated with antithyroid preparations (methyl-thiouracil, propyl-thiouracil and methimazole) a great increase of the excretion has been found and this also applies to some cases treated with iodine. Even the iodine content of the food should possibly be taken into consideration in some cases.

The renal function of the patients must be normal (Mason & Oliver, Arnott et al., 1949). Tests of normal function should therefore invariably be carried out when the results of the iodine test are to be assessed. Fever, sweat, reduced absorption, and possibly also excretion through the bile duct, are other sources of error to which attention should be paid.

The field within which the iodine urine test is of any use, is therefore very strictly limited. But taking everything into consideration, there is reason to believe that the method will prove to be a valuable, new diagnostic aid. For use in the laboratory it may be characterized as simple and satisfactory.
SUMMARY

A method for measuring small amounts of excreted radioactive iodine in the urine after oral administration is described. Extremely small doses (about 8 µc) of radioactive substance have been used.

41 subjects with presumed normal activity of the thyroid gland have been examined by fractional measurement of I^{131} excreted during 24 hours. 22 patients suffering from clinically verified thyroid hyperfunction have been examined by the same technique. The patients show a percentage excretion that is considerably reduced as compared with the normal, the reduction being especially marked in the time interval 6–24 hours. 5 patients suffering from myxedema showed no significant deviation from the normal values.

Treatment with goitrogens induces considerable increase in the excretion values of patients with thyroid hyperfunction.

ACKNOWLEDGMENTS

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REFERENCES