

CLINICAL
ASPECTS
OF
IODINE
META-
BOLISM

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CLINICAL ASPECTS OF IODINE METABOLISM

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PREFACE

Iodine occupies a unique position in human physiology since its only function is to take part in the synthesis of thyroid hormone. Iodine metabolism and thyroid physiology are therefore inextricably linked. The advent of radioactive isotopes of iodine has led to a great increase in our knowledge of the ways in which the body handles iodine and of the chemical pathology of thyroid disease. They have been used to provide tests of thyroid function which are in daily use throughout the world. On the other hand quantitative studies of stable iodine metabolism, although they provide much more information, have received comparatively little attention. Studies with radioisotopes are ideal for the measurement of the proportion of the body iodine which follows a particular metabolic pathway, and for the study of the rate of turnover of iodine, but it is only by using chemical methods that we can obtain information about the absolute quantities of iodine involved; when the two techniques are combined we are provided with a clear picture of the overall metabolism of iodine.

Hitherto technical difficulties have prevented most investigators from obtaining this type of quantitative data, but these have now been overcome, and parameters such as the plasma inorganic iodine and the absolute amount of iodine taken up by the thyroid in unit time can be measured with reasonable and reproducible accuracy.

Moreover, in the last decade the new techniques of chromatography and autoradiography together with a wider knowledge of the chemistry of the thyroid hormones and related compounds have greatly enlarged our knowledge of the production and physiological role of the organic derivatives of iodine.

In this volume we have attempted to describe both our own and other workers' attempts to obtain a complete picture of iodine metabolism in health and disease, and to show how such knowledge may influence diagnosis and treatment. The section which deals with the physiological aspects of the subject brings together much new material and includes many unpublished observations which we ourselves have made. In the second section we have continually kept the interests of the practising physician in mind and have not hesitated to include enough clinical description to make clear our views on the aetiology and pathogenesis of the diseases we are discussing.

The appendices provide detailed information about those established and more recently introduced techniques of which we have personal experience and for the accuracy of which we can vouch. We believe that these will be of value to both the newcomer and to the experienced worker in this important field of metabolism.

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ABBREVIATIONS AND TERMS USED

AIU	Absolute iodine uptake of the thyroid (normal range 0.5–6.0 $\mu\text{g/hr}$).
DIT	3,5-diiodotyrosine.
Iodide	This is used in the strict chemical sense to denote iodide ion or electrolytes containing the iodide ion, and not to mean iodine in general.
Iodine	Iodine is used to denote the element in either organic or inorganic form.
MIT	3-monoiodotyrosine.
PBI	Protein-bound iodine of serum (normal range 3.0–7.5 $\mu\text{g}/100\text{ ml}$).
PBI ¹³¹	Protein bound radioactivity of the plasma 48 hours after administration of the tracer dose.
PII	Plasma inorganic iodine (normal range 0.08–0.60 $\mu\text{g}/100\text{ ml}$).
R.Cl.	Renal clearance of iodide (normal range 15.0–55.0 ml/min).
T ₃	3,5,3'-triiodothyronine.
T ₄	3,5,3',5'-tetraiodothyronine (thyroxine).
TBG	Thyroxine-binding globulin.
TBP	Thyroxine-binding proteins.
Th. Cl.	Thyroid clearance rate of plasma inorganic iodine (normal range 8.0–40.0 ml/min).

Th. Upt.	Thyroid radioiodine uptake (normal range $2\frac{1}{2}$ hr 10-35%)
Thyroid hormone	This term is used to mean the sum of all the biologically active substances produced by the thyroid (i.e. both T_3 and T_4).
TSH	Thyroid stimulating hormone. Thyrotrophin.
Urinary iodine	Unless otherwise specified this refers to the absolute quantity of iodine in the urine (as estimated chemically).
\pm	Standard error of the mean unless otherwise specified. The use of standard deviations and standard errors is not entirely satisfactory in medicine, since many biological data do not fit a normal distribution curve, or even a log normal one. However, it has been customary to use them since, even if not entirely satisfactory, they still give some idea of the scatter of individual values (the standard deviation) or the accuracy of the mean (the standard error).

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PART I

IODINE METABOLISM IN HEALTH

CHAPTER I

METABOLISM OF INORGANIC IODINE

The iodine present in food and water is absorbed from the gastrointestinal tract and ultimately appears in the plasma as iodide ions. Part of the plasma inorganic iodine is lost in the urine, but part is retained by the thyroid where it is utilized for thyroid hormone synthesis. This hormone is released into the blood and so reaches the peripheral cells where it exerts its metabolic effects: a proportion is excreted in the bile and may appear in the faeces. The major part is deiodinated and the iodide released returns to the plasma iodide pool, and so the cycle is repeated. These basic aspects of iodine metabolism are illustrated in Fig. 1 and are described in detail in the subsequent sections.

Absorption of Iodine

Iodide is rapidly absorbed from the alimentary canal of normal persons if they are fasting. Thus Hamilton (1938) found that three minutes after the oral administration of radio-iodine, radioactivity could be detected in the hand, and that most of the tracer dose was absorbed within less than an hour. These observations have been confirmed by several other workers. Keating & Albert (1949) for example, showed that the rate of absorption is 5% per minute, and that in nearly all subjects, except perhaps in a few persons with hypothyroidism, absorption is virtually complete within two hours. However, absorption may be materially delayed if the subject is not fasting (Keating & Albert 1949), but three hours after the administration of the tracer dose there is little difference between fasting and non-fasting persons (Turell *et al* 1958). Part of the iodide is absorbed in the stomach, but the greater part in the small intestine (Small *et al* 1961).

If defective absorption of iodine were to take place it would lead to iodine deficiency, and so to goitre. While theoretically this could occur as part of a general 'malabsorption syndrome', or as the result of interference with iodine absorption by other substances, there is no satisfactory evidence that this in fact happens. It was at one time

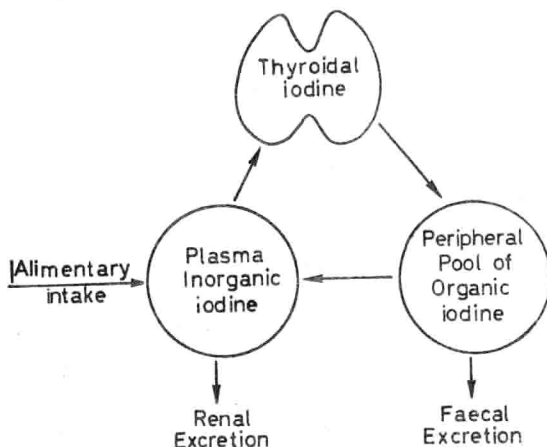


FIG. 1. Outline of iodine metabolism

Iodine is absorbed from the alimentary tract into the plasma inorganic iodine pool. Some is excreted by the kidneys, and some is taken up by the thyroid and converted into thyroid hormone. Thyroid hormone is secreted from the thyroidal iodine pool into the peripheral pool of organic iodine. The latter is made up of thyroid hormone in the plasma and tissues. Part of the iodine leaves this pool in the faeces but most is deiodinated and re-enters the plasma inorganic iodine pool. The cycle is repeated.

thought that calcium might decrease iodide absorption, but it certainly does not do so in rats (Taylor 1954). Similarly Halmi and co-workers (1956) have shown that the antithyroid substance potassium perchlorate does not reduce absorption of iodide.

Data derived from studies of the absorption of iodine in the form of iodide do not necessarily apply to the absorption of iodine in other forms. Cohn (1932) found that free iodine and iodate in dogs must first be converted to iodide within the gastrointestinal tract before being absorbed. However, iodinated thyronines may be absorbed intact, at least in part. Myant & Pochin (1950) gave radiothyroxine