THE CLINICAL USE OF SERUM IODINE DETERMINATION

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SIMPLIFICATION of the measurement of iodine in body fluids has resulted in increased use of the test and in demonstration of its importance in the study of patients suspected of having thyroid disease. Indeed, under certain circumstances, serum iodine determination may be the only laboratory test that shows with precision the abnormalities of thyroid function.* This is not surprising, since each of the three laboratory tests used in studying the thyroid—basal metabolic rate, thyroidal uptake of radioactive iodine and chemical determination of serum iodine—measures separate aspects of thyroid activity. Furthermore, each of the tests may be influenced by separate extrathyroidal factors. The purpose of this article is to outline the diagnostic uses and limitations of serum iodine determinations.

A simplified scheme (Fig. 1) shows the manner in which dietary iodine is made available for the production of thyroid hormone. In this diagram, it may be seen that the bulk of dietary iodine is first converted to iodide, mixing with the inorganic pool of the body, and then is taken up in part by the thyroid gland.

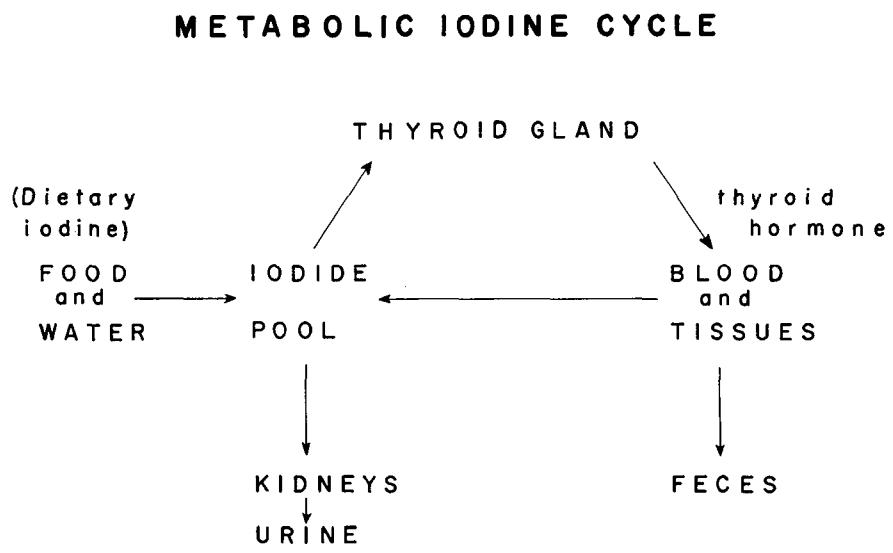

Fig. 1

*Representative reviews of iodine metabolism,[1] thyroid physiology[2] and clinical use of blood iodine determination[3] have appeared in recent years.

The remainder is made available for renal excretion. Besides the urinary excretion of iodide, an additional small proportion of body iodine is excreted as thyroid hormone glucuronide in the feces.

In the thyroid, iodine is affixed to tyrosine from which is synthesized the thyroid hormone. The hormone is stored within the gland as thyroglobulin but is released in a free form into the blood stream. Here it circulates combined with serum protein. Its discharge from the thyroid is under the influence of the thyrotropic substance of the anterior pituitary. The amount of this pituitary hormone in the serum is controlled, in turn, by the level of the circulating thyroid hormone. This is an example of the self-regulating relationship between pituitary hormones and their target organs, which is an important factor in endocrine homeostasis.

The Nature of Serum Iodine

From the preceding description of the iodine cycle, it can be seen that iodine is present in the serum in two forms, inorganic and protein bound (Fig. 2A); that inorganic iodide concentration is primarily dependent on dietary content; and that the protein-bound iodine is constituted largely of thyroid hormone which is available to the tissues. Chemically, serum inorganic iodide is entirely dialyzable, acid and water soluble. By precipitation, it may be easily separated from the clinically more significant protein-bound iodine. The protein-bound iodine consists almost entirely of thyroxine with traces of the more active triiodothyronine, and the biologically inactive diiodotyrosine. These substances are so weakly bound with serum protein that they easily dissolve in butanol. The diiodotyrosine accompanying thyroxine into the butanol is removed by washing with strong alkali. The remaining material is largely thyroxine and has been loosely termed the "butanol-extractable iodine" (BEI).[4]

Clinical Use of Serum Iodine Measurements

The minute concentration of serum iodine causes its determination to be a more difficult procedure than most other clinical laboratory procedures. However, it is not prohibitively tedious, and even the recently introduced fractionation of the protein-bound iodine does not place undue burden on the analyst. Both inorganic and protein-bound iodine should be determined routinely while the butanol fractionation of the latter need be done only when it will be of diagnostic value.

Because of the rapidity with which it is removed from the circulation, the inorganic iodide usually amounts to only a few micrograms per hundred milliliters of serum. It is not a direct measure of thyroid function. Nevertheless, it is of great value to the clinician since high values offer a clue to previous uses of iodine-containing substances, an historical point that patients are notoriously poor at recalling. Furthermore, it is well to remember that the inorganic fraction

may be falsely elevated by tincture of iodine used as a skin antiseptic prior to venipuncture.

The protein-bound iodine, of course, is the more important of the serum iodine fractions since its concentration usually parallels that of circulating thyroid hormone. Four to eight micrograms per hundred milliliters of serum is present in euthyroidism while values greater than 8 or perhaps 9 micrograms are found in hyperthyroidism, and less than 3 or 4 in myxedema. These normal limits, however, are not always clear-cut and must be evaluated in relation to other clinical information.

In certain cases, the protein-bound iodine values do not correctly define thyroid function. For example, elevated values unassociated with hyperthyroidism are found in certain cases of thyroiditis,[5] following radiation injury of the gland and after administration of iodine-containing substances [4,6-9] for therapeutic or radiologic purposes (Table). In most instances of abnormal values due to use of iodine compounds, the contamination appears in a butanol-insoluble fraction as shown in Figure 2B. The presence of this butanol-insoluble iodine leaves the thyroxine-like (butanol-soluble, alkali-insoluble) fraction as a precise measure of circulating thyroid hormone.

Abnormally low values of protein-bound iodine may be found in euthyroidism. Thus, patients who have hypoproteinemia do not sustain normal serum iodine concentrations, presumably because there is insufficiency of iodine-

TABLE
Sources and Duration of Artifactual Values of Serum Iodine

Source		Duration of effect	Remarks
Substance	Procedure		
Diodrast[6]	Urography[7]	4 weeks[7]	Unpredictably elevated[6]
Priodax*[6]	Cholecystography[7]	3 months[7]	Very high[6]
Pantopaque[6]	Bronchography[7]	9-12 months[7]	Elevated
Lipiodal[6]	Myelography[7]	1-5 years[7]	Unpredictably elevated[6]
Radioactive iodine	Destruction of thyroid tissue[8]	6-8 weeks	Elevated
Lugol's solution[4]		2-6 weeks	Elevated
Potassium iodide[9]		6-8 weeks	Elevated
Mercuhydrin[11]		24 hours	Lowered

**Priodax yields a butanol-soluble complex.*

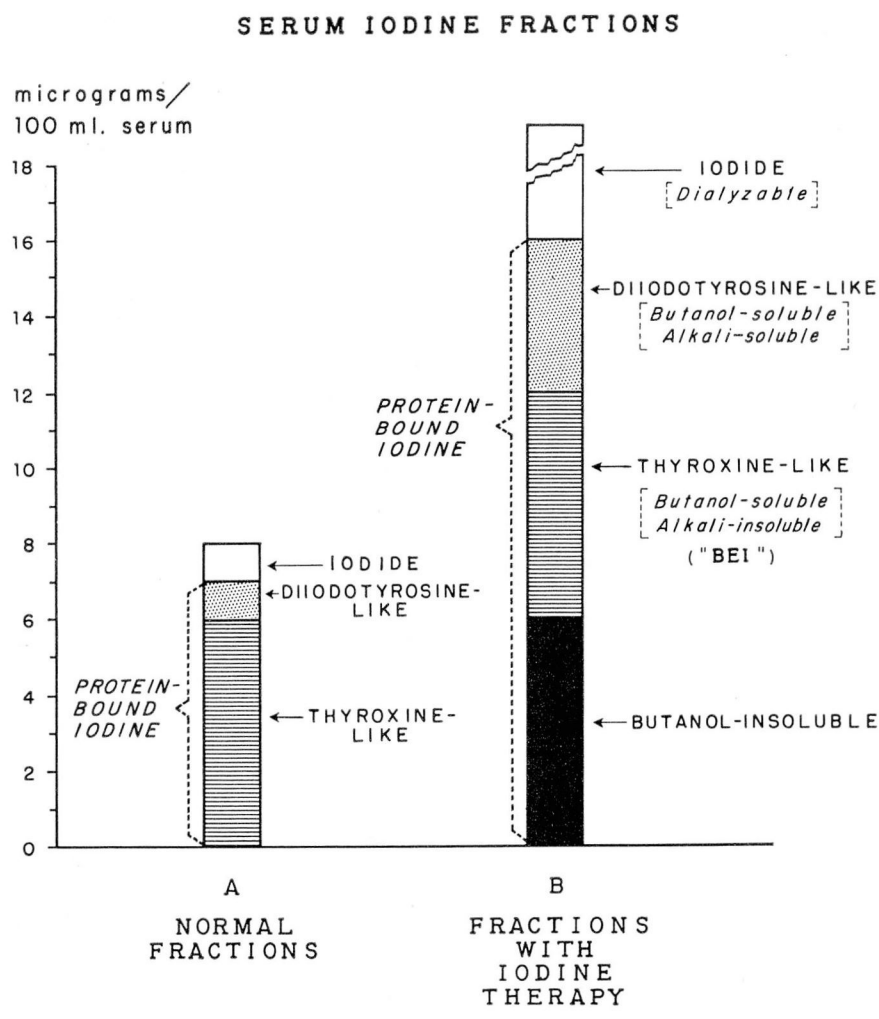

Fig. 2

carrying protein.[10] Falsely low values are found in patients receiving mercury-containing compounds, because iodine is removed by mercury during the chemical determination.[11]

In general, the unfractionated serum protein-bound iodine will indicate the true nature of the disease in hyperthyroidism and hypothyroidism as well as does the B.M.R. However, the protein-bound iodine is much more than a check on clinical judgment in uncomplicated cases. It fills a particular need as a precise measure of thyroid-hormone concentration in the serum. An example of the precise use of the test is in a case of factitious hyperthyroidism. Here, the

thyroidal uptake of radioactive iodine is low because of the antithyroid effect of large doses of thyroid substance and provides a false clue to thyroid status. However, the elevated serum protein-bound iodine will correctly measure the endocrine defect. Another example of the specific use of the test is in the study of thyroidectomized patients suspected of having recurrent thyrotoxicosis. In these cases, radioactive iodine uptake may be high even in the presence of euthyroidism; furthermore, the B.M.R. may be elevated because of the presence of other diseases that simulate hyperthyroidism. The serum protein-bound iodine, however, will furnish a true evaluation of the state of the thyroid.

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