Textbook of Nuclear Medicine: Clinical Applications

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PREFACE

The rapid advances in a highly technical specialty such as nuclear medicine require that textbooks be frequently updated. Associated fields which develop new correlative materials, such as ultrasonography, and the emergence of entirely new fields, such as computerized tomography, require additions to the standard nuclear medicine corpus. The declining interest in other areas, such as autoradiography (largely taken over by other specialties) warrants diminished emphasis. Within this volume we have tried to deal specifically and at length with all of the most important clinical applications of nuclear medicine. This book is intended for use by practicing nuclear physicians, for course work by students and residents in nuclear medicine, and as a reference text for clinicians who utilize nuclear medicine services.

This textbook is a companion volume to Nuclear Medicine—Basic Science, which deals extensively with such aspects as nuclear counting, instrumentation, radiopharmaceuticals, nuclear structure, radiation safety, and dosimetry as well as a host of special nuclear counting problems.

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CONTENTS

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The Thyroid

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TESTS OF THYROID FUNCTION

Anatomy and Physiology

The thyroid gland is situated in the anterior part of the neck immediately in front of the trachea and below the thyroid cartilage. Its two lobes, united by an isthmus, form the shape of a shield, hence its name from the Greek "thyro" meaning shield. In the adult the gland weighs 15 to 20 g.

Embryologically the thyroid has a dual origin. One part derives from an evagination of pharyngeal entoderm in the vertex of the laryngeal V. The other derives from bilateral ectodermal buds from the last branchial clefts, which ultimately fuse in the midline. Cell remnants along the tract of the lingual evagination often connect with the thyroid to produce a "pyramidal lobe," the so-called pyramid of Lalouette. Occasionally a lingual thyroid may persist, but it is almost never active in the presence of normal thyroid function. Lateral thyroid rests may occur, but also fail to function in the presence of normal thyroid activity. If they do demonstrate iodine uptake, they must always be considered metastases from well differentiated thyroid carcinoma. Another abnormal site for thyroid tissue is the ovary where such tissue occurs as a hamartoma called struma ovarii. This tissue may function and may occasionally give rise to thyrotoxicosis and malignancy.

The thyroid cells derived from the ectoderm form the follicle cells, while those stemming from the entoderm give rise to parafollicular or clear cells. The two types of cells have different functions as well as different pathologic characteristics. The follicle cell is well polarized; its base, which contains the nucleus, rests on the follicle basement membrane; and the apex, which contains microvilli, projects into the follicle lumen. The parafollicular cells also lie on the basement membrane, but do not come in contract with the lumen. They are generally larger than the follicle cells and do not stain with para-aminosalicylic acid (PAS), hence their name, clear cells.

Physiologically, the thyroid gland has only one function: to synthesize, store, and secrete the iodinated hormones so indispensable to cellular metabolism. For this role the thyroid cells must incorporate iodine into tyrosine. This process can be more readily understood by reference to the metabolism of iodine, which was first explained in 1938. Hertz et al. (1938) garnered these facts largely through the use of radioactive isotopes of iodine.

Iodine Metabolism

It is difficult to formulate a compartmental model of iodine metabolism that is on the one hand simple and clinically useful and on the other hand permits a quantitative reconstruction of the metabolic cycle. The model in Figure 1–1, although a compromise, does show the interrelationships among extrathyroid, intrathyroid, and hormonal iodine. The fractions lost transplacentally and by mammary excretion are excluded because of their transitory nature.

Extrathyroidal Compartment

This small compartment (40 to 60 μg for a 70-kg man) has a high turnover rate. Its principal inputs are the absorption of dietary iodine and the deiodination of thyroid hormones. Ingested iodine is rapidly reduced to iodide in the upper intestine, and approximately 90% is absorbed in the first 60 min after

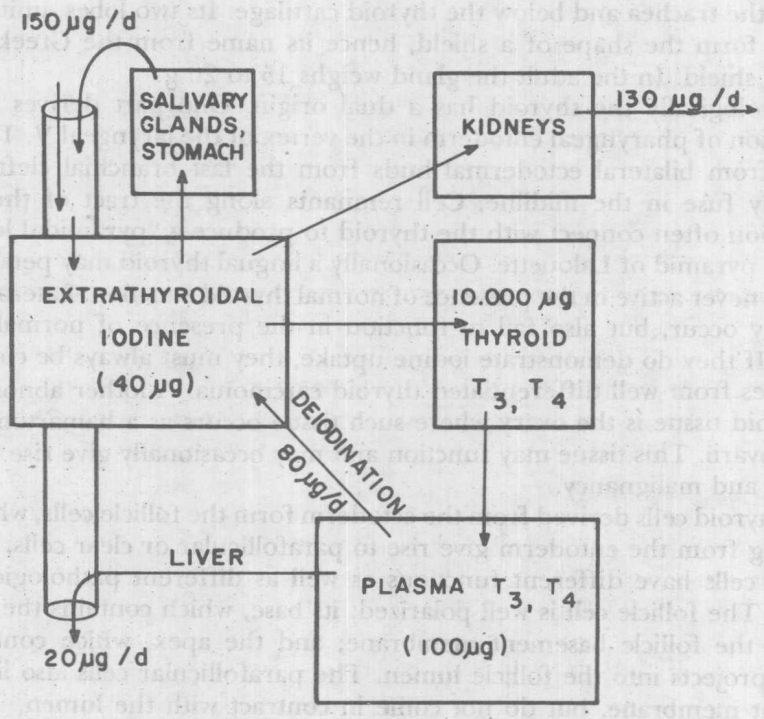

FIG. 1-1. Schematic model of iodine metabolism. (From Silva et al. 1973.)

ingestion. Once iodide reaches the blood, it is distributed similarly to chloride, which is essentially an extracellular ion. The iodide space, that is, the volume required to contain the total body iodide in the same concentration as in plasma, represents 35% of body weight. The plasma concentration of iodide fluctuates between 0.1 and 0.5 μg/100 ml, depending mostly on ingestion. Iodide leaves this compartment principally through thyroid uptake and urinary excretion. A small amount of plasma iodide is taken up by the salivary glands and gastric mucosa; this quantity soon enters the digestive tract and is recycled rather than lost. The rate of renal clearance of iodide normally varies between 20 and 40 ml per min. It is diminished in hypothyroidism, renal insufficiency, and cardiac failure. It is increased by hyperthyroidism and by the action of estrogens. Note that the renal clearance of iodide is not greatly affected by plasma iodide concentration, while thyroid clearance is. Under normal plasma concentrations, the thyroid clearance of iodide is 5 to 40 ml per min, or between 7 and 56 liters of plasma per day. In chronic iodine deficiency, thyroid clearance can increase to 100 ml per min, while with iodine excess, it may fall as low as 2 to 5 ml per min.

Thyroid Compartment

This compartment, which is formed by the iodide trapped and organified by the thyroid gland, is utilized in the synthesis of thyroid hormones. It also includes iodine liberated by the intrathyroidal deiodination of amino acids not utilized by the thyroid cells. This compartment is large (10,000 μg) and has a slow turnover. For didactic purposes the steps in iodine utilization are represented schematically in Figure 1–2.

Iodide Trapping. Iodide is trapped by the thyroid cells by means of a high energy metabolic process known as the thyroid "pump," which permits concentrations 25 to 500 times the plasma concentration depending upon the thyroid functional state. The trapping mechanism depends on oxidative phosphorylation, since it can be inhibited by anoxia, cyanides, dinitrophenol, or hypother-

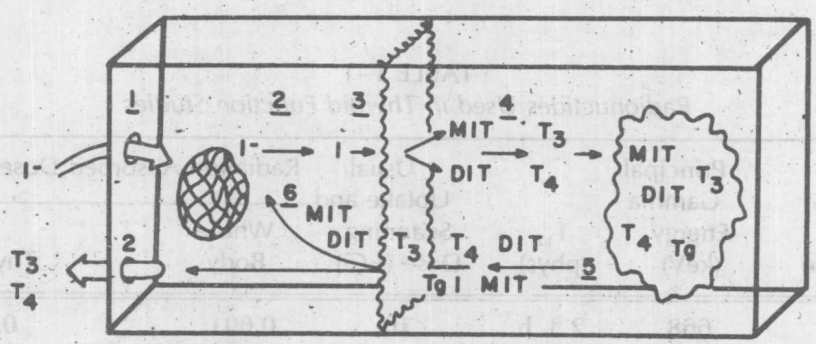

FIG. 1-2. Intrathyroidal iodine cycle: Iodine is first trapped (1), then oxidized to elemental I (2), after which it is organified to MIT and DIT (3), which are then coupled to form T_3 and T_4 and bound to thyroglobulin (4). When resorption occurs (5), it may be deiodinated and recycled (6), or secreted as thyroid hormone (7). I^- = iodide; DIT = diiodotyrosine; MIT = monoiodotyrosine; T_3 = triiodothyronine; T_4 = thyroxine; $T_g I$ = thyroglobulin.

mia. Iodide trapping can be blocked competitively by monovalent ions such as thiocyanate or perchlorate. An effect of this blocking action is to return unbound thyroidal iodide back into the plasma. This "washout" of thyroidal iodide serves as the basis for a clinical test of certain goiters caused by enzymatic defects. The fact that iodine can be displaced in this manner indicates that the trapping process is not unidirectional.

Organification. Once iodine has been incorporated into the cell, it is rapidly oxidized by enzymatic action. The oxidation process has not been well elucidated, but it is known that hydrogen peroxide is formed by a system of peroxidases and cytochrome oxidase and peroxide may be the oxidizing agent. Iodide is oxidized to neutral iodine, I, or to hypoiodide, IO^-, the only forms of iodine that can be utilized by the cells. Soon after oxidation, the iodine is incorporated by tyrosine, forming monoiodotyrosine (MIT) and diiodotyrosine (DIT), which are bound to thyroglobulin. This organification of iodine is stimulated by thyroid stimulating hormone (TSH) and blocked by thiourea. Thyroglobulin is a large glycoprotein (mol. wt. 600,000) composed of some 5000 amino acid elements, of which 125 are tyrosine, to which the iodine is fixed. Thyroglobulin is stored in the follicular lumen of the gland.

Coupling. MIT and DIT lose an alanine radical through an oxidative reaction (involving peroxidase) that links the two molecules, which then give rise to triiodothyronine (T_3) and tetraiodothyronine (T_4). These thyronines remain bound to thyroglobulin in the follicular lumen until needed. As in the previous steps, this coupling process is stimulated by TSH.

In Vivo Function Studies

Table 1–1 lists the most commonly used radionuclides in thyroid studies. While ^{131}I remains the most widely used for in vivo studies, ^{123}I and ^{99m}Tc are becoming increasingly accepted for thyroid uptakes and for scanning. The most commonly encountered tests of thyroid function are listed in Table 1–2.

Iodine 131. Using ^{131}I for thyroid studies has several disadvantages. The long half-life (8.1 days) and beta particle emission increase the radiation dose to the

TABLE 1–1
Radionuclides Used in Thyroid Function Studies

Nuclide	Principal Gamma Energy (keV)	$T_{1/2}$ (phys)	Usual Uptake and Scanning Dose (μCi)	Radiation Absorbed Dose (rads) Whole Body	Thyroid
^{132}I	668	2.3 h	10	0.001	0.01
^{131}I	364	8.1 d	50–80	0.04	25–150
^{125}I	27, 35	60 d	50–100	0.03	40–80
^{123}I	159	13.3 h	50–100	0.0003	0.5–2.0
^{99m}Tc	140	6 h	2000	0.03	0.2–2.0

TABLE 1–2
Summary of Thyroid Function Studies

Tests	Usefulness	Disadvantages
A. *"In Vivo" Studies*		
Radioiodine uptake		
Normal: Depends on dietary iodine	Easy to perfom. In normals, uptake is proportional to hormone production and release	Does not measure thyroid function directly because it often does not measure hormone production and release.
Plasma radioiodine		
Normal: Total ≦ 0.05%/l Organic Fraction ≦ 0.2%/l	Helps clarify the differential diagnosis of elevated uptakes	Organic fraction depends on plasma protein concentration. Not reliable in renal diseases
Urinary excretion of radioiodine		
Normal: Depends on dietary iodine	Permits indirect measure of thyroid function in incapacitated individuals or with very high dose levels	Depends on dietary iodine and renal function
TSH stimulation test		
Normal: 50% increase over baseline uptake value	Permits the differential diagnosis of primary and secondary hypothyroidism	Bovine TSH may rarely produce allergic reactions
T_3 suppression test		
Normal: 60% decrease from baseline uptake value	Permits differentiation of hyperthyroidism from euthyroidism	Some euthyroid patients with endemic goiter do not suppress. May exaggerate toxic symptoms, especially in elderly patients
Absolute iodine uptake		
Normal: less than 5 μg/h	Excellent index of thyroid functional activity especially in endemic goiter and oligosymptomatic (apathetic) hyperthyroidism	Difficult to measure. Requires blood and urine determinations. Limited utility in hypothyroidism
Perchlorate washout test		
Normal: no significant discharge	Useful in some forms of thyroiditis and congenital goiter. May be useful in controlling treatment with PTU	
B. *"In Vitro" Studies*		
Protein-bound iodine (PBI)		
Normal: 3.1–7.7 μg/100 ml	Useful in confirming iodine excess	Often does not accurately reflect level of serum thyroxine. Results strongly influenced by exogenous iodine
Butanol-extractable iodine (BEI)		
Normal: less than 2 μg/100 ml	Eliminates extraction of inorganic iodine	Tedious and expensive and subject to many of the errors of PBI
T_4 by column	Eliminates serum iodine from contrast agents	Same problems in general as PBI