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A MANUAL FOR NUCLEAR MEDICINE

With a Foreword by

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Foreword

THE development of the sub-specialty, nuclear medicine, has been one of the most fascinating events to occur in the medical profession during this century. In our naval hospitals all services have been affected by the progress which has been made in the clinical uses of radioactive isotopes and clinical radiobiology. Our research programs are affected to a similar degree. Even the planned trips of man into outer space will depend to a large extent on our solving the problems resulting from exposure to the ionizing radiation present in outer space.

Twelve years ago, as Commanding Officer of the Naval Medical School, I was instrumental in establishing the first Radioisotope School which later became the Department of Nuclear Medicine. Since then, I have followed the progress made in the study and uses of nuclear energy, especially as applied to medicine, and have been gratified by the advances made by the Navy's bio-medical radiation facilities.

This text, while written for the student and the practicing clinician, can also be applied to investigative animal research. I believe it to be a valuable addition to the library medical literature and hope that it will prove beneficial to all members of the medical and paramedical professions. It is another example of efforts made by the Navy Medical Department to disseminate acquired information to their colleagues, both civilian and military.

B. W. HOGAN
Rear Admiral, MC USN
Surgeon General of the Navy

Preface

THIS manual is intended as a laboratory guide for students studying radioisotope procedures in medicine, as well as for the practitioner. It is not intended as a complete text of nuclear medicine. The section on physics experiments is the same as offered to participants in our course in nuclear medicine for physicians. It is placed in the last half of the book for fear it would frighten away the casual reviewer. However, we would like to emphasize that the laboratory experiments in physics, listed in the last portion of the text, should be required work for all physicians before they apply the clinical studies in the first half of this manual.

The techniques and experiments described in this manual have been tested and applied at the National Naval Medical Center, Bethesda, Maryland. During the past several years, many individuals have served in the laboratories of the Department of Radiology, U. S. Naval Hospital, and the Department of Nuclear Medicine, U. S. Naval Medical School. Consequently, the authors owe a debt of gratitude to more individuals than is customary for a text of this size. Many of the technicians and physicians who have assisted in developing these procedures must, of necessity, remain unrecognized, since a hundred individuals have served in our departments over the past ten years.

Our special thanks are offered to the following: For the section on thyroid studies, Dr. Richard Spencer now of the University of Buffalo, School of Medicine, Dr. Ronald Koons now of University Hospital, Baltimore, and LT Ralph Cavalieri, MC USNR, who is serving with us; for the studies related to hematology, Dr. N. I. Berlin of the National Cancer Institute, Bethesda, and LCDR Howard Pearson, MC USN, of the Department of Pediatrics, U. S. Naval Hospital, Bethesda; for the sections on space and function studies and on tumor localization, LT William Fleming, MC USNR, of our laboratories, and Dr. William Maxfield now of the Johns Hopkins University Hospital; for the section

on autoradiography, the Medical Division of the Oak Ridge Institute of Nuclear Studies, from which much of the material was obtained, and LCDR Thomas Hartney, MC USN, of the Department of Pathology, U. S. Naval Medical School, Bethesda.

In addition, the following colleagues must be mentioned with their present addresses: Dr. T. G. Balbus of Episcopal Hospital, Philadelphia; Dr. Luther Brady of Hahnemann Hospital, Philadelphia; Dr. W. B. Looney of Johns Hopkins University, School of Public Health; Dr. B. J. Duffy of Seton Hall College of Medicine and Dentistry, New Jersey; Dr. Charles Henkelmann of Bakersfield, California; and Dr. Robert Druyan of the Biophysics Research Laboratory, Peter Bent Brigham Hospital, Boston. All assisted while serving as Medical Officers in the United States Navy. Likewise, LT Martin Colodzin, MC USN, and LT Armand Nice, MSC USN, aided in the section on physics.

Technicians furnishing invaluable aid include: William Beckner, HM1 USN, Richard C. Knoebel, HM1 USN, Norbert Konwinski, HMC USN, Paul Novak, now LTJG, MSC USN and Richard Baseman, now Ensign, USN.

For the clerical problems involved in assembling this manual, we offer our gratitude to Margaret Posipanka, HM1 USN, Virginia McLean, Bettie Jean Hessie, and Elaine Paris. Most of the illustrations were prepared by the Medical Illustration Section and the Medical Photography Department of the U. S. Naval Medical School.

E. R. K.
T. G. M.

Contents

A MANUAL FOR NUCLEAR MEDICINE

CHAPTER 1

Laboratory Studies of the Thyroid

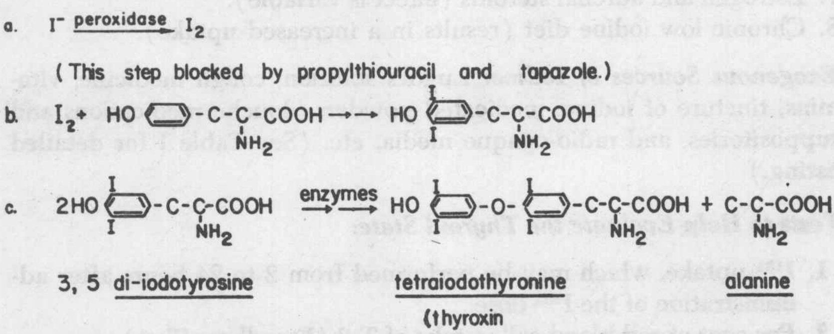
A. AN OUTLINE OF THYROID PHYSIOLOGY

THE most prevalent clinical application of radioisotopes is the use of radioiodine (most often I^{131}) in the study of thyroid function. Thus it behooves physicians learning clinical radioisotope procedures to acquaint themselves with the physiology of this very important endocrine gland. It should be stated that our knowledge of this subject is constantly changing. Following is a brief outline and charts of the present concept of thyroid physiology.

Function: To produce the hormones thyroxine and tri-iodothyronine which increase the rate of cellular metabolism.

Steps in Hormone Production by the Thyroid Gland:

1. *The trapping of iodide ions:* The thyroid can concentrate the iodide ion 50 – 500 × the concentration of this ion in the blood.
2. *Hormone synthesis:*



3. *Hormone storage and release:* After the hormone formation, a part is immediately released into the blood stream. The majority is stored in thyroid follicles where it combines with the thyroglobulin in the colloid. Release is under control of an enzyme and thyroid stimulating hormone (TSH).

Physiologic Factors Affecting Hormone Production:

1. The anterior pituitary produces thyroid stimulating hormone (TSH). This consists of:
   a. Growth hormone which controls size of thyroid gland.
   b. Metabolism hormone which controls thyroid hormone production.
2. Hypothalmus produces a neurotropic hormone which acts on the anterior pituitary to stimulate the growth hormone of TSH. (Cause of large glands in euthyroid people?)

Extraneous Factors That Affect Thyroid Function:

1. Perchlorates, thiocyanates, and nitrates interfere with the trapping mechanism.
2. Propylthiouracil and tapazole interfere with peroxidase and prevent iodination of tyrosine by blocking oxidation of iodide.
3. Iodine in large amounts blocks thyroid functions. (Iodine inhibits the anterior pituitary and blocks TSH.) In smaller amounts it tends to saturate thyroid tempcrarily. (Daily iodine requirements are about 75 μgm.)
4. Desiccated thyroid, thyroxine, and tri-iodothyronine, act by inhibiting the pituitary gland.
5. Exogenous Thyroid Stimulating Hormone (TSH) increases iodine uptake by the thyroid.
6. Aspirin in large doses.
7. Estrogen and adrenal steroids (effect is variable).
8. Chronic low iodine diet (results in a increased uptake).

Exogenous Sources of Iodine: Lugol's solution, cough medicine, vitamins, tincture of iodine, medicated powders, douche medications and suppositories, and radio-opaque media, etc. (See Table I for detailed listing.)

Tests to Help Evaluate the Thyroid State:

1. I^{131} uptake, which may be performed from 2 to 24 hours after administration of the I^{131} dose.
2. Per cent of red blood cell uptake of T-3 (Freedberg Test).
3. Thyroid clearance of I^{131}.
4. PBI-Conversion Ratio.
5. Saliva-PBI-Ratio.
6. Basal Metabolic Rate (BMR).

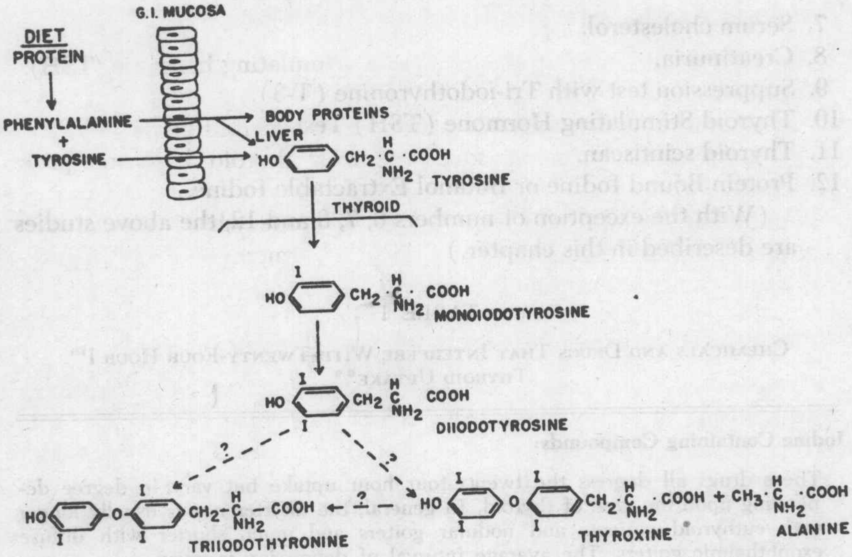


FIGURE 1. Thyroid biochemistry—the formation of the thyroid hormone complex.

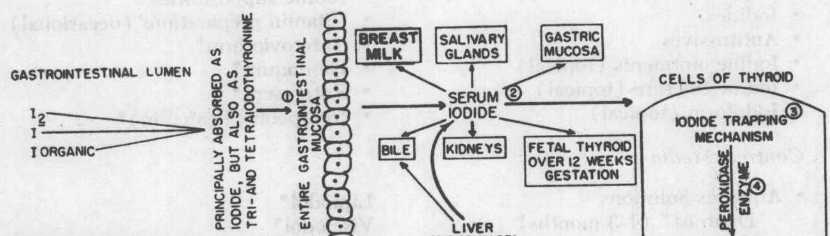


FIGURE 2. Schematic diagram of thyroid physiology. (Photo courtesy, U. S. Naval Medical School, Bethesda, Md.)

7. Serum cholesterol.
8. Creatinuria.
9. Suppression test with Tri-iodothyronine (T-3).
10. Thyroid Stimulating Hormone (TSH) Test.
11. Thyroid scintiscan.
12. Protein Bound Iodine or Butanol Extractable Iodine.

(With the exception of numbers 6, 7, 8 and 12, the above studies are described in this chapter.)

TABLE I

CHEMICALS AND DRUGS THAT INTERFERE WITH TWENTY-FOUR HOUR I^{131} THYROID UPTAKE**

Iodine Containing Compounds:

These drugs all depress the twenty-four hour uptake but vary in degree depending upon the type of thyroid. In general, the interference is usually longer with euthyroid patients and nodular goiters and much shorter with diffuse exophthalmic goiters. The average interval of depression is given.

General Preparations

(1-3 weeks)

- Lugol's solution
- Iodides
- Antitussives
- Iodine ointments (topical)
- Iodine tincture (topical)
- Iodoform (topical)
- Iodine suppositories
- Vitamin preparations (occasional)
- Enterovioform*
- Diodoquin*
- Enterosept*
- Neo-penil (Penicillin)*

Contrast Media

- Aqueous Solutions
  - Diodrast* (1-3 months)
  - Hypaque*
  - Medopaque*
  - Neo-iopax*
  - Urokon*
  - Miokon*
  - Thixokon*
  - Renografin (1-2 weeks)
  - Dionosil (British)* (2-4 months)
- Oily Solutions
  (Up to 1 year or more)
  - Lipiodol*
  - Visciodol*
  - Ethiodol*
  - Iodochlorol*
  - Pantopaque*
- Cholecystopaques and Cholangiopaques
  - Cholografin* (3 months)
  - Telepaque* (2 months)
  - Priodax* (1-3 months)
- Uterosalpingopaques
  - Skiodan acacia*
  - Salpix* (1 month)

Other Chemicals and Drugs:

These preparations all depress the twenty-four hour I^{131} uptake, usually less and for a shorter time in hyperthyroidism. The average interval of depression is given when known.

Antithyroid drugs (2-8 days)
- Thiouracil
- Propylthiouracil
- Methylthiouracil
- Iothiouracil (Itramil*)
- Muracil*
- Methimazole (Tapazole)*
- Mercazole*
- Carbimazole

Thyroid Medication (1-2 weeks)
- Desiccated thyroid
- Thyronine
- Thyroxine
- Thyroglobulin

Thiocyanates (1 week)
Perchlorate
Nitrate

Sulfonamides (1 week)
Orinase*
Progesterone
Adrenal Cortical Steroids (1 week or less)
- Cortisone, Corticosterone, Desoxycorticosterone, Prednisone, Prednisolone

ACTH
Resorcinol
Cobalt (1 week or less)
PAS and Isoniacid (1 week after prolonged use)
Butazolidin*
Amphenone (2-3 days)
Antihistamines (1 week or less)
Phenothiazine
Pentothal (1 week)

Compounds That Enhance the Twenty-four Hour I^{131} Thyroid Uptake

- Thyroid Stimulating Hormone (TSH)
- Estrogens (not persistently)

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* Other trademarks: Skiodan acacia, Telepaque, Pantopaque, Diodrast, Hypaque, Neo-iopax, Priodax, Urokon, Miokon, Thioxokon, Lipiodol, Visciodol, Ethiodol, Diodoquin, Iodochlorol, Salpix, Enterovioform, Itrumil, Tapazole, Orinase, Butazolidin, Enterosept, Neo-penil, Medopaque, Dionosil, Muracil, Mercazole.

** From Magalotti, Marion F., *et al.:* The Effect of Disease and Drugs on the Twenty-Four Hour I^{131} Thyroid Uptake. *Am. J. Roentgenol., 81*:54, January 1959. Courtesy, Charles C Thomas, Publisher.

B. THYROID STUDIES UTILIZING RADIOIODINE

Patients referred for thyroid studies are usually evaluated by means of the 24 hour thyroid uptake, the per cent red blood cell uptake of tri-iodothyronine (% RBC uptake T_3), the chemical PBI and a history and physical relative to the thyroid gland. A scintiscan of the neck is performed on all post-thyroidectomy patients (no matter how long ago the operation was performed); on all patients in whom a nodule is thought to be present; on all patients with abnormal 24 hour uptakes; and on all patients with known or suspected carcinoma of the thyroid. A 6 hour uptake is also performed on all patients when it is feasible.

Individuals showing laboratory values in the borderline hyperthyroid range may be further followed by having a "thyroid suppression study" using exogenous thyroxine or tri-iodothyronine.

A patient whose studies are in the hypothyroid range should be further evaluated to determine if the deficit is primarily in the thyroid gland or is secondary to pituitary dysfunction. This is done by following the routine tests a week later with a dose of TSH intramuscularly and repeating the studies. This procedure is known as the "thyroid stimulation study."

The patients are interviewed prior to beginning the tests. Studies with I^{131} are not done on pregnant women (the fetus accumulates iodine after the 12th week of gestation). Since radioiodine is also excreted via the mammary glands, nursing mothers are excluded from such studies. It is also important to elicit information on the use of any thyroid hormones, iodine, goitrogens, or radiopaque media because of their effects on the various tests. The PBI-Conversion ratio is occasionally performed and consists of counting the total amount of I^{131} activity in a sample of blood drawn 24 to 72 hours after the oral I^{131} is given, and comparing this with the amount of protein bound I^{131} activity in the same sample of blood. The ratio is usually above 50% in hyperthyroidism. Hypothyroid results are difficult to differentiate from euthyroid ones.

The Saliva-PBI ratio compares the amount of Iodine-131 in saliva with the amount of PBI-131. In hypothyroidism there is an increase in saliva I^{131} and decrease in PBI^{131}. The disadvantage of these two tests is that they require 50-100 μc of I^{131}, a dose that is larger than one would care to administer to many patients because of the resultant total body radiation dose. In the average individual this would be a dose in the order of 50-100 mr (milliroentgen).

C. IODINE-131 DOSES USED IN THYROID FUNCTION TESTS

In choosing the amount of radioactive material to use in each test, two criteria must be kept in mind. The dose should give as little radiation to the patient as possible but still give data which is statistically significant. Consequently, if possible, one should select the study utilizing the smallest possible dose of radioactivity.

The doses usually used in this laboratory are:

24 hour thyroid uptake of I^{131}	5 microcuries
Thyroid scans	10-25 microcuries
PBI-conversion ratio	50-100 microcuries
Saliva-PBI ratio	50-100 microcuries
Detecting metastatic uptake	100-1,000 microcuries
Thyroid clearance	40 microcuries

Comment

The 24 hour uptake of I^{131} appears to be the best overall study for thyroid function employing radioisotopes. The "Freedberg Test" and shorter time thyroid uptake of radioiodine show promise of becoming more safe and practical than this study however.

In establishing the diagnosis of hypothyroidism, it has been found that the Saliva-PBI ratio is of value, while in hyperthyroidism, the PBI-Conversion ratio is more useful (based on a series of 500 cases).

This laboratory prefers the Amberlite technique for conversion ratios. The next in preference is the Zinc Sulphate method. This preference was based upon the comparison of these techniques in the same patient, in a series of 50 patients. Normal values must be established in each laboratory for each type of test.

D. THE 24 HOUR THYROID I^{131} UPTAKE STUDY

Equipment

1. Sodium iodide, thallium activated crystal, scintillation detector, 2″ × 2″, shielded by 1″ of lead, with a "wide angle" collimator. For scanning, an automatic scanner with a 19 hole focussing collimator on a 2″ × 2″ crystal is used. A single channel gamma ray spectrometer is preferred to integral or scaler counting (see Chapters 20 and 21).
2. Suitable scaler or spectrometer.
3. I^{131} (obtained from Oak Ridge National Laboratory, Abbott, Squibb, etc.). The I^{131} is carrier free (fission product) in the form of NaI in a weak basic solution.

Discussion

Administered radio-iodine is accumulated by the thyroid gland, the daily requirement of iodine being about 75-100 micrograms per day for the adult. The ability of this organ to concentrate iodine is several hundred-fold greater than other tissues. The hyperactive gland takes up more iodine than normal, while the hypoactive gland takes up relatively little iodine.

Methodology

1. Five microcuries of I^{131} in distilled water is administered orally to the fasting patient through straws. The container is rinsed twice, and the patient drinks the rinse water. (If the patient is to be scanned, 25 microcuries are administered.)

2. A standard is prepared in identical fashion and measured in an ORINS type thyroid phantom (Abbott Radiopharmaceuticals).

3. A gamma ray spectrometer is used whenever possible so that the entire major peak of I^{131}, which is .364 mev., is counted in the "window." (See Chapters 20, 21.)

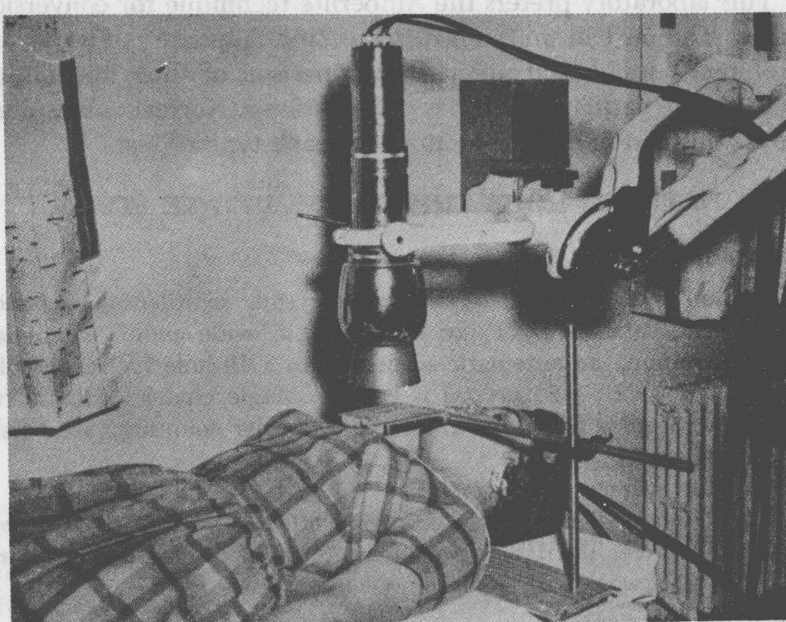

FIGURE 3. The use of the "B" Filter. A ¼ inch plate of lead is placed over the patient's thyroid, thus eliminating the radiation from radioiodine in other portions of the body. This is a correction for "body background." (See page 13.) (Photo courtesy, U. S. Naval Medical Center, Bethesda, Md.)