Evaluation of Diseases of the Thyroid Gland with the In Vivo Use of Radionuclides

Task Force on Short-lived Radionuclides for Medical Applications

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The thyroid gland is one of the organs frequently studied with nuclear medicine techniques. Over the past several decades, increased attention has been drawn to the association between ionizing radiation and the late development of nodules and cancer of the thyroid gland. Although no association has been reported between diagnostic doses of radiopharmaceuticals and thyroid nodules or cancer, it is advisable to minimize radiation exposure to the thyroid whenever clinical information will not be compromised.

Newer radionuclides and techniques yield better diagnostic information, with the delivery of lower radiation doses than techniques commonly used in previous decades. Therefore, recommendations are offered to encourage techniques that reduce radiation dose in thyroid studies with the most commonly used radiopharmaceuticals: [^{131}I] sodium iodide, [^{99m}Tc] sodium pertechnetate and [^{123}I] sodium iodide.

Radiopharmaceuticals for clinical evaluation of the thyroid gland.

The principal clinical use of I-131 continues to be for the study of the thyroid gland, both for determinations of function and to study the structure of the gland. Because of its availability, suitable half-life, and ease of measurement, I-131 as sodium iodide has been the radiopharmaceutical of choice for many years.

Technetium-99m as pertechnetate is widely employed for imaging studies. It has the advantage of being inexpensive and readily available. The absorbed radiation dose to the thyroid for a clinically effective administration of Tc-99m as sodium pertechnetate is the lowest of all radiopharmaceuticals used to study the gland. However, the dose to the lower large intestine, bone marrow, whole body, and gonads is greater with Tc-99m than with a comparable imaging dose of I-123. In the judgment of many physicians, Tc-99m is the preferred imaging agent for such studies.

A different viewpoint is expressed by some physicians who feel that an agent such as Tc-99m, which measures only equivalent ion transport (trapping), limits the effectiveness for evaluating the thyroid and its complex interrelationships. These physicians prefer I-123 or, if not available, I-131.

Many epidemiological studies have identified the thyroid gland, especially in children, as being particularly susceptible to radiation carcinogenesis. However, the majority of these studies have indicted external x-rays as being the factor commonly associated with carcinogenesis rather than the beta radiation of I-131. Possible reasons for the disparity between the reported carcinogenic potential of x-rays and radioiodines include the differences in distribution of ionization, dose, and dose rate when external sources of x-ray or gamma radiation are compared with the internal radiations produced by the different radioiodines (I-131, I-123) used in thyroid studies, or the use of high, ablation doses of radioiodine that have led to thyroid cell death before malignant changes could develop. External radiation exposes the entire gland uniformly and at higher dose rates, whereas the radiopharmaceuticals irradiate the gland in a nonuniform manner, depending on the degree of function of the acinar cells and the radiation characteristics of the emitter. The radiosensitivity of the thyroid strongly suggests that radiation to the thyroid should be minimized whenever possible. This goal can be accomplished in three ways: (a) in vivo radionuclide studies of the thyroid should be employed only when clearly indicated; (b) radionuclides delivering the lowest dose (i.e., I-123, Tc-99m) should be used whenever practical; and (c) when it is necessary to use I-131, the dose should be reduced to the minimum required to obtain the desired information.

Recommendations for the use of radioactive iodine in thyroid disease.

1. Radioactive iodine should not be used for the following thyroid diagnostic studies:

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a. Screening for thyroid disease in an apparently healthy population.

b. As a primary diagnostic test for hyperthyroidism and/or hypothyroidism.

c. During pregnancy and lactation, except under special circumstances.

d. In children, except under special circumstances.

2. Radioiodine uptake testing is important and useful in the diagnosis of thyroid disease, as follows:

a. To confirm the diagnosis of hyperthyroidism, i.e., to confirm that the thyroid gland is the source of elevated blood thyroid-hormone levels in clinical hyperthyroidism before instituting treatment, especially:

1. When the manifestations of hyperthyroidism are not clear as based on clinical findings and other laboratory tests.

2. To rule out thyrotoxicosis factitia.

3. To determine the existence of ectopic secretion of thyroid hormone.

b. To assist in the diagnosis of subacute and chronic thyroiditis and in the evaluation of various types of goiter.

c. For use in thyroid suppression tests to evaluate autonomy of functioning thyroid tissue.

d. For stimulation tests to assist in the differentiation of primary from secondary hypothyroidism, when determination of serum TSH is not available or appropriate.

e. For estimation of therapeutic doses of iodine-131 in the treatment of hyperthyroidism or thyroid cancer, or for thyroid ablation.

3. Thyroid imaging with radioiodine can provide useful information in the following circumstances:

a. Detection and evaluation of function of solitary or multiple thyroid nodules.

b. Evaluation of aberrant thyroid tissue such as substernal masses, possible lingual thyroid, functioning metastases of thyroid cancer, and other tumors containing thyroid tissue.

c. To assist in the estimation of thyroid size for radioiodine dosimetry.

d. In the management of thyroid cancer.

4. Technetium-99m, as sodium pertechnetate, is a suitable substitute for radioiodine for thyroid imaging in the following circumstances:

a. Detection and evaluation of function of solitary or multiple thyroid nodules.

b. It may be necessary to reimage the thyroid with radioiodine when:

1. The pertechnetate images demonstrate no abnormality corresponding to a palpable nodule(s).

2. The pertechnetate images demonstrate a hyperfunctioning nodule(s) (without suppression of extranodular thyroid tissue).

3. The thyroid pertechnetate concentration is low and image contrast is unsatisfactory.

4. Unexplained extrathyroidal uptake is suspected

TABLE 1. TYPICAL ABSORBED DOSES DUE TO THYROID DIAGNOSTIC RADIOPHARMACEUTICAL PROCEDURES (3,4) BASED ON ACTIVITIES RECOMMENDED IN THIS REPORT

Procedure for adults	Recommended administered activity	Critical organ	Critical organ (mrad/μCi)	Critical organ (actual mrads)	Whole-body dose (mrad)	Gonadal (6) dose (mrad)
Uptake						
I-123 (iodide)	10–20 μCi	Thyroid	11	110–220	0.3–0.6	M: 0.1–0.2 F: 0.2–0.4
I-131 (iodide)	6 μCi	Thyroid	1,100	6,600	2.6	M: 0.52 (5) F: 0.84
Scan						
Tc-99m (pertechnetate)	5–10 mCi	Thyroid†	0.20	1,000–2,000	60–120	M: 60–120
		L.L.I.‡	0.20	1,000–2,000		
		Stomach (7)	0.10–0.30	500–300		F: 90–180
I-123 (iodide)	100–400 μCi	Thyroid	11	1,100–4,400	3–12	M: 1–4
		L.L.I.		negligible		
		Stomach (5)	0.22	22–88		F: 2–8
I-131 (iodide)	30 μCi	Thyroid	1,100	33,000	14	M: 2.6 (5) F: 4.2

* The fraction of adult activity used for imaging procedures in children was chosen on the basis of proportionality to the ⅔ power of body weight following Webster (3). For the purpose of this calculation, adult values of 5 mCi Tc-99m and 100 μCi I-123 are assumed. See Table 7.

† Assumed a 1.6% uptake of pertechnetate for all ages except the newborn, where a 3.5% uptake is assumed, following Webster et al (3).

‡ Lower large intestine.

TABLE 2. TYPICAL ABSORBED DOSES DUE TO THYROID DIAGNOSTIC RADIOPHARMACEUTICAL PROCEDURES (3,4) BASED ON ACTIVITIES RECOMMENDED IN THIS REPORT

Procedure at age 15	Recommended administered activity	Critical organ	Critical organ (mrad/μCi)	Critical organ (actual mrads)	For administered activties: whole-body dose (mrad)	For administered activties: Gonadal (6) dose (mrad)
Uptake						
I-123 (iodide)	10–20 μCi	Thyroid	16	160–320	0.36–0.73	M: 0.12–0.24 F: 0.24–0.48
I-131 (iodide)	2 μCi	Thyroid	1,600	3,200	1.0	
Scan						
Tc-99m (pertechnetate)	4.2 mCi	Thyroid†	0.35	1,500	63	M: 59 F: 92
		L.L.I.*	0.20	840		
I-123 (iodide)	170 μCi	Thyroid	16	2,700	6	M: 2 F: 4
I-131 (iodide)	25 μCi	Thyroid	1,600	40,000	13	

* Lower large intestine.
† Assumed a 1.6% uptake of pertechnetate for all ages except the newborn where a 3.5% uptake is assumed, following Webster et al (3).

TABLE 3. TYPICAL ABSORBED DOSES DUE TO THYROID DIAGNOSTIC RADIOPHARMACEUTICAL PROCEDURES (3,4) BASED ON ACTIVITIES RECOMMENDED IN THIS REPORT

Procedure at age 10	Recommended administered activity	Critical organ	Critical organ (mrad/μCi)	Critical organ (actual mrads)	For administered activities: Whole-body dose (mrad)	For administered activities: Gonadal (6) dose (mrad)
Uptake						
I-123 (iodide)	10 μCi	Thyroid	22	220	0.5	M: 0.53 F: 0.37
I-131 (iodide)	2 μCi	Thyroid	2,200	4,400	1.6	
Scan						
Tc-99m (pertechnetate)	3 mCi	Thyroid†	0.47	1,400	65	M: 200 F: 100
		L.L.I.*	0.30	900		
I-123 (iodide)	120 μCi	Thyroid	22	2,600	6.2	M: 6.6 F: 4.4
I-131 (iodide)	18 μCi		2,200	40,000	15	

* Lower large intestine.
† Assumed a 1.6% uptake of pertechnetate for all ages except the newborn where a 3.5% uptake is assumed, following Webster et al (3).

of being an artifact.

5. Pertechnetate is generally a less satisfactory substitute for radioiodine for thyroid imaging in the following circumstances:

a. Evaluation of aberrant thyroid tissue, except in the lateral portion of the neck.

b. In the management of thyroid cancer.

c. Suppression and stimulation testing.

Recommendations to decrease administered doses of I-123 and I-131 as iodides, and Tc-99m as pertechnetate.

In this section we discuss some combinations of satisfactory imaging and measuring devices, together with some "routine" doses of the above radiopharmaceuticals for adults; they will yield adequate information and simultaneously will minimize radiation exposure of the patient (Table 1*).

It is to be emphasized that Tc-99m, I-123, and I-131 should not be used during pregnancy and their use should be limited in young children. Recommended oral doses for children are given in Tables 2–7*.

These recommendations should be posted where tracer doses of radiopharmaceuticals used for studies

TABLE 4. TYPICAL ABSORBED DOSES DUE TO THYROID DIAGNOSTIC RADIOPHARMACEUTICAL PROCEDURES (3,4) BASED ON ACTIVITIES RECOMMENDED IN THIS REPORT

Procedure at age 5	Recommended administered activity	Critical organ	Critical organ (mrad/μCi)	Critical organ (actual mrads)	For administered activties: Whole-body dose (mrad)	For administered activties: Gonadal (4) dose (mrad)
Uptake						
I-123 (iodide)	10 μCi	Thyroid	38	380	0.9	M: 0.9 F: 0.5
I-131 (iodide)	2 μCi	Thyroid	3,800	7,600	2.6	
Scan						
Tc-99m (pertechnetate)	2.2 mCi	Thyroid†	0.78	1,700	75	M: 160 F: 99
		L.L.I.*	0.40	880		
I-123 (iodide)	86 μCi	Thyroid	38	3,300	6.8	M: 5.4 F: 4.4
I-131 (iodide)	13 μCi	Thyroid	3,800	49,000	17	

* Lower large intestine.
† Assumed a 1.6% uptake of pertechnetate for all ages except the newborn where a 3.5% uptake is assumed, following Webster et al (3).

TABLE 5. TYPICAL ABSORBED DOSES DUE TO THYROID DIAGNOSTIC RADIOPHARMACEUTICAL PROCEDURES (3,4) BASED ON ACTIVITIES RECOMMENDED IN THIS REPORT

Procedure at age 1 yr.	Recommended administered activity	Critical organ	Critical organ (mrad/μCi)	Critical organ (actual mrads)	For administered activties: Whole-body dose (mrad)	For administered activties: Gonadal (6) dose (mrad)
Uptake						
I-123 (iodide)	10 μCi	Thyroid	81	800	1.3	M: 0.67 F: 0.83
I-131 (iodide)	2 μCi	Thyroid	8,100	16,000	4	
Scan						
Tc-99m (pertechnetate)	1.5 mCi	Thyroid†	1.30	2,000	76	M: 120 F: 110
		L.L.I.*	0.70	1,000		
I-123 (iodide)	60 μCi	Thyroid	81	4,900	7.8	M: 4.0 F: 5.0
I-131 (iodide)	9 μCi	Thyroid	8,100	73,000	18	

* Lower large intestine.
† Assumed a 1.6% uptake of pertechnetate for all ages except the newborn where a 3.5% uptake is assumed, following Webster et al (3).

of the thyroid are prepared. The physician should make certain that the prescribed tracer doses are of appropriate amounts in accordance with these recommendations except under special circumstances. For greater detail, reference may be made to the thyroid radionuclide uptake recommendations of the International Atomic Energy Agency (*1*) and the American National Standards Institute (*2*).

1. Iodine-131 as sodium iodide.

A principal concern in preparing these recommendations is the observation that doses of 100–500 μCi of I-131 for "routine" thyroid imaging are frequently used to decrease the time required for imaging a patient.

a. For uptake measurement using a single crystal, recommended doses are predicated upon a crystal with an average diameter of about 2 in. (5 cm), with a thickness of at least 1 in. (2.5 cm) at a standard distance of 10 in. (25 cm), measured from the surface of the neck at the thyroid isthmus to the front face of the crystal.

b. Based upon the instrumentation recommended

TABLE 6. TYPICAL ABSORBED DOSES DUE TO THYROID DIAGNOSTIC RADIOPHARMACEUTICAL PROCEDURES (3,4) BASED ON ACTIVITIES RECOMMENDED IN THIS REPORT

Procedure for newborn	Recommended administered activity	Critical organ	Critical organ (mrad/μCi)	Critical organ (actual mrads)	For administered activties: Whole-body dose (mrad)	For administered activties: Gonadal (6) dose (mrad)
Uptake						
I-123 (iodide)	10 μCi	Thyroid	160	1,600	3.7	M: 0.87 F: 2.4
I-131 (iodide)	2 μCi	Thyroid	16,000	32,000	20	
Scan						
Tc-99m (pertechnetate)	0.7 mCi	Thyroid†	3.40	2,400	100	M: 71 F: 150
		L.L.I.*	2.00	1,400		
I-123 (iodide)	28 μCi	Thyroid	160	4,500	9.8	M: 2.4 F: 6.8
I-131 (iodide)	4 μCi	Thyroid	16,000	64,000	42	

* Lower large intestine.

† Assumed a 1.6% uptake of pertechnetate for all ages except the newborn where a 3.5% uptake is assumed, following Webster et al (3).

TABLE 7. FRACTION OF ADULT ADMINISTERED RADIOACTIVITY RECOMMENDED FOR CHILDREN (3,4)

Age	Newborn	1 yr	5 yr	10 yr	15 yr	Adult
Body weight (kg)	3.54	12.1	20.3	33.5	55.0	70.0
Fraction of adult activity (based on (⅔) power of body weight)	0.14	0.30	0.43	0.60	0.85	1.00

maximum doses for uptake percentage measurement are as follows: for adults 6 μCi; for children of varying ages see Tables 2–7. In uptake measurements for children, consideration may be given for a shortened distance between detector and neck.

c. Recommended doses for imaging are predicated upon a crystal in a rectilinear scanner with an average diameter of 3–5 in. (8–13 cm) and a thickness of at least 2 in. (5 cm).

d. Imaging with the rectilinear scanner and/or scintillation camera is based upon percentage of iodine uptake and estimated thyroid gland weight for a euthyroid subject. For imaging, a dose of 30 μCi is recommended for euthyroid patients whose glands are of normal size. A dose of 100 μCi would be considered to be an upper limit, especially suitable for hypothyroid patients.

e. When a second dose is to be given for the completion of a "TSH stimulation test" or a "thyroid suppression test," and when the second part of the test immediately follows the first, the thyroid gland should always be "counted" and a repeat dose calculated to deliver to the thyroid gland between one and two times the number of microcuries of I-131 remaining in the gland from the first dose. If little or none of the first dose remains, the second dose need not exceed the first one.

f. After the diagnosis of hyperthyroidism or thyroid cancer has been made and when I-131 therapy is to be used, thyroid imaging studies can be done with I-131; here I-123 or Tc-99m offers no advantage.

2. Iodine-123 as sodium iodide.

a. For uptake measurements using a single crystal, the same system can be used as for I-131. For imaging with currently available I-123, the same rectilinear scanners and collimators can be used as for I-131. With the available gamma cameras, a pinhole collimator having an aperture 3–6 mm in diam. is recommended.

b. For uptake measurements with the above instruments, the following oral doses are recommended:

Measurement at 4–6 hr, 10 μCi

Measurement at 24 hr, 20 μCi.

c. For imaging either with the rectilinear scanner or gamma camera as described above, an oral dose range of 100–400 μCi is recommended.

3. Technetium-99m as pertechnetate.

a. The measurement of thyroid uptake with per-

technetate is more difficult than with the radioiodines, since the uptake must be measured within 20 min of administration, at which time the body background is high compared to the activity in the thyroid gland, enough to threaten the test's reliability. Although it is possible to develop appropriate ranges for this use, with the decreasing use of uptake measurements as a measure of thyroid function, either an in-vitro test or uptake with one of the radioiodines is preferable.

b. For imaging, the preferred method is the scintillation camera with a pinhole collimator having a 3- to 6-mm aperture.

c. An imaging dose of 3–10 mCi, given intravenously, is generally adequate. Recently, doses of 15–20 mCi have been used to improve visualization. At these dose levels the physician should consider the radiation dose delivered to the stomach, colon, and whole body, as well as that to the thyroid gland (see Tables 1–6).

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FOOTNOTE

* The table of absorbed doses lists the radiopharmaceuticals that are used in thyroid studies in relation to the recommended administered activities. The table illustrates the magnitude not only of critical-organ doses but also of the gonadal and whole-body doses where the information is available. Since pertechnetate is also concentrated in the stomach and lower large intestine, available data on these critical organs have been included. For different assumed administered activities or assumed uptake percentages, a simple ratio calculation may be applied for the critical-organ dose.

REFERENCES

1. International Atomic Energy Agency Panel: Thyroid radionuclide uptake measurements; Special Report number 7. *Brit J Radiol* 46: 58–63, 1973

2. American National Standards Institute: Thyroid radioiodine uptake measurements using a neck phantom. *ANSI* N44.3, 1973

3. WEBSTER EW, ALPERT NM, BROWNELL GL: Radiation doses in pediatric nuclear medicine and diagnostic x-ray procedures, as revised in July 1976, from *Pediatric Nuclear Medicine*, James AE, Wagner HN, Cooke RE, eds. W. B. Saunders Co., Philadelphia, 1974

4. KEREIAKES JG, WELLMAN HN, SIMMONS G, et al: Radiopharmaceutical dosimetry in pediatrics. *Semin Nucl Med* 2: 316–327, 1972

5. MIRD: Dose estimate report no. 5, *J Nucl Med* 16: 859, 1975

6. KEREIAKES JG, FELLER PA, ASCOLI FA, et al: Pediatric radiopharmaceutical dosimetry. Unpublished data, 1976

7. HINE GJ, SORENSON JA: A guide to the absorbed dose from internally administered radionuclides. In *Instrumentation in Nuclear Medicine* 2: 588–589, Academic Press, New York, 1974