Oak Ridge on
Symposium of the Soc. of Med. and
on "Pediatric Nuclear Medicine"
at Johns Hopkins Med. School
Baltimore, 18-19 Feb. 1972. To be
published in the
Proceedings,
Sponsored by
the Soc.

THYROID SCANNING IN THE PEDIATRIC PATIENT: THE ADVANTAGES
OF THE FLUORESCENT TECHNIQUE*

Ronald W. Hendrix and Paul B. Hoffer¹

Department of Radiology, Section of Nuclear Medicine, The University
of Chicago, and the Argonne Cancer Research Hospital (operated by
the University of Chicago for the United States Atomic Energy
Commission), Chicago, Illinois

ACRH-1000-328
CONF-720212--1

Imaging of the thyroid gland is only occasionally required for evaluation of the child with suspected thyroid disease. Indications include palpable nodules, suspected anatomic variation or absence of the gland and, in special circumstances, diffuse goiter. Although radionuclide techniques for thyroid scanning are well established in adults, many of these techniques are not considered suitable for use in children. The main objection to their use is the relatively high radiation dose delivered to the thyroid gland. Kereiakes, et al. (1) have shown that the radiation dose received by the juvenile thyroid gland from a scanning dose of ^{125}I or ^{131}I is substantial; Duffy (2) and Hempleman (3) have shown that the juvenile thyroid gland is very sensitive to radiation. Radiation doses to the thyroid of 200 rads or more received by children under age 4 have been clearly associated with an increased incidence of thyroid carcinoma (2,3). Pertechnetate-99m, because of its relatively low radiation dose to the thyroid gland (4) is

*This investigation was supported in part by The Junior Auxiliary of The University of Chicago Cancer Research Foundation and Goldblatt Brothers Employees Nathan Goldblatt Cancer Research Fund.

¹Scholar in Radiological Research of the James Picker Foundation.

NOTICE

This report was prepared as an account of work sponsored by the United States Government. Neither the United States nor the United States Atomic Energy Commission, nor any of their employees, nor any of their contractors, subcontractors, or their employees, makes any warranty, express or implied, or assumes any legal liability or responsibility for the accuracy, completeness or usefulness of any information, apparatus, product or process disclosed, or represents that its use would not infringe privately owned rights.

DISCLAIMER

This report was prepared as an account of work sponsored by an agency of the United States Government. Neither the United States Government nor any agency Thereof, nor any of their employees, makes any warranty, express or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by trade name, trademark, manufacturer, or otherwise does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof.

DISCLAIMER

Portions of this document may be illegible in electronic image products. Images are produced from the best available original document.

currently the preferred radionuclide for thyroid scanning in juveniles. Even with pertechnetate-99m, however, the radiation dose to the thyroid (100 mr - 600 mr per millicurie) and other organs (stomach 100 mr - 600 mr per mCi) is not insignificant.

We prefer to use the fluorescent scanning system for imaging of the thyroid in children. The radiation dose received by the thyroid is low, 15 mrad to the gland per scan (5). This radiation dose is approximately equivalent to the monthly background radiation received by children in the United States. Furthermore, no radionuclide is administered and therefore the radiation dose to the remainder of the body is virtually nil. An additional advantage of the fluorescent thyroid scan is the quantitation of intra-thyroidal iodine.

The Fluorescent Method (5-8)

When radiation of sufficient energy (above the K absorption edge) interacts with an element, characteristic radiation is produced. The radiation is referred to as "characteristic" because its energy spectrum is unique for each element. The incident photon displaces an electron from the K-shell orbit of the atom with which it interacts. This void is immediately filled by an electron from one of the outer electron shells of the atom. The electron loses energy in this process, the "lost" energy being given off in the form of characteristic radiation. The process is referred to as "X-ray fluorescence."

If the binding energy of the K-shell is weak, as for example in low atomic number molecules such as sodium (atomic #11) or calcium (atomic #20), the characteristic radiation is locally absorbed and difficult to detect. In materials with higher atomic numbers such as iodine (atomic #53), however,

the energy of the characteristic radiation is substantial ($K_2 = 28.5$ KeV) and only a small fraction is locally absorbed.

The concept of "X-ray fluorescence" has been adapted for thyroid scanning. An excitation source such as a sealed isotope source of ^{241}Am is used to stimulate characteristic X-ray production in iodine within the thyroid gland. A special radiation detector made of lithium drifted silicon is used to detect the characteristic X-rays produced and select them from the Compton scatter radiation also produced by the exciting beam interacting with neck tissue.

The collimated source and detector are scanned over the patient's neck in a manner similar to a conventional rectilinear scan, the characteristic X-rays being used to produce the gland image on a photographic film exposed to a light source. A total scan time of approximately 20 minutes is required to produce a satisfactory thyroid image.

Results in Adults

The fluorescent method has been used for thyroid scanning at our institution for the past three years. During that time over 600 fluorescent thyroid scans have been produced. The image quality of these scans is usually as good as scans obtained with radionuclides, although they do have somewhat more background activity due to incomplete scatter rejection.

The fluorescent scan is not significantly affected by the blood level of circulating inorganic iodides as in the radionuclide scan. Fluorescent scans can therefore be obtained on patients who have recently received iodine or iodinated contrast agents. We have found that administration of exogenous thyroid hormone to euthyroid patients does not affect the iodine content of the thyroid gland. Patients who have received exogenous thyroid for ten

years or longer will often have a gland that appears normal on fluorescent scan.

Nodules

Most nodules that are "cold" on a radionuclide scan also have low or no iodine on a fluorescent scan. The differential diagnosis of such nodules includes adenoma (either nonfunctioning or degenerative), carcinoma, focal regions of thyroiditis, hemorrhage or abscess.

Most nodules that are "hot" on radionuclide scans also have an increased iodine content on fluorescent scans. When however, a toxic autonomous nodule that is suppressing normal thyroid tissue is present, the suppressed tissue can also be seen on fluorescent scan.

The fluorescent scanning technique is useful in estimating the total iodine content of the thyroid gland. The production of a fluorescent scan is dependent on the presence of iodine within the thyroid gland. If only a small amount of iodine is present, only a small number of characteristic X-rays will be produced. Conversely, if the iodine content of the gland is high, the number of characteristic X-rays produced is larger. We purposely maintain constant scan speed and light intensity factors for all fluorescent scans. In consequence, the density of the thyroid scan is proportional to the number of characteristic X-rays produced, and this number is in turn proportional to the iodine content of the gland. Unfortunately, variations in the depth of the gland introduce a source of error. However, in the absence of thyroid nodules, or gross thyroid enlargement, this error is probably not large (9).

Analysis of thyroidal iodine content in adults (as determined by the fluorescent method) shows a strong correlation between iodine content and

various disease states. In primary hypothyroidism, the iodine content is always low. In secondary hypothyroidism, the iodine content is usually normal. Thus the fluorescent scan can serve to differentiate between these two forms of hypothyroidism. About three-quarters of patients with Hashimoto's thyroiditis (with or without hypothyroidism) have remarkably low iodine content in the gland. Ninety-seven percent (97 %) of euthyroid patients without thyroiditis have normal iodine content. In hyperthyroid patients (Graves' disease) most (60 %) have a normal iodine content, although a significant percentage (40 %) may have increased iodine content. More quantitative methods of determining iodine content by the fluorescent method are currently being explored.

We have reviewed fluorescent thyroid scans from 50 pediatric patients aged 4 to 19 years (mean age, 15 years) done at our institution since 1969. These scans were analyzed for morphological changes as well as total iodine content (Fig. 1). The results are listed in Table 1.

Nodules:

Four patients had detectable thyroid nodules on fluorescent scan. In three cases, the nodule was devoid of iodine and appeared "cold" on the scan. In two of these patients the nodule was surgically removed and proved to be a degenerative adenoma. In the other case, pathologic confirmation is not available.

In one patient, the nodule contained less iodine than the remainder of the gland but was not totally devoid of iodine. This patient also had a radionuclide (^{125}I) thyroid scan prior to surgery which demonstrated a completely "cold" nodule. At surgery a 3 cm follicular colloid cyst was removed.

One patient, post-thyroidectomy and post-neck irradiation for a rhabdomyosarcoma of the larynx, demonstrated a small midline remnant of

iodine-containing thyroid tissue. This area had evidently escaped surgery and irradiation (Fig. 2).

In general, morphological features of the thyroid gland were well demonstrated in those thyroid glands with normal or increased iodine content. Since comparable radionuclide scans were obtained in only a few of these patients, direct comparison between the two scan methods is not possible.

Iodine Content

As previously explained, the iodine content of the gland is recorded by the density of the scan image, the density of the exposed photographic film image being therefore a rough quantitative estimate of the iodine content in the thyroid.

A Macbeth Quanta Log Transmission Densitometer with a three-millimeter aperture was employed for the quantitative density measurement of our scan images. Four separate readings were taken for each gland (right upper and lower poles and left upper and lower poles) and averaged. Nodular glands (4 cases) were excluded from these measurements. Background readings adjacent to each upper and lower lobe were measured, averaged and then subtracted from the average readings over the gland. Kodak RP/L film was used. Since the H & D curve for this film is almost linear for the densities measured, no density correction was made.

The scans were evaluated for iodine content, with the results listed in Table 1.

In adult patients a diffusely enlarged gland with increased iodine content is associated with Graves' disease. Seven of the pediatric patients demonstrated these findings. Four of these patients had Graves' disease

which was either untreated or incompletely medically treated at the time of the scan. Two siblings with diffusely enlarged glands and markedly increased iodine content were determined to have hereditary end organ hormone receptor defects. In both of these patients total gland iodine estimates based on isotopic methods confirmed the increased iodine content. One patient was euthyroid and had a goiter of undetermined etiology.

In adults, low or absent iodine content is characteristically seen with thyroiditis, primary hypothyroidism and post-therapy with ^{131}I and anti-thyroid medication. Five of our pediatric patients had diminished thyroidal iodine. Two had received propylthiouracil or methimazole as treatment for Graves' disease. The other three patients had histories of slow growth and poor mental development, and one of them was known to have been hypothyroid since age 1-1/2 years. These patients had RAIU values in the hypothyroid range even after TSH stimulation, and are assumed to have primary hypothyroidism (Fig. 3a).

One patient had normal iodine content but a small gland (Fig. 3b). She had had a hypophysectomy for a suprasellar dysgerminoma. The fact that she has secondary hypothyroidism is reflected by the relatively normal iodine content of her gland as compared to the absence of iodine in the thyroid of primary hypothyroid patients.

Of special interest was a group of seven patients, 8 to 18 years old, who had taken steroids for three months to four years. Four had regional enteritis, two had ulcerative colitis, and one a presumptive diagnosis of Wegner's granulomatosis. The steroid doses ranged from 15 mg to 60 mg of prednisone daily at the time of the scan. One patient who had taken 5-20 mg of prednisone daily for three years was taken off steroids two months prior

to the date of the scan. Another patient was receiving 40 U of ACTH every two days in addition to her prednisone at the time of the scan.

These patients were scanned because of retarded growth, questionable thyroiditis or increased LATS. Prior to the scan the patients had symptoms of their primary disease for 3 months to 4 years.

The iodine content in the thyroid glands of this group was significantly higher ($p < .01$) than for the normals in the study (Fig. 4). The two differences between this group and the normals ~~was~~^{were} their inflammatory disease and steroid therapy.

TT₄, FTI, TRC and RAIU were done on these patients. The findings are listed in Table 2. The tanned red cell values were normal in six of the patients and not obtained in the seventh. The TT₄ and FTI values were either elevated or at the upper limits of normal for each patient. There was apparently no definite correlation between fluctuations of the steroid dose and the TT₄ and FTI values, neither were the quantitative estimates of iodine content definitely related to the level of steroid dose, the length of time the patients had received steroids nor the duration of their primary disease.

Nicoloff, et al. (10) have reported that euthyroid patients given pharmacological doses of glucocorticoids demonstrate acute suppression in both thyroidal iodine release and serum TSH values. They found an escape from glucocorticoid suppression in 2 to 3 days with resumption of a near normal thyroidal iodine release rate. However, they did not study the long-term effects of such pharmacologic doses as were present in our patients. McCaffery, et al. (11) studied 22 patients with inflammatory bowel disease 20 of whom were on steroids for 0.7 to 9 years. They did not find elevated PBI, RAIU or T₃ values. However, it is not related when these thyroid tests were performed in relation to the steroid therapy.

The present findings in these seven patients are interesting but the etiology of the increased iodine content of the thyroid is inconclusive.

Conclusion

Since 1969 we have routinely used the fluorescent thyroid scanning technique for pediatric and adult patients. Our findings in the pediatric age group are similar to those found earlier in adults.

Numerous advantages favor the fluorescent technique over radionuclide scanning in pediatric patients. The patient receives no total body or gonadal radiation, and the thyroid receives approximately 15 millirads as compared with multirad doses for a radionuclide scan. Specific information about iodine content of the gland is available only via the fluorescent technique. This information makes it possible to distinguish primary from secondary hypothyroidism. The image quality of the fluorescent scan appeared to be about the same as the nuclide scan whenever both were available.

We have found increased iodine content in the glands of seven patients who had been on steroid therapy for 3 months to 4 years. Six of these patients had inflammatory bowel disease and one presumably had Wegner's granulomatosis. The mechanism for this increased iodine content is unknown.

References

1. Kereiakes, J. G., Seltzer, R. A., Blackburn, B., and Saenger, E.L. Radionuclide Doses to Infants and Children: A Plea for a Standard Child. Health Phys. 11: 999, 1965.
2. Duffy, B. J. and Fitzgerald, P. J. Cancer of the Thyroid in Children: A Report of 28 Cases. J. Clin. Endocrinol. 10: 1296, 1950.
3. Hempelmann, L. H. Risk of Thyroid Neoplasms after Irradiation in Childhood. Science 160: 159, 1968.
4. Andros, G., Harper, P. V., Lathrop, K. A., and McCardle, R. J. Pertchnetate-99m Localization in Man with Applications to Thyroid Scanning and the Study of Thyroid Physiology. J. Clin. Endocrinol. Metab. 25(8): 1067, 1965.
5. Gottschalk, A. and Foster, V. Fluorescent Thyroid Scanning (Scanning Without Radioisotopes) Initial Clinical Results. Radiology 99: 117-123, 1971.
6. Hoffer, P. B., Bernstein, J., and Gottschalk, A. Fluorescent Techniques in Thyroid Imaging. Seminars in Nucl. Med. 1(3): 379-389, 1971.
7. Hoffer, P. B., Bernstein, Joel, and Gottschalk, A. Clinical Results of Fluorescent Thyroid Scanning. Chapter 16. In Semiconductor Detectors in the Future of Nuclear Medicine. Edited by P. B. Hoffer, R. N. Beck, and A. Gottschalk. New York: Society of Nuclear Medicine, 1971.
8. Hoffer, P. B., Jones, W. B., Crawford, R. B., Beck, R. N., and Gottschalk, A. Fluorescent Thyroid Scanning: A New Method of Imaging the Thyroid. Radiology 90(2): 342-344, February 1968.
9. Rollo, F. D. ^{125}I For Measuring the Radioiodine Uptake of the Thyroid. J. Nucl. Med. 12: 8-13, 1971.

10. Nicoloff, J. T., Fisher, D. A., and Appleman, M. D. The Role of Glucocorticoids in the Regulation of Thyroid Function in Man. J. Clin. Invest. 49: 1922, 1970.

11. McCaffery, T. D., Nasr, K., Lawrence, A. M., and Kirsner, J. B. Severe Growth Retardation in Children with Inflammatory Bowel Disease. Pediatrics 45: 386, 1970.

TABLE 1

Scan Findings		No. of Patients	Pathologic Abnormality
Gland Size	Iodine Content		
1. Diffusely increased	Increased	4	Graves' disease untreated or incompletely treated
		2	Hereditary end organ defect
		1	Euthyroid goiter of undetermined etiology
2. Diffusely increased	Normal	2	Goiter
		3	Treated Graves' disease
3. Increased	Decreased	1	Early thyroiditis
4. Normal	Nodular	4	Nodular thyroid
5. Normal	Increased	6	Inflammatory bowel disease
		1	? Wegner's granulomatosis
		3	Undetermined etiology
6. Normal	Normal	15	Normal
		1	Saturated iodine pool with decreased RAIU
7. Normal	Normal	1	Secondary hypothyroidism
8. Normal	Decreased	2	Treated Graves' disease
9. --	Absent	3	Primary hypothyroidism
10. Remnant of tissue	Normal	1	Post irradiation and thyroidectomy
TOTAL		50	

TABLE 2

Patients Initials	Clinical Diagnosis	TT ₄	FTI	TRC	Steroid Dose at Scan Date
DM	RE*	12.0	18.3	Negative	32.5 mg prednisone OD ACTH ge 40 U q 48 hrs
NH	Wegner's?	9.7	8.8	Negative	7.5 mg prednisone OD
BL	RE	8.9	7.3	Negative	10 mg prednisone OD
TM	UC**	9.7	11.3	Negative	25 mg prednisone OD
SB	RE	9.4	11.5	Negative	10 mg prednisone OD
TF	RE	9.1	7.6	--	Off steroids X 2 months
PF	UC	9.1	10.1	Negative	20 mg prednisone OD

*Regional enteritis.

**Ulcerative colitis.

- Fig. 1. Normal fluorescent thyroid scan on a 14-year-old male. Normal morphology and normal iodine content are demonstrated. The arrow marks the patient's thyroid cartilage.
- Fig. 2. Post surgical and irradiation changes. Only a small midline remnant of thyroid tissue remains after a thyroidectomy and irradiation for a rhabdomyosarcoma of the larynx. The thyroid remnant demonstrates normal iodine content. The superior margin of the functioning thyroid tissue is at the level of the thyroid cartilage. The sternal notch is marked by the arrow.
- Fig. 3. Primary and secondary hypothyroidism. The two scans above are examples of (a) primary and (b) secondary hypothyroidism. Note the total absence of iodine in (a) primary hypothyroidism as compared to (b) secondary hypothyroidism. The iodine content in (b) is relatively normal. The scans of all three patients with primary hypothyroidism were identical to (a). The fluorescent technique is a very convenient means of distinguishing primary from secondary disease. The straight line on each scan marks the thyroid cartilage and the V marks the sternal notch.
- Fig. 4. The effect of inflammatory bowel disease and/or steroids on the fluorescent thyroid scan. Notice the increased density of the scan image as compared to Fig. 1. The gland morphology is normal. The scan is of a 15-year-old female with symptomatic regional enteritis for one year who has received steroid therapy for 3 months. The arrow marks the thyroid cartilage.