Editorial: Comparison of Technetium-99m and Iodine-123 Nodules: Correlation with Pathologic Findings

It is refreshing to read a good article on "Comparison of Technetium-99m and Iodine-123 Imaging of Thyroid Nodules: Correlation with Pathologic Findings" (Kusic et al. in this issue) because of a growing trend in community hospitals to use contrast-enhanced CAT scans to picture the abnormal thyroid anatomy, and a fine-needle aspiration to define the pathology.

Indeed the new "scourge" of radionuclide scintigraphy of the thyroid today is a contrast-enhanced CAT scan within 6 wk of the requested thyroid scintigraphy.

Ultrasound will detect thyroid nodules 3–4 mm in size, does not require contrast enhancement, and is most helpful in pregnant patients who ideally should not receive radionuclide or contrast material intravenously. Ultrasound may also tell the surgeon treating medullary thyroid cancer whether or not cervical lymph nodes are enlarged.

As usual, radionuclide scintigraphy is based upon function rather than anatomy alone. The most common thyroid nodule evaluation problems are:

1. Solitary cold nodule.
2. Colloid nodular goiter, (endemic goiter), with hot and cold nodules, and its associated Plummer's disease and tracheal deviation and compression and thyroid cancer (*1–2*).
3. Hashimoto's struma.

In solving these problems in the Nuclear Medicine Department at St. John Hospital, we have learned that we cannot decide the diagnosis and therapy without radionuclide scintigraphy, serum antithyroid antibodies, and the immuno-radiometric TSH, to decide whether a fine-needle aspiration result is representative as a cause of the goiter if the fine-needle aspiration does not show a neoplasm.

Also, in Detroit, 85% of our thyroid nodules arise in colloid nodular goiter (*1–2*). Furthermore, throughout the United States the most common thyroid disease is colloid nodular goiter (*1–2*). The second most common thyroid disease is Hashimoto's struma.

Endemic goiter was "The adaptation of man to iodine deficiency" (*3*). The incidence of this goiter in Michigan decreased from 38.6% in school children in 1924 to 9.4% in 1928 with the introduction of iodine into the culture (*4–5*). By 1965, it existed in 10%–16% of women 20–40 yr of age in the Michigan town of Tecumseh (*6*). It was found in 33% of school children in a county in Kentucky in 1964 (*7*) and in 29% of the school children in a county in Virginia in 1967 (*8*), with proof of a more than adequate iodine intake, in each instance.

The introduction of more than adequate iodine intake also introduced Hashimoto's struma as a man-made environmental contribution to endemic goiter that does not exist in the presence of iodine deficiency (*9–11*). The major new second stress on the thyroid gland that has caused a return of colloid nodular goiter as the usual type of endemic goiter is more environmental chemical pollutants, both naturally occurring and man-made. These pollutants have been proved by Gaitan (*12–13*) in human thyroid peroxidase and in thyroid slices to be up to 23 times more active in inhibiting thyroid peroxidase than 6-propylthiouracil on a gram per liter basis.

During the period of 1972–1978, the NCI reported a doubling of the prevalence of human thyroid cancer (*14*) while the incidence of goiters in fish in the Great Lakes increased twofold to sixfold without change in iodine concentration in the Great Lakes water (*15*).

The fact that not everyone exposed to iodine deficiency or to goitrogenic chemicals in the environment develops a goiter tells us that a considerable portion of the population has an inherited or acquired biochemical defect that predisposes to these environmental stresses on the thyroid gland.

In a series of original experiments, Stanbury and coworkers described a number of inherited biochemical defects in the thyroid gland that predisposed a significant percent of the population to endemic goiter from iodine deficiency (*16*). Later, it was found that irradiation to the head, neck, and upper chest in childhood also leads to roughly a 23% incidence of colloid nodular goiter and ~7% of these patients operated upon had developed multicentric well-differentiated thyroid cancer, usually papillary, but often follicular or a mixture of the two (*17*).

In 1953, Selwyn Taylor (*18*) described in humans the evolution of a colloid nodular goiter. He performed thyroidectomies in 60 patients with simple and nodular goiters 48 hr after a tracer dose of ^{131}I was administered. He performed autoradiography on slices 2–5 mm thick to correlate function with morphology. He described five stages in evolution:

1. Diffuse hypertrophy and hyperplasia resulting in a U-shaped enlargement of the thyroid (whereas

Received Dec. 18, 1989; revision accepted Dec. 18, 1989.
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the isthmus of the thyroid is not visualized normally or only faintly visualized).

2. If not treated, one or more localized areas become more active in concentrating radioiodine than other areas and therefore become a radioactively "hot" nodule.
3. If not treated, one or more over-active hot nodules develop necrosis and hemorrhage and become a radioactively "cold" area. One or more of the "hot" nodules then become autonomous in function and are not suppressed by the administration of thyroid hormone and later may cause hyperthyroidism (Plummer's disease).
4. These steps 2 and 3 are repeated, leading to many hot and cold nodules.
5. These steps lead to large goiters commonly causing tracheal deviation and compression and a progressively increasing prevalence of thyroid cancer and substernal extension.

The generation of this genetic evolution leading to the production of thyroid cancer was originally described in great detail by Beierwaltes and Al Saadi (*19*) in the Fischer rat exposed to iodine-deficient diets and then transplants of the abnormal thyroid tissue to other iodine-deficient rats. Upon exposure of the Fischer rat to iodine deficiency, hyperplasia first occurred from TSH stimulation. Euploidy was replaced by aneuploidy, predominantly hyperploidy. The dropping out of the #15 chromosome was coincident with the escape from TSH dependency. When, additionally, 3–5 large marker chromosomes appeared in a high percent of thyroid cells, classical anaplastic thyroid cancer with very rapid growth was observed, resulting in death of the rat in as short a period of time as 13 days after transplant, with metastases to every organ in the body.

With the use of iodized salt, the increasing iodine uptake has resulted in the first appearance of Hashimoto's struma and then the increase in prevalence to around 14% of goiters (*11*).

Although most Hashimoto's struma goiters present on scan with little or no visualization of the isthmus in goiters up to 50 g in weight (the upper limit of normal thyroid weight is 20 g in persons 20 yr of age or over), some of these Hashimoto's struma goiters developed absolutely classical scan findings of Stage V colloid nodular goiters, that are U-shaped, contain many hot and cold nodules, and may cause tracheal deviation and compression. If such a goiter is associated with an elevated TSH and high anti-thyroid antibody titers, it usually regresses dramatically within two months after the administration of sodium-l-thyroxine in dosage of 0.125 mg/day, dropping the TSH to below the normal range without elevating the serum T4 and T3. Indeed, I no longer bother to get a fine-needle aspiration in such patients until I see the patient 2 mo after being started on adequate doses of thyroid hormone. If the goiter is no longer palpable, the patient has avoided a fine-needle aspiration. This beautiful response is rarely, if ever, seen with fully developed, Stage III to V colloid nodular goiter.

If a patient presents, however, with a solitary cold nodule in one lobe of the thyroid gland without enlargement of the rest of that lobe, or the opposite lobe, the occurrence of cancer in such a nodule has been found to be 35%–45%, especially in young individuals.

If the fine-needle reveals a "follicular neoplasm," then the entire nodule must be removed surgically to decide whether this neoplasm is a benign follicular adenoma or a follicular carcinoma. If every millimeter of the capsule is inspected and there is no invasion of the capsule, and there is no invasion of the blood vessels, then the neoplasm can be called a "benign" follicular adenoma.

In the article by Kusic et al., we find that the thyroid nodule imaging problem found today in Yugoslavia is no different than it is in the United States. Iodine deficiency no longer exists, yet colloid nodular goiter is common, Hashimoto's struma has appeared with iodine deficiency relief, and follicular adenomas exist which may be hot or cold to scanning in an otherwise "normal" thyroid gland. Thus this survey is relevant to all of us in the United States.

A major problem we face is that the pathologist commonly describes only the follicular neoplasm or the nodule of interest and does not record that the patient also has a colloid nodular goiter background. Ridgeway has stated that in autopsy studies, fully 50% of the general population will be found to have either single or multiple nodules in their thyroid glands.

Thus in the present study, discrepancies were found between ^{99m}Tc and ^{123}I images in 5%–8% of cases, but twice as often in "multinodular" goiters as in "single" nodules.

It would be of interest to know what the estimated (or true excised) weights of the thyroids were in these two categories of nodules. It is probable that multinodular goiters are just Stage III to V, while single nodules (with the exception of a follicular adenoma) are Stage I or II colloid nodular goiters. Evidence that this is true is that 12 carcinomas were found (4%) but "none in nodules showing a discrepancy." It is also of interest that the majority of the five readers in this study preferred ^{123}I, and in 42% to 72% of cases there was a difference in quality in the scintigram between the two radionuclides.

The principal advantages of ^{99m}Tc are that it is always available in the average nuclear medicine division or department in the United States, it is less expensive than ^{123}I, and it delivers a smaller radiation dose and a higher count rate. Its disadvantages are that it does not have the specificity of functional imaging of ^{123}I because

^{99m}Tc is concentrated but not organically bound and stored like ^{123}I.

Most of us are not willing to sacrifice "... the slightly better overall quality of ^{123}I scans ..." I have seen scans in thyroid cancer patients where the decision to treat or not treat with radioactive iodine was based on a "slightly better overall quality ..." of one scan as compared to another.

On the other hand, the routine use of ^{123}I only leads to undue rigidity in scheduling so that patients may have scans "only on Tuesdays and Thursdays" because those are "the only days that we receive ^{123}I." Under heavy thyroid scanning case loads, it might be better to accommodate the additional patients using ^{99m}Tc, especially in small goiters, (Stage I to III), and repeating them as necessary with ^{123}I when it is deemed of clinical importance.

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