

## Imaging the Thyroid Nodule

Five percent of the population have palpable thyroid nodules, and an additional 30% to 40% have nonpalpable nodules that can be found by imaging studies. However, thyroid cancer is found in only 8% of palpable thyroid nodules. Thus, the appropriate interpretation of incidentally discovered thyroid nodules found on imaging studies obtained for other indications is important.

### Thyroid Sonography

Sonographic examination of thyroid nodules is commonly performed for evaluation of thyroid glands that seem abnormal on palpation. Thyroid sonography is also indicated for case detection of malignancy in certain high-risk scenarios such as in patients with a history of head and neck irradiation or in some patients with a history of hereditary thyroid cancer. Ultrasonography can

- detect nodules with diameter larger than 3 mm
- demonstrate features of the nodule—cystic areas, character of the margin of the nodule (eg, a halo around the nodule), internal consistency, echo pattern, and calcifications
- provide accurate measurement of the size of the thyroid lobes
- display multiple nodules when only 1 nodule is noted clinically

Compared to a thyroid isotope scan, thyroid sonography is noninvasive, involves less time, allows serial examinations, and is usually less expensive. Up to 40% of thyroid nodules are found to be partially cystic.

Findings on ultrasonography that are consistent with a benign nodule (Figure 1) include

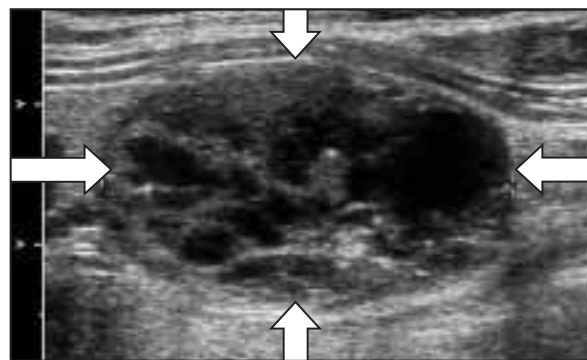
- a smooth, well-defined margin
- homogeneous internal consistency
- hyperechoic echo pattern
- complete halo
- coarse, large, scattered or peripheral (eggshell) calcifications
- low color Doppler flow

Diana S. Dean, MD, of the Division of Endocrinology, Diabetes, Metabolism, and Nutrition at Mayo Clinic in Rochester, explains: "A malignant



*Diana S. Dean, MD, and Vahab Fatourechi, MD*

lesion should be suspected if the margin is irregular and ill-defined or if heterogeneous internal consistency, a hypoechoic echo pattern, an incomplete halo, microcalcifications, high color Doppler flow, and pathologic cervical lymph nodes are present (Figure 2). However, none of these characteristics has a high specificity or sensitivity (about 80%-85% for both). Therefore, thyroid fine-needle aspiration (FNA) biopsy is recommended to confirm whether the thyroid nodule is benign or malignant. Ultrasound is also very useful for guiding FNA biopsy of palpable and nonpalpable thyroid nodules and is becoming the standard of care. Any nodule larger than 1 cm in diameter is usually evaluat-



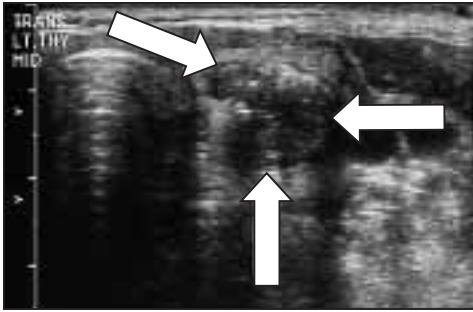
**Figure 1. Benign, partially cystic thyroid nodule (arrows). Note regular borders, spongiform appearance, and isoechoic echo texture of the solid components.**

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**Figure 2.** This thyroid ultrasound image is typical for papillary cancer (arrows). Note the microcalcification, hypoechoic echo texture, and irregular borders.

ed with an ultrasound-guided FNA biopsy, with the exception of those that are totally cystic. For nodules smaller than 1 cm in diameter, FNA biopsy is recommended if the patient has a history of head or neck irradiation, hereditary thyroid cancer, or sonographically suspicious features. In patients with multinodular goiter, sonographic features are used for selection of nodules needing FNA biopsy—up to 3 nodules may be biopsied if indicat-

ed. Ultrasound can also help differentiate Graves' disease versus Plummer's disease (toxic multinodular goiter)."

### Isotope Scan

Vahab Fatourechi, MD, of the Division of Endocrinology, Diabetes, Metabolism, and Nutrition at Mayo Clinic in Rochester, says: "The thyroid isotope scan received much attention in the past as an aid in the differential diagnosis of thyroid lesions. Before the advent of FNA biopsy, 'cold nodules' on thyroid isotope scan were selected for surgery. However, the specificity of this approach for thyroid cancer was low because the majority of cold nodules were benign. The 2 isotopes most commonly used are iodine 123 ( $^{123}\text{I}$ ) and technetium 99 ( $^{99\text{m}}\text{Tc}$ ) pertechnetate, the latter being preferable because of lower cost and greater availability. However, isotope imaging is no longer needed for the majority of thyroid nodules. For evaluation of a thyroid nodule, the serum thyrotropin (TSH) concentration should be measured—if serum TSH is suppressed, FNA biopsy may not be needed, and a hyperfunctioning nodule may be confirmed by isotope scanning. The likelihood of thyroid malignancy is extremely low if the scan demonstrates a hyperfunctioning nodule."

### Positron Emission Tomography Scan

$^{18}\text{F}$ Fluorodeoxyglucose (FDG) positron emission tomography (PET) delineates areas of increased metabolic activity by producing a map of FDG uptake. FDG-PET imaging has emerged as an accepted modality for detection, staging, and surveillance of a wide array of malignant tumors. Dr Fatourechi notes: "Although FDG-PET is not indicated for evaluation of thyroid nodules, incidentally discovered FDG-PET-positive thyroid nodules may be found on scans performed for detection and staging of other malignant lesions (Figure 3). Approximately 3% of FDG-PET scans have incidentally detected abnormalities in the thyroid

gland, and about 30% of these prove to be malignant. However, various benign conditions, including autoimmune thyroid disease, inflammatory and granulomatous processes, benign follicular neoplasms, and Hürthle cell adenomas, may be FDG-PET positive. Unilateral FDG-PET positivity warrants pursuit of a cytologic diagnosis. FNA biopsy is not needed in the presence of known autoimmune thyroid disease with bilateral FDG-PET positivity. Thyroid FNA biopsy should be considered in other situations on the basis of clinical presentation, sonographic characteristics, and risk factors."

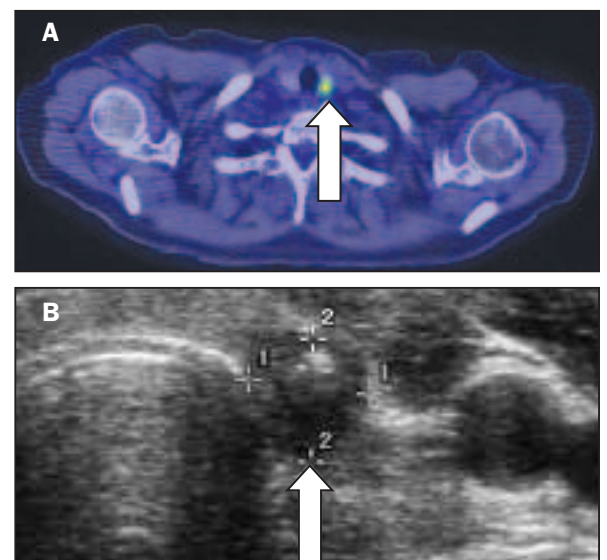
### Other Imaging Modalities

Although magnetic resonance imaging (MRI) and computed tomography (CT) obtained for other indications may incidentally detect thyroid nodules, we do not advocate MRI or CT for the evaluation of thyroid nodules, with a few exceptions:

- CT may be helpful in some cases of large nodular goiter before surgery and in cases of invasive malignant nodules for evaluation of tracheal invasion.
- MRI and magnetic resonance angiography may be helpful in assessing vascular involvement in large malignant lesions.

### Conclusion

Dr Dean concludes: "Thyroid ultrasonography has become an extension of the physical examination in the endocrinologist's office and should be the initial and primary imaging modality for thyroid nodules."



**Figure 3.** A, FDG-PET CT fusion scan performed in the evaluation of another malignancy showed a hypermetabolic area in the left lobe of thyroid (arrow). No nodules were palpable on physical examination. B, Thyroid ultrasound showed a thyroid nodule (arrow) with microcalcifications. Pathology revealed papillary thyroid cancer.

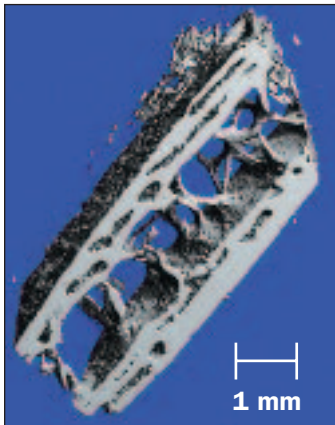
## Bone Histomorphometry in the Diagnosis and Management of Metabolic Bone Disease

The Mayo Clinic Bone Histomorphometry Laboratory is a full-service facility that offers bone histomorphometry and micro-computed tomography (micro-CT) analysis for clinical and research purposes. With its unique database of sex-specific reference ranges for iliac crest biopsies, the laboratory has recently undergone comprehensive validation and has become a core laboratory within Mayo Clinic. Scientists and clinicians who specialize in metabolic bone disease prepare and analyze the bone biopsy specimens in a collaborative effort.

Michael J. Yaszemski, MD, PhD, Department of Orthopedic Surgery at Mayo Clinic in Rochester, says: "Bone histomorphometry may be used in the evaluation of metabolic bone disease—it provides qualitative information and quantitative histomorphometric measures of static and dynamic bone properties, including rates of bone formation and resorption. Bone biopsy with these analyses may be considered when osteomalacia is suspected or in several metabolic bone disorders such as those associated with chronic kidney disease (CKD), refractory osteoporosis, or unusual forms of osteoporosis." Theresa E. Hefferan, PhD, of the Division of Orthopedic Research, Department of

Orthopedic Surgery at Mayo Clinic in Rochester, says: "Micro-CT analysis (Figure 1) of bone biopsy specimens provides further insight into bone microarchitecture, an important determinant of bone strength that cannot be assessed with most conventional measures of bone mass. This is primarily a research tool at this point but may have clinical application in the future."

Chronic kidney disease results in complex metabolic bone disease. The National Kidney Foundation estimates that 20 million people are at risk for CKD and that the number of patients with end-stage renal disease will double by 2010. Robert A. Wermers, MD, of the Division of Endocrinology, Diabetes, Metabolism, and Nutrition at Mayo Clinic in Rochester, explains: "Bone histomorphometry is helpful in distinguishing high-turnover bone disease (osteitis fibrosa) from low bone turnover (adynamic bone disease). Adynamic bone disease has become increasingly more prevalent—estimated to be present in 30% to 40% of bone biopsies from dialysis patients. Furthermore, the value of standard bone miner-



**Figure 1.** Image of a micro-CT-scanned transiliac crest bone biopsy showing cortical and cancellous bone.



*The bone histomorphometry team. From left to right, standing: Julie A. Burgess, Glenda L. Evans, James L. Herrick, and Donna E. Jewison. Seated: Robert A. Wermers, MD, and Theresa E. Hefferan, PhD. Not pictured: Michael J. Yaszemski, MD, PhD.*

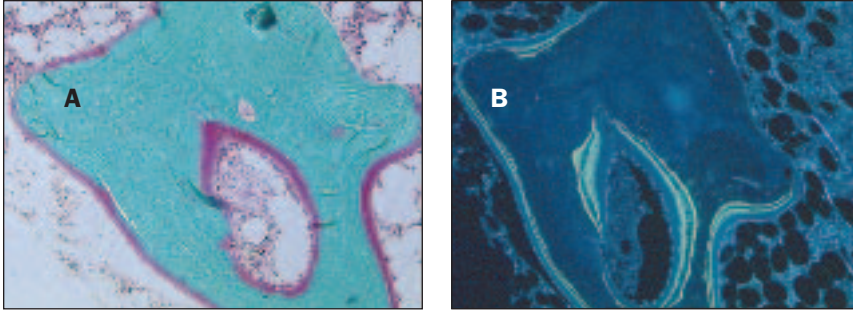
al density (BMD) measurement to assess bone disease in patients with CKD is not well established, and the correlation of BMD results to fracture risk in patients with CKD is inconsistent."

Osteomalacia is a disorder of the newly formed collagen matrix of bone that results in excessive accumulation of unmineralized bone (osteoid). Dr Wermers notes: "Although BMD is reduced in patients with osteomalacia, it is a nonspecific finding. Furthermore, there are no specific laboratory tests for osteomalacia. Clinically, osteomalacia results in structurally weakened bone and can lead to fracture, bone deformity, muscle weakness, hypocalcemia, and bone pain. There are multiple causes of osteomalacia (eg, vitamin D deficiency, phosphate depletion, and toxic inhibition of mineralization). The diagnosis of osteomalacia is clinically important—proper treatment is based on the etiology and avoids the use of medications, such as bisphosphonates, that are contraindicated in this setting."

Bone biopsy histomorphometry can also be helpful in directing the appropriate therapy in patients with osteoporosis. For example,

- when osteoporosis is refractory to standard treatments
- when there appears to be an unusual form of osteoporosis (such as that seen in young individuals)
- when assessing response to therapy (see Figure 2)

Dr Hefferan explains: "Bone samples are typically obtained from the anterior iliac crest. We recommend both quantitative and qualitative analysis of the specimen. Quantitative analysis can measure bone volumes, osteoid volumes, osteoclast and osteoblast numbers, eroded surface area, and with



**Figure 2.** Iliac crest bone biopsy images from a patient who was receiving anabolic therapy for osteoporosis. **A,** The bone biopsy specimen prepared with Goldner trichrome stain shows normal mineralized bone (green) with abundant osteoid (pink)—findings consistent with increased bone formation. The inner portion of the osteoid is covered by cuboidal and robust young osteoblasts. **B,** Double tetracycline-labeled bone biopsy specimen shows well-resolved double labels indicating normal bone mineralization during the labeling interval. In addition, there is a notable amount of unmineralized osteoid consistent with an increased amount of remodeling space.

the administration of tetracycline derivatives, which are incorporated into mineralizing bone, dynamic rates of bone formation (Figure 2). Demeclocycline hydrochloride, 150 mg, should be administered orally 4 times daily for 3 days (days 1 to 3) and then repeated on days 18 to 20.

## Graves' Disease in Children

Graves' disease accounts for 10% to 15% of all childhood thyroid disorders. Girls are 4 to 5 times more likely to be affected than boys. Aida N. Lteif, MD, of the Division of Pediatric Endocrinology and Metabolism, Department of Pediatric and Adolescent Medicine at Mayo Clinic in Rochester, says: "Typically the signs and symptoms of hyperthyroidism develop gradually. The symptoms may be subtle over several months before hyperthyroidism is diagnosed. Anxiety, hyperactivity, and declining school performance may be attributed to other causes, especially in adolescents. The main clinical manifestations, however, are comparable to those present in adults. Nocturia is also frequently reported in children. Fetal hyperthyroidism can result in intrauterine growth retardation, fetal tachycardia, and premature birth. Newborns with hyperthyroidism have poor weight gain, vomiting, diarrhea, and tachypnea, which may lead to heart failure. Craniosynostosis and mental retardation have been reported."

On physical examination, thyromegaly is present in more than 95% of children with Graves' disease. Ophthalmic findings are more common but less severe in children than in adults with Graves'

Alternatively, tetracycline, 250 mg, can be given 4 times daily for 3 days for both or one of the labeling cycles to give a different autofluorescence. The bone biopsy should be performed anytime from day 23 to day 27."

Qualitative assessment involves evaluating several features of bone histology, including the following:

- What is the quality of the bone biopsy specimen?
- Is the bone lamellar in nature or woven?
- Is there evidence of osteomalacia?
- Is there evidence of a marrow dyscrasia?
- Is marrow fibrosis present?
- Is a double or a single label noted in cortical and/or trabecular bone?

The Mayo Clinic Mayo Medical Laboratories Web site (<http://www.mayoreferenceservices.org/it-mmfiles/BoneHistoFactSheet1006.pdf>) has specific information about bone histomorphometry. The Bone Histomorphometry Fact Sheet outlines the procedures for patient preparation for a bone biopsy, processes for handling the biopsy specimen, and where to send the biopsy specimen.

disease—the findings include proptosis, lid lag, lid retraction, stare, chemosis, conjunctival injection, periorbital edema, excess lacrimation, pain, and diplopia. Pretibial myxedema is much more common in adults than in children. Bone age may be advanced, although final height does not appear to be affected. Costochondral calcifications may be present.

### Laboratory Findings

In Graves' disease, circulating levels of thyroid hormones—thyroxine ( $T_4$ ) and triiodothyronine ( $T_3$ )—are increased while thyroid-stimulating hormone (TSH) is suppressed.  $T_3$  thyrotoxicosis—where primarily serum  $T_3$  is increased—may be seen early in the course of the disease. Thyroid hormone receptor antibodies are usually increased at the time of diagnosis and can be measured by 2 types of assays:

- Receptor assays assess the capacity of Graves' immunoglobulins to inhibit labeled TSH from binding to thyroid membranes. Assay sensitivity is about 94% in children with untreated active Graves' disease.
- Bioassays assess the ability of immunoglobulin



Peter J. Tebben, MD, Aida N. Lteif, MD, and Geoffrey B. Thompson, MD

concentrates to stimulate the production of cyclic AMP from thyroid cells. Assay sensitivity is 73% to 91% in children with untreated active Graves' disease.

Peter J. Tebben, MD, of the Division of Endocrinology, Diabetes, Metabolism, and Nutrition and Division of Pediatric Endocrinology and Metabolism at Mayo Clinic in Rochester, notes: "Untreated children with negative thyroid receptor antibodies usually have mild hyperthyroidism. The majority of patients in remission have negative findings with both thyroid receptor assays. Levels of thyroid-stimulating antibodies are typically higher in young patients with ophthalmopathy than in those without ophthalmopathy. Antibodies to thyroperoxidase are present in the majority of pediatric patients with Graves' disease."

### Treatment

Treatment options for children with Graves' disease include antithyroid medications, thyroidectomy, or radioactive iodine ( $^{131}\text{I}$ ). Children with moderate to severe symptoms often have symptomatic improvement if a  $\beta$ -adrenergic blocking agent, such as propranolol, is administered before initiation of specific therapy to reduce thyroid hormone concentrations. As with adults, no single therapy is appropriate for all patients. Although these options are the same as those available to adults with Graves' disease,  $^{131}\text{I}$  is used considerably less often in children.

Antithyroid medications methimazole and propylthiouracil have been used extensively in children and are effective in the management of hyperthyroidism due to Graves' disease. Dr Lteif explains: "These drugs block the production of thyroid hormone, and propylthiouracil also inhibits the conversion of  $T_4$  to  $T_3$ . Although these medications are generally well tolerated, rash or gastrointestinal tract disturbance occasionally requires their discontinuation. Agranulocytosis and severe hepatic toxicity are rare yet serious adverse effects that need to be discussed with the child and the parents. Long-term remission after treatment with antithyroid

medications occurs in fewer than 25% of children—the remission rate is even lower when TSH receptor antibody levels are exceedingly high."

### Radioactive Iodine

The use of  $^{131}\text{I}$  to treat Graves' disease in children was first reported about 50 years ago. Dr Tebben comments: "Despite many subsequent reports, the use of  $^{131}\text{I}$  in children remains quite controversial. As with adults, a smaller dose of  $^{131}\text{I}$  and a larger thyroid gland are predictive of recurrent or persistent hyperthyroidism after  $^{131}\text{I}$  therapy. The short- and long-term safety data regarding  $^{131}\text{I}$  use in children are reassuring and do not suggest a subsequent increased risk of thyroid malignancy or issues with fertility when compared with outcomes in children treated surgically or with medications. Also, progression of ophthalmopathy does not appear to be more frequent in children treated with  $^{131}\text{I}$ . However, the available data are limited, and long-term follow-up is documented in relatively few children."

### Surgery

Thyroidectomy is seldom chosen as definitive therapy for treatment of Graves' disease in adults. Geoffrey B. Thompson, MD, of the Department of Surgery at Mayo Clinic in Rochester, says: "In our practice, children undergoing definitive therapy for Graves' disease are treated with total or near-total thyroidectomy. Children are prepared preoperatively with antithyroid medications,  $\beta$ -adrenergic blockers, or both. Lugol's solution (saturated solution of potassium iodide) is added to the regimen approximately 10 days before surgery to reduce gland vascularity. Transient or permanent hypoparathyroidism and recurrent laryngeal nerve injury can result after thyroidectomy. Perioperative morbidity and mortality are low when the procedure is performed by an experienced surgeon. Our experience in 78 children treated with thyroidectomy between 1986 and 2003 resulted in no deaths, no permanent hypoparathyroidism, and no recurrent laryngeal nerve injury. Only 2 patients had recurrent hyperthyroidism—both having received bilateral subtotal thyroidectomies early on in the experience."

### Summary

Graves' disease remains the most common cause of hyperthyroidism in children. No one treatment available is appropriate for every patient. A thorough discussion with the child and parents regarding the advantages and disadvantages of each treatment modality is essential to provide appropriate individualized treatment.

## Laboratory Testing in Thyroid Cancer for Diagnosis and Follow-up—the Old and the New

In 2008, at least 32,000 new thyroid cancer cases will be diagnosed in the United States. Most of these patients will require long-term follow-up surveillance for tumor recurrence. Recent developments are changing some long-established patterns of thyroid cancer–related laboratory testing.

### Current Laboratory Testing in Thyroid Malignancies

Thyroglobulin (Tg) is the key tumor marker to detect recurrence of follicular cell–derived tumors, while calcitonin and carcinoembryonic antigen are used for the much rarer C-cell–derived medullary thyroid carcinoma (MTC). Stefan K. Grebe, MD, Division of Clinical Biochemistry and Immunology, Department of Laboratory Medicine and Pathology at Mayo Clinic in Rochester, says: “Tg measurements should always be interpreted in the context of simultaneous measurement of Tg autoantibodies (TgAB). TgAB occur in about 20% of thyroid cancer patients and can lead to falsely low Tg measurements.” Bryan McIver, MBChB, PhD, of the Division of Endocrinology, Diabetes, Metabolism, and Nutrition at Mayo Clinic in Rochester, adds: “Although the presence of TgAB after thyroid surgery has been interpreted as an indicator of persistent thyroid cancer, there is uncertainty about the time course of TgAB decay in cured patients; the wide variability in detection sensitivity between different TgAB assays; and the cut-offs for normality in this setting. Thus, persistence of TgAB is a qualitative indicator of possible persistence of thyroid-derived tissue and should be interpreted with extreme caution.”

### New Developments in Tg Testing

Serum concentrations of Tg are highly specific for the presence of thyroid tissue in the body, but they are not specific for malignancy. The value of Tg measurement in thyroid cancer follow-up is therefore compromised in patients with more than a minimal amount of postsurgical thyroid tissue (remnant). Dr Grebe explains: “Each gram of thyroid remnant contributes approximately 1 ng/mL to serum Tg in patients with a detectable thyrotropin (TSH) level and 0.5 ng/mL in those with a suppressed serum TSH concentration. Consequently, many physicians recommend postsurgical radioiodine (RAI) remnant ablation to make Tg a better assessment tool to follow patients with thyroid cancer.” Dr McIver adds: “However, low-risk patients following near-total thyroidecto-



*Stefan K. Grebe, MD, Christine L. H. Snozek, PhD, and Bryan McIver, MBChB, PhD*

my can have low levels of Tg—consistent with a small normal thyroid remnant—and might not require RAI ablation.”

The success of RAI ablation has been traditionally assessed by diagnostic RAI scanning sometime after ablation, or by postablation stimulated Tg measurements—either after thyroid hormone withdrawal or, more commonly in recent years, after recombinant human TSH (rhTSH) administration. However, these unpleasant (thyroid hormone withdrawal) or costly (rhTSH) procedures may no longer be necessary. The newest-generation Tg assays—which have been available for the past 6 years and are used routinely at Mayo Clinic—have 4- to 10-fold better detection sensitivity than the older assays, obviating the need for stimulated Tg measurements in many cases. Our recent data suggest that a 4- to 8-week postablation unstimulated serum Tg concentration less than 0.1 ng/mL indicates complete remnant ablation. Similarly, we have recently demonstrated that unstimulated serum Tg levels less than 0.1 ng/mL during follow-up exclude thyroid cancer recurrence, except in patients with TgAB and in very rare individuals with highly dedifferentiated tumors.

One immediate practical benefit from this observation is that most patients with serum Tg level less than 0.1 ng/mL might not require fine needle aspiration (FNA) biopsy of enlarged neck nodes, unless these are deemed highly suspicious by experienced ultrasonographers. However, those patients with detectable serum Tg or TgAB should undergo FNA biopsy of most enlarged or questionable neck nodes. The FNA biopsy specimen is then examined by an experienced cytopathologist. While FNA biopsy is considered the diagnostic gold standard, it is not infallible, with the most common problem being nondiagnostic biopsies because of paucicellu-

lar or acellular aspirates. Christine L. H. Snozek, PhD, Division of Clinical Biochemistry and Immunology, Department of Laboratory Medicine and Pathology at Mayo Clinic in Rochester, says: “Tg measurement on needle washes can resolve many of these problem cases. Normal lymph nodes do not contain Tg, and therefore any detectable Tg in a node is highly suspicious for metastatic thyroid cancer. We have recently reviewed our experience with Tg measurements in 122 cases of lymph node FNA biopsies. We were able to provide a diagnosis in all 119 cases that also had cytology performed;

cytopathology was nondiagnostic in 16 of these cases. The FNA biopsy Tg measurement with a cut-off of 1 ng/mL had a sensitivity of 100% and specificity of 96.2% (2 false positives). In the 103 cases with both diagnostic cytology and FNA biopsy Tg measurements, the results of both methods agreed in all but 5 cases; in 4 of these 5 cases, the final clinical and histopathologic diagnosis agreed with the FNA biopsy Tg measurement, rather than with the cytopathologic assessment.”

#### Calcitonin Testing and Procalcitonin as an Alternative

Unlike Tg, which is used primarily for follow-up of patients with follicular cell–derived thyroid carcinomas, calcitonin plays a role in both initial diagnosis and follow-up of MTC. Its role in the initial diagnosis is based on the fact that baseline secretion of calcitonin by normal C cells is very low. However, a number of conditions other than MTC can lead to calcitonin elevations (Table). Thus, modest elevations (2- to 4-fold

elevations above the upper limit of normal) in serum calcitonin concentrations often do not indicate the presence of a C-cell tumor. Other limitations of calcitonin assays include

- Variability between different assays—mandat-

ing that serial measurements on the same patient should, if possible, always be obtained with the same assay.

- Instability of the analyte—about 20% of a given amount of calcitonin will decay into fragments every 2 hours at room temperature or in a refrigerator. Samples for calcitonin measurements should be frozen immediately.

Calcitonin and its multiple decay fragments and precursor fragments interact in complex ways with the antibodies in calcitonin assays, making accurate quantification of very high calcitonin levels (eg, >800 pg/mL) difficult.

Dr Grebe explains: “For these reasons, we have recently started evaluating procalcitonin (PCT), a calcitonin precursor, as an alternative to calcitonin for diagnosis and follow-up of MTC patients. PCT is a much more stable analyte and does not seem to be affected by assay interference of calcitonin fragments. Our preliminary data show a good correlation between calcitonin and PCT levels in patients with suspected or confirmed MTC, as well as in normal individuals. If these data are confirmed, we may start recommending PCT as an analytically superior alternative to calcitonin in the near future.”

#### Novel Molecular Tests

Dr McIver explains: “Detection of the tumorigenic BRAF V600E mutation is highly specific for papillary thyroid carcinoma, and we have recently shown that circulating tumor cells with this mutation can be detected in some patients with papillary thyroid cancer.” Clinical validation studies are under way to determine how these observations can best be introduced into clinical practice to augment existing laboratory testing in thyroid cancer. We hope that this type of cancer-specific surveillance method might eliminate many of the uncertainties that currently complicate the interpretation of measurement of Tg and TgAB and simplify the management of patients with differentiated thyroid cancer.”

#### Table. Causes of Increased Serum Calcitonin Levels Unrelated to MTC

- Active autoimmune thyroiditis
- Hyperparathyroidism
- Lactation
- Mastocytosis
- Neonates
- Nonthyroid neuroendocrine neoplasms (eg, islet cell tumors, carcinoid tumors, small cell carcinomas of the lung) and (rarely) leukemias
- Renal failure
- Sepsis
- Severe noninfectious inflammatory conditions and massive trauma

### Endocrinology Update

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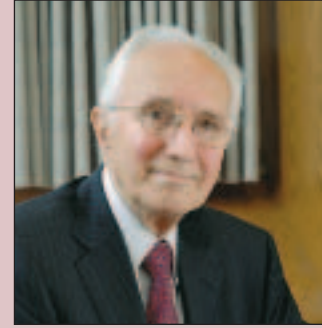
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### Education Opportunities

**11th Mayo Clinic Endocrine Course**, April 16-19, 2008, Palma de Mallorca, Spain. This course, created for endocrinologists and interested internists and surgeons, will cover selected topics in endocrinology through short lectures, case-based debates, clinicopathologic sessions, and clinical pearls sessions. For more information about this course please visit <http://endocourse.mayo.edu>.

**Mayo Clinic Nutrition in Health and Disease**, October 9-10, 2008, Chicago, Illinois. This course, designed for physicians, dietitians, nurses, and pharmacists, will provide a full-spectrum, in-depth overview of challenging nutritional issues that clinicians encounter in the ambulatory and hospital settings. For more information about this course, please call 800-323-2688 or visit [www.mayo.edu/cme/endocrinology.html](http://www.mayo.edu/cme/endocrinology.html).



### Richard F. Emslander, MD—50 Years at Mayo Clinic

Dr Emslander earned his bachelor's degree at Oberrealschule Eichstätt

in Eichstätt, Germany, and his medical degree from Würzburg University in Würzburg, Germany. He completed residency training at University Hospital in Würzburg, Germany, St. Joseph's Hospital in New Jersey, and USA Hospital in Munich, Germany. Fifty years ago, Dr Emslander came to Mayo Clinic for further clinical and research training. Since 1962, he has been a full-time clinical member of the Mayo Clinic Division of Endocrinology, Diabetes, Metabolism, and Nutrition.

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### Pediatric Endocrinologists at Mayo Clinic Rochester

From left to right: Seema S. Kumar, MD, Siobhan T. Pittock, MD, Aida N. Lteif, MD, W. Frederick Schwenk II, MD, and Peter J. Tebben, MD, shown here in the new T. Denny Sanford Pediatric Center.

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