Focus on Subspecialties, Endocrinology

Focus on Subspecialties: Guidelines aid in management of children with thyroid nodules, cancer
by Clifford A. Bloch M.D., FAAP

Dr. Bloch Until recently, no evidence-based guidelines were available to help clinicians manage children and adolescents with thyroid nodules and differentiated thyroid cancer (DTC).

Recognizing that management of thyroid cancer has become more sophisticated and complex and children differ from adults in their biological responses to thyroid cancer, the American Thyroid Association convened a task force of experts in pediatric thyroid cancer, and they produced the AAP-endorsed Management Guidelines for Children with Thyroid Nodules and Differentiated Thyroid Cancer (Francis GL, et al. Thyroid. 2015;25:716-759, http://bit.ly/20qAVKU).

Since no large, comprehensive, long-term, prospective trials compare various evaluation and management strategies in this population, the task force culled the best evidence from retrospective studies to produce the guidelines. They acknowledge that children differ from adults in their presentation, biology, response to, tolerance of and compliance with therapy as well as prognosis.

Following are some of the recommendations in the report:

• The American Joint Committee on Cancer Tumor-Node-Metastasis (TNM) classification system should be used to stage patients at diagnosis.

• After undergoing surgery, children should be stratified into high, intermediate or low risk.

• Based on their surgical and pathology findings and their thyroglobulin responses to recombinant human TSH (rhTSH) stimulation, treatment should be customized based on their stage and risk category to eradicate disease and minimize risks of therapy.

The report also provides recommendations for management of children with distant metastases and discusses the role of ultrasound, random and rhTSH-stimulated thyroglobulin, and 123I radiiodine whole body scanning in post-operative surveillance for metastatic disease.

The task force recommends that children with DTC be followed for life because recurrences have been noted to occur up to 40 years after initial therapy. It also recommends that evaluation and management be conducted by physicians and teams who are trained and skilled in the management of thyroid nodules and cancer.
Management of thyroid cancer has become more sophisticated and complex. AAP News photo by Jeff Knox
Recent advances in tumor biology have shed some light on the molecular genetics of papillary thyroid cancer (PTC), including the discovery of the RAS-RAF-MEK-ERK mitogen-activated protein kinase pathway and how it influences tumor biology. These genetic advances have been used commercially in adults for mutational analysis of DNA extracted from nodules and tumors. While this has the potential to allow the customization of therapy to influence decisions on how aggressive management ought to be, its role in children remains to be determined.

Given the observation that PTC in children is associated with a "higher prevalence of gene rearrangements and a lower frequency of point mutations" (Fenton CL, et al. J Clin Endocrinol Metab. 2000;85:1170-1175; Penko K, et al. Thyroid. 2005;15:320-325) in the associated proto-oncogenes compared to adults, it stands to reason that management guidelines in children ought to follow pediatric-specific protocols. These protocols should be forthcoming if/when justified by the results of current research.

While most of the report focuses on PTC, it also briefly discusses the management of children with follicular thyroid cancer (FTC). Because FTC is much less common than PTC in children, there is even more of a paucity of prospective studies on evaluation, management and outcome. Hence, the recommendations are weak, based mainly on adult data.

Although the report does not discuss medullary thyroid cancer (MTC), there is general consensus that genetic mutational analysis ought to be performed on all confirmed cases and their first-degree relatives to detect mutations in the ret proto-oncogene. These mutations are highly specific markers for MTC. If ret proto-oncogene mutations are found, children ought to undergo a prophylactic, total thyroidectomy because the incidence of MTC approaches 100%.

*Dr. Bloch is a member of the AAP Section on Endocrinology.*