# Initial Management and Follow-up of Differentiated Thyroid Cancer in Children

Steven G. Waguespack, MD,[a] and Gary Francis, MD, PhD,[b] *Houston, Texas, and Richmond, Virginia*

## Abstract

Children with differentiated thyroid cancer (DTC) often present with metastatic disease and have a high risk for recurrence, but rarely die of the disease. This article reviews DTC in children and discusses current approaches to their initial care and follow-up. These recommendations take into account the greater risk for recurrence and lower disease-specific mortality in these patients. Total thyroidectomy and central compartment lymph node dissection are appropriate for most children, but should be performed by a high-volume thyroid surgeon. Radioactive iodine (RAI) should generally be prescribed for those at very high risk for recurrence or known to have microscopic residual disease, and those with iodine-avid distant metastases. RAI should be considered in other patients only after carefully weighing the relative risks and benefits and the aggressiveness of the clinical presentation, because RAI may be associated with an increased risk for second malignancies and an increase in overall morbidity and mortality. All patients should be treated with thyroid hormone suppression, and follow-up should be lifelong. However, the degree of thyroid hormone suppression and frequency of disease surveillance usually decrease over time as patients are determined to be disease-free. (*JNCCN* 2010;8:1289–1300)

From the [a]Departments of Endocrine Neoplasia & Hormonal Disorders, and Pediatrics, University of Texas MD Anderson Cancer Center, Houston, Texas, and [b]Division of Pediatric Endocrinology and Metabolism, Virginia Commonwealth University, Richmond, Virginia.

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Correspondence: Gary Francis, MD, PhD, Division of Pediatric Endocrinology and Metabolism, Virginia Commonwealth University, 1001 East Marshall Street, Richmond, VA 23298. E-mail: glfrancis@vcu.edu

## Background

Only 1.8% of thyroid cancers develop in persons younger than 20 years, but the incidence may be increasing.[1–3] Adolescents have a 10-fold greater incidence than younger children, and a female:male preponderance (5:1) occurs during adolescence that is not seen in young children.[2–7] Most thyroid cancers in children are papillary (PTC), followed by follicular (FTC) and, more rarely, medullary carcinoma.[5,8–10] Subtypes of PTC include follicular variant, tall cell, columnar cell, diffuse sclerosing, and encapsulated variants.[11] PTC in children younger than 10 years may be unencapsulated, be widely invasive throughout the gland, and have a follicular and solid architecture with unique nuclear features and abundant psammoma bodies.[12,13] Histologic variants of FTC include Hürthle cell (oncocytic), clear cell, and insular (poorly differentiated) carcinoma.[11] PTC and FTC exhibit major clinical differences.[14] PTC is frequently multifocal and bilateral, and metastasizes to regional neck lymph nodes. Hematogenous metastases are much less common and generally occur only with significant regional lymph node metastases.[10,15] FTC is typically a unifocal tumor and more prone to initial hematogenous metastases to lungs and bones; metastases to regional lymph nodes are uncommon.

The major risk factor for the development of PTC is radiation exposure to the thyroid.[16,17] Children, especially those younger than 5 years, are most sensitive.[18,19] The clinical behavior of radiation-induced PTC does not seem to differ from sporadic PTC.[20] Activation of the RAS-RAF-MEK-ERK (mitogen-activated protein kinase) pathway is critical in thyroid malignancies.[21–23] An estimated 5% of patients with PTC have a family history of this disease,[18,24] which may portend a worse prognosis and require more aggressive treatment.[25]

## Unique Features of Childhood Thyroid Cancers

In children, the most common presentation for differentiated thyroid cancer (DTC) is that of a palpable thyroid nodule. However, PTC also frequently presents as cervical adenopathy with or without a palpable thyroid lesion, or as an incidental finding after imaging or surgery for an unrelated condition.[26] Occasionally, it may be diagnosed only after the discovery of distant metastases.[27–29]

The evaluation, treatment, and follow-up of children with DTC have generally followed available guidelines for adults.[30–33] However, several important differences in DTC have been described in children. First, although thyroid nodules are uncommon in children, they are 5-fold more likely to be malignant in children (26.4%) than adults (5%).[34,35] Second, when controlled for histology and tumor size, children with PTC are more likely to have regional lymph node involvement, extrathyroidal extension, and distant pulmonary metastasis.[9,10,13,26,28,29,36–40] Third, despite having extensive disease, children are less likely to ultimately die of the disease than are adults.[40,41] Molecular studies also show that, although mutations in *BRAF* are the most common finding in adult PTC (36%–83% of cases),[21] they are rare in childhood PTC,[42] in which *RET/PTC* rearrangements are more common and possibly contribute to a more favorable clinical course.[5,23,43]

## Initial Preoperative Staging and Prognosis

Similar to adults, DTC, specifically PTC, is usually diagnosed based on fine-needle aspiration of an asymptomatic thyroid nodule or metastatic lymphadenopathy. Preoperative staging should be performed to direct management of all children with DTC (Figure 1), and applies to overt and incidental DTC. DTC becomes overt when it is palpable, involves cervical lymph nodes, is 1 cm or larger in diameter, has suspicious ultrasound features, or invades surrounding tissues. Incidental DTC is identified through imaging or pathology for an unrelated condition. It is generally smaller than 1 cm in diameter and does not have suspicious ultrasound features, direct extension, or regional metastases.

At a minimum, preoperative staging (Figure 1) should include a chest radiograph to assess for mac-

roscopic pulmonary metastases and a comprehensive neck ultrasound to interrogate the contralateral thyroid lobe and the lymph nodes in the central and lateral neck compartments.[44] Most children with PTC have cervical node involvement.[9,10,13,26,28,29,36]

To facilitate surgical planning, the authors also consider cross-sectional imaging (CT or MRI) of the neck in children with bulky metastatic lymphadenopathy. Nuclear scintigraphy is not recommended for the initial evaluation of DTC in children with an intact thyroid and a normal thyroid-stimulating hormone (TSH) level. Radioactive iodine (RAI) uptake in the lungs after initial surgery seems to be the most sensitive indicator of pulmonary metastatic disease,[38] and chest CT is usually only obtained after pulmonary metastases are demonstrated to minimize diagnostic radiation exposure. DTCs in children are well-differentiated tumors with robust RAI uptake and, in the authors' experience, PET scanning at the outset seems to have no benefit.

Several staging systems to estimate the risk of death have been used for thyroid cancer, specifically PTC,[30,45–47] but none seems to offer significant advantages over the TNM classification.[48] Most young patients (< 45 years) will be TNM stage I, and only those few with distant metastases will be stage II. However, stage I is highly diverse and would include incidental PTC, PTC with cervical lymph node metastases, and PTC invading the surrounding tissues. Despite similar stage and low risk for mortality, the risk of recurrence is much greater for patients with cervical node involvement or direct extension.[15,49] Children with PTC who have palpable cervical lymph node metastases are more likely to experience recurrence (53% vs. 0%), have persistent disease (30% vs. 0%), show diffuse sclerosing histology (63% vs. 4%), have multifocal disease (89% vs. 16%), and have a higher incidence of pulmonary metastasis (20% vs. 0%) than children without nodal disease.[15] Therefore, the absence of cervical node involvement is an important indicator of low recurrence risk.

Most children with DTC have an excellent prognosis, and survival over decades is generally the norm, even in the presence of distant metastases at diagnosis.[9,10,13,40,41,50,51] Cure rates are high, and 10-year survival is almost universally 100% in this age group.[7,10,13,37,40,41,50,52,53] For patients with stage II disease, micronodular lung metastases and iodine-avid disease (i.e., the cells that retain good expression of
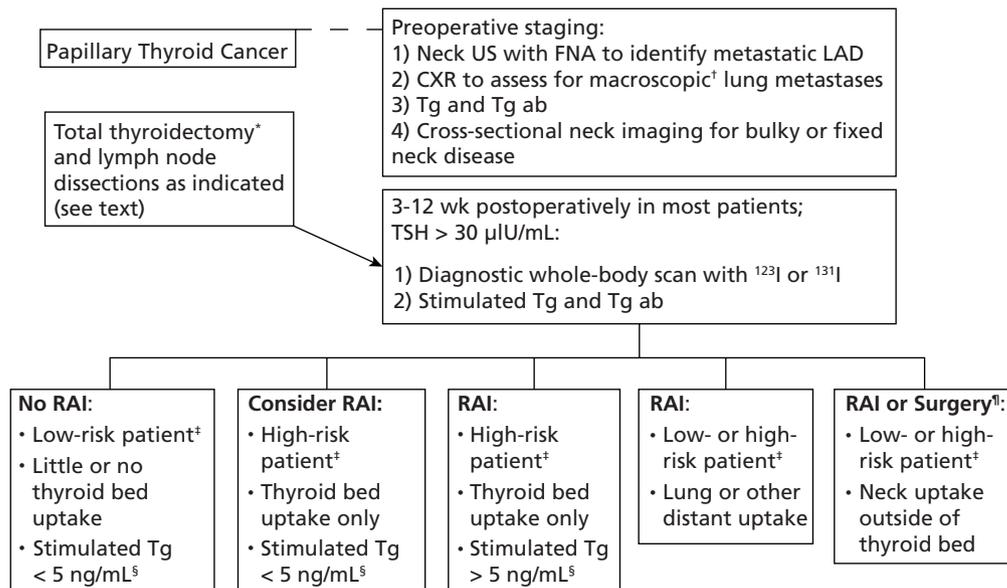
**Figure 1** Initial evaluation and treatment of papillary thyroid cancer.
Abbreviations: CXR, chest radiography; FNA, fine-needle aspiration; LAD, lymphadenopathy; RAI, radioactive iodine; Tg, thyroglobulin; Tg ab, thyroglobulin antibody; TSH, thyroid-stimulating hormone; US, ultrasound.
*Rare cases where lobectomy may suffice.
†Macroscopic lesions are considered to be larger than 1 cm.
‡Low-risk: primary tumor does not grossly invade the trachea, recurrent laryngeal nerve, esophagus, or other vital structures; non-bulky lymph node presentation; no evidence of distant metastatic disease. High risk: any of the previous features present.
§Assumes negative Tg ab.
¶RAI if no macroscopic disease on US; surgery if macroscopic disease on US.

the sodium-iodide symporter) confer the best prognosis.[38,53,54] Some children with DTC will ultimately succumb to the disease or die of treatment-related complications.[41,55] Children diagnosed before 10 years of age seem to have a higher risk for recurrence and ultimately death,[51,56,57] but not all studies support this observation.[39,58]

Based on these data, the authors prefer to use TNM staging, but also take into account patient age, the presence of cervical lymph node disease, and direct extension of the primary tumor into surrounding tissues to predict the risk of residual/recurrent disease. All patients younger than 10 years and any patient with palpable cervical lymph node disease or direct extension are considered at higher risk for recurrence but still at low risk for short-term mortality. Preoperative staging helps identify children who do not have cervical lymph node involvement and thus have a reduced risk of distant metastases and recurrence. These children can generally be treated with total thyroidectomy and close follow-up for cervical node recurrence.

## Initial Thyroid Surgery for Overt PTC

Because surgical complication rates are higher in children, thyroid surgery should ideally be performed by a high-volume thyroid surgeon (at least 30–50 thyroidectomies annually).[59–61] Most surgeons perform a total thyroidectomy for children with overt PTC for several reasons. First, 40% of children have multifocal PTC and a higher risk for recurrence if less than a total thyroidectomy is performed.[7,10,14,26,30,40,50,51,60,62–65] Second, most children with PTC have regional lymph node disease and a greater risk for distant metastasis. Total thyroidectomy will facilitate the future use of RAI as indicated. Third, sensitive assays for thyroglobulin (Tg) are used as a marker for disease but are most sensitive after total thyroidectomy and RAI ablation.[66–68]

Lobectomy and isthmusectomy alone may suffice in the low-risk adolescent with a small (< 1 cm) unifocal PTC but only if ultrasound shows no evidence of contralateral lobe or regional lymph node disease.[7,30,31,60,64] Clinician assessment of adherence to life-long levothyroxine therapy may also help determine the extent of initial surgery in low-risk patients.

Therefore, the authors recommend that surgery in all children with DTC be performed by a high-volume thyroid surgeon. They advocate total thyroidectomy for patients younger than 10 years and for those with overt disease, a history of radiation exposure, a family history of thyroid cancer, or unusual histology. They consider lobectomy for low-risk patients with incidental micro-PTC or small (< 1 cm) unifocal tumors as long as pre- and postoperative staging fail to identify multifocal disease in the thyroid or cervical lymph node involvement.

## Lymph Node Dissection

Lymph node dissection reduces recurrence risk for children with PTC and improves progression-free survival.[69,70] The extent of lymph node dissection is based on the type and clinical presentation of PTC.[47] All lymph node dissections should be comprehensive and compartment-focused because higher recurrence rates occur with "berry picking."[71] Although total thyroidectomy and central compartment dissections are associated with greater risks for hypoparathyroidism and recurrent laryngeal nerve injury,[10,64,72] these risks are minimized when a high-volume surgeon performs the surgery.[59,60]

Based on these data, the authors recommend that central compartment neck dissection be performed by a high-volume thyroid surgeon for children with overt PTC. They waive central compartment dissection for children with small PTC and no evidence of metastatic lymphadenopathy on ultrasound, or if the risks outweigh potential benefits because of the lack of availability of a high-volume surgeon. A compartment-focused lymph node dissection of the lateral neck should be performed only if metastatic disease is confirmed through preoperative staging and fine-needle aspiration.

## Postoperative Staging

After surgery, patients are evaluated for persistent disease. In patients at very low risk for recurrence, this is primarily based on ultrasound of the thyroid bed and cervical lymph nodes along with a suppressed serum Tg. Low-risk patients can generally be followed up expectantly (Figure 2). Postoperatively, patients at high risk for residual/recurrent disease are taken off thyroid hormone to prepare for a stimulated Tg test

and diagnostic RAI scan (Figure 1). Patients with pulmonary or distant metastases should be treated with RAI, whereas RAI use in patients with documented cervical lymph node disease is generally determined by the stimulated Tg, diagnostic thyroid scan, and extent of disease identified at surgery and pathologically (Figure 1).

## RAI Treatment

Except for in patients with iodine-avid pulmonary or distant metastases, routine RAI treatment for children with DTC has been debated. RAI may lower recurrence and cancer-related mortality in patients with iodine-avid tumors.[53,63,73] However, low-risk adults do not seem to benefit from RAI.[74,75] This issue has not been well addressed in children, and the possible benefits must be weighed against the potential risks of RAI on an individual basis. A few authors support routine RAI therapy in children.[14,76] Studies that lack support for RAI show similar recurrence rates for children treated with surgery or surgery plus RAI.[26,40] Unfortunately, these are all retrospective data, and why RAI was prescribed for only some patients, who might have had more extensive disease, is unclear.

Recently, strong data against the universal prescription of RAI therapy were published.[40] In that study, children previously treated with radiation (external-beam radiation, RAI, or radium implants) developed various second cancers and had increased overall mortality compared with the general population.[40] Whether this represents a direct treatment effect or an underlying predisposition to cancer is unknown. Long-term, a real concern exists for the development of other cancers (chiefly leukemia, but also stomach, bladder, colon, salivary gland, and breast carcinomas),[77–83] particularly when RAI is administered at a young age. However, an analysis of approximately 30,000 cases in the SEER database failed to substantiate an increase in second malignancy for patients treated with RAI.[84]

If RAI is prescribed, the TSH should be greater than 30 μIU/mL.[7,30,65,85] In patients at high risk for disease, this will generally be induced through 14 days of thyroid hormone withdrawal.[86] Recombinant human TSH (rhTSH) can be used for remnant ablation in low-risk patients[87,88] and may result in a lower absorbed dose to the blood.[89] Although experience
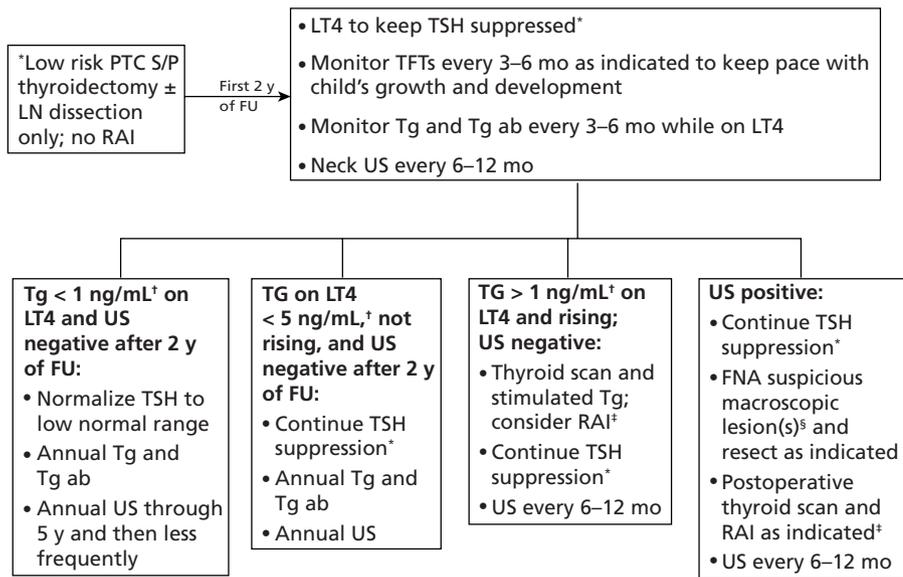
**Figure 2** Approach to surveillance and treatment in pediatric patients treated with surgery alone.
Abbreviations: FNA, fine-needle aspiration; FU, follow-up; LN, lymph node; LT4, levothyroxine; PTC, papillary thyroid carcinoma; RAI, radioactive iodine; S/P, status post; TFTs, thyroid function tests; Tg, thyroglobulin; Tg ab, thyroglobulin antibody; TSH, thyroid-stimulating hormone; US, ultrasound.
*See text.
†Assumes negative Tg ab.
‡See Figure 1.
§Macroscopic lesions are considered to be larger than 1 cm.

with rhTSH is increasing, data regarding its use in children remain limited and retrospective in nature.[90,91] To facilitate RAI uptake, a low iodine diet is generally recommended for 2 weeks before therapy. In children who received intravenous contrast as part of their preoperative staging, waiting 2 to 3 months or confirming normal 24-hour urinary iodine values before performing a diagnostic thyroid scan is advisable.

No standardized doses of RAI exist for children. Some clinicians adjust $^{131}$I dose according to weight or body surface area and give a fraction (e.g., child's weight in kg per 70 kg) based on the typical adult dose used to treat similar disease extent.[7,14,85] Others suggest that $^{131}$I doses should be based on body weight alone (1.0–1.5 mCi/kg).[92,93] A posttreatment thyroid scan, sometimes coupled with single photon emission CT (SPECT) imaging, should be obtained 5 to 8 days after $^{131}$I treatment to identify potential sites of disease that were not apparent on the diagnostic study.[30,38] Dosimetry may be used to limit whole-body retention to less than 80 mCi at 48 hours and blood and bone marrow exposure to less than 200cGy,[30,94,95] and is most useful in selecting an appropriate dose of RAI for small children, children

with diffuse lung uptake or significant distant metastases, and those undergoing multiple RAI treatments. Although total body dosimetry calculates the absorbed dose to bone marrow and blood, the lung is actually the dose-limiting organ in 10% of cases.[96] Lesional dosimetry could also be performed to select optimal doses of RAI for children with substantial lung involvement.[97–100]

From these data, the authors conclude that prospective randomized clinical trials would be required to determine any true benefit or risk from routine RAI ablation of the thyroid remnant in children. Lacking proper evidence to guide decision-making, the authors consider RAI treatment for children at greatest risk for distant metastases and locoregional recurrence (children with extensive cervical lymph node metastasis, locally invasive cancers, or aggressive histology; Figure 1). In the absence of data suggesting residual or metastatic disease, RAI is not routinely prescribed for lower-risk children whose primary surgery was performed by a high-volume thyroid surgeon. RAI treatment is appropriate in children with distant metastatic disease, but the use of high-dose $^{131}$I to treat macroscopic cervical lymph node disease is not recommended because surgical

removal seems to be the better option.

In preparation for evaluation and possible therapy with ^{131}I, the authors perform thyroid hormone withdrawal and measure a stimulated serum Tg and obtain a diagnostic ^{123}I or ^{131}I whole-body scan. In rare cases when the initial stimulated Tg test (assuming negative Tg antibodies) and diagnostic scan are negative, the authors defer RAI. Initial doses of ^{131}I are typically based on body weight alone or body weight and extent of disease identified on the diagnostic scan. In more advanced cases, dosimetry can be performed, and consideration should be given to referral to a tertiary care facility with expertise in treating this disease in children.

## Evaluation and Treatment of FTC in Children

FTCs are more prone to hematogenous metastases to lungs and bones than are PTCs. FTCs are diagnosed based on the pathologic identification of capsular or vascular invasion of a resected lesion, and are subdivided into those with capsular invasion only (minimally invasive FTCs) and those with capsular and widespread vascular invasion. Vascular invasion increases the risk for recurrence and metastasis.

Only a few data compare outcomes for FTC and PTC in children. Mortality and recurrence rates were similar, but most patients were treated with total thyroidectomy and RAI.[26] Because angioinvasion and hematogenous spread can occur even without regional lymph node disease, most patients with invasive FTC are treated with total thyroidectomy and RAI.[101] Lymph nodes in more aggressive variants of FTC are managed similarly to PTC.[46]

The management of minimally invasive FTC is controversial, even in adults, and the optimal management for children is unknown.[102,103] Many surgeons perform lobectomy alone and consider this sufficient surgery with close follow-up and possible TSH suppression. In patients of all ages with minimally invasive FTC, 10-year disease-free survival was 92% and none of the 37 patients younger than 45 years developed distant metastases,[102] suggesting that it might be less aggressive in young patients.

Based on the minimal data available regarding FTC in children, the authors are unable to make strong recommendations regarding therapy. In the authors' opinion, widely invasive FTC should be treated with total thyroidectomy and probable RAI ablation because of the high risk for distant metastases. Minimally invasive FTC should be treated on an individual basis. Families should be informed that, unlike what is seen in PTC, absence of regional lymph node disease does not preclude distant metastases. Similar to PTC, measurement of Tg will help guide decisions regarding RAI therapy (Figure 1).

## TSH Suppression

TSH suppression is a cornerstone of DTC treatment, but the optimal level of suppression is debated.[104] The recent American Thyroid Association (ATA) guidelines recommend that TSH should be 0.1 to 0.5 µIU/mL in low-risk patients and less than 0.1 µIU/mL in high-risk patients.[30] However, children were not defined as low- or high-risk patients. Some experts have recommended initial suppression of TSH to less than 0.1 µIU/mL, followed by relaxation of TSH suppression to 0.5 µIU/mL once children enter remission.[92] Although unstudied, the potential risks of long-term TSH suppression (e.g., negative effects on childhood growth, bone mineralization, and the heart) are likely to be minimal in the otherwise healthy pediatric population.

In the absence of data to the contrary, the authors generally follow the ATA recommendation and administer thyroid hormone suppression in most children with a goal of achieving and sustaining a serum TSH level ranging from 0.1 to 0.5 µIU/mL in the absence of symptoms of hyperthyroidism. More complete suppression is recommended in children at greatest high risk for morbidity and mortality (i.e., those with locally advanced or distantly metastatic disease). Over time, suppression may be relaxed in children with no sign of recurrent disease to reduce the long-term risks of hyperthyroxinemia.

## Disease Surveillance

Although some series suggest most recurrence in young patients occurs during the first decade,[26] other series have equal recurrence rates in the first and second decades,[105] and all series show some recurrence after 20 to 30 years.[40] Therefore, follow-up should be lifelong (Figures 3 and 4).

Most data on DTC in children are retrospective and used diagnostic RAI scans as the gold-standard for disease surveillance. Unfortunately, these scans are suboptimal for detecting disease in all cases. In adults, assessment for persistent/progressive disease usually entails measurement of suppressed Tg, neck ultrasound, and TSH stimulated Tg test values (with or without diagnostic RAI scan) in patients previously treated with [131]I.[30] Patients with a negative stimulated Tg test and ultrasound are considered as having "no evidence of disease," and suppressive therapy and follow-up interval are ultimately relaxed. Approximately 20% of adults with suppressed Tg less than 1 ng/mL will have Tg greater than 2 ng/mL after TSH stimulation, indicating possible disease.[106] However, the clinical importance of a low-level disease burden identified by Tg testing alone is not clear.[106,107] A serial increase in serum Tg levels indicates disease that might achieve clinical importance.[106,107]

Whether similar Tg levels have the same prognostic value for children is unclear. Children generally have well-differentiated disease, and most survival data for children are based on undetectable RAI uptake on a diagnostic scan.[108] The authors do not know the serum Tg levels of these children nor how aggressive treatment should be of disease that is detected solely through abnormal serum Tg levels. Another reason to be cautious in treating Tg-positive patients who have negative diagnostic whole-body scans is that almost 50% of children with pulmonary metastases develop stable but persistent disease after ^{131}I therapy.[109] Whether they benefit from additional therapy is unknown, but the extent of disease does not seem to change over short-term follow up in most cases.

The ATA guidelines recommend that rhTSH not be considered for Tg stimulation.[30] However, rhTSH is not yet FDA-approved for use in children, and adequate TSH levels can be achieved in children after short-term cessation (only 14 days) of levothyroxine therapy.[86] Nevertheless, the limited yet growing data available on rhTSH use in children show that the typical adult dose seems to be safe and can generate TSH levels similar to those seen during thyroid hormone withdrawal.[91,110,111]
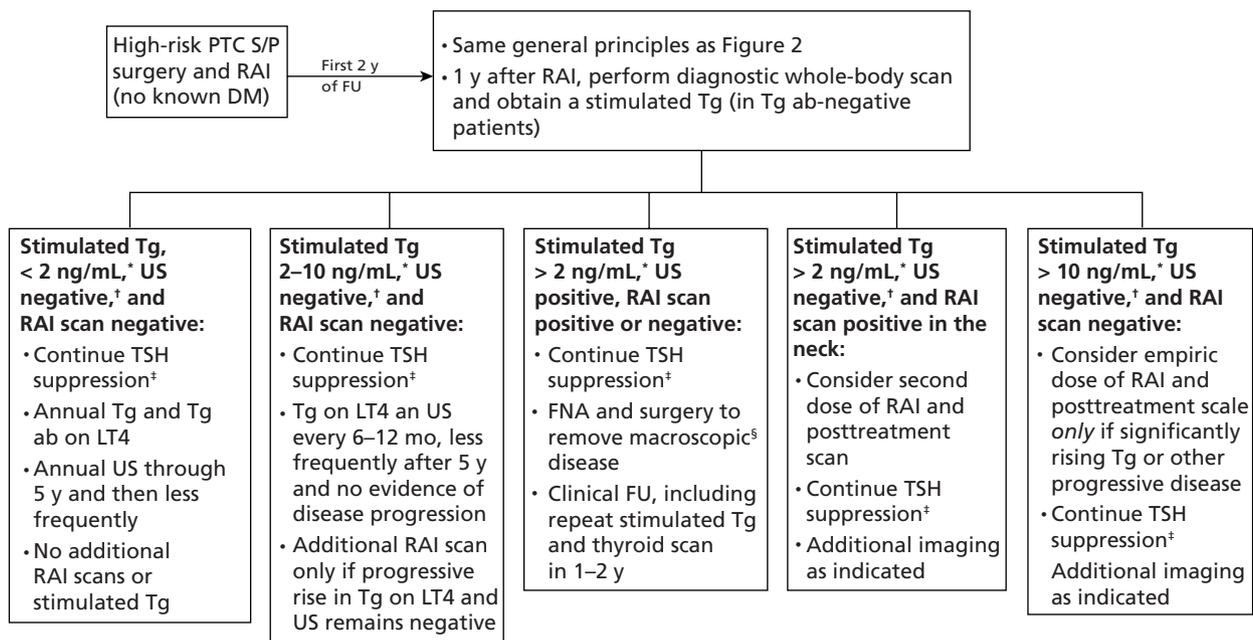


**Figure 3** Approach to surveillance and treatment in pediatric patients treated with surgery and radioactive iodine in the absence of known distant metastases.

Abbreviations: DM, distant metastases; FNA, fine-needle aspiration; FU, follow-up; LT4, levothyroxine; PTC, papillary thyroid cancer; RAI, radioactive iodine; S/P, status post; Tg, thyroglobulin; Tg ab, thyroglobulin antibody; TSH, thyroid-stimulating hormone; US, ultrasound.

*Assumes negative Tg ab.

†When US is positive for macroscopic disease, surgery should be considered.

‡See text.

§Macroscopic lesions are considered to be larger than 1 cm.
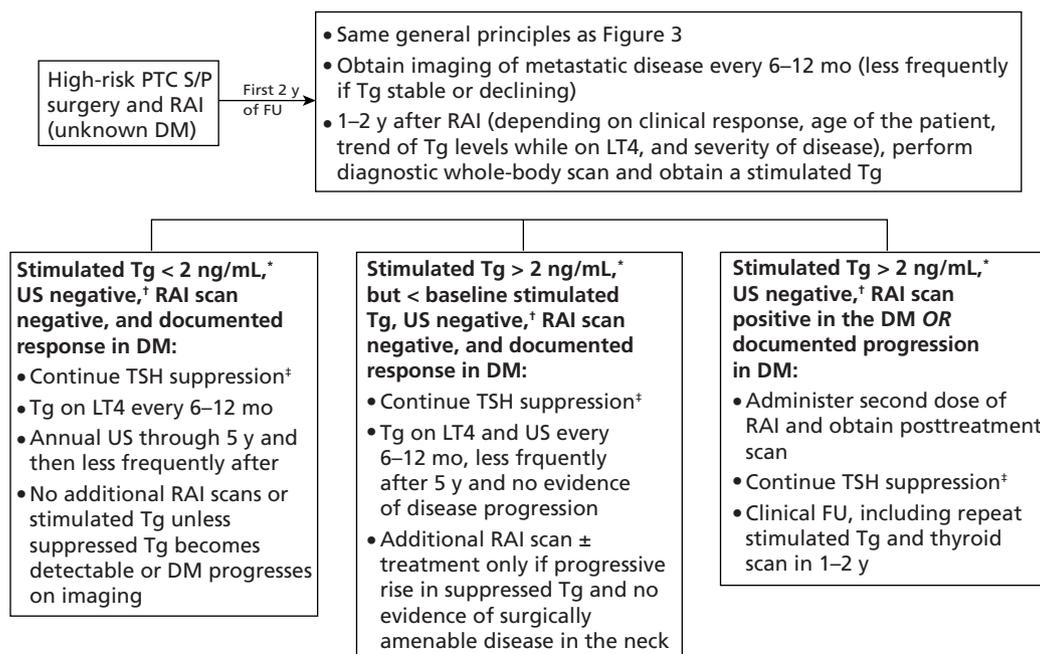
Waguespack and Francis



**Figure 4**    Approach to surveillance and treatment in pediatric patients treated with surgery and RAI with known distant metastases.

Abbreviations: DM, distant metastases; FU, follow-up; LT4, levothyroxine; PTC, papillary thyroid cancer; RAI, radioactive iodine; S/P, status post; Tg, thyroglobulin; Tg Ab, thyroglobulin antibody; TSH, thyroid-stimulating hormone; US, ultrasound.

*Assumes negative Tg ab.

†When US is positive for macroscopic disease, surgery should be considered.

‡See text.

Some clinicians choose to treat young patients until they have a negative ^{131}I scan.[53] This approach is commonly used but does not take full advantage of thyroid ultrasound, given that ultrasound has detected disease in 23% of children when the Tg and scan were negative.[112] Furthermore, Tg levels may slowly continue to decline in children previously treated with RAI, and undetectable Tg levels in children with pulmonary metastases may not be a tenable goal in all cases.[5,52,81,113]

The authors' practice is to determine suppressed serum Tg and Tg antibodies every 3 to 6 months after initial therapies. They also perform neck ultrasound every 6 to 12 months during the first 1 to 2 years of follow-up, and then decrease the frequency to annually or less frequently, depending on the patient history. A stimulated Tg test and a whole-body scan are obtained at least once in patients previously treated with ^{131}I, usually a year after RAI therapy. If there is no evidence of disease at 1 year, the authors do not routinely obtain subsequent stimulated Tg levels or RAI scans, as long as the patient has no other evidence of recurrent/progressive disease. They stratify patients according to the risk for detecting disease based on age (< 10 years is high risk), tumor size (> 2 cm is high risk), previous disease in the cervical nodes (high risk), or pulmonary metastases (high risk). Patients at high risk for disease are prepared with thyroid hormone withdrawal in anticipation of a possible need to retreat with ^{131}I one year after initial therapy. Lower-risk patients are prepared with either thyroid hormone withdrawal or rhTSH stimulation, depending on patient preference and available resources.

In patients with a detectable suppressed Tg greater than 1 ng/mL, the authors monitor the suppressed Tg because obtaining a stimulated Tg seems to have little benefit in this setting. In patients with a negative suppressed but positive stimulated Tg (> 2 ng/mL) and no other evidence of disease, the authors consider repeating the stimulated Tg in the future, because some patients will experience improvement without additional therapy. After 5 years, the interval between assessments is lengthened for those who remain disease-free, but at least annual assessments are recommended for life.

## Follow-Up of Children with Tg Antibodies

Tg antibodies are detected in approximately 25% of patients with thyroid cancer and interfere with serum Tg assays, rendering the Tg level uninterpretable.[114] For these patients, a decline in Tg antibody titer indicates declining disease burden but Tg antibody levels take a median of 3 years to clear after cure of DTC.[115] Once the child becomes Tg antibody–negative, a stimulated Tg can be considered to document the absence of disease. A significant rise in Tg antibodies may suggest disease progression and warrant further evaluation as clinically indicated.

It is the authors practice to assess serum Tg and Tg antibody levels concomitantly, preferably using the same laboratory used for prior measurements. In children with detectable Tg antibodies, the authors monitor the antibody titer. A steady decline in titer suggests response to treatment, whereas a rise in antibody warrants additional evaluation and possible treatment. Imaging is performed similar to in children who do not have Tg antibodies, but TSH-stimulated Tg and Tg antibody levels are not clinically useful in this setting.

## Conclusions

Although children with DTC typically present with locoregional metastases and a high rate of distant metastatic disease, they rarely die from their disease. Treatment should be based on their increased risk for recurrence but overall low mortality, and lifelong follow-up is required because recurrence and death may not occur for decades after diagnosis. Initial treatment will generally include total thyroidectomy and central compartment lymph node dissection. RAI should generally be reserved for those with iodine-avid distant metastases, children at high risk for locoregional recurrence or known to have residual microscopic disease, and others on an individual basis. As in any rare malignancy, these children are best treated by physicians and surgeons experienced in the management of pediatric thyroid carcinoma. Large multicenter studies are needed to better understand optimal treatment approaches to this unique population.

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