

# Pediatric Differentiated Thyroid Cancer

## (Papillary and Follicular)

### WHAT IS THE THYROID GLAND?

The thyroid gland is a butterfly-shaped endocrine gland that is located in the lower front of the neck, just above the collarbone. The thyroid's job is to make thyroid hormones, which are released into the blood and then carried to every tissue in the body. In children, thyroid hormone helps to ensure that growth and development occur normally and that the body's energy, metabolism, heart, muscles, and other organs are working properly.

### CANCER OF THE THYROID

Thyroid cancer is less common in children and adolescents when compared to adults, with an annual incidence of approximately 4-5 in 100,000 cases. Within pediatrics, thyroid cancer is most commonly diagnosed in teenage girls, for whom it is estimated to be the 2nd most commonly diagnosed cancer.

Compared to adults, childhood thyroid cancers have higher rates of metastases and recurrence. However, for the majority of children and adolescents, thyroid cancer is very treatable and the prognosis for children with thyroid cancers is usually excellent. Thus, the goal of treatment is to get rid of the cancer with the fewest complications from treatment.

Surgery is the initial step in therapy (see [Thyroid Surgery brochure](#)), in some cases followed by radioactive iodine (see [Radioactive Iodine brochure](#)). Even when thyroid cancer is more advanced, effective treatment is available for the most common forms of thyroid cancer.

### WHAT ARE THE TYPES OF PEDIATRIC THYROID CANCER?

**Papillary thyroid cancer (PTC):** PTC is the most common form, making up about 90% of all thyroid cancers. PTC usually presents as a solitary nodule. It tends to grow slowly and often spreads to the lymph nodes in the neck. Unlike many other cancers, PTC typically has an excellent prognosis, even if there is spread to the lymph nodes.

**Follicular thyroid cancer (FTC):** FTC makes up about 5-10% of all thyroid cancers in children. FTC can spread to lymph nodes in the neck, but it is also more likely than PTC to spread to distant organs, particularly the lungs and bones. Metastases to distant organs are very uncommon in pediatric patients.

PTC and FTC are known as well-differentiated thyroid cancers (DTC). DTC in children tends to behave differently than in adults. At diagnosis, approximately 40-60% of children with PTC will have thyroid cancer that has spread to the lymph nodes in the neck, and approximately 10-15% of patients with lymph node metastases will have thyroid cancer that has spread to the lungs. However, even when DTC has spread (metastasized), children have much better outcomes because the cancer grows slowly and maintains the ability to absorb radioactive iodine (explained below).

OTHER FORMS OF THYROID CANCER (DISCUSSED IN OTHER ATA PATIENT EDUCATION BROCHURES) ARE DESCRIBED HERE:

**Medullary thyroid cancer (MTC):** MTC accounts for approximately 2% of all thyroid cancers. Approximately 25% of all MTC runs in families and is associated with other endocrine tumors (see [Medullary Thyroid Cancer brochure](#)). In family members of an affected person, a blood test for a genetic mutation in the RET proto-oncogene can lead to an early diagnosis of medullary thyroid cancer and, as a result, to curative surgery. The likelihood of cure is dependent on the specific RET mutation as well as the age of diagnosis and surgery.

**Anaplastic thyroid cancer (ATC):** ATC is an extremely rare type of thyroid cancer that occurs almost exclusively in older adults. (See [Anaplastic thyroid cancer brochure](#).)

### WHAT ARE THE SYMPTOMS OF DTC IN CHILDREN?

Thyroid cancer often presents as a lump in the thyroid and usually does not cause any symptoms (see [Thyroid Nodule brochure](#)). Blood tests are generally not helpful in the diagnosis of thyroid cancer, since they are usually normal even when a cancer is present. Neck examination by a medical provider is a common way in which thyroid nodules and thyroid cancer are found. Often, thyroid nodules are discovered incidentally on head and neck imaging done for unrelated reasons. Occasionally, children themselves find thyroid nodules by noticing a lump in their neck during routine daily activities. Thyroid cancer may also present as 'swollen glands' (enlarged lymph nodes in the neck) that are hard, slowly increase in size and do not go away. Uncommon signs and symptoms include pain, difficulty with breathing or swallowing or hoarseness of the voice.

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### WHAT CAUSES PEDIATRIC DTC?

Pediatric thyroid cancer is more common in children who have a history of exposure to radiation that was used for treatment of other cancers. DTC can also be familial (inherited), with the risk increasing when two or more first degree relatives have a history of PTC or FTC. However, for the majority of children who develop thyroid cancer, there is no known risk factor and nothing that could have been done to prevent it from developing.

Exposure to radioactivity released during nuclear disasters (the 1986 power plant accident in Chernobyl, Russia or the 2011 nuclear disaster in Fukushima, Japan) has also been associated with an increased risk of developing thyroid cancer, particularly in exposed children. Thyroid cancers can be seen in exposed individuals up to 40 years later (see [Nuclear Radiation and the Thyroid Brochure](#) and [www.thyroid.org/web-links-for-important-documents-about-potassium-iodide/](http://www.thyroid.org/web-links-for-important-documents-about-potassium-iodide/)).

### HOW IS PEDIATRIC THYROID CANCER DIAGNOSED?

Thyroid cancer usually presents in the form of nodule(s) in the thyroid. Thyroid ultrasound (US) is used to determine which nodule(s) should be further evaluated. The size of the nodule is only part of the selection process and there are several other important US features that your physician will use to select which nodules should be evaluated. For patients with a thyroid nodule, it is very important that the US exam include images of the lymph nodes from the lateral (side) neck. The next step after US is to perform a fine needle aspiration (FNA) biopsy to obtain cells from the nodule and look at them under the microscope. The FNA is performed with a very skinny needle (smaller than that used to draw blood). The procedure can be mildly painful and many pediatric thyroid centers will offer some technique to decrease the pain and anxiety of the procedure. US is typically used to ensure the needle is in the proper location. FNA of the thyroid nodule(s) and abnormal lymph nodes can be performed at the same time. The results may take up to one week to return and are divided into four possible categories; unsatisfactory (not enough cells to make a diagnosis), benign (not cancer), malignant (papillary thyroid cancer) and a grey-zone result where the cells are not clearly normal (benign) and not clearly cancer. (see [Thyroid Nodule brochure](#)). In children and teenagers, up to 25% of nodules will end up with a diagnosis of thyroid cancer.

### WHAT IS THE SURGICAL TREATMENT FOR PEDIATRIC DTC?

The initial therapy for all types of thyroid cancer is surgery (see [Thyroid Surgery brochure](#)). The extent of surgery will depend on the location and number of nodules, a history of autoimmune thyroid disease, and the FNA biopsy results of the nodule and lymph nodes. Either a total thyroidectomy (removal of the entire thyroid gland) or lobectomy (removal of half of the thyroid gland) will be recommended. Surgical removal of lymph nodes from behind the thyroid (central neck) or lateral neck will be determined based on the FNA biopsy results. The goal is to have an accurate surgical plan based on pre-surgery imaging and FNA to decrease the need for more than one surgery. However, for some patients, a second surgery is unavoidable. For all children, referral to a center with experienced thyroid surgeons (one who performs 25 or more thyroidectomies per year) is important in an effort to reduce complications.

After surgery, children who have their entire thyroid removed will need to take thyroid hormone for the rest of their lives (see [Thyroid Hormone Treatment brochure](#)). Children that have half of the thyroid removed (lobectomy) may also need follow-up testing to ensure that the remaining thyroid tissue is producing adequate amounts of thyroid hormone.

### DO ALL PATIENTS RECEIVE RADIOACTIVE IODINE?

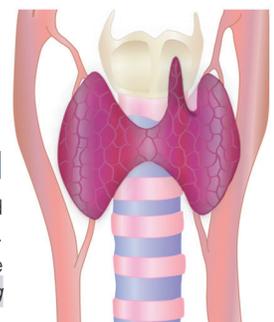
Radioactive iodine (RAI) therapy, also referred to as I-131 therapy, is used to treat any thyroid cancer that is left after a total thyroidectomy. This may include either a small amount of cancer remaining in the neck (residual) or metastases that cannot be removed with surgery, including cancer that has spread to the lungs. RAI is not used after a lobectomy.

Thyroid cells have the ability to absorb and concentrate iodine and use iodine to make thyroid hormone. Since differentiated thyroid cancer develops from normal thyroid cells, most DTC also have the ability to absorb iodine. Thus, RAI is used as a targeted form of treatment

### FURTHER INFORMATION

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to eliminate all remaining normal thyroid tissue and destroy (ablate) residual cancerous thyroid tissue (see [Radioactive Iodine brochure](#)). Since most other tissues in the body do not absorb iodine, RAI administered for ablation usually has little or no effect on organs outside of the thyroid. However, in some patients who receive larger doses of RAI for treatment of thyroid cancer, the salivary glands that produce saliva can be affected and result in dry mouth. In addition, for some children, it may be necessary to re-treat remaining DTC tissue. If higher doses of RAI are used more than once, there may also be a small risk of developing other cancers later in life. The potential risks of treatment can be minimized by using the smallest, effective dose of RAI and waiting as long as possible between RAI treatments to ensure that more RAI is necessary. A single RAI treatment may continue to destroy the cancer for 12 months or more after administration. So, waiting is not a risk, and may be a benefit, to see if additional treatment is necessary. Balancing potential risks against the benefits of RAI therapy is an important discussion to have with your child's doctor before this therapy and a very important reason to have your child cared for in a high-volume pediatric thyroid cancer center if possible.

The amount of spread (metastases) outside of the thyroid gland and to lymph nodes is used to select patients where the benefit from RAI is greater than the risk of treatment. Patients with small tumors and patients with no or minimal evidence of spread to lymph nodes behind the thyroid are considered to be at low-risk and these patients may be followed without receiving RAI. For patients with evidence of significant spread to tissue next to the thyroid, into lymph nodes or lungs, RAI is administered.

**PREPARING FOR RAI:** Two to three weeks before the RAI, patients are placed on a low iodine diet and most are asked to stop taking thyroid hormone medication in order to have the TSH increase. This is an important step to increase the effectiveness of the RAI treatment (see [Low Iodine Diet FAQ](#)). For patients that cannot tolerate stopping thyroid hormone, there is an injectable form of TSH that may be used. Several days before the RAI, a blood test is done to evaluate the TSH and the tumor marker, thyroglobulin. A diagnostic whole body scan (Dx-WBS) is performed to determine how much thyroid cancer is present. This information is used to help decide on the size of the treatment dose of RAI. About seven days after the RAI treatment, a repeat WBS may be performed. This post-treatment WBS (Rx-WBS) takes advantage of the

larger amount of RAI used for treatment, and in 10-15% of patients there may be new areas of thyroid cancer seen on the post-treatment WBS. This is important information for surveillance but no additional immediate treatment is typically necessary.

## WHAT IS THE FOLLOW-UP FOR CHILDREN WITH DTC?

Lifelong follow-up is essential for all children with thyroid cancer because thyroid cancer can recur (come back) years after successful initial treatment. These follow-up visits include a careful history, physical examination, blood tests, and imaging that may include ultrasound of the neck, chest CT scan and/or nuclear medicine whole body scans. Visits and blood tests are typically every 3 months after the initial treatment for the first 1 to 2 years, with decreasing frequency if the results are consistent with remission from disease. Repeat imaging is usually on a 6 month interval, decreasing to every year or longer if remission is achieved. More frequent surveillance is continued if there is any concern that the cancer is still present or is progressing.

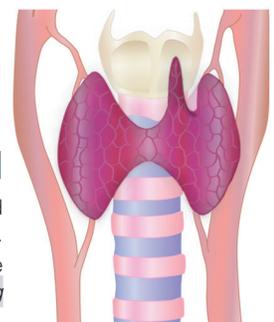
For the patient who has had a total thyroidectomy, he or she will need to take thyroid hormone (also referred to as levothyroxine) for the rest of his/her life to replace the hormone the thyroid produced. During this active surveillance time, many patients will be placed on higher doses of levothyroxine (LT4) to keep the TSH below the lower end of the normal range for this measurement (this is called TSH suppression). This is a very important part of treatment as we do not want any remaining cancer cells to be stimulated to grow by having an elevated thyroid stimulating hormone (TSH). The dose may be decreased if signs or symptoms of hyperthyroidism develop (some symptoms include: anxiousness, jitteriness, heart beating fast at rest and others) as well as after your provider is comfortable that the cancer is gone (that the patient is in remission).

In addition to measuring the TSH, another important blood test to monitor is the thyroglobulin (Tg), a protein produced by normal thyroid tissue as well as by most DTC cells. Tg is not a 'cancer' protein, but it is used as a marker in

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the blood to determine if the thyroid cancer has been completely eliminated. This lab test is extremely sensitive and there are times when the cancer cannot be found by imaging even though the Tg is measurable. A single Tg level is not as important as looking at the differences between measurements over time. After surgery and/or RAI, it may take months (even up to 2 years) for the Tg level to become undetectable. Thus, a decreasing Tg level is reassuring that the cancer is being destroyed as a result of the RAI treatment. About 25-40% of pediatric patients with DTC will have antibodies directed against Tg (anti-thyroglobulin antibodies (TgAb)). If present, the TgAb may make the Tg level less reliable. The Tg and TgAb testing should be performed in the same laboratory each time if at all possible with the same testing method to allow for the most accurate comparative results.

### TREATMENT OF ADVANCED PEDIATRIC THYROID CANCER

Advanced or progressive thyroid cancer is cancer that continues to grow after attempts to get rid of it with repeat surgery and RAI. New chemotherapeutic agents targeted to certain cell receptors and proteins have shown promise and are becoming more widely available at advanced cancer centers. These drugs are usually not curative, but they can slow down the growth of the cancer. These treatments are usually given by an oncologist (cancer specialist) and require care at a regional or university hospital that has a high-volume pediatric thyroid cancer center. This type of thyroid cancer occurs more frequently in adult patients and your pediatric thyroidologist should consider discussing if and when these medications are indicated with a specialist that has experience with these chemotherapeutic agents.

### WHAT IS THE PROGNOSIS OF PEDIATRIC THYROID CANCER?

Overall, the prognosis for children with DTC is excellent, with a survival rate of greater than 95% over 20 to 30 years of follow-up. Outcomes are best with early detection and treatment. Even for patients with spread to the lymph nodes and/or distant metastases, the outcome is still excellent. For some, repeat surgery and repeat RAI treatment may be necessary to achieve an excellent outcome. It is important for families to know that the response to radioactive iodine can be slow and may require years of ongoing surveillance in order to determine if the cancer has been destroyed. For the patients that achieve remission, there is an approximately 20-30% risk of recurrence that may occur decades later. Because of the high risk of recurrence, most children will need lifelong follow-up. For patients with lung metastases, up to 1/3 may have disease that remains but does not grow ('stable, but persistent disease'). One additional RAI treatment may be attempted, but, if there continues to be no decrease or growth, then long-term surveillance with labs and imaging (usually chest CT) is the best option.

The vast majority of children with differentiated thyroid cancer are able to lead healthy lives. As with any cancer, psychosocial and behavioral health support should be considered for the patient and family. Any cancer, even cancers that are treatable, can be associated with post-traumatic stress disorder. Regular follow up with a primary care pediatrician and eventual transition to an adult endocrinologist is extremely important.



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