Thyroid Cancer in Children

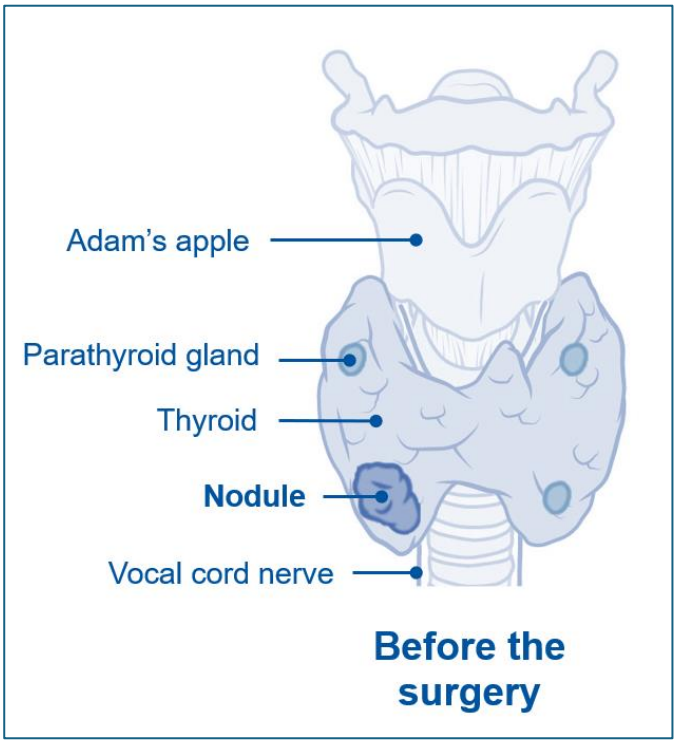
INTRODUCTION

A lump (nodule) has been discovered in your child's thyroid that is strongly suspected to be malignant or has already been confirmed as thyroid cancer. This leaflet is about thyroid cancer in children and its treatment. Every child is unique, which means that the treatment or care pathway may differ from what is described in this leaflet. Please read the information at your own pace, and if you have any questions or unclear points, discuss them with the treatment team.

Disclaimer: This leaflet is a general information guide, written from a Dutch hospital according to European guidelines. Certain procedures or practices may differ locally in other countries or hospitals. The leaflet is written in the 'you' form and is aimed at the patient, but it can also be read by family members, caregivers, and other loved ones involved in the child's care, or by anyone who wants to learn more about thyroid cancer and its treatment in children. No rights can be derived from the information provided in this leaflet.

WHAT IS THYROID CANCER?

The thyroid is a butterfly-shaped organ located at the front of the neck. The thyroid produces hormones that play an important role in metabolism, brain development, and growth in height. A lump (nodule) in the thyroid can arise due to uncontrolled division of thyroid cells or fluid buildup (cyst). The cells of a thyroid nodule may be benign or malignant. If a thyroid nodule is malignant, it is called thyroid cancer. Another term for thyroid cancer is thyroid carcinoma. Thyroid cancer in childhood is rare. The majority of these children are teenagers at the time of diagnosis.



The cause of thyroid cancer is usually unknown, although in some forms a hereditary predisposition plays a role. Radiation to the neck in the past increases the risk of developing thyroid cancer.

TYPES OF THYROID CANCER

In childhood, two different types of thyroid cancer can occur:

- Differentiated thyroid cancer
- Medullary thyroid cancer

The tissue of the thyroid gland is made up of a kind of small sacs: follicles. The follicles contain follicular cells that produce thyroid hormone. Between the follicles lie the C-cells. These produce the hormone calcitonin. In this leaflet, we focus on thyroid cancer that arises from the follicular cells: differentiated thyroid cancer. There are two types of differentiated thyroid cancer: the papillary and the follicular form. The papillary type is the most common, occurring in about 90% of cases. Medullary thyroid cancer originates in the C-cells of the thyroid and is very rare in childhood. It follows a different course and requires a different treatment than differentiated thyroid cancer.

SYMPTOMS

Differentiated thyroid cancer usually presents itself as a swelling or lump in the neck without other symptoms. Sometimes it presents with complaints such as pain in the neck, difficulty swallowing, difficulty breathing, or hoarseness of the voice. Occasionally, the lump is discovered incidentally during another examination and cannot be felt from the outside. Thyroid cancer can also present through one or more enlarged lymph nodes in the neck that feel firm, increase slowly in size, and do not go away. The amount of thyroid hormone produced is almost always normal in cases of thyroid cancer. Therefore, there are usually no symptoms of an excess or shortage of thyroid hormone.

HOW IS THYROID CANCER DIAGNOSED?

The examination of a thyroid nodule almost always consists of blood tests, an ultrasound of the thyroid, and a fine needle aspiration. Sometimes, a special thyroid scan is also performed.

Blood Tests

The thyroid produces various hormones that can be measured in the blood. With a nodule in the thyroid, these hormone levels may be elevated, decreased, or normal. Depending on the blood test results, a further plan is developed.

Ultrasound

An ultrasound is an examination performed in the radiology department. The procedure takes place while lying down on an examination table. A clear gel is applied to the neck, and the radiologist then moves an ultrasound probe over the area. The thyroid can then be seen on the screen as black-and-white images. The ultrasound is used to examine the exact appearance of the thyroid nodule, to take measurements, and to look at all the lymph nodes in the neck. You do not need to be fasting for the ultrasound. The procedure is not painful and takes about 30 minutes.

Fine needle aspiration of the thyroid

To determine whether a thyroid nodule is benign or malignant, a needle biopsy may be necessary. This is called a fine needle aspiration or biopsy. Using ultrasound guidance, the radiologist locates the thyroid nodule and inserts a thin needle to collect cells for examination. Cells are aspirated from the nodule with the needle. It is not always possible to collect enough cells in a single attempt, so sometimes another aspiration is needed. During the procedure, your child will need to lie very still. A local anaesthetic cream is usually applied to reduce discomfort, making the procedure generally tolerable. In children who are very anxious about needles, the biopsy can sometimes be performed under general anaesthesia.

Note: Procedures may differ slightly depending on the hospital or country. Your doctor or care team will explain exactly how it will be done for your child.

The cells collected during the aspiration are examined by a pathologist under the microscope.

After about seven to ten days, your treating physician will provide the results. There are three possible outcomes:

1. Only healthy thyroid cells without abnormalities are found (benign nodule);
2. Cells are found that are (very likely) malignant (thyroid cancer);
3. The result is uncertain.

Unfortunately, the result of the aspiration is not always clear, and an uncertain outcome occurs regularly. If the result is uncertain, or if too few cells were collected to allow proper evaluation, the aspiration will be repeated at a later time. In some cases, thyroid surgery is needed to obtain more clarity.

TREATMENT OF THYROID CANCER

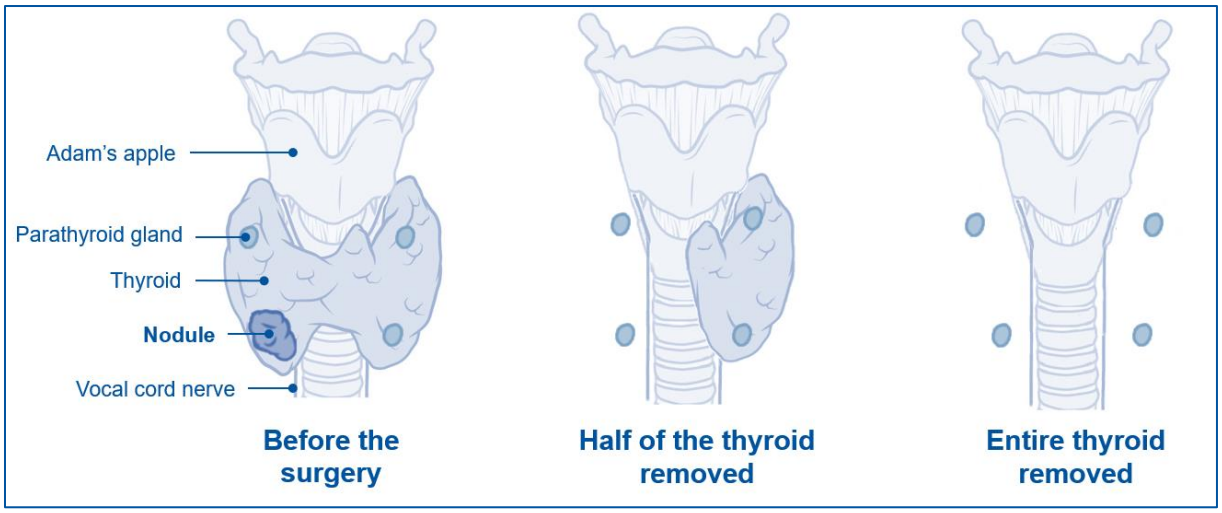
Differentiated thyroid cancer can be treated effectively with surgery, usually followed by treatment with radioactive iodine. In most cases, the thyroid is completely removed during the operation, after which lifelong treatment with thyroid hormone is necessary. With this treatment, the prognosis for children is very good. There are special treatment protocols for children because differentiated thyroid cancer behaves differently in children compared to adults. At the time of diagnosis, thyroid cancer has already spread (metastasized) to the lymph nodes in the neck in 40–60% of children, and in about 10–15% of those children, the cancer has also spread to other parts of the body (most commonly to the lungs or liver). Even when thyroid cancer has spread, the prognosis is still very good. This is because differentiated thyroid cancer in children grows slowly and is very sensitive to treatment with radioactive iodine. Because the disease can recur, regular follow-up is necessary after treatment. Chemotherapy is not part of the treatment for differentiated thyroid cancer.

SURGERY

The most common thyroid surgeries are:

- Hemithyroidectomy: half of the thyroid is removed.
- Total thyroidectomy: the entire thyroid is removed.
- Neck dissection: the lymph nodes in the neck that (are suspected to) contain metastases, as well as surrounding lymph nodes, are removed.

The surgeon will provide detailed information about the surgery and the possible complications during the outpatient consultation. If only the thyroid is operated on, a horizontal scar is made in the neck, about two to three centimeters above the breastbone. In most cases, this scar heals nicely and becomes barely visible in a natural skin fold of the neck. If a neck dissection has to be performed, the scar might be extended on one or both sides. To prevent too much fluid or blood from accumulating, a drain may be left in the wound. After a hemithyroidectomy, the hospital stay usually lasts one to two days. After a total thyroidectomy or a neck dissection, discharge is generally possible after two to four days.



POSSIBLE COMPLICATIONS OF SURGERY

No surgery is without risks. The possible complications and the likelihood of them occurring depend on the extent and course of the surgery. The more complex the operation, the greater the risk of damage to the structures located close to the thyroid (such as the vocal cord nerves and the parathyroid glands).

The most common complications are:

- Damage to the vocal cord nerve (recurrent laryngeal nerve), which may result in a hoarse and weaker voice. Fortunately, damage to this nerve is rare, and in most cases recovery occurs within three months after the surgery. In rare cases, hoarseness persists. In such cases, you will be referred to an ENT specialist and a speech therapist. With the help of the speech therapist, speech can be improved, although shouting or speaking loudly may no longer be possible.
- Damage to the parathyroid glands. The parathyroid glands lie adjacent to the thyroid. During the surgery, the parathyroid glands may be damaged. These glands regulate the calcium levels in the blood. When there is hypoparathyroidism (a low level of parathyroid hormone), a calcium deficiency can occur in the blood. This can lead to tingling (in the hands, feet, and around the mouth) and muscle cramps. To prevent low calcium levels, every child undergoing thyroid surgery receives extra vitamin D beforehand. After every thyroid surgery, calcium levels are closely monitored through blood tests every few hours immediately after the procedure. If the calcium level is low after surgery, there is a good chance that the function of the parathyroid glands will recover spontaneously within a few days to months after the surgery. If this does not

happen, lifelong treatment with active vitamin D (and often also calcium tablets) is necessary.

- After every surgery, there is a small chance of postoperative bleeding. In thyroid surgery, postoperative bleeding is very rare, but if it does occur, a second surgery is often required quickly to stop the bleeding.
- A numb sensation in the skin near the scar may occur, especially after a neck dissection. Over time, at least partial sensation usually returns.
- Several important nerves run through the neck, including the nerve that controls shoulder movement (accessory nerve). During a neck dissection, these nerves may be closely involved with tumor tissue and can be damaged or bruised during surgery. After the surgery, you may experience tingling in the arm, a dull aching pain in the shoulder, and reduced strength in the shoulder muscles. These symptoms often improve over time.
- After a total thyroidectomy, the body no longer produces thyroid hormone, leading to a thyroid hormone deficiency. Therefore, it is necessary to take thyroid hormone tablets daily for the rest of your life. Regular blood tests are required to ensure the dosage is appropriate. After a hemithyroidectomy (removal of half the thyroid), the chance of developing a thyroid hormone deficiency is approximately 30%.

RADIOACTIVE IODINE (I-131)

After the surgery of the thyroid (total thyroidectomy), most cases are followed by additional treatment with radioactive iodine (I-131). This is necessary because, even after removing the thyroid, a small amount of (microscopic) thyroid tissue or cancer may still remain in the neck. The treatment with radioactive iodine ensures that this remaining tissue is also removed. Thyroid cells (both benign and malignant) absorb iodine. The radioactive iodine will therefore be taken up by any remaining thyroid cells (both benign and malignant), and in doing so, these cells are irradiated and destroyed from the inside out. This form of radiation primarily targets thyroid cells and does not significantly affect other tissues. However, small amounts may be taken up by other iodine-avid tissues, such as the salivary glands, which can potentially cause mild side effects, like a dry mouth.

The radioactive iodine is taken by swallowing a capsule containing the iodine. The dose administered varies and depends on the age, weight, and extent of the disease at diagnosis. Temporary hospital admission (five to seven days) is necessary because, during the first few

days, the level of radiation released by the body may be harmful to others. Once the radiation levels have decreased sufficiently, you may leave the hospital.

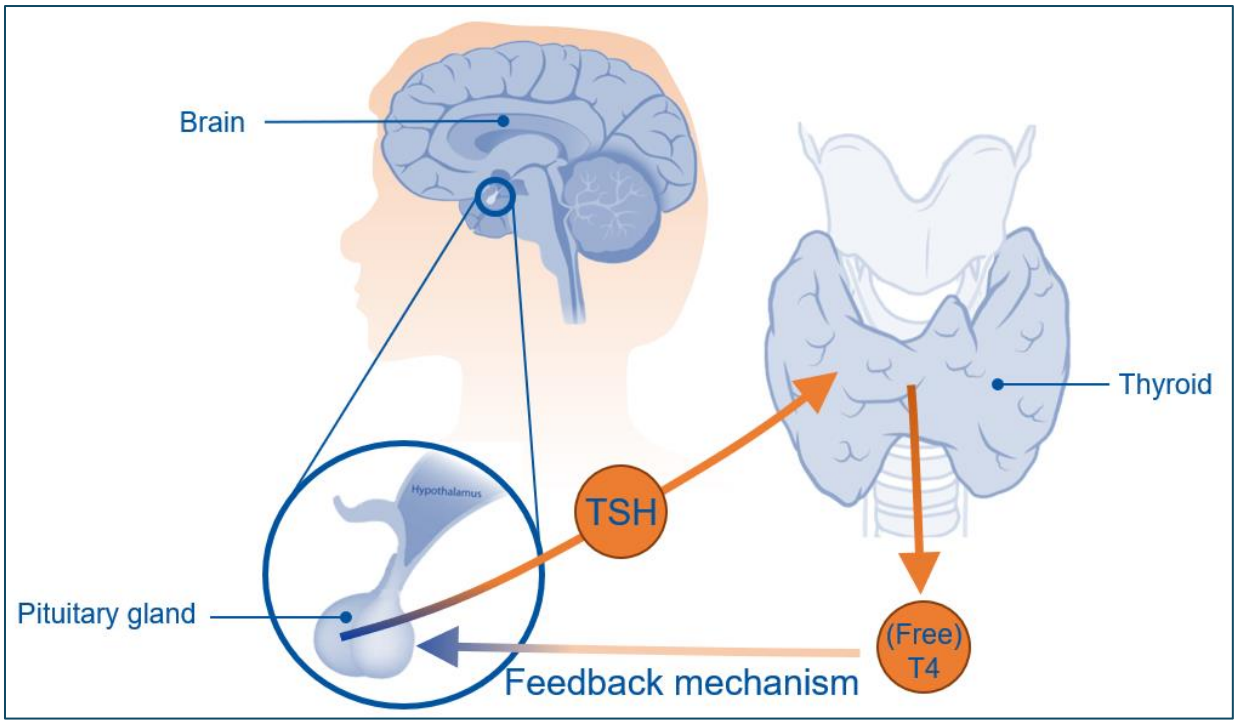
In the first weeks after the treatment, it is important to follow certain precautions (living guidelines) to minimize the exposure of household members to the residual radioactive radiation. Detailed information about the preparation, admission, treatment, and safety measures will be provided by the nuclear medicine specialist.

SCAN

Approximately one week after the treatment with radioactive iodine, a scan of the body and the neck is performed at the department of nuclear medicine. With this scan, we can see where in the body the radioactive iodine has been taken up. During the scan, you will lie on a table that slowly moves through a scanning device. The camera takes images of the entire body; in many cases, the camera will also rotate around you. This examination takes between 30 and 90 minutes.

TREATMENT WITH THYROID HORMONE

If the thyroid gland is completely removed during surgery (total thyroidectomy), you no longer produce thyroid hormone yourself. That is why from that moment on you receive thyroid hormone in tablet form. Treatment starts the day after the surgery or the day after administration of the radioactive iodine, and you must take it for life. The amount of thyroid hormone you need depends, among other things, on your weight and is monitored through blood tests. In the first year after the surgery, you receive a relatively high dose of thyroid hormone. This is necessary to suppress the levels of TSH (Thyroid Stimulating Hormone). This is called TSH suppression. TSH is produced by the pituitary gland, a small gland in the brain that stimulates the thyroid gland to release thyroid hormone (T4). Because of this stimulating effect, TSH can be a potential growth factor for any remaining thyroid (cancer) cells. After one year, TSH usually no longer needs to be suppressed, and the thyroid hormone dose will be adjusted accordingly.



FOLLOW-UP

After the surgery (and treatment with radioactive iodine), you will remain under follow-up care for at least 10 years with the pediatric endocrinologist or, after the age of 18, with the internal medicine endocrinologist. In the first year, check-ups take place every three months. If the disease does not return, the frequency of follow-up visits can be reduced to every six months or once a year.

OUTPATIENT FOLLOW-UP AFTER HEMITHYROIDECTOMY

The follow-up consists of two parts:

1. Monitoring thyroid function

In most cases, thyroid function remains normal after the removal of one half of the thyroid. This is checked after the surgery. In about 30% of children, however, the remaining half does not produce enough thyroid hormone (T4), leading to a condition we call hypothyroidism. This is well treatable with thyroid hormone replacement therapy in tablet form. It is important to treat hypothyroidism, as untreated it can lead to symptoms such as fatigue, sensitivity to cold, constipation, weight gain, and sad feelings, and because having enough thyroid hormone is essential for normal growth and development.

2. Neck ultrasound

At least once a year, we check whether the thyroid cancer has returned. This is done through an ultrasound of the neck. The radiologist uses the ultrasound to examine the area where half of the thyroid was removed, the remaining part of the thyroid, and all lymph nodes in the neck. If any suspicious findings are detected, a needle biopsy will be performed. If the disease has not returned after five years, the likelihood of recurrence becomes very low. In such cases, further follow-up may no longer be necessary. If you had a hemithyroidectomy because it was unclear whether the thyroid nodule was malignant, and it later turned out to be benign, then no further ultrasound examinations are required after the surgery.

OUTPATIENT FOLLOW-UP AFTER TOTAL THYROIDECTOMY (AND TREATMENT WITH RADIOACTIVE IODINE)

The follow-up consists of three parts:

1. Monitoring thyroid function

Blood tests are used to measure the levels of TSH and T4 (thyroid hormone). Based on these values, we can ensure the correct dosage of the replacement hormone. These check-ups will take place every 3 months during the first year, after which they may be extended to (semi-)annual check-ups.

2. Monitoring the tumor marker (thyroglobulin)

The protein thyroglobulin, which is produced by thyroid (cancer) cells, is used as a marker for the presence of thyroid cancer cells (i.e., a tumor marker) after surgery to remove the thyroid gland. Thyroglobulin can be measured in the blood. Depending on the levels, your doctor can provide more information about the presence of thyroid cancer cells. In general, the lower the value, the fewer thyroid cells are present. During the first three years of follow-up, thyroglobulin is monitored every six months; after that, it will be checked annually.

3. Ultrasound of the neck

In addition to measuring thyroglobulin, an ultrasound of the neck may occasionally be performed to check whether the thyroid cancer has returned. The radiologist examines the area where the thyroid was removed and all lymph nodes in the neck. If thyroglobulin is no longer detectable in the blood, the risk of recurrence is very low. In that case, annual ultrasound examinations are often no longer necessary.

ABNORMAL ULTRASOUND FINDINGS AND/OR DETECTABLE THYROGLOBULIN

If the ultrasound shows abnormalities and/or the thyroglobulin level rises or remains detectable, there are several options. The best course of action will be discussed in a multidisciplinary team meeting with various specialists. It is possible that a watchful waiting approach with strict monitoring will be taken, that a new surgery may be needed, and/or that a new treatment with radioactive iodine will be required. The treating physician will ultimately discuss the recommended course of action with you and your parents

PROGNOSIS

In general, the prognosis for children with differentiated thyroid cancer is very good (20- to 30-year survival rate is >98%). Even if the disease has spread to the lymph nodes in the neck or to other parts of the body, it can still be effectively treated with radioactive iodine. For some children, repeated surgery or multiple treatments with radioactive iodine are necessary to completely eliminate the disease. Among children who have been fully cured, there is a 20-30% risk of the disease returning, sometimes even years after the initial treatment. Recurrences can also be treated successfully. Because of the risk of recurrence, long-term follow-up with the pediatric endocrinologist and, after the age of 18, with the internal medicine - endocrinologist is necessary.