THYROID DISEASE

A Patient's Guide

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1.

A note from Dr. Van Lier Ribbink

The following information has been written for the patient with thyroid disease. I have attempted to provide a general overview of thyroid anatomy, function, disease and it's treatment. A description of what the patient should expect regarding thyroid surgery is provided. Finally, a list of suggested questions the patient should ask their surgeon is given.

Thank you.

J. Van Lier Ribbink, M.D., F.A.C.S.

2.

<u>What is the anatomy of the thyroid gland?</u>

The normal adult thyroid gland is located in the anterior (front part) neck and weighs about 17 grams. It is soft and dark wine-red in color. It consists of a right thyroid lobe, left thyroid lobe, and thyroid isthmus. The right and left lobes are connected to each other by the thyroid isthmus.

The right and left thyroid lobes lie next to the trachea (windpipe) and esophagus (food pipe). The thyroid isthmus lies anterior (in front of) to the trachea. These relationships to the trachea and esophagus explain why masses in the thyroid gland can compress the trachea and esophagus thereby causing trouble breathing, coughing, and trouble swallowing.

The right and left recurrent laryngeal nerves (RLN) course from inferior to superior along the posterior surfaces of the right and left thyroid lobes to enter the lower part of the larynx (voice box). Masses in the thyroid gland can press on these nerves and sometimes can invade them. Since these nerves innervate the vocal cords, this can cause weakness or paralysis of the vocal cords resulting in hoarseness and difficulties with aspiration and cough.

The external branches of the superior laryngeal nerves (EBSLN) also innervate muscles associated with the vocal cords. These nerves course from superior to inferior along with the superior thyroid vessels towards the superior thyroid poles. Generally before reaching the thyroid gland, the nerves course medially (inward) to innervate the muscles associated with the vocal cords. The anatomy of the EBSLN's is quite variable, and therefore the surgeon should be quite careful to be sure to identify these nerves. If they are injured, then the patient will have a problem with the pitch of their voice and difficulties with the strength of the voice.

Adjacent to the posterior aspect of the right and left superior thyroid lobes are the right superior and left superior parathyroid glands. Next to the anterior-lateral surface of the inferior right and left thyroid lobes are the right inferior and left inferior parathyroid glands. In unusual circumstances, the parathyroid glands can be found in unusual locations relative to abnormal descent during embryologic development in the mother's womb. They might be found near the angle of the mandible, behind the larynx, behind the esophagus, in the carotid sheath that encases the carotid artery and jugular vein and vagus nerve, within the thyroid gland, in the thymus, or even down in the mediastinum (chest). These four parathyroid glands are totally separate both anatomically and by function from the thyroid gland. The parathyroid glands produce parathyroid hormone (PTH) which basically controls the levels of calcium in the body.

Within the neck there are many lymph nodes that receive lymphatic fluid drainage from the thyroid gland. The endocrine surgeon must have an extensive knowledge of these lymph nodes and their drainage patterns. The neck lymph nodes are divided into 11 neck lymph node compartments as follows:

1. Right Level 1
2. Right Level 2
3. Right Level 3
4. Right Level 4
5. Right Level 5
6. Level 6 (Central Neck Compartment)
7. Left Level 1
8. Left Level 2
9. Left Level 3
10. Left Level 4
11. Left Level 5

Often, surgery for thyroid cancer will be accompanied by lymph node dissections of some of these compartments to be sure to remove any areas of lymph nodal metastatic disease. The endocrine surgeon must have extensive experience to have a mastery of the relationship of these various lymph node compartments with vital anatomic structures that run through and in close proximity to them.

As can be appreciated from the above discussion, the neck which contains the thyroid gland contains many vital structures that either reside in the neck, or pass through the neck. The endocrine surgeon who performs thyroid surgery must have the expertise to perform the right operation well while avoiding injury to vital adjacent structures.

3

What Is the Function Of The Thyroid Gland?

The thyroid gland produces two biologically active thyroid hormones, tetraiodothyronine (thyroxine or T4) and triiodothyronine (T3). The synthesis of these hormones depends upon the supply of iodine from the diet.

Iodine is a chemical element that has the symbol I. When freed from its compounds, it never occurs alone, but does form diatomic molecules, I2.

Daily iodine intake varies from less than 10 mcg in areas of extreme deficiency to several hundred milligrams in people receiving medicinal iodine. The average intake in the United States is 150mcg per day. Virtually 100% of ingested iodine in the diet is absorbed from the small intestine into the bloodstream. Most of the ingested iodine is separated from its compounds by digestion within the gastrointestinal tract before its absorption into the bloodstream. The concentration of iodide in the bloodstream is usually less than 10mcg/L.

The thyroid gland follicular cells extract and concentrate iodide from the blood. Through this process, the thyroid gland stores 90% of total body iodine. The protein responsible for this active transport process of iodine from the blood into the follicular thyroid cell is the membrane bound protein, sodium/iodide symporter (NIS). This protein consists of 618 amino acids coded for by a gene on chromosome #19.

Once within the follicular cell, the iodide is oxidized by the enzyme thyroperoxidase (TPO). The TPO then organifies the iodine within the cytoplasm of the follicular cell by binding the oxidized iodine to tyrosine amino acid residues in the thyroglobulin molecule to form monoiodotyrosine (MIT) and diiodotyrosine (DIT). The gene coding for TPO is located on chromosome #2. T3 is formed from the binding of MIT with DIT on the thyroglobulin molecule. T4 is formed from the binding of DIT with DIT on the thyroglobulin molecule in the thyroid follicular cells.

The thyroglobulin protein is produced exclusively by the thyroid gland. It functions primarily as the protein backbone for the synthesis and storage of thyroid hormone within the thyroid gland. It consists of 2,749 amino acids and is coded by a gene on chromosome #8. The thyroglobulin containing MIT, DIT, T3, and T4 is then transported by exostosis from the thyroid follicular cell into the follicle lumen for storage as material called colloid.

The thyroid follicular cell generates free thyroid hormones initially by the process of endocytosis which transfers the thyroglobulin/iodinated tyrosine molecules from the follicular lumen into the follicle cell cytoplasm. Within the follicle cell, the thyroglobulin is hyrolized with complete degradation of the thyroglobulin and the release of free T3 and T4 into the cytoplasm of the cell. The T3 and T4 then exit the thyroid cell into the bloodstream.

The half-life of T4 in the bloodstream is about 7 days and the half-life of T3 is only 8-12 hours.

The thyroid hormones have multiple effects upon body metabolism including:

1. Thyroid hormone is necessary for normal growth and development. It is essential for normal development of the nervous system, brain, and bones.
2. Thyroid hormone regulates the "burning of calories" by controlling oxygen consumption and the basal metabolic rate.
3. Thyroid hormone affects protein, carbohydrate, and fat metabolism.
4. Thyroid hormone affects the heart rate and contractility of the heart.
5. Thyroid hormone affects bone turnover.
6. Thyroid hormone affects red blood cell production.
7. Thyroid hormone affects steroid hormone release.

4.

<u>What is Fine Needle Aspiration Biopsy?</u>

Fine needle aspiration biopsy (FNAB) of the thyroid gland is a diagnostic procedure involving a tiny needle attached to a syringe being passed through the skin of the neck into a lesion in the thyroid gland. This can be performed with or without local anesthesia (numbing medication). Ultrasound guidance should be used to ensure accurate placement of the needle into the lesion. Cells from the lesion are aspirated (sucked) through the needle into the syringe. The cells are then squirted onto slides or into liquid in a specimen jar.

A pathologist examines these cells underneath a microscope and will usually report his findings in one of four different categories:

1. Non-diagnostic
2. Benign
3. Suspicious (indeterminate)
4. Malignant

The non-diagnostic category account for about 15% of all FNAB's performed. A diagnosis cannot be made either due to not enough cells in the sample to look at, due to inadequate preservation of the sample, or due to blood cells in the sample obscuring adequate view of the thyroid lesion cells.

The benign category account for about 70% of FNAB's performed. FNAB from multinodular goiters, benign microfollicular adenomas, and normal thyroid are commonly referred to as colloid nodules on the cytology report, and therefore benign. Hashimoto's thyroiditis, a benign chronic autoimmune inflammatory condition of the thyroid gland, can also be diagnosed by FNAB. Sub acute (granulomatous) thyroiditis is a rare benign condition that can be diagnosed by FNAB.

The suspicious (indeterminate) FNAB cytology category is seen in about 20% of the samples. The most common reading in this group is the follicular lesion. This finding indicates that the nodule has an 80% chance of being benign, and a 20% chance of being malignant.

Finally, the malignant category is seen in about 5% of FNAB samples. Papillary, medullary, anaplastic thyroid carcinomas can be diagnosed in this category. Follicular and Hurthle cell thyroid carcinomas cannot be diagnosed by FNAB.

The false negative rate with FNAB, defined as the percentage of patients with "benign" cytology in whom malignant lesions are later confirmed by surgery is less than 5%.

The false positive rate with FNAB, defined as the percentage of patients with a "malignant" FNAB result having the lesion removed and found to actually be benign, is 3%.

The sensitivity of FNAB is 83%, specificity 92%, predictive value of a positive or suspicious cytologic result is 50%, and the overall accuracy for cytologic diagnosis approaches 95%. Sensitivity is the likelihood that the patient

who has disease has positive test results. The specificity is the percentage of patients without disease having negative test results. The positive predictive value is the percentage of patients who have a positive test who have disease.

FNAB of the thyroid gland is very safe. The procedure is usually associated with little discomfort. Minor bleeding with a small noticeable hematoma is unusual. The FNAB can be done without stopping anticoagulants or aspirin. No severe complications such as tumor seeding in the FNAB needle tract, nerve injury, or major blood vessel bleeding have been reported.

5.

<u>What is Hashimoto's Thyroiditis?</u>

Hashimoto's thyroiditis was first described in four patients in 1912 by Dr. Hakaru Hashimoto. The disease has also been called struma lymphomatosa, chronic thyroiditis, lymphocytic thyroiditis, lymphadenoid goiter, and autoimmune thyroiditis.

Hashimoto's thyroiditis is a disease of the thyroid gland seen 20 times more often in women than in men. It is seen in patients of any age, but most commonly between 30 to 50 years of age. It is the cause of the vast majority of hypothyroidism diagnosed in the USA.

The cause of this disease is an autoimmune process that the body mounts against the thyroid gland. High blood levels of anti-thymoglobulin antibody and anti-TPO antibody are seen in most patients. Other antibodies against the thyroid gland are seen in high levels in the blood also. T and B lymphocytes infiltrate the thyroid gland as part of the autoimmune process. The thyroid follicular cells turn into larger, eosinophilic cells that are known as Hurthle cells that are packed with mitochondria and have high metabolic activity. The thyroid follicular cells are destroyed, and fibrosis can develop in the gland.

The cause of this autoimmune process is still unclear. There does appear to be a genetic inherited component with an association of the HLA-DR3 gene and HLA-DR5 gene with the atrophic and goitrous forms of the disease. Viral infection has been proposed as an inciting event. Smoking, long term iodine exposure, and selenium deficiency have also been associated with an increased risk of the disease.

Usually Hashimoto's thyroiditis is discovered as a goiter (enlarged thyroid gland) in a patient with no symptoms. The patient might complain of a feeling of fullness or vague discomfort in the neck. Usually, the gland will enlarge slowly over years. Occasionally it can enlarge rapidly and be painful, causing compression symptoms of hoarseness, trouble swallowing (dysphasia), or difficulty breathing (dyspnea). Hypothyroidism (low thyroid function) is seen in 20% of patients at the time of diagnosis. The other 80% of patients with normal thyroid function (euthyroid) at diagnosis will develop hypothyroidism at a rate of 5% per year. Mild hyperthyroidism (elevated thyroid function) may be seen at diagnosis in 5% of patients. These patients eventually progress to hypothyroidism. Eventually, thyroid atrophy (reduction in size) may occur.

The thyroid gland usually is non-tender, firm, nodular, and enlarged on exam. Lymph nodes in the neck may also be enlarged.

The diagnosis of Hashimoto's thyroiditis depends on a correlation of symptoms, examination, and primarily laboratory work-up. The levels of antibody against thyroid peroxidase (TPOAb) in the blood is elevated in 90% of patients. Elevated levels of antibody against thyroglobulin are seen in 20 to 50% of

patients. Radioactive iodine uptake (RAIU) is not of much value in the diagnosis since it may be elevated, normal, or low. Nuclear medicine thyroid scanning usually just shows patchy uptake. Ultrasound of the thyroid gland usually shows marked hypoechogenicity. Fine needle aspiration biopsy of the thyroid gland is seldom required to make the diagnosis.

   Many patients require no treatment since they may have no symptoms and the goiter may be small. If the goiter is large, then thyroid hormone treatment is indicated since it often causes significant reduction in the size of the goiter after several months of treatment. Thyroid hormone treatment is also necessary if hypothyroidism is present. Surgery for thyroid resection is indicated when severe symptoms and/or large goiter do not respond to medical therapy.

   The question of whether Hashimoto's thyroiditis is associated with an increased risk of thyroid malignant disease remains controversial. A recent study suggests that patients may be 3 times more likely to develop thyroid cancer. The risk of developing thyroid lymphoma may also be increased.

6.

What is Grave's Disease?

Grave's disease is the most common cause of hyperthyroidism. It is also the most common autoimmune disorder in the United States.

The hyperthyroidism is caused by thyroid-stimulating antibodies which bind to and activate the receptors for thyroid stimulating hormone on the membranes of thyroid follicular cells. This stimulates the production of cyclic adenosine monophosphate (cAMP), which stimulates the production of thyroid hormone. Inflammatory cells infiltrate the thyroid gland and produce inflammatory mediators that stimulate the production of stimulating antibodies to the TSH receptors, again causing increased production of cAMP and thyroid hormone. These mediators bind to other thyroid follicular cell membrane receptors causing further increased inflammatory mediator production and increased production of thyroid stimulating antibodies.

The thyroid stimulating antibodies also cause hypertrophy (enlargement) and hyperplasia (multiplication) of thyroid follicular cells leading to the thyroid goiter (enlargement of thyroid gland).

Grave's disease is a multisystem disease. The most common symptom is thyroid goiter. Seventy-five to ninety percent of patients develop this. The goiter is usually symmetrical, smooth, firm, and rubbery. The gland can be normal in size however, especially in patients over 50 years of age.

The most common symptoms present in more than 50% of patents are nervousness, fatigue, irritability, palpitations, rapid heartbeat, heat intolerance, tremor, weight loss, and decreased menstrual periods in women.

Less commonly, patients may present with myxedema where the skin is warm and moist, with a silky texture. Patients might have graying of hair, thinning of hair, or alopecia (hair loss). Vitiligo (uneven patches of skin lacking color with colorful borders) or onycholysis (separation of the nail from its bed) can develop.

Ophthalmopathy (eye changes) occur in 50% of Grave's disease patients. Seventy-five percent of these patients develop these changes within one year before or after the diagnosis of Grave's disease is made. The cause of these changes is an inflammatory infiltrate composed mostly of activated T-lymphocytes within the connective tissues and muscles that surround the eye. These lymphocytes produce cytokines which stimulate the production of glycosaminoglycans causing further edema and fibrosis. These changes displace the eyeball forward due to increase tissue volume within the orbit and may interfere with eye muscle function. As a result, patients may have photophobia (sensitivity to light), eye irritation, diplopia (double vision), and change in visual acuity. Patients may have eye lid retraction, eyelid lag, or periorbital edema. Proptosis (exopthalmos) occurs in up to 33% of patients. Eyelid erthema (redness), conjunctival injection (redness), and eyelid swelling may occur.

Dermopathy (skin changes) occur in 1-2% of Grave's patients, and almost always in the presence of Grave's ophthalmopathy. This is most frequent over the anterolateral aspects of the shin, but can occur in other sites. The pretibial myxedema over the shin consists of scaly, thickened, indurated skin usually with an orange peel texture.

The current treatment options for Grave's disease include antithyroid drugs, radioactive iodine treatment, and thyroid resection surgery.

The antithyroid medication treatment involves methimizol or propylthiouracil (PTU). Both inhibit the enzyme within the thyroid follicular cell, thyroid peroxidase (TPO). This results in inhibition of thyroid hormone synthesis. PTU also blocks the extrthyroidal conversion of T4 to T3. This may allow for a more rapid resolution of hyperthyroid symptoms as compared to methimizol.

The antithyroid medications can generally be given as a titration regimen or block-replace regimen. With the titration regimen, the dosage is decreased as euthyroidism (normal thyroid function) is achieved. Prolonging this treatment beyond 18 months offers no benefit to the patient. The block-replace regimen involves a high daily dose of drug together with thyroxine. Treatment for more than 6 months with this regimen offers no benefit for the patient.

With anti-thyroid drug therapy, the patient will usually develop the euthyroid state within 6-12 weeks after starting treatment. The recurrence rate of Grave's disease is 60% after completion of a 6 month treatment course with remission. The recurrence rate is 40% after completion of a 2 year treatment course with remission.

The adverse effects of the anti-thyroid drugs are as follows:

1. Fifteen to 30% of patients develop skin rash, arthralgias (joint aches), fever, and urticaria within the first several weeks of treatment.
2. Fifteen to 30% develop elevated abnormal levels of transaminases (liver enzymes) in the blood within the first two months of treatment.
3. Fifteen percent of patients develop hypo-thyroidism.
4. 0.2 to 0.5% develop agranulocytosis (decreased type of white blood cell) within the first 3 months of treatment.
5. Rarely develop fulmanent hepatitis, acute liver necrosis, ANLA-mediated vasculitis, glomerulonephritis, and lupus-like syndrome.

Patients that are unlikely to have permanent remissions with anti-thyroid drug therapy and are therefore generally not offered this option include young patients, and those with large goiters, ophthalmopathy, or high blood levels of thyrotropin-receptor antibody at the time of diagnosis. Anti-thyroid treatment with the intent to cure is indicated with better results in patients with the following features:

1. Small (less than 40mg) non-toxic (mild symptoms) goiter.
2. Mildly elevated thyroid hormone levels
3. Those who exhibit rapid remission with reduction in gland size.

Radioactive iodine therapy involves the oral ingestion of iodine-131 (I-131) which is selectively taken up by the thyroid gland and destroys the thyroid follicular cells. The dosage of I-131 given varies among endocrinologists treating this disease. The dosages given have been categorized as low, medium, or high dose therapy. It generally takes 2 to 6 months following treatment for the hyperthyroidism to convert gradually to the euthyroid (normal thyroid function) state.

High dose therapy with I-131 in the range of 16mCi per gram of estimated thyroid weight results in a very high percentage of patients being converted to the euthyroid state. However, the development of hypothyroidism is quite high, reaching 20 to 40% the first year after treatment, and increases at a rate of about 2.5% per year, so that by 10 years 50 to 80% of patients have hypothyroidism which needs to be treated with lifelong daily thyroid hormone replacement.

Low dose treatment with I-131 results in after one year following treatments 60% of patients being converted to the euthyroid state, 30% remaining hyperthyroid and only 10% of patients being hypothyroid. At 10 years following treatment only 40% are euthyroid, and 60% are hypothyroid. About 25% of patients require a second treatment, and 5% require a third treatment.

The moderated dose treatment program involves a dosage of about 9mCi per gram of thyroid weight. The success rate of conversion to the euthyroid state is higher, and therefore the need for repeat treatments is lower. However, as expected, the ultimate development of hypothyroidism is higher.

I-131 treatment obviously does expose the patient to radiation. There does not however, appear to be an associated increased significant risk of developing thyroid cancer, leukemia, or other cancers in adults. Children are not generally candidates for I-131 treatment for Grave's disease due to evidence that in the age group I-131 does increase the risk of the development of thyroid cancer. There is no evidence for an increased risk of birth defects in the children of patients treated with I-131.

Patients should not be treated with I-131 if they are pregnant. The fetus which has increased sensitivity to radiation is exposed to significant radiation from I-131 in the mother's system and from migration of I-131 through the placenta. Also, after the twelfth week of pregnancy, the thyroid of the fetus takes up the I-131 and the fetal thyroid gland may be destroyed. Women treated with I-131, should avoid pregnancy for at least 6 months since it usually takes that long to be sure that re-treatment will not be needed.

Recent studies have indicated that no patients with Grave's ophthalmopathy treated with I-131 have subsequent improvement in the eye disease. Among those patients with Grave's disease treated with I-131, 15% developed ophthalmopathy or had subsequent worsening ophthalmopathy 2-6 months after treatment. If prednisone (steroids) is added to the I-131 treatment, then 67% of patients with ophthalmopathy will have improvement, and no patients have progression. Steroids of course have their own side effects.

The following are general contraindications to I-131 treatment for Grave's disease:

1. Pregnancy
2. Lactation
3. Children
4. Possible Malignant thyroid tumor
5. Very large thyroid glands
6. Ophthalmopathy

Surgery for Grave's disease involves thyroidectomy. The extent of thyroidectomy ranges from subtotal thyroidectomy, to near total, to total thyroidectomy.

A subtotal thyroidectomy (STT) for Grave's disease involves leaving a thyroid remnant 4 grams in size. This is thought to result in an 8% rate of persistent or recurrent hyperthyroidism. Up to 20% of patients develop recurrence after STT during long term follow up, likely related to a thyroid remnant more than 4 grams in size left behind. The majority of patients who proceed with surgery have either rejected or have contraindications to antithyroid medications or I-131 treatment. Recurrence after STT forces the patient back to previously declined treatment modalities or to re-operation that carries increased risk of complications. Post operative hypothyroidism after STT ranges from 4 to 75% depending on how much thyroid tissue remains.

In the surgical treatment of Grave's disease, total thyroidectomy has gained favor. IT basically results in a 0% risk of recurrence of hyperthyroidism. All patients become hypothyroid, and are treated with thyroid hormone replacement. Seventy-two % of patients with ophthalmopathy have improvement in their eye disease following TT.

The risks of thyroid resection are injury to the recurrent laryngeal nerves causing hoarseness and of injury to the four parathyroid glands causing permanent hypocalcemia. The risks of these complications should be less than 1% in the hands of an experienced thyroid surgeon.

The surgical treatment option is indicated in patients with coexisting thyroid malignancy, pregnancy, patients who are breast feeding, very large thyroid goiter, children, severe ophthalmopathy, those patients who have failed antithyroid treatment and I-131 treatment, those patients who want to get pregnant within one year, and those patients who want to avoid the radiation exposure with I-131.

7

What is thyroid cancer?

The main types of thyroid cancer are:

1. Papillary thyroid cancer (PTC)

2. Follicular thyroid cancer (FTC)

3. Hurthle cell thyroid cancer (HTC)

4. Medullary thyroid cancer (MTC)

5. Anaplastic thyroid cancer (ATC)

6. Primary lymphoma of thyroid gland

7. Metastatic cancer to thyroid gland

These cancers usually are caused by spontaneous mutations in the DNA of a thyroid cell which leads to it being unable to control its growth and multiplication, thereby forming a malignant tumor. Less commonly some of these cancers can be hereditary in origin. The metastatic cancers to the thyroid gland are primary cancers of other organs that spread to the thyroid to form tumors there.

These cancers pose a threat to the patient by growing locally in the neck to invade adjacent structures, and by metastasizing (spreading) to other sites.

The treatment of these various types of cancers varies and often requires physicians from multiple different specialties taking part in the care of the patient.

8

What is Papillary Thyroid Cancer?

Papillary thyroid cancer (PTC) is most commonly seen in patients in their 20's and 30's. It is seen 3 times more frequently in women than in men. It is the most frequent thyroid cancer, accounting for 60-75% of all thyroid cancers.

PTC can be diagnosed by fine needle aspiration biopsy. Once diagnosed, the patient should undergo preoperative staging with ultrasound of the neck lymph nodes, levels I-VI in the right, left and central neck. IF, there are abnormal lymph nodes seen, then these should undergo ultrasound guided FNAB to see if they are involved with metastatic disease.

The treatment of PTC is surgery. This involves removal of half of the thyroid gland called thyroid lobectomy, or removal of the entire gland, called total throidectomy. The amount of thyroid removed depends upon the size of the cancer, the number, and distribution of thyroid cancers within the gland, the presence of extension of tumor outside of the gland, the presence, or absence of lymph nodal involvement, the presence of distant metastatic disease, and upon prognostic risk factors.

The same above factors will determine whether or not a Level VI central neck lymph node dissection will be performed. Also, if a preoperative ultrasound guided FNAB of a level VI lymph node shows metastasis to that lymph node, or if these lymph nodes are found to have cancer at the time of surgery, then the Level VI dissection will be performed.

A lateral neck lymph node dissection is performed if ultrasound guided FNAB reveals metastic disease to those lymph nodes (Levels II-V).

If PTC metastasizes (spreads), it usually spreads to lymph nodes in the neck and mediastinum (chest). More rarely it can spread to lungs and bone, in addition to other organs.

Depending upon the stage of disease and other prognostic factors, the patient with papillary thyroid cancer might be treated with I-131 thyroid remnant ablative therapy. This involves taking Iodine-131 tablets orally usually 6 weeks following surgery. The Iodine-131 is selectively taken up by any residual normal thyroid cells and papillary thyroid cancer cells and destroys them. Ten days later, a whole body Iodine-131 nuclear medicine scan is performed to detect any residual activity from thyroid cells.

The patient subsequently is followed long term with regular physician evaluations, routine laboratory evaluation, serial blood thyroglobulin levels, possible nuclear medicine Iodine-131 whole body scans, and possible ultrasound of neck lymph nodes.

Papillary thyroid cancer is generally not treated with chemotherapy or external beam radiation therapy. These modes of treatment are offered to patients with locally advanced papillary thyroid cancer in the neck not amenable to surgical removal and for some patients with distant metastatic disease.

Generally speaking, the overall prognosis in patients with papillary thyroid cancer is very good. However, this cancer can recur, can metastasize, and can take patients' lives.

What is Follicular Thyroid Cancer?

Follicular thyroid cancer (FTC) is the second most common thyroid cancer accounting for about 15% of all thyroid cancers. Women are 2.5 times more likely to develop FTC than men. The median age at diagnosis is 48 years in women and 53 years in men.

Most FTC's are sporadic (not inherited). They appear to be caused by mutations is the DNA of a thyroid follicular cell. This causes the cell to lose the ability to regulate its growth and multiplication, thereby forming the cancerous tumor.

Rarely, FTC may be inherited (familial syndrome). IT is seen with increased frequency in Cowden Syndrome. This is associated with hamartomas, and other tumors of the breast, colon, endometrium, and brain. Carney Complex is a genetic syndrome associated with myxomas of soft tissues, and skin. Mucosal pigmentation, schwannomas, and tumors of the adrenal glands, pituitary, and testicles are also seen. The incidence of FTC is increased in this syndrome.

A benign follicular adendoma cannot be distinguished from FTC by fine needle aspiration biopsy cytology evaluation alone. FTC is defined as having capsular and or lumphovascular invasion. Therefore, the only way to determine if a nodule is a FTC, is to remove it surgically. In this fashion the pathologist can look at the entire nodule to see if the above features are present.

There are two main types of FTC. The minimally invasive type has microscopic capsular invasion and perhaps blood vessel invasion. Invasive FTC has more extensive invasion of the nodule capsule into the surrounding thyroid tissue.

Minimally invasive FTC less than 4.0 cm in size can potentially be treated with thyroid lobectomy (removing one half of the thyroid gland) with a following excellent prognosis. Invasive FTC usually must be treated with total thyroidectomy (removal of the entire thyroid gland).

Following surgery, the patient may be treated with long term thyroid hormone replacement therapy (THRT) to treat post thyroidectomy hypothyroidism and to suppress TSH production by the pituitary gland which could otherwise stimulate growth of any other remaining thyroid cancer cells. The risks of THRT and thyroid hormone suppressive therapy (THST) are related to bone loss and heart rhythm problems. These side effects are small.

Patients may also be treated with I-131 thyroid remnant ablative therapy 6 weeks following surgery. This involves taking oral I-131 tablets. The radioactive iodine is taken up by any residual benign or malignant thyroid tissue in the neck and taken up by distant metastatic malignant FTC and destroys it. This treatment also improves the ability to follow the patient in the future with thyroglobulin tumor marker monitoring and/or whole body scanning (WBS) with I-131 for recurrence of the FTC.

The I-131 therapy is generally well tolerated. Acute side effects include sialadenitis (inflammation and tenderness in salivary glands), xerostomia (dry mouth), loss of taste, and lacrimal duct stenosis (narrowing of tear duct). Chronic side effects associated with large cumulative doses of I-131 include damage to salivary glands, gonads, bone marrow, lungs, and rarely secondary malignancies including leukemia, bladder cancer, and others.

There are numerous staging systems for FTC. The two most commonly used are the TNM (tumor-node-metastasis) system from the American Joint Committee on Cancer (AJCC) and MACIS (metastasis, age, completeness of resection, invasion, and size) system from the Mayo Clinic, Rochester, Mn. These systems allow physicians to predict overall prognosis following surgery, and help guide choices of treatment and follow up.

While most patients with FTC have an excellent prognosis, the cancer can recur. Up to 25% of patients with FTC develop distant metastasis, usually by a hematogenous (via blood stream) route to bone, lungs, brain, and liver. This spread to distant sites is the usual cause of death from FTC.

Chemotherapy and radiation therapy is rarely used in the treatment of FTC, and are used to treat markedly advanced local or distant metastatic disease.

Novel targeted therapies against molecular pathways in the development of FTC are the focus of much research regarding compounds such as axitinib, sorafenib, depsipeptide, 17-AAG, and PS-341.