

Hyperparathyroidism

Questions and Answers

To the Patient and Family

This booklet is for individuals who have received a diagnosis of hyperparathyroidism or those being tested for this illness.

If you have questions that are not answered in this booklet, please ask a member of your healthcare team or visit mdanderson.org and search under hyperparathyroidism.

For your own record-keeping purposes, always ask your doctor for copies of your pathology reports, operative notes, and laboratory evaluations.

Words that may be new to you appear in *italics*. You can find the meanings of these terms in the glossary.

What are the parathyroid glands, and what do they do?

Parathyroid glands are pea-sized glands that are located near each corner of the thyroid gland (Figure 1). Most people have four parathyroid glands, but sometimes a person is missing a gland or has an extra gland. Sometimes parathyroid glands are located inside the *thyroid gland*, *thymus gland*, *mediastinum*, or other places. These misplaced glands can still work normally.

Even though parathyroid glands are near the thyroid gland, their function is unrelated to the thyroid gland. Parathyroid glands produce a substance called “parathyroid hormone” (also known as “PTH”). This hormone controls the levels of calcium and phosphorous in the blood. This hormone also helps the body make vitamin D and helps prevent loss of too much calcium in the urine.

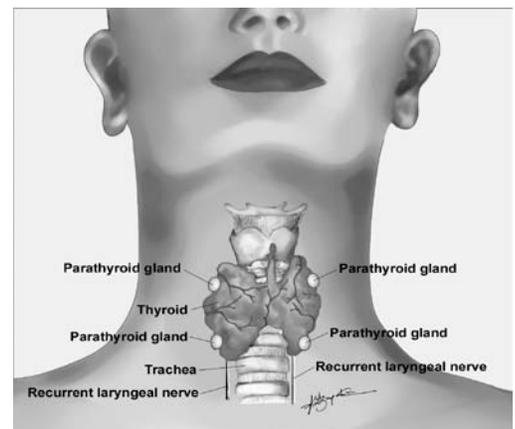


Figure 1: Thyroid and parathyroid glands in the neck

What is hyperparathyroidism (HPT)?

Hyperparathyroidism (abbreviated as "HPT") occurs when one or more parathyroid glands enlarge and produce too much parathyroid hormone. The extra amount of parathyroid hormone tricks the body into thinking that the level of calcium in the blood is too low. As a result, calcium moves into the bloodstream from places in the body where it is normally stored, namely the bones. This movement of calcium into the bloodstream has several undesirable consequences. First, the level of calcium in the bloodstream will become too high, causing a condition known as "hypercalcemia." Second, over time too much borrowed calcium from bones can cause weakness and thinning of the bones (a condition called "osteoporosis"). Osteoporosis may even cause bones to break. Among many other consequences, excess calcium can form stones in the kidneys.

Approximately 90 percent of patients, HPT, a single, benign (non-cancerous) tumor called an "adenoma" in one of the four parathyroid glands are the cause. Occasionally patients with HPT have parathyroid hyperplasia - a condition involving enlargement of more than one parathyroid gland. Some patients with parathyroid hyperplasia have a hereditary (*genetic*) form of HPT, such as multiple endocrine neoplasia.

What are the symptoms of HPT?

Patients with HPT may have kidney stones, bone loss, and/or digestive complaints. Mild symptoms of HPT may include:

- Problems with sleeping
- Difficulty concentrating
- Low energy
- Feeling tired (fatigue)
- Loss of appetite
- Muscle weakness
- Bone or joint pain
- Constipation
- Anxiety

Untreated HPT may cause nausea, vomiting, and abdominal pain as well as more serious problems such as osteoporosis, bone fractures, memory loss, and depression.

Almost 75 to 80 percent of patients with HPT have no obvious symptoms or will not realize that their mild symptoms are actually caused by HPT. This is because the mild symptoms of HPT are similar to symptoms of other common conditions such as menopause, mid-life crisis, stress, depression, and even early dementia.

What causes HPT?

The cause of HPT in most people who have a single adenoma is unknown. HPT is more common

in women and older people. About one out of every 1,000 people 60 years and older will have HPT. The risk of HPT may be higher in people who take certain medications such as thiazide diuretics and lithium. Previous radiation exposure to the neck (radiotherapy) is another risk factor for the development of parathyroid adenomas. A deficiency of Vitamin D can also cause a false picture of HPT and is usually corrected prior to further diagnosis.

HPT is the result of a hereditary condition in about five to 10 percent of cases. The risk of a hereditary condition is higher for people with parathyroid hyperplasia and/or recurrent problems with HPT.

Hereditary conditions that cause HPT and/or hypercalcemia include:

- Multiple endocrine neoplasia syndromes (MEN1, MEN2A)
- Familial isolated HPT
- HPT-jaw tumor syndrome
- Familial hypocalciuric hypercalcemia (FHH)

It is important for patients to tell their doctors about any family history of HPT or other tumors, especially tumors of the jaw, thyroid, pancreas, pituitary, or adrenal glands, which can occur more often in people with some of these hereditary conditions.

How is HPT diagnosed?

HPT is usually diagnosed by a blood test that measures an elevated level of calcium in the blood. Sometimes HPT is discovered unexpectedly during routine checkups when a blood test reveals high calcium levels. Patients may be surprised to find they have HPT, especially if they feel well.

An additional blood test to measure the level of parathyroid hormone ("intact PTH assay") will be needed to make sure the patient has HPT, because this is only one cause of a high calcium level in the blood. Other tests will likely include:

- A 24-hour urine collection to measure the amount of calcium in the urine.
- DEXA Scan.
- A bone density test to detect early bone loss. This test, which should include an examination of the spine, hip, and forearm, is recommended for all patients with HPT.

What is a sestamibi scan?

Once it is certain that a patient has HPT, one or more imaging tests may be done to identify how many tumors are present and where they are located. The best test for this is the sestamibi scan.

In this scan, a radioactive agent called "technetium sestamibi" is given through an IV (through a vein), which is absorbed by abnormal parathyroid glands.

Here are two examples of sestamibi images of a patient with a parathyroid adenoma. The image in Figure 2 was obtained right after the sestamibi was administered, and the image in Figure 3 was obtained about two hours later. In the image in Figure 2, both the healthy thyroid gland and the adenoma within the parathyroid gland have absorbed the sestamibi. In the image in Figure 3, however, the sestamibi has “washed out” of the thyroid gland, but it can still be seen inside the adenoma. Images such as these can help the surgeon determine the exact location of a parathyroid adenoma.

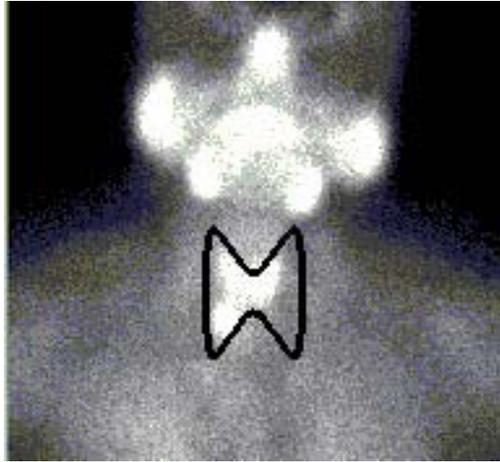


Figure 2: Sestamibi scan obtained right after the administration of the sestamibi agent. The image shows a diffuse bright spot throughout much of the thyroid gland (see butterfly-shaped area).



Figure 3: Sestamibi scan obtained two hours after the administration of the sestamibi agent. The image shows a single intense spot typically seen when there is a single parathyroid adenoma.

A sestamibi scan is usually done along with an ultrasound study, but both tests may fail to identify a parathyroid adenoma in 10 to 20 percent of patients. Therefore, other tests sometimes need to be done. Additional tests may include *magnetic resonance imaging (MRI)*, *computerized tomography (CT scan)*, and *venous sampling*.

On occasion, the CT scan can be combined with the sestamibi scan in order to evaluate the location of the parathyroid adenoma(s) and the surround anatomical structures.

How is HPT treated?

A surgical procedure called “parathyroidectomy” is currently the only way to cure HPT, although surgery may not be necessary for patients who have a mild form of the disease. Occasionally, mild cases of HPT cause only a small rise in the calcium level in the blood, no kidney or bone problems, and no symptoms. Because the disease can worsen over time in the remaining 25 percent of patients, all patients with mild disease still need to see their doctors periodically.

Surgical Guidelines

Patients with HPT should have surgery when they have:

- Pancreatitis caused by hypercalcemia
- Kidney stones
- Evidence of bone disease (osteoporosis or recent fractures)
- Severe hypercalcemia
- A calcium level in the blood that is more than one mg/dL above the normal level
- A calcium level in urine that is more than 400 mg/day
- Significant kidney dysfunction
- Young age (less than 50 years)

Although the doctor will use these guidelines to plan the best treatment for a patient, both the patient and doctor should be comfortable with the final treatment decision.

Abnormal parathyroid glands are surgically removed in a procedure called “parathyroidectomy.” There are two ways to perform a parathyroidectomy: the conventional technique and a minimally invasive technique.

The method and difficulty of surgery are determined by two factors:

- Whether the patient is having parathyroid surgery for the first time or having repeat surgery.
- Whether the doctors can determine the exact location of the abnormal parathyroid gland(s) before surgery using a sestamibi scan or other imaging test.
- If more the single gland disease is suspected.

What does surgery of the parathyroid glands involve?

Patients traveling to Houston from out of town should plan to stay in Houston for at least two to three days. At the outpatient office visit before surgery, patients are told how to prepare for the surgery. Patients also meet with a member of the anesthesia team and have blood and imaging tests. Most of the time, patients are admitted to the hospital on the day of surgery and may stay in the hospital anywhere from several hours to one day, depending on the type of surgery performed.

When patients are discharged after surgery, they are given pain medication. Patients will return to see the surgeon one to two weeks later for a checkup. At that visit, patients are given a copy of the surgical and pathology reports.

Conventional Parathyroidectomy

In a conventional parathyroidectomy, patients are given *general anesthesia*. The surgeon examines all four parathyroid glands during surgery. Rarely, the abnormal gland(s) cannot be

found and more extensive surgical exploration is needed. For example, the abnormal gland may be located inside the thyroid gland, thymus gland, or upper mediastinum (the front part of the chest). When this happens, part of the thyroid or thymus may be removed or the upper mediastinum may need to be explored.

The location and length of the incision depend on several factors – the natural creases in the skin,

the location of any prior incisions, the size of the tumor(s), and the surgeon's preference. If both sides of the neck have to be explored, the incision may be as long as two to four inches, as shown in Figure 4. The surgeon will give the patient a more specific description of the incision they are likely to have. The incision is closed with stitches that often dissolve on their own. The incision is covered with "steri-strips" that can become wet during bathing, but patients should let them fall off on their own (usually in five to seven days). Patients who have more extensive surgery may need to have a small drain (tube) placed near the incision to collect fluid from the surgery site.

Right after surgery, patients are carefully watched in a recovery room until they are fully alert. Patients are then moved to a hospital room for the rest of their hospital stay, which is usually one night. If a drain is used, it is usually removed before the patient leaves the hospital, but sometimes it is removed during a follow-up visit.



Figure 4: Typical incisions for parathyroidectomy (solid line: conventional, dashed line: minimally invasive surgery)

Minimally Invasive Parathyroidectomy

When the location of the abnormal parathyroid gland(s) is known ahead of time, the surgeon may be able to use a minimally invasive approach during surgery. This involves the removal of the abnormal parathyroid gland(s) without examining the other glands. The benefits of this approach may include a shorter hospital stay (generally four hours or less) and sometimes a smaller incision (Figure 4).

In addition, patients who have the minimally invasive form of parathyroidectomy are usually given general anesthesia, but may be given either *local anesthesia*. If local anesthesia is used, medication is given to patients through an IV to make them sleepy but not completely asleep. Local anesthesia may allow patients to recover and become alert more quickly after surgery. In addition, patients who have local anesthesia may have fewer side effects such as nausea and vomiting, which can sometimes occur after general anesthesia.

In about five percent of cases, the abnormal parathyroid gland is not easily found during minimally invasive surgery. If this happens, the surgeon may need to switch the patient to general anesthesia so that other parts of the neck can be explored.

After surgery, patients are closely watched for about three to four hours before they are released from the hospital. Complications are rare, but they can include nausea, vomiting, pain, swelling, or bleeding. If any one of these complications occurs, the patient will be admitted to the hospital for overnight observation. Patients are allowed to bathe the day after surgery, and the incision can get wet. As with the conventional method, stitches will dissolve on their own, and "steri-

strips" are used to protect the incision as it heals.

Quick PTH Assay

The quick PTH assay is a blood test that is done during both conventional and minimally invasive parathyroid surgery. This test rapidly measures the level of parathyroid hormone before the abnormal parathyroid is removed and five to 10 minutes after the abnormal parathyroid gland(s) is removed. If the parathyroid hormone level drops by at least 50 percent after removal of the abnormal parathyroid gland(s), the surgeon can be confident that the other parathyroid glands are normal and do not need to be surgically examined. This allows the operation to be less extensive.

Parathyroid Autografting

Sometimes the blood flow to one or more of the healthy parathyroid glands is affected during neck surgery. If this happens, the healthy parathyroid gland is carefully preserved when possible and placed in the neck or forearm muscle in a procedure called "parathyroid autografting" or "parathyroid autotransplantation." This is done because it is important to preserve the parathyroid glands to maintain a normal level of calcium in the blood and prevent hypoparathyroidism – a condition in which the level of parathyroid hormone is too low.

Sometimes patients may need to take calcium and/or vitamin D pills for a short time after surgery and only occasionally for a longer time. Rarely, lifelong calcium replacement is required in addition to the regular supplements that are recommended for all normal adults, especially post-menopausal women. In patients who have bone loss, the need for calcium after surgery is more likely due to "bone hunger" (See page 9, "hungry bone syndrome").

Thyroid Lobectomy

If an abnormal parathyroid gland is located inside the thyroid gland, one of the thyroid lobes (right or left) may have to be removed in a procedure called a "thyroid lobectomy." Patients are usually given general anesthesia if a thyroid lobectomy is required.

What are the complications of parathyroid surgery?

Rare complications of parathyroid gland surgery include:

- Nausea and/or vomiting
- Pain
- Swelling of the neck
- Infection
- Bleeding
- Hoarseness caused by damage to one or both of the recurrent laryngeal nerves, which control the vocal cords (Figure 1)
- Hypocalcemia (low calcium levels), which may be temporary or permanent

The exact risk of complications depends on several factors, including the extent and severity of disease, the type of parathyroid surgery performed, and the number of surgeries, if any, the patient has had in the past. In addition, surgeons and hospitals performing a large volume of

endocrine surgery (for example, M. D. Anderson Cancer Center) tend to have lower rates of complications.

Will surgery cure my HPT?

Parathyroidectomy cures HPT 95 percent of the time. Failure to cure the condition may be related to an unidentified parathyroid tumor outside of the neck, an unidentified tumor in more than one parathyroid gland, or the formation of another parathyroid tumor long after the first operation.

What are the possible long-term benefits of parathyroid surgery?

- Less bone pain and joint ache
- For patients with kidney stones, prevention of forming new stones and damage in the kidneys
- For patients with reduced bone density, major improvements can be seen over a period of one to four years

Are there any alternative non-surgical treatments for HPT?

Parathyroidectomy is the only treatment that will cure HPT. If patients have other health problems, they may not be able to have a parathyroidectomy and may want to consider non-surgical treatments. Patients who do not have a parathyroidectomy should see their physicians periodically so that their blood calcium levels and bone density can be checked.

Non-surgical treatments for HPT include:

- Following drug therapy as prescribed by the doctor
- Drinking plenty of water to avoid dehydration
- Avoiding prolonged bed rest
- Avoiding long-term use of medications that may increase the calcium level in blood (for example, lithium and thiazide diuretics)

These safety precautions will help keep the hypercalcemia from getting worse. Despite having hypercalcemia, patients should still take an adequate amount (approximately 1,200 mg/day) of calcium in their diet. This is because a very low calcium diet can cause bone disease associated with HPT to worsen.

Estrogens (female hormones) and bisphosphonates are some of the drugs that are used to treat HPT. These drugs may lower the level of calcium in blood and slow the amount of bone loss. Researchers have also recently discovered a group of drugs called “calcimimetics” that can directly stop the production of parathyroid hormone. One such drug, Cinacalcet, has recently become available for the treatment of HPT in patients with kidney failure and parathyroid carcinoma. It may also be used in the future to treat patients with HPT who are not cured by surgery or who cannot have surgery.

Can I live without my parathyroid gland(s)?

Yes. Many people who have had one or more of their parathyroid glands removed live completely normal lives. Patients should, however, have the levels of parathyroid hormone and calcium in their blood checked periodically. Most patients can expect to live a long and healthy life without some or even all of their parathyroid glands, as long as they follow medical advice and take the appropriate medication.

More Information on Related Diseases

What is hypoparathyroidism?

Hypoparathyroidism occurs when the level of parathyroid hormone and calcium in the blood are below normal. This condition is usually caused by neck surgery or damage to one or more parathyroid glands. Symptoms of hypocalcemia include numbness, tingling, and muscle cramps or spasms. Cramps and spasms are more common when patients have had most or all of their parathyroid glands removed or their parathyroid glands damaged. To help prevent hypoparathyroidism as a complication of neck surgery, surgeons often also perform a parathyroid autografting procedure. (See Parathyroid Autografting on page 10.)

Hypoparathyroidism is usually temporary and easily treated by taking calcium and vitamin D pills for a short time after surgery. Rarely hypoparathyroidism is permanent, and when this happens, patients must take calcium and vitamin D pills for the rest of their lives.

Sometimes, hypocalcemia may occur after parathyroidectomy in patients with severe HPT as the bones try to heal themselves. This cause of hypocalcemia is due to a condition called "hungry bone syndrome". Hungry bone syndrome is usually temporary and is treated the same way as hypoparathyroidism due to other causes.

What is parathyroid cancer?

Cells are the body's basic unit of life. Normally they grow, divide, and are replaced by new, healthy cells in an orderly, controlled fashion. Cancer occurs when cells grow out of control. The

resulting growth forms a mass, which may also be called a "tumor," "lesion," or "nodule." These growths can be benign (non-cancerous) or malignant (cancerous). Benign tumors do not spread to other parts of the body. Malignant tumors can spread (*metastasize*) to other parts of the body. This can cause more serious health problems.

Cancer of the parathyroid glands is extremely rare. Less than one percent of all patients with HPT have cancer of one of the parathyroid glands. Symptoms of parathyroid cancer may include a lump in the neck, difficulty speaking or swallowing, muscle weakness, and the sudden development of a very high blood calcium level.

Glossary

Computerized Tomography (CT) Scan - A CT scan is an imaging test that uses x-rays and computers to show internal organs in detail. It can show the complete shape and

inside of organs.

Familial hypocalciuric hypercalcemia (FHH) - FHH may be confused with HPT because the parathyroid hormone level, although often within the normal range, is inappropriately high for the level of calcium in the blood. FHH can usually be distinguished from HPT by a low calcium level in urine collected over a 24-hour period. Patients with FHH have no symptoms of hypercalcemia, and parathyroid surgery is not recommended.

General Anesthesia - Anesthesia means “without feeling” and refers to the use of drugs that block pain during surgery. All patients who have surgery receive some type of anesthesia. The drugs used in anesthesia are called “anesthetics”; they work by blocking pain messages that go to the nervous system. General anesthesia affects the entire body and puts patients to sleep. It is given before surgery so that the patient’s muscles relax and the body loses all feeling and sense of movement. The patient’s heartbeat, breathing, and other body functions are carefully monitored during general anesthesia. As general anesthesia wears off after surgery, the patient slowly wakes up.

Genetics - This term refers to information located in individual messages called “genes,” which instruct the body how to look and function. Genes are located in all of the cells in our bodies and are inherited from our parents and passed onto our children. Sometimes misspellings called “mutations” occur in a gene. When a mutation causes a health problem, the resulting condition is considered “genetic” or “hereditary.” Not all mutations result in health problems, however.

Local Anesthesia - In local anesthesia, the skin is numbed with a local anesthetic like Xylocaine or Novocain. The patient remains awake during the procedure but does not feel any pain. After the surgery, the medication wears off and full feeling comes back to the area.

Magnetic Resonance Imaging (MRI) - An MRI is an imaging test that uses magnetic fields and radio (sound) waves to create pictures of internal organs. MRI is similar to CT.

Mediastinum - The mediastinum is the middle of the chest cavity. The anterior mediastinum is located directly below the sternum (breast bone) and in front of the heart. Parathyroid glands can occasionally be found here and may require a surgical procedure called “mediastinal exploration.” This type of surgery can require partial or complete opening of the sternum.

Metastasize - This is the spread of malignant cancer from the first (primary) tumor to a second cancer site or multiple cancer sites. Cancer cells usually spread through the bloodstream or lymphatic system away from the original site of cancer. Parathyroid cancer is extremely rare.

Thymus Gland - The thymus gland, which is located in the chest behind the sternum, has a role in the immune system. The thymus gland is largest during childhood and normally shrinks after puberty when it is no longer needed. When extra parathyroid glands are present, they may be located inside the thymus gland. If an abnormal parathyroid gland is found there, the thymus is usually removed in a procedure called “thymectomy.”

Thyroid Gland - The thyroid gland is a butterfly-shaped gland that wraps around the front of the trachea (windpipe) just below the Adam's apple in the neck (Figure 1). The thyroid gland helps control the body's metabolism and other functions important to keeping a person healthy. Sometimes the abnormal parathyroid gland(s) are located inside the thyroid gland. If this happens, part of the thyroid gland may have to be removed in a surgical procedure called "thyroid lobectomy."

Ultrasound - Also called a "sonogram." This is an imaging test in which sound waves are used to create a picture of internal organs. The scanner has a device called a "transducer" that sends out sound waves and receives the echoes as they bounce off structures inside the body. These echoes create electronic pictures on a small television screen.

Venous Sampling (with possible arteriography) - This is an invasive imaging test that is used only when abnormal parathyroid glands cannot be found using non-invasive methods. A catheter (tube) is placed through the femoral vein in the upper leg or groin area and threaded into the patient's neck. Using the catheter, blood samples are then obtained from specific locations in the body. These blood samples are used to check parathyroid hormone levels. A very high level in a certain place can indicate the location of the abnormal parathyroid gland. Injection of a small amount of dye into specific blood vessels can also help identify the location of the parathyroid gland. This procedure is rarely used at MD Anderson Cancer Center.