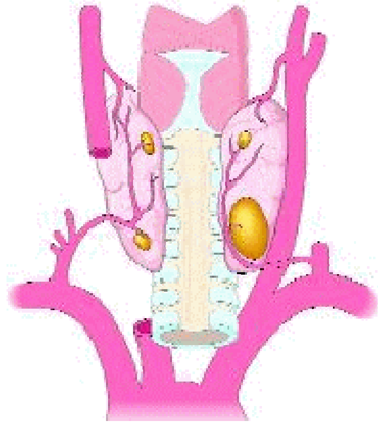
Your Parathyroid



Parathyroid glands are small glands of the endocrine system which are located behind the thyroid. There are four parathyroid glands which are normally about the size and shape of a grain of rice. They are shown in this picture as the **mustard yellow** glands behind the pink thyroid gland. This is their normal color. The sole purpose of the parathyroid glands are to regulate the **calcium** level in our bodies within a very narrow range so that the nervous and muscular systems can function properly. Although they are neighbors and both part of the endocrine system, the thyroid and parathyroid glands are otherwise **unrelated.** The single major disease of parathyroid glands is overactivity of one or more of the parathyroids which make too much parathyroid hormone causing a potentially serious calcium imbalance. This is called hyperparathyroidism.

Parathyroid Function
Normal and Abnormal

The sole purpose of the parathyroid glands is to control calcium within the blood in a very tight range between 8.5 and 10.5. In doing so, parathyroid glands also control how much calcium is in the bones, and therefore, how strong and dense the bones are. Although the parathyroid glands are intimately related to the thyroid gland anatomically, they have no related function. **The thyroid gland regulates the body's metabolism and has no effect on calcium levels while parathyroid glands regulate calcium levels and have no effect on metabolism.** Calcium is the primary element which causes muscles to contract. Calcium levels are also very important to the normal conduction of electrical currents along nerves. Knowing these two major functions of calcium helps explain why people can get a tingling sensation in their fingers or cramps in the muscles of their hands when calcium levels drop below 8.5 (like immediately after a successful parathyroid operation). Likewise, too high a calcium level can cause a person to feel run down, cause them to sleep poorly, make them more irritable than usual, and even cause a decrease in memory. **Even though half of patients with this hyperparathyroidism (Parathyroid**

Disease) will state that they feel just fine, after a successful parathyroid operation more than 85 percent of these patients will claim to "feel much better"! Some say its like "someone turned the lights on".

NORMAL PARATHYROID ACTIVITY

Although the four parathyroid glands are quite small, they are very vascular. This suits them well since they are required to monitor the calcium level in the blood 24 hours a day. As the blood filters through the parathyroid glands, they detect the amount of calcium present in the blood and react by making more or less parathyroid hormone (PTH). When the calcium level in the blood is too **low**, the cells of the parathyroids sense it and make **more** parathyroid hormone. Once the parathyroid hormone is released into the blood, it circulates to act in a number of places to increase the amount of calcium in the blood (like removing calcium from bones). When the calcium level in the blood is too **high**, the cells of the parathyroids make **less** parathyroid hormone (or stop making it altogether), thereby, allowing calcium levels to decrease. This feed-back mechanism runs constantly, thereby maintaining calcium (and parathyroid hormone) in a very narrow "normal" range.

HOW DOES PARATHYROID HORMONE INCREASE BLOOD CALCIUM ?

Like all endocrine glands, parathyroids make a hormone (a small protein capable of causing distant cells in the body to react in a specific manner). Parathyroid hormone (PTH) has a very powerful influence on the cells of the bones which causes them to release their calcium into the bloodstream. Calcium is the main structural component of bones which give them their rigidity. Under the presence of parathyroid hormone, bones will give up their calcium in an attempt to increase the blood level of calcium. Under normal conditions, this process is very highly tuned and the amount of calcium in our bones remains at a normal high level. Under the presence of too much parathyroid hormone, however, the bones will continue to release their calcium into the blood at a rate which is too high resulting in bones which have too little calcium. This condition is called osteopenia and osteoporosis and is illustrated in the bone segment on the top which has larger "pores" and less bone mass. When bones are exposed to high levels of parathyroid hormone for several years they become brittle and much more prone to fractures. Another way in the parathyroid hormone acts to increase blood levels of calcium is through its influence on the intestines. Under the presence of parathyroid hormone the lining of the intestine becomes more efficient at absorbing calcium normally found in our diet.

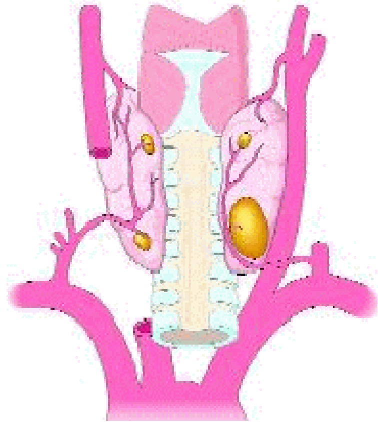
Hyperparathyroidism

Over-activity of the parathyroid glands

This parathyroid page was updated January 16, 2005.

The primary disease of parathyroid glands is overactivity...too much parathyroid hormone is produced. This is called hyperparathyroidism. Under this condition of hyperparathyroidism, one or more of the parathyroid glands behaves inappropriately by making excess hormone regardless of the level of calcium. In other words, the parathyroid glands continue to make large amounts of parathyroid hormone even when the calcium level is normal and they should not be making hormone at all. Remember as you read these pages, its a hormone problem, not a cancer problem. We'll say it again--Hyperparathyroidism is a parathyroid hormone problem, NOT a parathyroid cancer problem! HOWEVER, over-production of parathyroid hormone by over-active parathyroid glands (hyperparathyroidism) can rob you of your health, making you feel run down and tired, causing osteoporosis and many other serious problems. KEEP READING--Hyperparathyroidism can be fixed with new mini-surgery techniques in most people in under 20 minutes! (often--under 15 minutes!).

WHAT CAUSES EXCESS HORMONE PRODUCTION?



The most common cause of excess hormone production is the development of a benign tumor in one of the parathyroid glands. This enlargement of one parathyroid gland is called a parathyroid **adenoma** which accounts for 96 percent of all patients with primary hyperparathyroidism (see chart below). This situation is illustrated here: one of the parathyroid glands has developed a tumor which is secreting all the hormone...the other three glands are small and responding appropriately to the high calcium by becoming dormant (the parathyroids are yellow and are situated behind the larger thyroid lobes shown in light pink). This out of control parathyroid gland is essentially never cancerous (less than one in 2500), however, it slowly causes damage to the body because it induces an abnormally high level of calcium in the blood which can slowly destroy a number of tissues. Parathyroid adenomas typically are much bigger than the normal pea-sized parathyroid (shown to scale) and will frequently be about the size of a walnut.

Approximately 3 or 4 percent of all patients with primary hyperparathyroidism will have an enlargement of all four parathyroid glands, a term called parathyroid **hyperplasia.** In this instance, all of the parathyroid glands become enlarged and produce too much parathyroid hormone. This is a much less common scenario but the end results on the tissues of the body are identical. An even rarer situation occurs in less than 1% of the people who have two parathyroid adenomas while having two normal glands. This is a very uncommon situation and can make the diagnosis and treatment of this disease a bit tricky. This is why you have to choose your parathyroid surgeon very wisely. You should NEVER let a surgeon operate on you that does not do at least one parathyroid operation per month. Ideally, (and this is very important), you should not let a surgeon operate on your parathyroid glands if they do not do one parathyroid operation per week. The location of the parathyroid glands can be extremely variable and to make matters worse, every patient has a different problem. Do you want to be your surgeon's first case of strange parathyroid anatomy? Its not like gallbladder surgery where every person's gallbladder is in the exact same place. Please, choose your surgeon wisely!

HOW MANY OF MY PARATHYROIDS ARE BAD ???

A recently conducted a scientific study of 6331 patients with primary hyperparathyroidism examined their final diagnosis to determine how many glands typically go bad in this disease. This study includes data collected on a portion of patients with this disease for the past 10 years (1987 - 1997). The complete data and statistical analysis was published in March, 1998 by Dr. Norman's group in the *Journal of the American College of Surgeons*. The results are as follows:

- 95.5 % = one enlarged, overactive gland (termed a single adenoma)
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- 0.5 % = two or three large glands (termed multiple adenomas)...(many think this group is over-reported)
- <1 % = cancer of the parathyroid (EXTREMELY uncommon!!)

Some experts believe the incidence of multi-gland disease (hyperplasia and multiple adenomas) is slightly over reported. This data is obtained from surgical specimens from patients who have undergone a full neck exploration and had all of the glands biopsied. Therefore the data is based on a microscopic examination and not on whether any hormone is produced or not. We simply do not know if these other glands would be clinically active (produce hormone). The only way to know this answer is to remove only one gland while leaving the others untouched and then following these patients for a number of years. A number of groups are in the process of doing this now. The bottom line... somewhere between 94 and 96 % of all patients with hyperparathyroidism have 1 bad gland and 3 normal glands.

SYMPTOMS OF HYPERPARATHYROIDISM. Smart Info!

Since hyperparathyroidism was first described in 1925, the symptoms have become known as "moans, groans, stones, and bones". Although most people with primary hyperparathyroidism claim to feel well when the diagnosis is made, the majority of these will actually say they feel better after the problem has been cured. This can only be known retrospectively when patients are allowed to comment on how they feel several months after the operation. Many patients who thought they were asymptomatic preoperatively will claim to sleep better at night, be less irritable, and find that they remember things much easier than they could when their calcium levels were high (**nervous system problems**). In some studies, as many as 92% of patients claim to feel better after removal of a diseased parathyroid gland, even when only 75% claim they felt "bad" before the operation. Patients with persistently elevated calcium levels due to overproduction of parathyroid hormone also can have complaints of bone pain. In the severe form, bones can give up so much of their calcium that the bones become brittle and break (**osteoporosis** and **osteopenia**). This problem is even more of a concern in older patients. Bones can also have small hemorrhages within their center which will cause bone pain.

Smart Info!

Other symptoms of hyperparathyroidism are the development of gastric ulcers and pancreatitis. High levels of calcium in the blood can be dangerous to a number of cells including the lining of the stomach and the pancreas causing both of these organs to become inflamed and painful (**ulcers** and **acute pancreatitis**). Another common presentation for persistently elevated calcium levels is the development of **kidney stones**. Since the major function of the kidney is to filter and clean the blood, they will be constantly exposed to high levels of calcium in patients with hyperparathyroidism. The constant filtering of large amounts of calcium will cause the collection of calcium within the renal tubules leading to kidney stones. In extreme cases the entire kidney can become calcified and even take on the characteristics of bone because of deposition of so much calcium within the tissues. Not only is this painful because of the presence of kidney stones, in severe cases it can cause kidney failure.

POTENTIAL DANGERS OF HYPERPARATHYROIDISM

- **Severe osteoporosis and osteopenia**
- **Bone fractures**
- **Kidney stones**
- **Peptic ulcers**
- **Pancreatitis**
- **Nervous system complaints**

The incidence of these problems depends primarily on the duration of the disease and its severity. ***Everybody* will lose bone density, which is progressive.** Pancreatitis and

ulcers are much more rare. Even though the majority of patients claim they feel "just fine" when this disease is diagnosed, all most 80 percent of them claim to feel better (sleep better, etc) three months after the problem has been fixed. DO NOT elect to undergo surgery (or decide not to do so) based upon how you feel. Remember, the typical patient has had this disease for several years before it was ever found...because it does its bad things so silently. The good news is that it can be cured with a routine operation which caries a success rate of about 95% and a complication rate of around 1% or less. Some centers are even performing minimal surgery for this disease which can be accomplished under local anesthesia.

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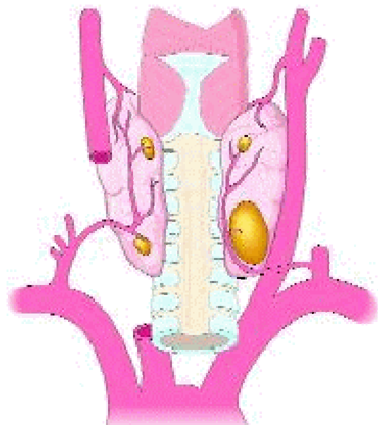

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Hyperparathyroidism
Diagnosis and Treatment

Since parathyroids are glands of the endocrine system, we can detect disease in these glands by measuring the appropriateness of their hormone production.

Under normal conditions, a normal calcium level will be associated with a normal parathyroid hormone level. Also under normal conditions, a low serum calcium level will be associated with a high parathyroid hormone level; and a high calcium level will be associated a with low parathyroid hormone level. These are all appropriate ways in which a parathyroid gland will react to calcium which is circulating in the blood as the parathyroid glands attempt to regulate calcium in the narrow "normal" range. A better explanation of the normal function of parathyroid glands is covered in more detail on our "function" page.

Hyperparathyroidism is relatively easy to detect because the parathyroid glands will be making an inappropriately large amount of parathyroid hormone in the face of an elevated serum calcium. This is straightforward and simple to measure. Another way to confirm this diagnosis is by measuring the amount of calcium in the urine over a 24-hour period of time. If the kidneys are functioning normally they will filter much of this calcium in an attempt to rid the body of calcium leading to an and an abnormally large amount of calcium in the urine. Measuring calcium in the urine, however, is an indirect measure of parathyroid activity and is only accurate in about 25 to 40 percent of the time. The most accurate and definitive way to diagnose primary hyperparathyroidism is by showing an elevated parathyroid hormone level in the face of an elevated serum calcium.

TREATMENT OPTIONS FOR PRIMARY HYPERPARATHYROIDISM

The only two choices available for patients with primary hyperparathyroidism are to do nothing, or to have surgical removal of the diseased parathyroid gland (or infrequently, more than one diseased parathyroid gland). Some physicians will elect to not refer their patients for an operation if they have a mild form of primary hyperparathyroidism. Much of this management style stems from the fact that ***standard*** parathyroid surgery in the past required the use of general anesthesia and was a major operation. THIS IS NOT GOOD ADVICE! Parathyroid disease will ALWAYS get worse. It will NEVER go away on its own. Remember, it is caused by a tumor that has developed from one of the parathyroid glands. Waiting will just allow the parathyroid tumor to grow bigger. It will NEVER get better on its own. It will NEVER stay the same.

The standard "Old Fashioned" operation that is still performed by nearly all general surgeons and ENT surgeons can be dangerous, thus everywhere you read you will see people advise you to "pick an expert surgeon". This is because the old fashioned operation requires that the surgeon dissect all the structures in your neck to "find" the bad parathyroid gland. All of this dissection increases the chances of bleeding and requires general anesthesia and a large incision. An inexperienced surgeon also has a much lower rate of finding the tumor... Most importantly, however, is that this big operation performed by an inexperienced general surgeon has a risk of injury to the voice box nerve of about 2-5%. Sounds like a pretty low risk??? Well, if the nerve to your voice box is injured, then you will likely never be able to talk again. Trust us, this will ruin your life! Furthermore, if this surgeon is inexperienced and he/she operates on both sides of your neck and injures the voice box nerve on BOTH sides, then you will require a tracheostomy just to be able to breathe, and of course, you can't talk! YES, we are referred patients to our clinic about every 4 DAYS that cannot talk, and a patient that has a tracheostomy comes seeking our help about every 3-4 WEEKS. Finally, AT LEAST ONCE PER DAY we get a referral for a patient that is not cured, thus needing a second operation, after an inexperienced general surgeon or ENT surgeon operated on them.

HOWEVER, if you find an expert surgeon, then these operations are not nearly as "involved" as they once were. An expert parathyroid surgeon (one that performs at least 100 of these operations per year) will have a MUCH lower rate of complication and will usually cure you. Some new techniques of ***radioguided parathyroidectomy*** (the MIRP operation) is DRAMATICALLY better than the old operation. The MIRP operation typically takes less than 20 minutes and you can go home in an hour!

Smart Info!

HOW CAN YOU TELL IF YOUR SURGEON IS AN EXPERT AT PARATHYROID SURGERY?

Simple, ask these questions to tell if your surgeon is an expert and is up with the latest and greatest available to you in 2005. Listen to their answers... they should be clear and concise, look for avoidance or excuses...

The answer to the FIRST 3 questions SHOULD BE YES...
if they say NO to ANY of these, then go somewhere else.

1. Do you perform MORE THAN 50 parathyroid operations per year? (do not let them count thyroid operations, it is NOT the same thing).
2. Are you trained in Mini-Parathyroid surgery? Do you routinely perform Mini-parathyroid surgery at least 85% of the time?
3. Do you check the status of the parathyroid glands in the operating room? (by measuring radioactive ratios of the glands or using PTH assays in the operating room).

The answers to the last 4 questions should be NO.
If they say YES, go somewhere else!

4. Do you put a drain in all or most of your patients to drain blood? (experts almost never do this!)
5. Do you require most or all of your patients to spend the night in the hospital after the operation? (experts send home nearly 100% of their patients... find another doctor!).
6. Do you use a nerve stimulator to help you find the voice box nerve? (this is a sign of low experience... someone who is unsure of the anatomy... RUN!!).
7. Do you require that every patient is intubated with "general endotracheal anesthesia"?

Parathyroid Surgery
The Standard Technique

Overview of Parathyroid Surgery

Since 1925, the gold standard treatment for primary hyperparathyroidism has been to surgically remove the parathyroid gland (or glands) which are overproducing hormone. Remember, this is a hormone problem, so the goal is to remove the source of the excess hormone (remove the bad parathyroid gland, leave the normal parathyroid glands). The '*standard parathyroid operation*' has not changed since its invention in 1925, and is performed by putting the patient to sleep under general anesthesia, an incision is made in the neck and the thyroid gland is mobilized to allow the surgeon to identify the four parathyroid glands which reside moderately deep in the neck behind the thyroid. Patients are typically hospitalized over night, and occasionally as long as a day or two. The incision has to be made of sufficient length to allow the surgeon adequate exposure of the

numerous important structures in the neck, and thus it is typically five to seven (or even 10) inches long. These wounds eventually heal quite nicely.

Because of the numerous small nerves and other important structures within the neck which reside around the parathyroid glands, this standard parathyroid operation can be technically challenging and is usually only performed by experienced endocrine surgeons or surgeons with extensive head and neck operative experience. Numerous publications in medical journals have shown that the success rate following parathyroid surgery is directly related to the number of parathyroid operations the surgeon has performed. During this operation, the surgeon must identify all four parathyroid glands and remove whichever one(s) is enlarged. As covered in the section describing hyperparathyroidism in detail, approximately 96 % of the time there is one large parathyroid gland (an **adenoma**) and three normal parathyroid glands. In this situation the one large gland (the parathyroid adenoma) would be removed leaving the three normal ones to function in a normal fashion indefinitely. If the surgeon found all four parathyroid glands to be enlarged (called: parathyroid hyperplasia), he/she would typically take out 3 or 3-1/2 of these glands leaving some parathyroid tissue behind to function normally in the future. In experienced hands, this operation has a cure rate of about 94 percent, but can be as low as 85% for surgeons who operate on parathyroid patients infrequently.

To complete a 'standard parathyroid operation' safely with a high rate of success, the operation occurs on both sides of the neck (a standard bilateral neck exploration), and is always performed using general anesthesia. General anesthesia, however, is extremely safe for nearly all patients. Because of the concern over general anesthesia in some elderly patients, and concerns about a 6 to 8 inch incision on the neck, and the risks of damage to the nerves to the voice box, some endocrinologists and family doctors elect not to send patients for this operation until the patients develop hyper-parathyroid symptoms or have a significant loss of bone density (osteoporosis). This means of management of parathyroid disease may or may not be in the best interests of the patient based upon the potential risks (small, but real) of the standard parathyroid operation. You need to discuss the pros and cons of this safe and routine operation with your endocrinologist and weigh the risks of surgery versus continued monitoring of your body calcium stores and your bone density. **NOTE:** Minimal parathyroid surgery is dramatically changing the way endocrinologists treat hyperparathyroidism, sending many more patients for surgery. Read a recent survey of endocrinologists (Click Here) to see how 96% of them would have a MIRP instead of a standard parathyroid operation.

Overview of Standard Parathyroid Surgery For Primary Hyperparathyroidism

- You have 4 parathyroids, so all 4 are examined to see which ones are over producing hormone

- If one bad (overactive) parathyroid found, it is removed

- If 4 overactive glands are found, 3 or 3 1/2 are removed

- High rate of cure is the norm (~93%) for experienced endocrine (parathyroid) surgeons, but can be as low as 84% for general surgeons who perform parathyroid surgery only a few times per year.

- Cure rates are extremely dependent upon the experience of the surgeon.

- Requires general anesthesia (extremely safe these days)

- Risks are very low (~1% chance of injury to the nerve to the voice box).

- Complication rates extremely dependant upon the experience of the surgeon.

- Expected blood loss is extremely low (less than 1/4 cup...no need to prepare for possible transfusions)

UPDATED JANUARY 2005.
EDITOR'S NOTE: The standard operation for parathyroid disease as discussed on this page is no longer the preferred method of removing parathyroid glands for patients with primary hyperparathyroidism. It is a very safe and effective operation, but typically is a **MUCH** larger and more complex operation than is needed for most patients. Since the invention of Minimally Invasive Radioguided Parathyroid surgery in 1996, many universities in the US and around the world have documented that minimal parathyroid surgery has a cure rate that is higher, a complication rate that is less than 1/2 of the old way (near zero), and it can be done with local anesthesia typically in less than 20 minutes. There are several pages on minimal parathyroid surgery on this web site, including surveys from endocrinologists and summaries of journal articles showing statistical evidence of the benefit of minimal parathyroid surgery. Before you have surgery, make sure you understand your options.

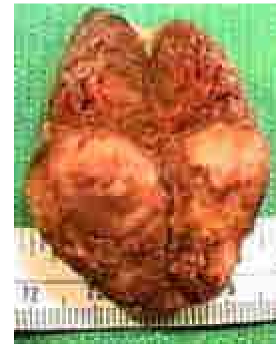
Parathyroid Anatomy
Why are they so hard to find?

The key to these questions is to understand where parathyroids come from. When you understand this, you will understand why parathyroid anatomy is some of the most variable anatomy in the human body--and why it is VERY important to get a very experienced parathyroid surgeon to perform your parathyroid surgery (read more).

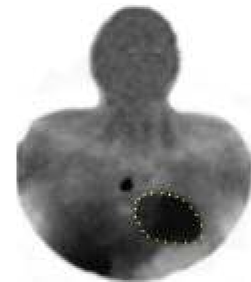
Technically speaking, the four parathyroids arise from the third and forth branchial pouches. This means that they are formed early in embryogenesis along with other organs of the neck. **The lower 2 parathyroids** come from the third brachial pouch which is also responsible for producing the thymus gland (not thyroid) which is important for the development of a normal immune system. The thymus eventually sits behind the breast bone (sternum). **The upper 2 parathyroids** come from the fourth branchial pouch which also produces the **thyroid** gland.

Normally, as the larger thymus and thyroid glands migrate from the upper neck (where they are formed) into the lower neck and upper chest, they take the small "passenger" parathyroids with them. The lower parathyroids usually getting stuck in the neck next to the thyroid during this migration and rarely make it all the way into the chest with the thymus. Therefore, under normal circumstances, the lower parathyroids will usually be found just below and behind the bottom of the thyroid. Likewise, the upper parathyroids will be found behind the middle of the thyroid gland. That is to say, normally, all four parathyroids are found around the back side of the thyroid (like in our main parathyroid picture).

BUT, it doesn't always go as planned !



It is this migration of the parathyroid glands through the neck during our gestation in the womb that makes finding them tricky. Occasionally, the **upper parathyroid glands** are formed with the thyroid to such a high degree that they never become separated. Under these circumstances, an upper parathyroid will actually be found WITHIN the thyroid gland. This picture shows the right half of the **thyroid** gland of a recently operated patient. I cut the thyroid in half to demonstrate the large parathyroid tumor (adenoma) which was inside the thyroid. This young patient had primary hyperparathyroidism with a very high calcium and parathyroid hormone. The sestamibi scan showed that it was completely buried within the thyroid gland and the only way to adequately get the entire adenoma out and cure her disease was to remove the right lobe of the thyroid. Her remaining thyroid (the isthmus and left lobe) will make enough thyroid hormone so she will not have to take thyroid hormone pills. Keep in mind that this situation is uncommon (about 1 percent of all cases). But your surgeon should have enough experience and knowledge to deal with these difficult circumstances should they arise. This picture was taken after the specimen was in preservatives overnight (prior to being sliced and stained by the pathologist) that is why the colors have all turned brown. ✔ Normally, the thyroid is a deep **brown** color and the parathyroid adenoma is a **mustard yellow** color. Even though the colors are not well preserved, you can easily see the large round parathyroid adenoma completely within the thyroid gland.



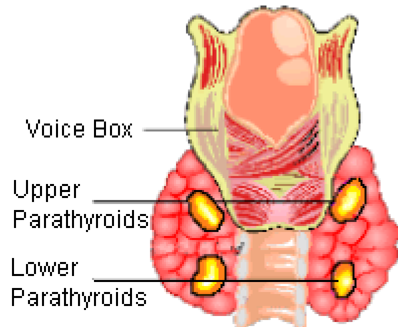
When the **lower parathyroids fail to migrate**, they can reside very high in the neck, several inches above the top of the thyroid. This is quite rare. A more common migration problem occurs when the lower parathyroids fail to separate from the thymus as the thymus makes its way to the chest (although still uncommon, this happens in about 1% of patients with primary hyperparathyroidism). Instead of the parathyroids ending up just below the lower edge of the thyroid, they will go all the way into the chest and reside next to the heart. This picture shows just this case. There is a very "hot" parathyroid adenoma which shows up on this sestamibi scan just to the right of the patient's heart (outlined in yellow).

HYPOPARATHYROIDISM

Too little parathyroid hormone production

Hypoparathyroidism is the combination of symptoms due to inadequate parathyroid hormone production. This is a VERY rare condition, and most commonly occurs because of damage or removal of parathyroid glands at the time of parathyroid or thyroid surgery. If this is the first parathyroid page you have read from our site, we strongly

recommend that you read our introduction to the parathyroid gland first! Remember, hyperparathyroidism is much more common than hypoparathyroidism.



Hypoparathyroidism is the state of decreased secretion or activity of parathyroid hormone (PTH). This leads to decreased blood levels of calcium (hypocalcemia) and increased levels of blood phosphorus (hyperphosphatemia). Symptoms can range from quite mild (tingling in the hands, fingers, and around the mouth) to more severe forms of muscle cramps leading all the way to tetany (severe muscle cramping of the entire body), and convulsions (this is very rare!).

Parathyroid gland insufficiency is quite rare, but it can occur in several well defined ways. The most common cause of hypoparathyroidism is the loss of active parathyroid tissue following thyroid or parathyroid surgery. More rare is a defect present at birth (congenital) where a person is born without parathyroid glands. Occasionally, the specific cause of hypoparathyroidism cannot be determined.

Three Categories of Hypoparathyroidism (each discussed below)

[1] Deficient Parathyroid Hormone Secretion.

[2] Inability to make an active form of PTH.

[3] Inability of the kidneys & bones to respond to PTH.

[1] Deficient Parathyroid Hormone Secretion.

This type of hypoparathyroidism is the easiest to understand. A patient afflicted with this condition simply has too little (or a complete absence of) parathyroid tissue therefore, inadequate PTH is produced. There are two major causes of this problem:

A) Post Surgical. The first (and most common) mechanism by which inadequate parathyroid hormone is produced is due to the removal of parathyroid glands at the time of surgery. The operations which are typically associated with this problem are operations designed to remove parathyroid glands for hyperparathyroidism. The goal of this operation is to remove those parathyroid glands which are overproducing PTH, however, occasionally, (less than 1%) too much parathyroid tissue is removed. The

second operation which is associated with postoperative hypoparathyroidism is total thyroidectomy. This operation is performed for a number of reasons, but because of the close relationship that the thyroid and parathyroid have to one another (including sharing the same blood supply) the parathryoid glands can be injured or removed. This is very rare and occurs in much less than 1% of thyroid operations. In many patients, the inadequate secretion of PTH is transient following surgery on the thyroid or parathyroid glands, so this diagnosis cannot be made immediately following surgery.

B) Idiopathic. Deficient PTH secretion without a defined cause (e.g. surgical injury) is termed Idiopathic hypoparathyroidism. This disease is rare and can be **congenital** or **acquired** later in life.

Congenital. Patients in this category are born without parathyroid tissues. Most patients with congenital hypoparathyroidism have no family history of the disease. Those who do may have any one of a number of congenital causes. The pattern of inheritance is as varied as the kinds of genetic abnormalities that cause the disease. The children in some families are at a 50% risk for disease (dominant gene defect) while others are at a risk of 25% or less (recessive gene defect). In some families only the boys suffer from disease. This sex-linked inheritance pattern indicates the presence of a genetic defect on the X chromosome. The inherited forms tend to arise from abnormal genes that either: 1) encode abnormal forms of PTH or its receptor, 2) prevent normal conduction of cell signals from the PTH receptor to the nucleus, or 3) prevent normal gland development before birth.

Hypoparathyroidism with onset during the first few months of life can be permanent or temporary. The cause is usually unknown and if spontaneous resolution occurs. If it does not, it will usually become manifest by 24 months of age. Finally, mothers who have overactive parathyroid glands may have high calcium levels. The excess ionized calcium can enter the baby and suppress the baby's parathyroid gland function. If suppression of the gland is not released quickly enough after birth, low calcium levels can be a temporary problem for the baby. This will **not** result in permanent parathyroid gland dysfunction in the child.

Acquired. The acquired form of this disease typically arises because the immune system has developed antibodies against parathyroid tissues in an attempt to reject what is sees as a foreign tissue, much as it would a transplanted organ. This disease can affect the parathyroid glands in isolation or can be part of a syndrome that involves many organs. An antibody that binds to the calcium sensor in the parathyroid gland has been discovered in the blood of patients with autoimmune hypoparathyroidism. It has been proposed that such binding "tricks" the parathyroid gland into believing that the blood level of ionized calcium is high. Responding to this signal, the parathyroid stops making PTH.

C) Hypomagnesemia. The element magnesium is closely related to the action of calcium in the body. When magnesium levels are too low, calcium levels may also fall. It appears that magnesium is important for parathyroid cells to make PTH normally.

Once recognized, this is usually very easy to fix. Chronic alcoholism is a frequent cause of low calcium and magnesium levels.

[2] Secretion of Biologically Inactive Parathyroid Hormone.

This section is placed here for completion sake only. There have only been a few cases of this syndrome ever reported, but one can see that if the PTH which is produced is actually a defective hormone, it would not have the same biologic strength as its normal counterpart.

[3] Resistance to Parathyroid Hormone (pseudo-hypoparathyroidism).

This disease is also VERY RARE! Like all patients with hypoparathyroidism, this disease is characterized by hypocalcemia (too low calcium levels), hyperphosphatemia (too high phosphorus levels), but they are distinguished by the fact that they produce PTH but their bones and kidneys do not respond to it. Even if PTH is given to them in their veins, they do not respond to it. Therefore, these rare individuals have plenty of PTH, but their organs do not behave appropriately to it (so they look to be hypoparathyroid but they are not...thus the name "pseudo-hypoparathyroid").

Treatment of Hypoparathyroidism

- Vitamin D and calcium supplements are the primary treatments for this disease regardless of the cause. The only exception is when the inactivity of PTH is due to hypomagnasemia which is readily treated with magnesium supplementation. At this time, a replacement form of PTH is not available.