

PRIMARY HYPERPARATHYROIDISM:

A Patient's Guide

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A Note from Dr. Van Lier Ribbink

The following information has been written for the patient with Primary Hyperparathyroidism. I have attempted to provide a general overview of the disease and its treatment. In addition, a list of suggested questions that every patient should ask is included.

I hope this will provide a balanced overview of the disease and its treatment. A patient deserves nothing less. Hopefully, this will help empower patients with Primary Hyperparathyroidism to be the true managers of the choices they make.

Thank you

J. Van Lier Ribbink

Introduction

Primary Hyperparathyroidism (pHPT) is a disorder of the parathyroid glands. These glands produce too much parathyroid hormone (PTH), which causes elevated blood levels of calcium (Ca) called hypercalcemia. This can be associated with severe, moderate or mild symptoms (symptomatic). This can be associated with no symptoms (asymptomatic). Almost every organ system of the body can be adversely affected.

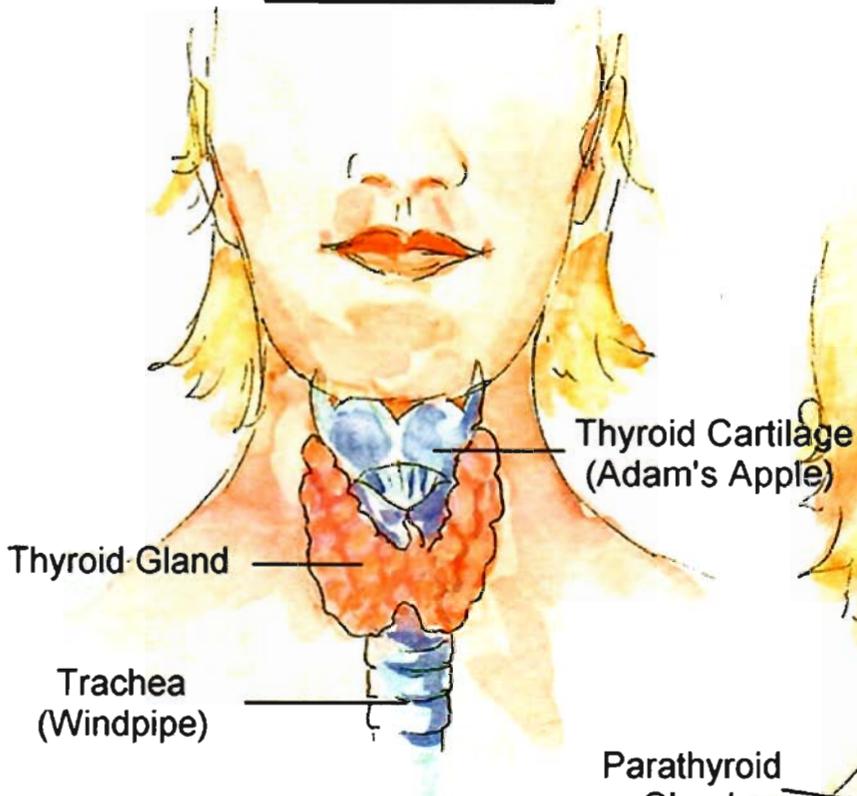
The only cure for this disease is surgery. There are a number of different accepted surgical procedures that can be utilized. The choice of any one of these approaches will depend upon the patient's overall clinical condition, past medical history, actual cause of the pHPT, and whether an abnormal parathyroid gland is localized by preoperative tests.

The chance for cure of pHPT with surgery in the hands of an experienced endocrine surgeon should be 97.5%. The risk of complications in the hands of an experienced endocrine surgeon should be less than 1%. It is well recognized that the most important step a patient with HPT must make is the initial one: finding an experienced endocrine surgeon.

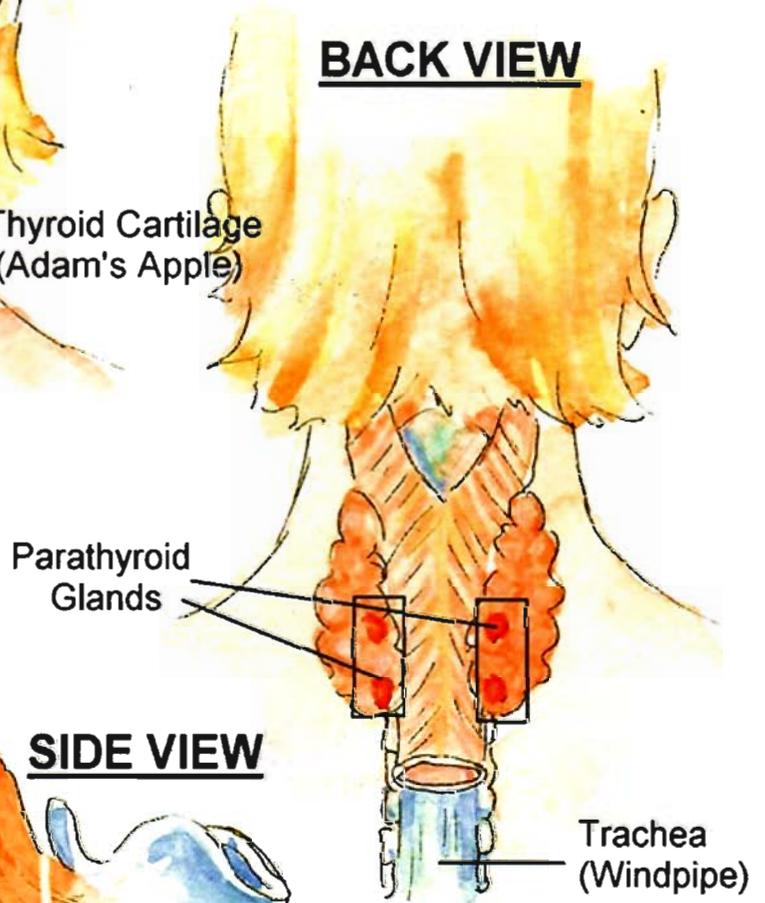
What is the Anatomy of the Parathyroid Glands?

Each normal parathyroid gland is quite small, weighing about 40 mg. and measuring 4 mm in size. There are normally four parathyroid glands, and all of them are usually located in the neck adjacent to the surface of the thyroid gland. The parathyroid glands are designated as the right superior, left superior, right inferior, and left inferior parathyroid glands. These glands are separate from the thyroid gland and have an entirely different function. (Figure 1)

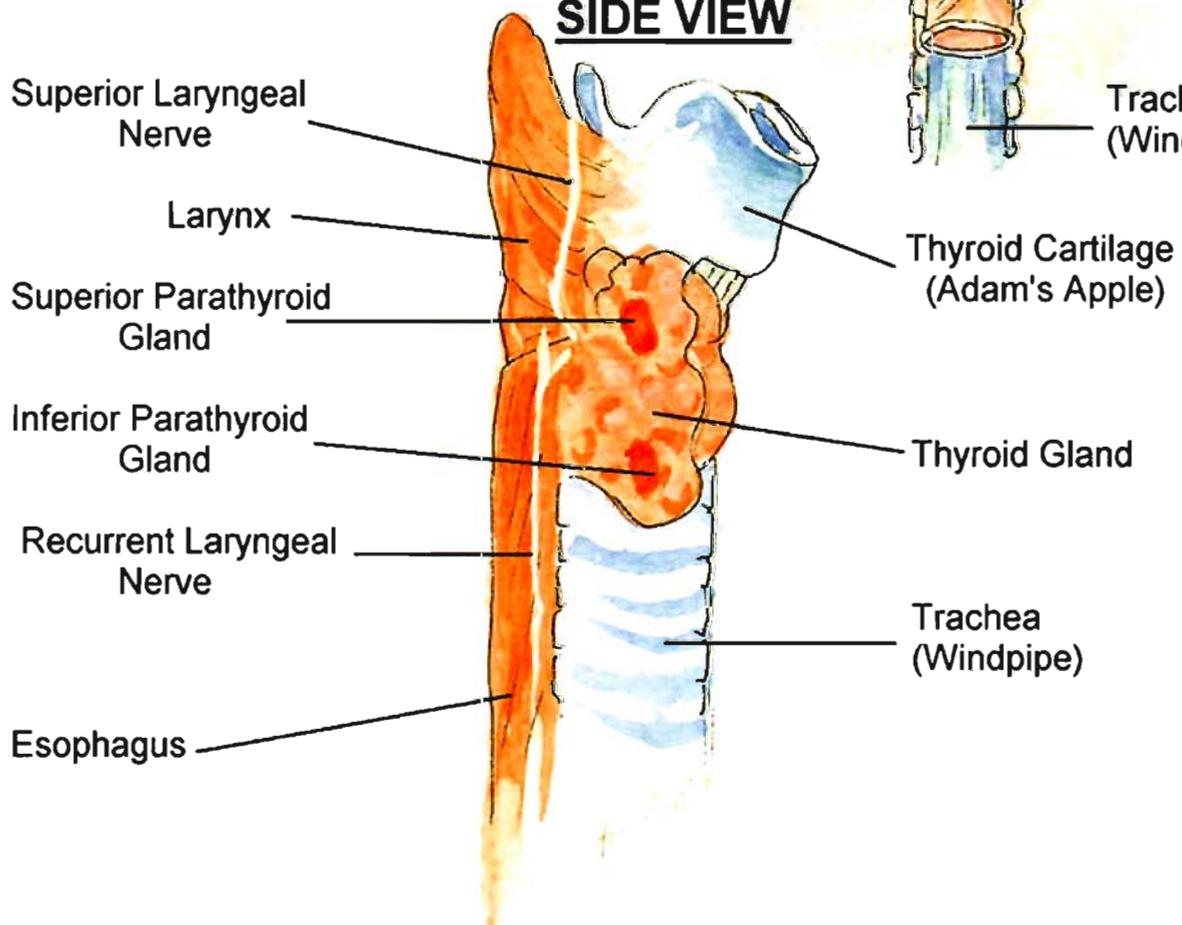
FRONT VIEW



BACK VIEW



SIDE VIEW



What is the Normal Function of the Parathyroid Glands?

The parathyroid glands produce a hormone called parathyroid hormone (PTH). The hormone is secreted into the bloodstream and has effects upon bone, kidneys, and the small intestine.

With normal function of the parathyroid glands, PTH influences bone formation and bone loss to maintain normal bone density and strength.

PTH affects the kidneys in two ways. First, it stimulates the conversion in the kidneys of inactive Vitamin D to active Vitamin D. Second, it regulates how much Ca is taken out of the blood by the kidneys and excreted out of the body in the urine. Finally, PTH affects the absorption of Ca in food through the small intestine and into the bloodstream. It does this in an indirect fashion by stimulating the kidneys to produce the active form of Vitamin D. This Vitamin D then travels in the bloodstream to the small intestine where it increase the amount of Ca absorbed from the small intestine into the bloodstream.

The parathyroid gland maintains normal blood Ca levels via the above mechanisms.

What is Primary Hyperparathyroidism?

In pHPT, the parathyroid glands produce and secrete too much PTH into the bloodstream. This causes Ca to be drawn out of bone and transferred into the blood stream. The bone density and strength decreases thereby increasing the risks of fracture. The conversion of an inactive to active Vitamin D in the kidney is increased. This leads to increased absorption of calcium into the bloodstream from the small intestine. These processes all ultimately lead to elevation of the blood calcium levels. This hypercalcemia causes most of the varied symptoms of HPT.

What is the Cause of Primary Hyperparathyroidism?

Primary hyperparathyroidism is most often caused by spontaneous mutations within the DNA of parathyroid cells that lead to benign parathyroid gland enlargement and increased secretion of PTH.

A history of radiation therapy exposure to the neck is known to increase the risk of hyperparathyroidism. This is unusual however.

Rarely, primary hyperparathyroidism may be an inherited condition associated with the following syndromes:

- A) Familial Non-Men Hyperparathyroidism
- B) Multiple Endocrine Neoplasia Syndrome, Type 1 (MEN1)
- C) MEN2A

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Who Gets Primary Hyperparathyroidism?

Primary hyperparathyroidism is a relatively common disease. Approximately 100,000 new cases are diagnosed each year in the United States. One in every 500 women and one of every 2,000 men older than 40 years of age have this disease. About 2% of postmenopausal women have this disease.

What are the Characteristics of the Parathyroid Glands in Primary Hyperparathyroidism?

In more than 99% of patients with primary hyperparathyroidism, the condition is benign. Less than 0.1% of patients with HPT have cancer of the parathyroid glands.

Eighty-nine percent of patients have only one abnormal parathyroid gland called a parathyroid adenoma. Four percent of the patients have 2 abnormal parathyroid glands (double adenoma). In 7% of patients, all four of the glands are abnormal. This is called parathyroid hyperplasia.

What are the Symptoms of Primary Hyperparathyroidism?

HPT affects nearly every organ system of the body and is associated with a wide variety of symptoms:

1. Brain – Neurologic

Headaches, agitation, anxiety, depression, poor motivation, nervousness, memory problems, mood changes, lethargy, hearing loss, problems with balance, poor concentration, confusion, seizures, coma.

2. Cardiovascular

High blood pressure, decreased heart function, and heart rhythm abnormalities. A study from the Scandinavian countries suggests that premature death from heart related complications may be increased in patients with HPT.

3. Kidneys

Kidney stones (nephrolithiasis), kidney damage, urinating large amounts (polyuria).

4. Bones

Calcium loss from bone. This bone loss is measured by a Dual Energy X-ray Absorptiometry (DEXA) scan. This study shows if the patient has osteopenia or osteoporosis, which are increasing levels of bone loss. The corresponding decreased strength of bone leads to an increased risk of fractures, e.g. hip fractures.

5. Gastrointestinal

Constipation, peptic ulcer disease, pancreatitis (inflammation of pancreas), loss of appetite, nausea, vomiting, weight loss, abdominal pain.

6. Skin

Ulcerating skin lesions, itching.

7. Other Systems

Weakness, fatigue, muscle aches (myalgias), joint aches (arthralgias), drinking large amounts of water (polydypsia), muscle cramping, brittle nails, vision changes, blood clots.

How is Primary Hyperparathyroidism Diagnosed?

Hyperparathyroidism is diagnosed by a blood test usually showing an elevated ionized calcium (Ca) level associated with an elevated or inappropriately normal parathyroid hormone level.

A 24 hour urine collection for calcium and creatinine levels also needs to be performed to rule out a very rare condition called Familial Hypocalciuric Hypercalcemia (FHH). A patient with FHH should not have surgery.

Other tests may be necessary depending upon each individual patient's clinical situation.

The Technetium-99 Labelled Nuclear Medicine Parathyroid Scan is not a test used to diagnose pHPT. It is a test used to locate a solitary parathyroid adenoma in the patient already diagnosed with pHPT.

What is the Treatment for Primary Hyperparathyroidism?

The only treatment that can cure primary HPT is surgery.

Prior to surgery, a Technetium-99 Labelled Sestamibi Nuclear Medicine Parathyroid Scan is performed. This study is not performed to make the diagnosis of HPT. The diagnosis is made prior to this study by blood tests and a 24-hour urine collection. The role of the Sestamibi Scan is to try to localize where an abnormal parathyroid gland is located. In this new millennium with globalization, expert nuclear medicine radiologists and the necessary technology are available in every major metropolitan area in the United States and most other developed countries. Basically, any patient with HPT in any geographic region of the United States can therefore obtain an expertly performed Sestamibi Scan in their own region. Fortunately, there is no longer a need for a patient to travel a long distance to obtain this scan.

If the Sestamibi Scan fails to identify the location of an abnormal parathyroid gland, then the explanation may be that there are multiple abnormal parathyroid glands. The other explanation may be that a single abnormal parathyroid gland simply is not taking up the Sestamibi. This is unusual. In these uncommon situations, it appears that the mitochondria (basically the power plants of the cell) of the abnormal parathyroid glands do not take up an excessive amount of Tc-99-Sestamibi as compared to normal parathyroid cells. Therefore, the scan does not show the abnormal glands and does not localize them for the endocrine surgeon.

In this uncommon situation of having the diagnosis of HPT, yet not knowing the location of the abnormal parathyroid glands, the endocrine surgeon cannot perform an open minimally invasive parathyroidectomy, a minimally invasive radioguided parathyroidectomy (MIRP), or an endoscopic videoscopic minimally invasive parathyroidectomy (EVMIP). The endocrine surgeon in this situation will offer a standard classic open neck incision approach (using a longer incision) designed to allow for examination of all four of the parathyroid glands in the right and left sides of the neck. This involves a horizontal low incision in the front of the neck that extends to the left and right of the midline. The endocrine surgeon will then remove the abnormal parathyroid gland or glands in the neck.

The procedure is performed under general anesthesia (asleep), and the patient usually stays only one night in the hospital. In the hands of an experienced endocrine parathyroid surgeon, the chance of him finding the abnormal parathyroid gland or glands, removing them, and curing the patient of the HPT is excellent at 97.5%. The cosmetic appearance of the scar from the incision usually turns out to be very good.

Now, if the Tc-99-Sestamibi parathyroid scan does identify the location of the abnormal parathyroid gland, then the patient is an excellent candidate for a minimally invasive parathyroidectomy. There are a number of different forms of this operation which include the open minimally invasive parathyroidectomy (OMIP), and the minimally invasive radioguided parathyroidectomy (MIRP). These approaches are not truly minimally invasive; however, since they do not utilize endoscopic videoscopic techniques and; therefore, require longer incisions through which instruments can be used. However, to avoid confusion regarding these two procedures, the minimally invasive connotation will be used.

The open minimally invasive parathyroidectomy (OMIP) involves a small incision made on the side of the neck where the Sestamibi scan localized the abnormal parathyroid gland to. Basically, using the same instruments one would use for the classic standard neck exploration already described, the abnormal parathyroid gland is identified and removed. This operation can be performed under general anesthesia, or with the patient awake with local anesthesia and intravenous sedation. The patient can be discharged home on the same day of surgery. This approach has a 97.5% success rate of curing HPT in the hands of an experienced endocrine surgeon.

The minimally invasive radioguided parathyroidectomy (MIRP) procedure basically uses the same approach with the same incision as the OMIP described above. The difference is that the patient is given Tc-99-Sestamibi by intravenous line in the holding area just prior to the MIRP procedure. During surgery, a specialized hand held head and neck gamma probe (like a Geiger counter) is placed into the incision to “help localize” the abnormal parathyroid gland. The procedure can be performed under general anesthesia or under local anesthesia with intravenous sedation. Patients are generally discharged home on the same day of surgery. The success rate in curing patients of HPT with this approach is also 97.5% in the hands of an experienced endocrine surgeon. It has been shown in multiple published studies from different endocrine surgery groups inside and outside the United States, that in the hands of experienced endocrine surgeons, the MIRP procedure does not offer any real advantage in finding the

abnormal parathyroid glands. These published studies that have been subjected to peer review, also show no decrease in operative time associated with the use of the MIRP operation. Clearly, the ability to find the abnormal parathyroid glands and the time it takes to find them depend upon having an experienced endocrine parathyroid surgeon performing the surgery who knows where and how to find abnormal parathyroid glands in their normal and abnormal positions. After incorporating the MIRP procedure into their practices, most endocrine surgeons in and outside the U. S. now infrequently use it due to the above findings.

One disadvantage associated with the OMIP and the MIRP procedures that must be appreciated is that the recurrent laryngeal nerves (RLN) that innervate the muscles of the vocal cords are usually not identified due to the smaller incision and reduced exposure. If the nerve is injured, the patient can potentially suffer permanent hoarseness.

Finally, the Endoscopic Videoscopic Minimally Invasive Parathyroidectomy (EVMIP) is a procedure performed worldwide by relatively few endocrine surgeons. A surgeon who performs this operation must have a large amount of experience with all of the above outlined procedures before performing the EVMIP. The endocrine surgeon should also have extensive experience with endoscopic videoscopic surgery which has usually been obtained through laparoscopic gastrointestinal-abdominal surgery.

EVMIP is the only truly “minimally invasive” approach to parathyroid surgery. Therefore, this approach has the best cosmetic results of all the surgeries for parathyroidectomy. The procedure requires two 2.5 millimeter (mm) incisions on the neck for placement of the 2.5mm cannulas (metal tubes) through which the surgeon uses endoscopic micro-instruments to perform the operation. These two incisions are so small that they basically disappear and leave no obvious scar. A 1.5 centimeter (cm) incision is made also on the lateral neck through which a 1.0 cm cannula is passed into the neck. The endoscope transmits pictures to a large video screen. The surgeon then performs the operation while looking at the video screen, much like playing a videogame on a home computer. The abnormal parathyroid gland is removed through the 1.0 cm cannula and the incisions are closed with glue. No sutures have to be removed. The only incision that leaves a scar is smaller than any incision that is used for other approaches to parathyroidectomy. The EVMIP is performed under general anesthesia. Patients are discharged home on the same day of surgery from the recovery room and patients return to work and/or their normal daily activities by the next day after surgery. The success rate for EVMIP for curing HPT is 97.5%.

One advantage of EVMIP is the excellent exposure of the parathyroid glands, recurrent laryngeal nerve, inferior thyroid artery, carotid artery, and lymph nodes in the neck. As one can imagine, these small structures in the neck appear enormous on the video screen. In contrast to the other “minimally invasive” approaches, the recurrent laryngeal nerve is almost always seen, and therefore, clearly kept out of harms way. Another advantage of EVMIP is that a parathyroid gland located in the chest (mediastinum) can be removed via the EVMIP approach. Although this is unusual (less than 1% of patients with HPT), every experienced endocrine surgeon has seen this. The cosmetic advantage of EVMIP over the other approaches has already been discussed.

The complications of any of the above surgical approaches include bleeding, infection, injury to the RLN causing permanent hoarseness, or injury to the parathyroid glands causing permanent low blood calcium levels (hypocalcemia). The risk of any of these complications; however, developing in the hands of an experienced endocrine surgeon should really be less than 1%.

During any of the above surgeries, rapid intraoperative parathyroid hormone (IOPTH) monitoring can be performed. Blood levels of PTH are drawn during the surgery, and if the levels drop adequately after removal of the abnormal parathyroid gland, this indicates that there is a 97.5% chance of cure.

Nerve monitoring can be performed during any of the above parathyroid surgeries. With monitoring of the RLN, identification of that nerve may be easier and the chances of nerve injury may be lessened.

Which Patients With Primary Hyperparathyroidism Should Have Surgery?

The American Association of Clinical Endocrinologists and the American Association of Endocrine Surgeons Position Statement on the Diagnosis and Management of Primary Hyperparathyroidism issued in 2005 states that:

“Operative management is clearly indicated for all patients with classic symptoms or complications of Primary Hyperparathyroidism. ...operative management should be considered and recommended for all asymptomatic patients with Primary Hyperparathyroidism who have a reasonable life expectancy and suitable operative and anesthesia risk factors.”

What is the Patient to Expect after Surgery for Primary Hyperparathyroidism?

Postoperative instructions and care will vary depending upon the surgeon. The following information therefore will relate to Dr. Van Lier Ribbink's patients.

1. Endoscopic Videoscopic Minimally Invasive Parathyroidectomy
 - A. Patients are discharged home on the same day of surgery from the recovery room.
 - B. The incisions are closed with glue. No sutures have to be removed.
 - C. A prescription for a mild narcotic for discomfort will be provided.
 - D. A prescription for an outpatient blood draw for a tCa level the day following surgery will be provided.
 - E. No bandages are placed on the incisions postoperatively.
 - F. No restrictions on talking, eating or moving neck beginning immediately postoperatively.
 - G. May get wounds wet with shower, soap, and shampoo the day after surgery.
 - H. No immersing wounds under water with bathing, hot tubbing, or swimming for three weeks after surgery.
 - I. May return to work and/or normal level of activity the day after surgery.
 - J. May drive once off the narcotic pain medication, when the head can be turned adequately, and when the patient feels up to it.
 - K. Patient to see Dr. Van Lier Ribbink for follow up in office in three weeks.
 - L. A follow up tCa and iPTH level will be drawn in six months.

2. OMIP and MIRP Procedures

The postoperative instructions and care following the OMIP and the MIRP procedures are the same as those outlined above for EVMIP, except for the following:

- A. The incision is closed with sutures beneath the skin. No sutures have to be removed.
- B. A strip of tape called a Proxy-Strip is placed over the incision. This tape is removed three weeks after the surgery. If the Proxy-Strip comes off before that time, that is not a problem.
- C. A bandage is also placed over the incision and Proxy-Strip at the conclusion of the surgery. The patient will remove this bandage the day after surgery.

3. Classic Parathyroidectomy with Neck Exploration

- A. The patient is usually discharged from the hospital the day following surgery.
- B. The incision is closed with sutures beneath the skin. No stitches have to be removed.
- C. A strip of tape called a Proxy-Strip is placed over the incision. This tape is removed three weeks after surgery. If the Proxy-Strip comes off before that time, that is not a problem.
- D. A bandage is also placed over the incision and Proxy-Strip at the conclusion of the surgery. This bandage is removed the day after surgery.
- E. A prescription for a mild narcotic for discomfort will be provided.
- F. A tCa level will be drawn in the hospital the day after surgery.
- G. No restrictions on talking, eating, or moving neck beginning immediately postoperatively.
- H. May get incision wet with shower, soap, shampoo the day after surgery.
- I. No immersing incision under water with bathing, hot tubbing, or swimming for three weeks after surgery.

- J. May return to work and/or to normal level of activity three to five days after surgery.
- K. May drive once off the narcotic pain medication, when the head can be turned adequately, and when the patient feels up to it.
- L. The patient will need to see Dr. Van Lier Ribbink for follow up in the office three weeks after surgery.
- M. A follow up tCa level and PTH level will be drawn six months after surgery.

What Questions Should the Patient Ask the Surgeon Before Proceeding with Parathyroid Surgery?

- 1) How long have you been performing parathyroid surgery?
- 2) How many parathyroid surgeries have you performed?
- 3) How many parathyroid surgeries did you perform over the past year?

The following classification system measuring the expertise of a surgeon performing parathyroid surgery has been proposed by Dr. W.B. Inabnet of the Columbia University Department of Surgery on their web site (cpmcnet.columbia.edu/dept/thyroid/parasurg).

- “An expert thyroid and/or parathyroid surgeon performs at least 50 thyroid/parathyroid operations per year.”

<u>Total Number of Career Thyroid and Parathyroid Operations</u>	<u>Experience Level</u>
Less than 200	Inexperienced
200 – 500	Intermediate
501 - 1,000	Experienced
More than 1,000	Expert

- 4) What are your success and complication rates?
- 5) How long will the surgery take? You should hope that the surgeon answers with a general estimate followed by, “As long as it takes to do a good operation.” There will always be variation in surgery time between surgeons, but the most important determinant of surgery time is usually based on the difficulty of the surgery. There is generally a significant degree of inaccuracy when a surgeon estimates the amount of time it takes him to perform any surgical procedure.

- 6) Do you perform parathyroid surgery under local anesthesia and intravenous sedation?
- 7) Do you perform minimally invasive parathyroidectomy?
- 8) Does your hospital have radioguidance capability?
- 9) Does your hospital have rapid intraoperative intact parathyroid hormone monitoring capability?
- 10) Do you perform nerve monitoring during surgery?
- 11) Will you be performing the entire operation yourself?
- 12) Will you be taking direct care of me postoperatively, or will someone else be?
- 13) Will I go home on the same day of surgery?
- 14) Are you Board Certified?

Explanation of Abbreviations

1.	Ca	Calcium
2.	cm	Centimeter
3.	EVMIP	Endoscopic Videoscopic Minimally Invasive Parathyroidectomy
4.	FHH	Familial Hypocalciuric Hypercalcemia
5.	iCa	Ionized calcium
6.	IOPTH	Intraoperative Parathyroid Hormone
7.	MEN	Multiple Endocrine Neoplasia
8.	MIRP	Minimally Invasive Radioguided Parathyroidectomy
9.	mm	Millimeter
10.	OMIP	Open Minimally Invasive Parathyroidectomy
11.	pHPT	Primary Hyperparathyroidism
12.	PTH	Parathyroid Hormone
13.	RLN	Recurrent Laryngeal Nerve
14.	tCa	Total Calcium