QUESTIONS AND ANSWERS

ABOUT

PRIMARY HYPERPARATHYROIDISM

A PUBLICATION OF

THE PAGET FOUNDATION
FOR PAGET'S DISEASE OF BONE AND RELATED DISORDERS

Primary Hyperparathyroidism is a hormonal problem due to one or more of the parathyroid glands producing too much parathyroid hormone. When this happens, the blood calcium becomes higher than normal. Bones may lose calcium, and too much calcium may be excreted by the kidneys.

1. Q. What are the parathyroid glands?
A. They are four small glands located in the neck, close to the thyroid gland. Rarely there are more than four, and they may be located in other parts of the neck, or even in the chest.

2. Q. What is their purpose?
A. The glands produce parathyroid hormone (PTH) which plays a critical role in maintaining normal blood calcium levels.

3. Q. How do these small glands maintain normal calcium levels in the blood?
A. PTH, released by these glands, keeps the amount of calcium in the blood from falling below normal in three ways:

1) By conserving calcium at the kidneys.
2) By releasing calcium from the bones.
3) By increasing absorption of calcium from food.

4. Q. What goes wrong in primary hyperparathyroidism?
A. One or more of the glands becomes enlarged and overactive, producing too much PTH. This leads to a rise in the blood calcium. In most patients (80-85%), a single parathyroid gland becomes enlarged and develops into a benign tumor, known as an adenoma. In nearly all other patients (15-20%), two or more glands enlarge, again in a benign fashion, a condition called hyperplasia. Parathyroid cancer is an extremely rare cause of primary hyperparathyroidism.

5. Q. What are the harmful effects of primary hyperparathyroidism?
A. When the blood calcium is very high the most common symptoms are loss of appetite, thirst, frequent urination, lethargy, fatigue, muscle weakness, joint pains, and constipation. Symptoms can also include nausea, vomiting, abdominal pain, memory loss, and depression. These problems are not usually present unless the blood calcium is very high. Most patients with primary hyperparathyroidism in the United States do not have blood calcium levels in the range where these signs typically occur. In fact, many patients with primary hyperparathyroidism have no symptoms at all. They are said to be asymptomatic. Even so, patients with primary hyperparathyroidism who are asymptomatic can lose bone density and be at risk for fractures because of a loss of calcium from the skeleton. Primary hyperparathyroidism can also lead to kidney stones and calcification of the kidney.

6. Q. Do all patients with primary hyperparathyroidism have symptoms?
A. No. Most patients are discovered to have primary hyperparathyroidism incidentally, in the course of a routine blood test.

7. Q. Do all patients with primary hyperparathyroidism develop complications including bone loss, kidney stones, weakness, fatigability, etc?

A. No. Many patients do not develop obvious complications, but bone loss is not uncommon.

8. Q. Does the physician know who will develop complications?

A. At the time of diagnosis, the physician cannot predict who will develop complications. However, complete biochemical and radiological evaluation over time will identify individuals who may exhibit the first signs of these complications before they progress to a more serious stage.

9. Q. What is a complete evaluation?

A. Blood is tested for calcium and PTH to establish the diagnosis and assess severity. Blood is also tested for 25-hydroxyvitamin D (the main form of vitamin D in blood) and creatinine (a test of kidney function) to ensure that the disease is not being made worse by vitamin D deficiency or poor kidney function. Measuring "bone markers", such as alkaline phosphatase and collagen breakdown products in blood and urine can assess the effect of primary hyperparathyroidism on bone. Kidney x-rays or ultrasound tests are obtained to assess for the presence of kidney stones. Bone mineral density (spine, hips, forearm) is measured to detect bone loss. It is important to measure the forearm as well as the lumbar spine and hip because the forearm can be the first site where bone is lost in people who have primary hyperparathyroidism.

10. Q. What causes primary hyperparathyroidism?

A. In most cases the cause is unknown. Previous x-ray treatments of the face or neck years before may be a cause in some patients. Treatment with drugs such as lithium and thiazide diuretics may lead to a higher risk for developing primary hyperparathyroidism. In some patients there is a family history of primary hyperparathyroidism. However, the great majority of patients do not have any relatives with the disorder.

11. Q. How common is primary hyperparathyroidism?

A. Estimates are difficult to obtain. Between 1983-1992 a study at the Mayo Clinic in Rochester, Minnesota found that the annual number of newly diagnosed patients was 20.8 per 100,000. In 1999 approximately 12,000 patients had parathyroid surgery in the United States. Women patients outnumber men by three to one. Primary hyperparathyroidism can occur at any age but is more common with aging and its highest occurrence is in people over the age of 50.

12. Q. Is there a cure for primary hyperparathyroidism?

A. Yes, if the surgery is done for a patient with a single abnormal gland (adenoma). When the surgery is performed by an experienced parathyroid surgeon the operation is successful in about 95% of cases. In patients with four abnormal glands surgery usually produces a normal blood calcium, but the abnormal remaining gland may enlarge over time and a high blood calcium may return. The surgery usually leaves a thin, faint horizontal scar in the lower neck. The size of the scar depends upon the kind of surgery, but generally it is one to three inches.

13. Q. Should all patients with primary hyperparathyroidism undergo surgery?

A. Not necessarily. Although surgery may be considered an appropriate treatment even in patients without signs or symptoms, such patients are not always operated upon because the disease is mild. In these patients the disease may not get worse. If surgery is not performed, these patients should be monitored regularly with blood testing every 6 - 12 months and bone mineral density testing yearly. These tests will allow the physician to identify those patients who show signs of progression and who require active treatment.

14. Q. Who should have surgery?

A. Patients who have symptoms of primary hyperparathyroidism are generally recommended for surgery unless they have other medical problems that might make the surgery too risky. Patients who have no symptoms may also have surgery suggested if their physicians, after careful analysis of their condition, feel that the surgery would likely prevent future complications.

15. Q. Is there a way to locate the enlarged parathyroid gland(s) before surgery is performed?

A. Preoperative localization technology has advanced to the point where it has become standard to obtain a preoperative imaging test prior to surgery. This type of test should be mandatory for patients who have had previous neck surgery and for patients who elect to have minimally invasive surgery (see question 17). Localization studies do not always find the abnormal gland/s. At times, the localization study incorrectly indicates that a parathyroid gland is at a location when it is not present. This is called a "false positive test."

16. Q. What preoperative localization tests are available?

A. There are a number of non-invasive imaging tests to locate abnormal parathyroid glands. They include ultrasound, computerized tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), and the sestamibi scan. Tc99m-sestamibi is an imaging agent that localizes in the abnormal parathyroid gland. The sestamibi scan, especially when used with another scanning agent ^{123}I and with computerized tomography (SPECT), is the most sensitive and specific test available to identify the parathyroid glands. In unusual situations, the quest to find the parathyroid gland requires invasive tests (arteriography and blood sampling of veins in the neck for PTH) that require great expertise and are more difficult. Patients who are considering minimally invasive parathyroid surgery (see question 17) require successful preoperative imaging to localize the abnormal parathyroid glands.

17. Q. What is the standard surgical approach for primary hyperparathyroidism and are there alternative approaches?

A. The traditional approach is to perform the operation under general or local anesthesia. All four glands are identified. The enlarged gland(s) is removed. If all four glands are enlarged, a 3 to 3 1/2½ gland parathyroidectomy is performed.

In additional to the traditional approach, less invasive techniques have been developed. They go under the term "minimally invasive parathyroidectomy". These approaches require successful preoperative localization.

1) A small incision is made in the neck in the area where the gland was identified by

the imaging study and the gland is removed. This approach is combined with the use of PTH measurements done while the patient is still in the operating room. If the blood PTH, which can be measured within 10 minutes after gland removal, falls to below 50% of the level before surgery and into the normal range, the surgery is nearly always successful. The other glands are not examined. If the post-operative PTH level does not fall to below 50% of the preoperative value and is not in the normal range, this may be an indication that there is more overactive parathyroid tissue and the search has to be continued.

2) A second approach is to do the sestamibi scan a few hours before surgery and use a radioactivity detector to more rapidly identify the abnormal gland(s). Once more, an appropriate 50% decline in blood parathyroid hormone into the normal range confirms the success of the procedure.
3) A third, much less common, approach is to use an endoscopy tube through a small incision to locate the gland(s) that have been identified by the sestamibi test. These three approaches should be undertaken only by surgeons with great experience in parathyroid surgery.

18. Q. Can the standard parathyroid operation be performed under local anesthesia?

A. Yes. Parathyroid surgery can be performed under general, regional (spinal nerve block), or local anesthesia. In many centers local anesthesia has become routine. In all cases, an experienced surgeon is strongly recommended, regardless of the kind of operation that is performed.

19. Q. What is parathyroid autotransplantation?

A. Parathyroid autotransplantation may be used in patients when all four parathyroid glands are abnormal. It is also of benefit in patients who have previously had an unsuccessful operation to treat hyperparathyroidism since these patients are more likely to develop postoperative hypoparathyroidism, a condition in which the blood calcium is low because of inadequate secretion of parathyroid hormone. After all four glands are removed, a small remnant of one gland is transplanted in the muscle of a forearm. If a high blood calcium develops because the transplanted parathyroid tissue enlarges over time, this can be corrected by removing some of the tissue in an outpatient procedure under local anesthesia. Parathyroid autotransplantation should only be performed by surgeons with experience in this technique.

20. Q. Is surgery always successful?

A. Not always. The abnormal gland may not be found at surgery. There are several reasons for this:

1) Many abnormal glands are small and hard to find.
2) The gland may not be in its normal location in the neck but instead may be in the chest or in an unusual neck location.
3) The surgeon is not highly experienced in the operation.
4) In patients with four abnormal glands the patient may not be cured because not enough parathyroid tissue was removed, or after apparent cure the growth of the residual overactive parathyroid tissue produces a recurrence of high blood calcium.
5) The diagnosis is not correct.

21. Q. Are there alternatives to surgery?

A. There are no other cures for primary hyperparathyroidism other than surgery. Estrogen therapy in post-menopausal women reduces the blood calcium to some extent and increases bone mineral density, but does not control the increased secretion of the parathyroid gland. Drugs are being developed to reduce PTH secretion. One such drug, Sensipar® (cinacalcet) is approved by the U. S. Food and Drug Administration (FDA) for the treatment of patients with parathyroid cancer and for patients who have chronic renal failure and are on dialysis. This drug has also proven effective in clinical studies for treating primary hyperparathyroidism. Though this drug has not been approved by the FDA for treating primary hyperparathyroidism, it has been used "off-label" to treat primary hyperparathyroidism patients.("Off-label" means that the drug is used for a condition other than the condition approved by the FDA.). Alendronate, one of the bisphosphonates, a group of drugs used to treat osteoporosis and Paget's disease, increases the bone mineral density in patients with primary hyperparathyroidism but does not affect the level of calcium or PTH.

22. Q. What general measures should patients with primary hyperparathyroidism follow?

A. Patients should always maintain good hydration by drinking enough fluids. (Dehydration will lead to an increase in the blood calcium). Immobilization, which can also cause increased blood calcium, should be avoided. A low level of calcium intake should be avoided since this may stimulate the parathyroid glands further. On the other hand, it is not advisable for patients to receive too much calcium. A daily intake of about 1000 mg daily from food and/or supplements is recommended. Patients whose vitamin D level is below normal should discuss vitamin D supplementation with their physician. Many experts think that the present recommendation of 400-800 units of vitamin D daily is not adequate for people who do not have adequate exposure to sunlight.

23. Q. Which types of physicians are specialists in treating primary hyperparathyroidism?

A. Specialists include endocrinologists, physicians who specialize in hormonal disorders, and surgeons who specialize in endocrine surgery.

The Paget Foundation for Paget's Disease of Bone and Related Disorders provides information and programs for consumers and health professionals on several bone disorders including Paget's disease of bone, primary hyperparathyroidism, fibrous dysplasia, osteopetrosis, and the complications of certain cancers on the skeleton.

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A copy of the Foundation's annual report is available by writing to the Foundation office or the Office of the Attorney General, Charities Bureau, 120 Broadway, New York, NY 10271.

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