Prolactinoma

National Endocrine and Metabolic Diseases Information Service

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What is a prolactinoma?

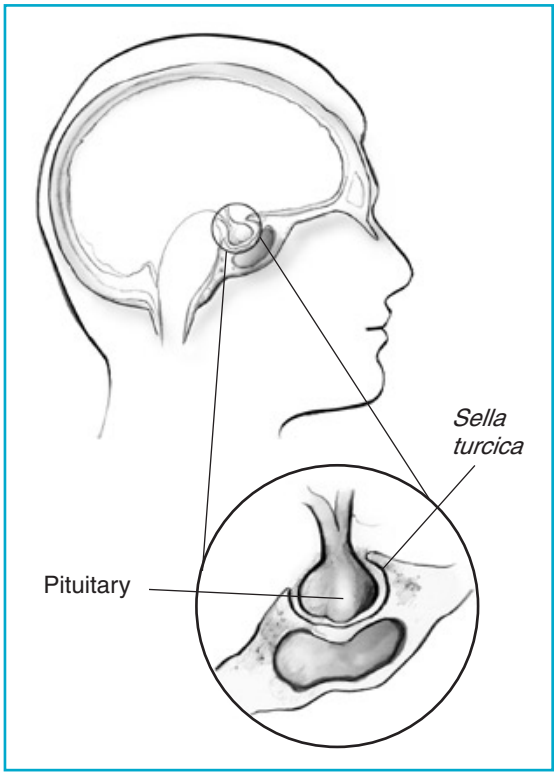
A prolactinoma is a benign—noncancerous—tumor of the pituitary gland that produces a hormone called prolactin. Prolactinomas are the most common type of pituitary tumor. Symptoms of prolactinoma are caused by hyperprolactinemia—too much prolactin in the blood—or by pressure of the tumor on surrounding tissues.

Prolactin stimulates the breast to produce milk during pregnancy. After giving birth, a mother's prolactin levels fall unless she breastfeeds her infant. Each time the baby nurses, prolactin levels rise to maintain milk production.

What is the pituitary gland?

The pituitary gland, sometimes called the master gland, plays a critical role in regulating growth and development, metabolism, and reproduction. It produces prolactin and other key hormones including

- growth hormone, which regulates growth
- adrenocorticotropin (ACTH), which stimulates the adrenal glands to produce cortisol, a hormone important in metabolism and the body's response to stress
- thyrotropin, which signals the thyroid gland to produce thyroid hormone, also involved in metabolism and growth



The pituitary gland sits in the *sella turcica*.

- luteinizing hormone and follicle-stimulating hormone, which regulate ovulation and estrogen and progesterone production in women and sperm formation and testosterone production in men

The pituitary gland sits in the middle of the head in a bony box called the *sella turcica*. The optic nerves sit directly above the pituitary gland. Enlargement of the gland can

cause symptoms such as headaches or visual disturbances. Pituitary tumors may also impair production of one or more pituitary hormones, causing reduced pituitary function, also called hypopituitarism.

How common is prolactinoma?

Although small benign pituitary tumors are fairly common in the general population, symptomatic prolactinomas are uncommon. Prolactinomas occur more often in women than men and rarely occur in children.

What are the symptoms of prolactinoma?

In women, high levels of prolactin in the blood often cause infertility and changes in menstruation. In some women, periods may stop. In others, periods may become irregular or menstrual flow may change. Women who are not pregnant or nursing may begin producing breast milk. Some women may experience a loss of libido—interest in sex. Intercourse may become painful because of vaginal dryness.

In men, the most common symptom of prolactinoma is erectile dysfunction. Because men have no reliable indicator such as changes in menstruation to signal a problem, many men delay going to the doctor until they have headaches or eye problems caused by the enlarged pituitary pressing against nearby optic nerves. They may not recognize a gradual loss of sexual function or libido. Only after treatment do some men realize they had a problem with sexual function.

What causes prolactinoma?

The cause of pituitary tumors remains largely unknown. Most pituitary tumors are sporadic, meaning they are not genetically passed from parents to their children.

What else causes prolactin to rise?

In some people, high blood levels of prolactin can be traced to causes other than prolactinoma.

Prescription drugs. Prolactin secretion in the pituitary is normally suppressed by the brain chemical dopamine. Drugs that block the effects of dopamine at the pituitary or deplete dopamine stores in the brain may cause the pituitary to secrete prolactin. These drugs include older antipsychotic medications such as trifluoperazine (Stelazine) and haloperidol (Haldol); the newer antipsychotic drugs risperidone (Risperdal) and molindone (Moban); metoclopramide (Reglan), used to treat gastroesophageal reflux and the nausea caused by certain cancer drugs; and less often, verapamil, alpha–methyldopa (Aldochlor, Aldoril), and reserpine (Serpalan, Serpasil), used to control high blood pressure. Some antidepressants may cause hyperprolactinemia, but further research is needed.

Other pituitary tumors. Other tumors arising in or near the pituitary may block the flow of dopamine from the brain to the prolactin-secreting cells. Such tumors include those that cause acromegaly, a condition caused by too much growth hormone, and Cushing's syndrome, caused by too much cortisol. Other pituitary tumors that do not result in excess hormone production may also block the flow of dopamine.

Hypothyroidism. Increased prolactin levels are often seen in people with hypothyroidism, a condition in which the thyroid does not produce enough thyroid hormone. Doctors routinely test people with hyperprolactinemia for hypothyroidism.

Chest involvement. Nipple stimulation also can cause a modest increase in the amount of prolactin in the blood. Similarly, chest wall injury or shingles involving the chest wall may also cause hyperprolactinemia.

How is prolactinoma diagnosed?

A doctor will test for prolactin blood levels in women with unexplained milk secretion, called galactorrhea, or with irregular menses or infertility and in men with impaired sexual function and, in rare cases, milk secretion. If prolactin levels are high, a doctor will test thyroid function and ask first about other conditions and medications known to raise prolactin secretion. The doctor may also request magnetic resonance imaging (MRI), which is the most sensitive test for detecting pituitary tumors and determining their size. MRI scans may be repeated periodically to assess tumor progression and the effects of therapy. Computerized tomography (CT) scan also gives an image of the pituitary but is less precise than the MRI.

The doctor will also look for damage to surrounding tissues and perform tests to assess whether production of other pituitary hormones is normal. Depending on the size of the tumor, the doctor may request an eye exam with measurement of visual fields.

How is prolactinoma treated?

The goals of treatment are to return prolactin secretion to normal, reduce tumor size, correct any visual abnormalities, and restore normal pituitary function. In the case of large tumors, only partial achievement of these goals may be possible.

Medical Treatment

Because dopamine is the chemical that normally inhibits prolactin secretion, doctors may treat prolactinoma with the dopamine agonists bromocriptine (Parlodel) or cabergoline (Dostinex). Agonists are drugs that act like a naturally occurring substance. These drugs shrink the tumor and return prolactin levels to normal in approximately 80 percent of patients. Both drugs have been approved by the U.S. Food and Drug Administration for the treatment of hyperprolactinemia. Bromocriptine is the only dopamine agonist approved for the treatment of infertility. This drug has been in use longer than cabergoline and has a well-established safety record.

Nausea and dizziness are possible side effects of bromocriptine. To avoid these side effects, bromocriptine treatment must be started slowly. A typical starting dose is one-quarter to one-half of a 2.5 milligram (mg) tablet taken at bedtime with a snack. The dose is gradually increased every 3 to 7 days as needed and taken in divided doses with meals or at bedtime with a snack. Most people are successfully treated with 7.5 mg a day or less, although some people need 15 mg or more each day. Because bromocriptine is short acting, it should be taken either twice or three times daily.

Bromocriptine treatment should not be stopped without consulting a qualified endocrinologist—a doctor specializing in disorders of the hormone-producing glands. Prolactin levels rise again in most people when the drug is discontinued. In some, however, prolactin levels remain normal, so the doctor may suggest reducing or discontinuing treatment every 2 years on a trial basis.

Cabergoline is a newer drug that may be more effective than bromocriptine in normalizing prolactin levels and shrinking tumor size. Cabergoline also has less frequent and less severe side effects. Cabergoline is more expensive than bromocriptine and, being newer on the market, its long-term safety record is less well defined. As with bromocriptine therapy, nausea and dizziness are possible side effects but may be avoided if treatment is started slowly. The usual starting dose is .25 mg twice a week. The dose may be increased every 4 weeks as needed, up to 1 mg two times a week. Cabergoline should not be stopped without consulting a qualified endocrinologist.

Recent studies suggest prolactin levels are more likely to remain normal after discontinuing long-term cabergoline therapy than after discontinuing bromocriptine. More research is needed to confirm these findings.

In people taking cabergoline or bromocriptine to treat Parkinson's disease at doses more than 10 times higher than those used for prolactinomas, heart valve damage has been reported. Rare cases of valve damage have been reported in people taking low doses of cabergoline to treat hyperprolactinemia. Before starting these medications, the doctor will order an echocardiogram. An echocardiogram is a sonogram of the heart that checks the heart valves and heart function.

Because limited information exists about the risks of long-term, low-dose cabergoline use, doctors generally prescribe the lowest effective dose and periodically reassess the need for continuing therapy. People taking cabergoline who develop symptoms of shortness of breath or swelling of the feet should promptly notify their physician because these may be signs of heart valve damage.

Surgery

Surgery to remove all or part of the tumor should only be considered if medical therapy cannot be tolerated or if it fails to reduce prolactin levels, restore normal reproduction and pituitary function, and reduce tumor size. If medical therapy is only partially successful, it should be continued, possibly combined with surgery or radiation.

Most often, the tumor is removed through the nasal cavity. Rarely, if the tumor is large or has spread to nearby brain tissue, the surgeon will access the tumor through an opening in the skull.

The results of surgery depend a great deal on tumor size and prolactin levels as well as the skill and experience of the neurosurgeon. The higher the prolactin level before surgery, the lower the chance of normalizing serum prolactin. Serum is the portion of the blood used in measuring prolactin levels. In the best medical centers, surgery corrects prolactin levels in about 80 percent of patients with small tumors and a serum prolactin less than 200 nanograms per milliliter (ng/ml). A surgical cure for large tumors is lower, at 30 to 40 percent. Even in patients with large tumors that cannot be completely removed, drug therapy may be able to return serum prolactin to the normal range—20 ng/ml or less—after surgery. Depending on the size of the tumor and how much of it is removed, studies show that 20 to 50 percent will recur, usually within 5 years.

Because the results of surgery are so dependent on the skill and knowledge of the neurosurgeon, a patient should ask the surgeon about the number of operations he or she has performed to remove pituitary tumors and for success and complication rates in comparison to major medical centers. The best results come from surgeons who have performed hundreds or even thousands of such operations. To find a surgeon, contact The Pituitary Society (see For More Information).

Radiation

Rarely, radiation therapy is used if medical therapy and surgery fail to reduce prolactin levels. Depending on the size and location of the tumor, radiation is delivered in low doses over the course of 5 to 6 weeks or in a single high dose. Radiation therapy is effective about 30 percent of the time.

How does prolactinoma affect pregnancy?

If a woman has a small prolactinoma, she can usually conceive and have a normal pregnancy after effective medical therapy. If she had a successful pregnancy before, the chance of her having more successful pregnancies is high.

A woman with prolactinoma should discuss her plans to conceive with her physician so she can be carefully evaluated prior to becoming pregnant. This evaluation will include an MRI scan to assess the size of the tumor and an eye examination with measurement of visual fields. As soon as a woman is pregnant, her doctor will usually advise her to stop taking bromocriptine or cabergoline. Although these drugs are safe for the fetus in early pregnancy, their safety throughout an entire pregnancy has not been established. Many doctors prefer to use bromocriptine in patients who plan to become pregnant because it has a longer record of safety in early pregnancy than cabergoline.

The pituitary enlarges and prolactin production increases during pregnancy in women without pituitary disorders. Women with prolactin-secreting tumors may experience further pituitary enlargement and must be closely monitored during pregnancy. Less than 3 percent of pregnant women with small prolactinomas have symptoms of tumor growth such as headaches or vision problems. In women with large prolactinomas, the risk of symptomatic tumor growth is greater, and may be as high as 30 percent.

Most endocrinologists see patients every 2 months throughout the pregnancy. A woman should consult her endocrinologist promptly if she develops symptoms of tumor growth—particularly headaches, vision changes, nausea, vomiting, excessive thirst or urination, or extreme lethargy. Bromocriptine or, less often, cabergoline treatment may be reinitiated and additional treatment may be required if the woman develops symptoms during pregnancy.

How do oral contraceptives and hormone replacement therapy affect prolactinoma?

Oral contraceptives are not thought to contribute to the development of prolactinomas, although some studies have found increased prolactin levels in women taking these medications. Because oral contraceptives may produce regular menstrual bleeding in women who would otherwise have irregular menses due to hyperprolactinemia, prolactinoma may not be diagnosed until women stop oral contraceptives and find their menses are absent or irregular. Women with prolactinoma treated with bromocriptine or cabergoline may safely take oral contraceptives. Similarly, postmenopausal women treated with medical therapy or surgery for prolactinoma may be candidates for estrogen replacement therapy.

Is osteoporosis a risk in women with high prolactin levels?

Women whose ovaries produce inadequate estrogen are at increased risk for osteoporosis. Hyperprolactinemia can reduce estrogen production. Although estrogen production may be restored after treatment for hyperprolactinemia, even a year or 2 without estrogen can compromise bone strength. Women should protect themselves from osteoporosis by increasing exercise and calcium intake through diet or supplements and by not smoking. Women treated for hyperprolactinemia may want to have periodic bone density measurements and discuss estrogen replacement therapy or other bone-strengthening medications with their doctor.

Points to Remember

- A prolactinoma is a benign tumor of the pituitary gland that produces the hormone prolactin. Prolactin stimulates the breast to produce milk during pregnancy.
- In women, high levels of prolactin in the blood often cause infertility and changes in menstruation. Women who are not pregnant or nursing may begin producing breast milk. In men, the most common symptom of prolactinoma is erectile dysfunction.
- Prolactinoma is diagnosed through a blood test. Additional tests rule out other causes of high prolactin levels, such as medications or thyroid problems. Magnetic resonance imaging (MRI) is then used to detect pituitary tumors and determine their size.
- The first line of treatment is usually medication to shrink the tumor and return prolactin levels to normal. Sometimes surgery or radiation may be necessary.
- Women with prolactinoma should be carefully evaluated before becoming pregnant and monitored during pregnancy by an endocrinologist.

Hope through Research

Researchers are working to identify a gene or genes that may contribute to the development of pituitary tumors, including sporadic tumors. They are also investigating certain side effects of long-term treatment for prolactinomas with cabergoline.

Participants in clinical trials can play a more active role in their own health care, gain access to new research treatments before they are widely available, and help others by contributing to medical research. For information about current studies, visit *www.ClinicalTrials.gov.*

For More Information

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- searching the NIDDK Reference Collection at *www.catalog.niddk.nih.gov/resources*
- visiting MedlinePlus at *www.medlineplus.gov*

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