

Pituitary Tumors (adenoma, craniopharyngioma)

Overview

Tumors that grow from the pituitary gland can affect the whole body by interfering with normal hormone levels. They can also cause headaches and vision problems. There are various kinds of pituitary tumors: adenomas, craniopharyngiomas, and Rathke's cleft cysts. Most are benign (not cancer) and are often curable. Treatment options aim to remove the tumor or control its growth and correct hormone levels with medications.

Anatomy of the pituitary and sella

The pituitary gland is a small, bean-shaped organ that sits at the base of the brain, behind the bridge of the nose (Fig. 1 and 2). It has a large anterior lobe (gland cells that produce hormones) and a smaller posterior lobe (nerve cells that release hormones). It sits in a small pocket of bone in the base of the skull called the sella turcica. The gland is connected to the hypothalamus in the brain by the pituitary stalk. The pituitary gland is bordered on either side by the cavernous sinuses and below by the sphenoid sinus. The sphenoid sinus is an air-filled sinus that drains into the nose. The internal carotid arteries and the nerves that control eye movement lie on the sides of the pituitary. Directly above the pituitary gland is the optic chiasm, which is responsible for vision. When pituitary tumors grow they can compress the above-mentioned structures and cause symptoms.

Known as the master gland, the pituitary controls the other endocrine glands in the body. It releases secretions into the bloodstream and provides feedback to the hypothalamus. The hypothalamus then regulates pituitary hormone levels, depending on the needs of the body.

Hormones made by the pituitary gland include:

- Prolactin hormone: causes a woman's breasts to make milk after pregnancy.
- Growth hormone: helps control body growth and the metabolism of sugar and fat.
- Adrenocorticotrophic hormone: causes the adrenal glands to make cortisol. Cortisol helps control the use of sugar, protein, and fats in the body and helps the body deal with stress.
- Thyroid-stimulating hormone: causes the thyroid gland to make other hormones that control growth, temperature, and heart rate.

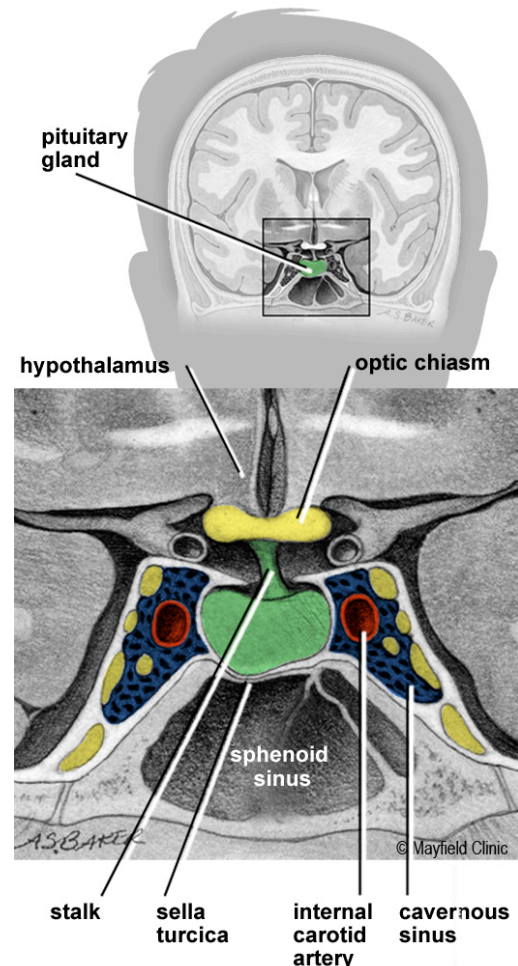


Figure 1A. A cross-section of the pituitary gland (green) shows its relationship to the optic chiasm, the sphenoid sinus, and the cavernous sinuses on each side.

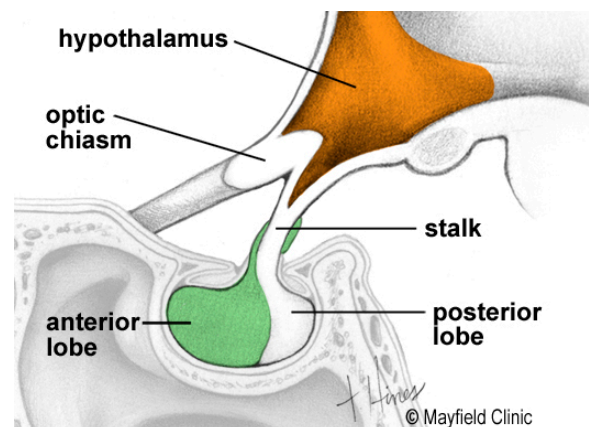


Figure 1B. Side view of the pituitary gland sitting inside the bony sella.

- Antidiuretic hormone (ADH or vasopressin): regulates water balance. Too little of this hormone can cause diabetes insipidus. Too much of this hormone can cause syndrome of inappropriate ADH secretion. Both of these conditions affect the kidneys' ability to regulate the balance of water and electrolytes.
- Luteinizing hormone and follicle-stimulating hormone: control the menstrual cycle in women and sperm production in men.

What is a pituitary tumor?

A tumor that grows from the pituitary gland is called an adenoma. Most adenomas are benign, slow growing, and relatively common. Tiny tumors or cysts are often found on an MRI scan performed for another reason. Most of these never grow or cause symptoms.

Functioning pituitary tumors secrete high levels of hormones and interfere with other body organs. These tumors behave according to their cell of origin and are named for the specific hormone they produce. For example, a prolactinoma grows from prolactin-producing cells.

Nonfunctioning pituitary tumors do not secrete hormones. Instead, they grow until their size and mass effect cause headache, vision loss, nausea, vomiting, or fatigue. These tumors may compress the normal pituitary gland and decrease hormone production (hypopituitarism).

Based on size, pituitary tumors may be classified as microadenomas (less than 10mm) or macroadenomas (larger than 10mm). Large tumors can press on the optic nerves and invade the cavernous sinuses, which house the carotid arteries and the nerves involved in eye movement.

Closely related to pituitary adenomas are craniopharyngiomas and Rathke's cleft cysts. These grow from embryonic remnant cells in the pituitary gland. Craniopharyngiomas typically grow from the pituitary stalk upward into the third ventricle and cause symptoms similar to pituitary adenomas.

What are the symptoms?

Symptoms of a pituitary tumor vary depending on its size and hormone secretion; many are asymptomatic. About 25% of pituitary tumors are nonfunctional; 75% are functional. Of hormonally active adenomas, about 50% secrete prolactin, 20% secrete growth hormone, 20% secrete adrenocorticotrophic hormone, and 10% secrete multiple hormones.

Prolactin-producing tumors. The most common pituitary tumor, a prolactinoma, causes an overproduction of the hormone that helps control sexual function. In women, the tumor can cause menstruation to stop (amenorrhea) or inappropriate

production of breast milk (galactorrhea). In men, prolactinomas may cause enlarged breasts (gynecomastia), erectile dysfunction or impotence, infertility, decrease in body hair, and low sex drive.

Growth hormone-producing tumors. More common in men, these pituitary tumors may cause gigantism in children or acromegaly in adults. Symptoms include enlargement of the bones in the hands, feet, or face. Other symptoms include excess sweating, high blood pressure, heart disease, diabetes, and arthritis.

Adrenocorticotrophic hormone (ACTH)-producing tumors. More common in women, these tumors stimulate the adrenal gland to secrete cortisol. Excess cortisol causes Cushing's disease, a fatty hump between the shoulders; weight gain in the face, neck, and trunk of the body; and pink or purple stretch marks on the skin. Cushing's can also cause diabetes, menstrual irregularities, excessive hair growth, bruising, hypertension, and bone fractures from calcium depletion.

Thyroid-stimulating hormone-producing tumors. TSH-secreting tumors can cause hyperthyroidism. Hyperthyroidism can accelerate the body's metabolism, causing sudden weight loss, irregular heartbeat, and nervousness or irritability.

Non-secreting tumors have few symptoms and are difficult to recognize until they grow quite large. These tumors can press against nearby optic nerves, causing headaches or vision loss. They can also impair hormone secretion from the pituitary gland, which can cause fatigue, weakness, loss of body hair, and pale skin.

Pituitary apoplexy. In rare instances, a pituitary tumor can suddenly bleed (hemorrhage). Symptoms include sudden onset of a severe headache and vision changes, including vision loss, double vision, or drooping of an eyelid. Pituitary apoplexy requires emergency treatment, usually with corticosteroids and often surgery.

What are the causes?

The cause of pituitary tumors is unknown. Some researchers believe they occur when a cell in the pituitary gland becomes abnormal or mutates.

Multiple endocrine neoplasia type 1 (MEN 1) is a rare condition with simultaneous tumors of the pituitary, pancreas and parathyroid glands. Pituitary adenomas develop in 25% of patients with MEN 1.

Who is affected?

Pituitary tumors are common and occur in 15% of adults; most do not cause symptoms. They can occur at any age, but are more common after puberty.

How is a diagnosis made?

If you have symptoms that suggest a pituitary tumor, your physician will work with a team of specialists to confirm the diagnosis. This team may include a neurosurgeon, otolaryngologist (ear, nose, and throat surgeon), endocrinologist, ophthalmologist, radiologist, and pathologist.

First, the doctor will obtain your personal and family medical history and perform a physical examination. In addition to checking your general health, the doctor performs a neurological exam to check mental status and memory, cranial nerve function, muscle strength, coordination, reflexes, and response to pain. Other tests may include:

- **Magnetic Resonance Imaging (MRI) scan** uses a magnetic field and radiofrequency waves to give a detailed view of the soft tissues of the brain. A dye (contrast agent) may be injected into your bloodstream (Fig. 3).
- **Endocrine evaluation** measures hormone levels in the blood or urine to detect abnormal levels caused by pituitary tumors.
- **Visual field acuity test** detects vision loss and missing areas in the field of view. This test measures both central and peripheral vision.
- **Petrosal sinus sampling** is a procedure to draw blood from the veins that drain the pituitary gland. Similar to an angiogram, flexible catheters are inserted into the femoral veins in the groin. The catheters are advanced to the petrosal veins near the pituitary. Blood is taken and tested for ACTH levels to help diagnose Cushing's disease.

What treatments are available?

Treatment options vary, depending on the type, grade, size, and location of the tumor, and your age and general health. Medication, surgery, and radiation either alone or in combination, are used to treat pituitary tumors and return hormone levels to normal. It is important to seek treatment at a center that offers the full range of options including surgery, radiation, and endocrine therapy. A neurosurgeon, ENT surgeon, endocrinologist and radiation oncologist work as a team to treat pituitary tumors.

Medication

The goal of medication is to block the tumor from making abnormal quantities of hormones.

Prolactinomas can be controlled with the drugs cabergoline (Dostinex) or bromocriptine (Parlodel), which reduce the size of the tumor while maintaining normal prolactin levels. About 80% of patients will have prolactin levels restored to normal with cabergoline. Many will have marked tumor shrinkage on their MRI, making surgery unnecessary.

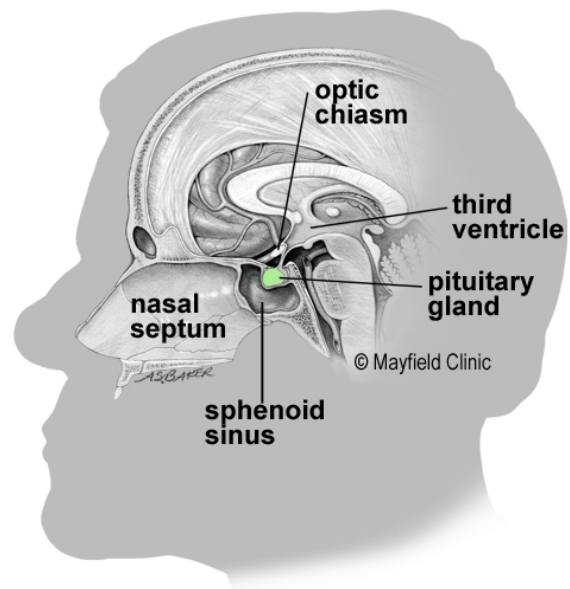


Figure 2. Side view. The pituitary gland (green) is located deep within the skull in an area called the sella. The pituitary gland is related to the optic chiasm above and the sphenoid sinus below.

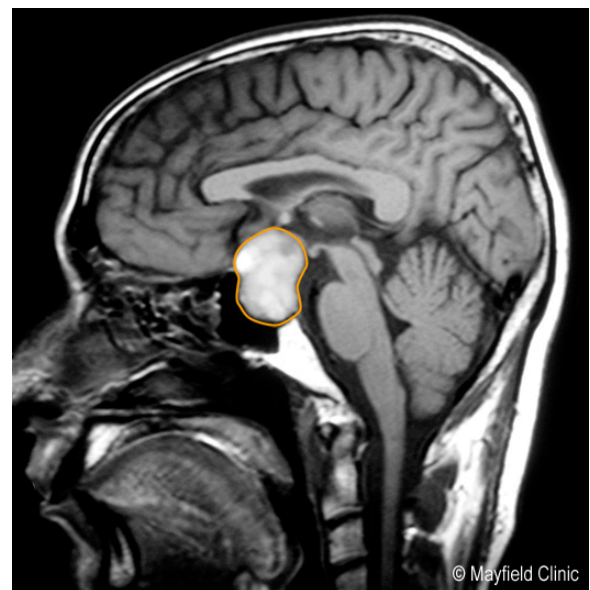


Figure 3. An MRI scan of a pituitary macroadenoma (orange line) that has grown upward to compress the optic chiasm.

Tumors that make growth hormone can be controlled with the drugs octreotide (Sandostatin) or pegvisomant (Somavert), which are used in conjunction with surgical removal. These drugs are also used to treat recurrent tumors.

In Cushing's disease, drugs used to control the production of ACTH and excess cortisol may include mitotane (Lysodren), ketoconazole (Nizoral), aminoglutethimide (Cytadren), and pasireotide (Signifor).

Surgery

Surgical removal of a pituitary tumor may be performed with a minimally invasive endoscopic transsphenoidal, traditional transsphenoidal, or a craniotomy approach. The best option varies for each patient, depending on the tumor size, type, and location. For growth hormone-producing and ACTH-producing tumors, surgery is the treatment of choice to reverse endocrine problems. If a tumor is located near critical areas, surgeons may remove only part of it. A partial removal can still relieve symptoms. Radiation may be used to treat the remaining tumor.

- **Endoscopic transsphenoidal surgery.** An ENT surgeon inserts an endoscope through the nostril to reach the sphenoid sinus. An endoscope is a thin, tube-like instrument with a light and a camera. Video from the camera is viewed on a monitor. An opening is made in the sphenoid sinus to access the sella and pituitary gland (Fig. 4). Next, the neurosurgeon removes the tumor by passing long instruments through the nostril while watching the monitor. Surgery is usually carried out with the aid of computer image guidance (an anatomical navigation system akin to a GPS). The goal is to precisely expose the tumor and to avoid nearby carotid arteries or optic nerves.
- **Traditional microscopic transsphenoidal.** This technique is performed through an incision made under the upper lip (sublabial) along with removal of the nasal septum to access the tumor. The endoscopic technique is replacing the traditional microscopic approach as it reduces the trauma to the nasal tissues and the recovery time for the patient.
- **Expanded endoscopic transsphenoidal surgery** involves opening more bone into the anterior skull base. This enables the surgeon to safely expose very large tumors that extend beyond the boundaries of the transsphenoidal approach. It provides the surgeon with direct visualization of compressed structures, such as the optic nerves or anterior cerebral arteries.
- **Craniotomy.** A skin incision is made in the scalp. A small bone flap above the eye (supraorbital craniotomy) is cut and removed to access the brain (Fig. 5). The brain is gently retracted to locate and remove the tumor. The bone flap is replaced and secured with tiny plates and screws. A craniotomy is required for large tumors that have invaded nearby tissues and cannot be removed through a transsphenoidal approach.

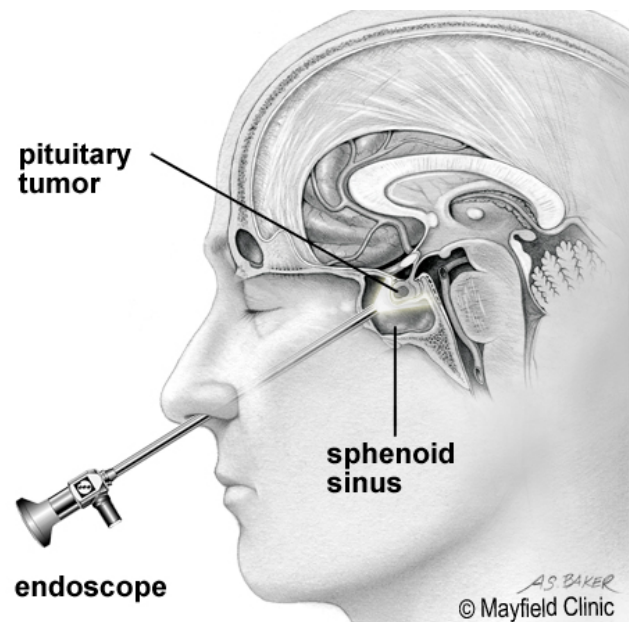


Figure 4. Endoscopic transsphenoidal surgery, performed through the nose, creates a minimally invasive path to a pituitary tumor. An opening is made in the sphenoid sinus to access the sella and remove the tumor.

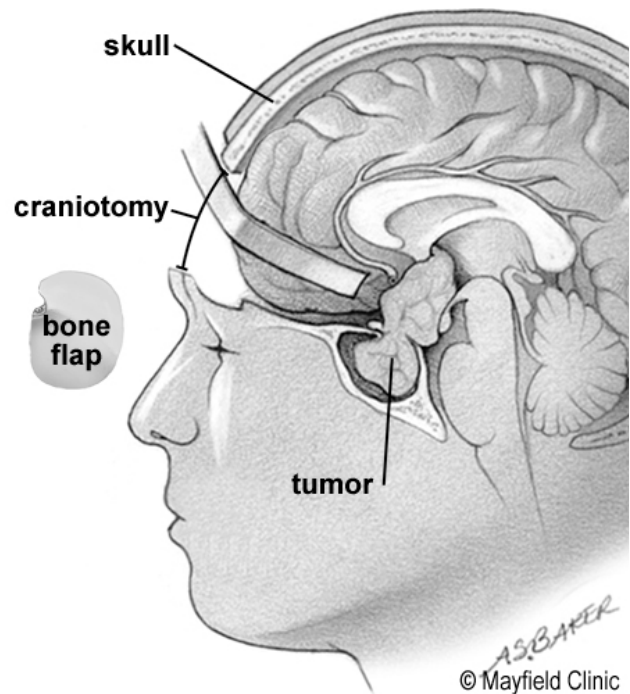


Figure 5. Craniotomy approach to a pituitary macroadenoma that extends down into the sphenoid sinus and up into the third ventricle. A bone flap is cut above the eye (supraorbital) to expose the brain. Retractors gently open a corridor to the tumor.

Radiation

Radiation therapy uses controlled high-energy rays to treat pituitary tumors. Radiation damages the DNA inside cells, making them unable to divide and grow. The benefits of radiation are not immediate but occur over time. Gradually, the tumor stops growing, shrinks, and in some cases disappears.

The goal of radiation therapy is to maximize the dose to abnormal tumor cells and minimize exposure to normal healthy cells (Fig. 6).

External beam radiation is delivered from outside the body by a machine that aims high-energy rays (x-rays, gamma rays) at the tumor. Ways to deliver radiation include:

- **Stereotactic radiosurgery** delivers a high dose of radiation during a single session or 5 daily sessions. The two main technologies are the Leksell Gamma Knife and linear accelerator systems such as the BrainLab Novalis. Although it is called surgery, no incision is made. Because a single radiosurgery dose is more damaging than multiple fractionated doses, the target area must be completely immobilized with a head frame or facemask (Fig. 7).
- **Fractionated radiotherapy** delivers lower doses of radiation daily over 5 to 6 weeks. A facemask is used to accurately reposition the patient for each treatment session. Delivering a fraction of the total radiation dose allows normal cells time to repair themselves between treatments. It also reduces side effects.
- **Proton beam therapy** delivers accelerated proton energy to the tumor at a specific depth. The radiation beam does not go beyond the tumor.

Radiation is most often used to treat residual tumor after surgery or for tumor recurrence. Some people who have radiation treatment will need pituitary hormone replacement.

Observation ("watch and wait")

Sometimes the best treatment is observation. Small, slow-growing tumors that produce few symptoms may be observed with routine MRI scans until their growth or symptoms necessitate surgery. Observation may be the best option for older patients with other health conditions. You and your doctor can weigh the risk that symptoms will develop versus the risk of treatment intervention.

Clinical trials

Clinical trials are research studies in which new treatments – drugs, diagnostics, procedures, vaccines, and other therapies – are tested in people to see if they are safe and effective. Research is always being conducted to improve the standard of medical care and to explore new drug and surgical treatments. Information about current clinical trials,

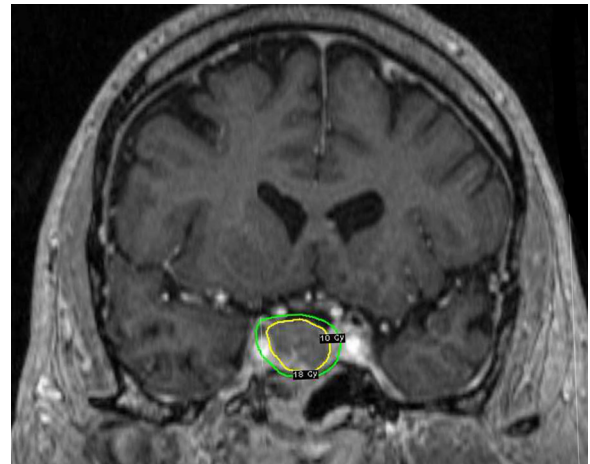


Figure 6. Radiation treatment plan for a pituitary adenoma. Colored lines around the tumor indicate radiation dose to the tissue.

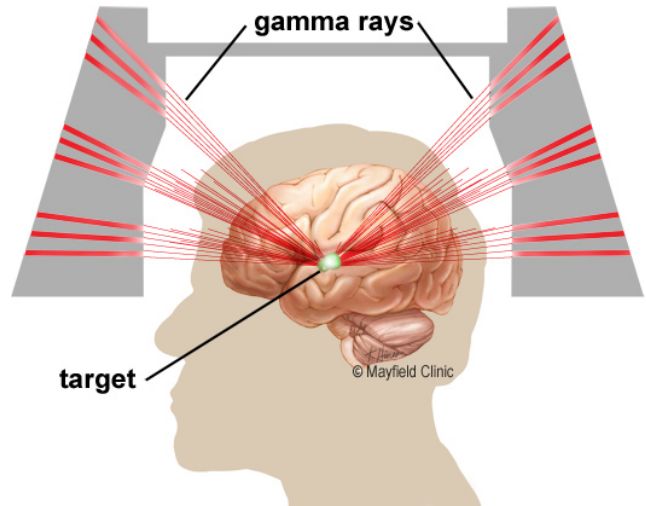


Figure 7. Gamma Knife utilizes 192 low-dose beams of radiation that intersect at the tumor to produce a high dose while minimizing exposure to nearby healthy brain.

including eligibility, protocol, and locations, are found on the web. Studies can be sponsored by the National Institutes of Health (www.clinicaltrials.gov) as well as private industry and pharmaceutical companies (www.centerwatch.com).

Recovery and prevention

The size and location of the tumor is the most important factor in determining the outcome. Since it is impossible to predict whether or when a pituitary tumor may recur, periodic monitoring with MRI scans is needed to watch for changes or regrowth.

Many people with pituitary tumors are followed long-term by an endocrinologist. Hormone imbalances can be caused by the tumor itself, or may result from the treatment. An endocrinologist will monitor your hormone blood levels, outline a treatment plan and make drug adjustments when needed.

Sources & links

If you have more questions, please contact New England Neurological Associates at 978-687-2321.

Support

Support groups provide an opportunity for patients and their families to share experiences, receive support, and learn about advances in treatments and medications. Contact the Pituitary Network Association for support groups in your area.

Links

Pituitary Network Association, www.pituitary.org
National Brain Tumor Society, www.braintumor.org
American Brain Tumor Association, www.abta.org

Glossary

acromegaly: enlargement of the hands, feet or face in adults due to overproduction of growth hormone; often from a growth hormone-secreting pituitary tumor.

adenoma: a tumor that grows from a gland.

apoplexy: sudden bleeding inside an organ.

Cushing's syndrome: an endocrine disease caused by increased levels of cortisol in the body; often from an adrenocorticotrophic hormone (ACTH)-secreting pituitary tumor. Hallmark signs include a fatty hump between the shoulders, a rounded face, and pink or purple stretch marks on the skin. Also caused by excessive use of corticosteroid medication.

diabetes insipidus: a disorder in which there is an abnormal increase in urine output, fluid intake, and often thirst. Caused by a decrease in vasopressin hormone due to damage of the posterior pituitary lobe.

gigantism: excessive growth and height in children caused by overproduction of growth hormone; often from a growth hormone-secreting pituitary tumor.

hyperthyroidism: increased heart rate, weight loss, nervousness, and sleeplessness caused by excess thyroid hormone; can be caused by thyroid-stimulating hormone (TSH) pituitary tumor.

prolactinoma: a benign pituitary tumor that overproduces the hormone prolactin. Too much prolactin causes abnormal milk production in the breasts, lack of menstruation, infertility, and decreased sex drive.



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