All About Pituitary Adenomas

What is the pituitary gland?

The pituitary is a small gland, approximately the size and shape of a pea. It is located between the eyes, behind the bridge of the nose, just below the brain. The pituitary lies within a bony depression in the skull called the sella turcica, which sits below the optic chiasm, the area where nerves from the eyes (the optic nerves) cross and enter the brain. It is often referred to as the "master" gland of the body, because it produces hormones (proteins that are released into the body that influence the function of other organs) that control several other glands throughout the body, including the thyroid and adrenal glands, and the sex organs (ovaries and testicles).

The pituitary gland is divided into two main portions: the larger anterior pituitary (at the front) and the smaller posterior pituitary (at the back). Each of these portions has different functions, producing different types of hormones. It is rare for tumors to develop in the posterior lobe of the pituitary gland.

The pituitary itself is controlled by another gland called the hypothalamus, which sits just above the pituitary gland. In response to various signals from the body, the hypothalamus sends hormones directly down a channel to the pituitary gland, telling the pituitary to produce and release its hormones into the bloodstream so they can act on various organs throughout the body.

What hormones are produced by the pituitary gland?

In the posterior lobe, two different hormones are produced:

- **Anti-diuretic hormone** (ADH, also called vasopressin): acts on the kidneys and signals them to retain water, rather than releasing water through the urine. Without ADH, excessive amounts of water can be lost through the urine. This is seen in a condition called central diabetes insipidus.
- **Oxytocin**: primarily acts on the uterus to stimulate contractions. It can also act on the breasts to stimulate the secretion of milk.

In the anterior lobe, several different hormones are produced:

- **Growth hormone** (GH, also known as somatotropin): stimulates growth in children and plays an important role in regulating the metabolism and processing of proteins, fats, and carbohydrates in the body. Abnormal levels of GH in children can lead to dramatic growth defects including dwarfism (when GH levels are too low) and gigantism (when GH levels are too high). In adults, a small amount of GH is normally produced; however, excess production of GH in adults can lead to excessive growth of bone and tissues, particularly in the face, hands, and feet (a condition known as acromegaly).
- **Prolactin**: primarily acts on the breast to stimulate the production of milk. It also plays a role in development of eggs in a woman's ovaries and may help to regulate the immune system.
- **Adrenocorticotropic hormone** (ACTH, also known as corticotropin): stimulates growth of the adrenal glands, which are located just above the kidneys. ACTH triggers the adrenal glands to produce steroid hormones such as cortisol. Excessive production of steroid hormones by the adrenal glands is called Cushing's disease, and leads to a number of symptoms, including weight gain, increased fat around the neck and back, poor wound healing, high blood pressure, increased blood sugar, excessive hair growth, and erratic mood changes.
- **Thyroid-stimulating hormone** (TSH, also known as thyrotropin): acts on the thyroid gland to stimulate the production of thyroid hormone. Thyroid hormone is the main regulator of overall metabolism in the body. Too much thyroid hormone (called hyperthyroidism) can lead to weight loss, irritability, and cardiac arrhythmias. Too little thyroid hormone...
Hypothyroidism can lead to weight gain, excessive sleepiness, and fatigue.

- **Luteinizing hormone (LH) and follicle-stimulating hormone (FSH)** (known as gonadotropins): act on the gonads (the testes in men and the ovaries in women). In men, LH causes the testicles to produce testosterone, the primary male hormone, while FSH regulates the production of sperm. In women, LH causes the ovaries to produce estrogen, the primary female hormone, and also plays an important role in stimulating the release of eggs from the ovary. LH has a critical role during pregnancy by regulating hormone levels so that the pregnancy is maintained. FSH in women primarily acts to regulate the maturation of eggs within the ovary. Decreased levels of FSH and/or LH (known as hypogonadism) can lead to failure of sperm production in men and cessation of the menstrual cycle in women.

**What is a pituitary adenoma?**

Normally, cells in the body will grow and divide to replace old or damaged cells. This growth is highly regulated, and once enough cells are produced to replace the old ones, normal cells will stop dividing. Tumors occur when there is an error in this regulation, and cells continue to grow in an uncontrolled manner. Tumors can either be benign or malignant. Benign tumors represent uncontrolled growth. However, unlike malignant tumors, they typically do not invade into surrounding tissues or break off and spread beyond where they started. Malignant tumors will grow uncontrolled in such a way that they invade and damage other tissues around them. They also gain the ability to break off from where they started and spread to other parts of the body, usually through the blood stream or through the lymphatic system where the lymph nodes are located.

Pituitary adenomas are benign growths of glandular tissue that almost always grow from the anterior lobe of the pituitary gland. Pituitary adenomas can be either non-secreting adenomas, meaning that they do not produce excess levels of hormones, or they can be secreting adenomas, meaning they produce an excessive level of one or more of the hormones normally produced by the pituitary gland.

There are two general types of pituitary adenomas.

- **Macroadenomas**: adenomas that are at least 1 cm in maximum dimension. These can exert pressure on nearby structures due to their increased size.
- **Microadenomas**: These are small adenomas, less than 1 cm, in maximum dimension. Most pituitary adenomas are microadenomas.

The vast majority of tumors in the pituitary gland are benign, and most of these are pituitary adenomas. Other types of tumors (both benign and malignant) can develop in the pituitary gland. These include teratomas, germinomas, and choriocarcinomas. Although malignant cancers can develop in the pituitary gland, they are very rare. In fact, only about 100 cases of malignant pituitary cancer have been reported in the medical literature.

**What causes pituitary adenomas and am I at risk?**

Pituitary adenomas are indolent (slow growing) tumors, and account for 10–15% of all tumors in the brain. Each year, there are approximately 13,210 cases of pituitary tumors in the United States; of these only about 60 will be malignant. The cause of most pituitary adenoma is unknown, although some genetic abnormalities are associated with these tumors. Pituitary adenomas develop in 30% percent of patients with multiple endocrine neoplasia type 1 (MEN-1). Individuals with Carney complex may also be at higher risk for development of pituitary adenoma. Familial isolated pituitary adenoma (FIPA) is another genetic condition influenced by changes in the AIP gene. In FIPA, adenomas seem to only present in the pituitary, while with MEN-1 or Carney complex tumors can occur in other organs/glands.

Another gene called gsp may be involved in sporadic cases of pituitary tumor. Mutations in the gsp gene have been found in 10% of non-secreting pituitary adenomas, 40% of pituitary adenomas secreting growth hormone, and 5% of pituitary adenomas secreting ACTH.

Aside from these genetic mutations, no other cause is known for pituitary tumors. Pituitary tumors are not associated with smoking or drinking and have not been linked with any viral infections. The risk of pituitary adenomas does increase with age, and they are slightly more likely to occur in women than men.
How can I prevent pituitary adenomas?

There are no methods to prevent pituitary adenomas for occurring.

What are the signs of pituitary adenomas?

Most commonly, because the pituitary gland sits right underneath the optic chiasm, macroadenomas can affect vision. This usually presents as loss of peripheral vision on both sides, but can also present as other patterns of vision loss. The pressure of pituitary macroadenomas can also lead to headaches, and invasion into nearby nerves can cause other neurologic signs, such as loss of motion of the eye.

If microadenomas cause symptoms, it is because they produce excessive amounts of hormones, although macroadenomas can also secrete and produce hormones. Depending on which hormones they secrete, the signs and symptoms of these adenomas can differ. For example, prolactin-secreting adenomas can result in milk production from the breast, while growth hormone-producing adenomas can cause acromegaly.

Some adenomas do not produce any symptoms at all. Most are found incidentally during the workup of another unrelated problem. Many people may have pituitary adenomas and never know it because they do not have symptoms.

How are pituitary adenomas diagnosed?

Most pituitary adenomas are discovered because they produce symptoms, either from direct pressure due to their large size (in the case of macroadenomas), or due to the hormones that they secrete. Occasionally, pituitary adenomas are detected when the brain is imaged for an unrelated reason. When a pituitary adenoma is suspected, the healthcare provider will perform a thorough history and physical examination. The physical exam should consist of a complete neurologic evaluation and examination for signs of excessive hormone secretion.

A number of blood tests can be performed to look for excess production of hormones. Often, these hormones can be measured directly from a blood sample. In some cases, additional tests are needed to distinguish if abnormalities on a blood test are due to a pituitary adenoma or due to some other cause. These tests include a glucose suppression test used to detect pituitary adenomas that produce growth hormone, and a cortisol-stimulation test used to distinguish if abnormal blood cortisol levels are due to a secreting pituitary adenoma or due to a problem in the adrenal glands.

In addition to blood tests, imaging of a suspected pituitary adenoma may be ordered. The most common type of imaging used is Magnetic Resonance Imaging (MRI), which uses magnets to produce a very sharp picture of the inside of the head. Despite the high resolution of MRIs, small microadenomas may not be detectable on an MRI. In those cases, the only way to confirm the diagnosis is by obtaining a biopsy or by removing the tumor and examining it underneath a microscope.

Less commonly, computed tomography (CT or CAT) scans are used. CT scans use x-rays to form a three-dimensional picture of the inside of the body. The ability to detect pituitary tumors on CT scan is significantly worse than on MRI; however, large macroadenomas can sometimes be seen on CT scan. With the use of modern imaging techniques, the diagnosis of pituitary adenoma is increasing.

Ultimately, the only way to confirm a diagnosis of a pituitary adenoma is to examine the tissue underneath a microscope. In most cases of tumors or cancers in other parts of the body, this is done by obtaining a biopsy of the tumor. A biopsy is where a small piece of the suspected tumor is removed (i.e. with a needle, etc.) and examined underneath a microscope. Pituitary adenomas are an exception to this general rule. The accuracy of diagnosing pituitary adenomas through blood tests and radiographic imaging is very good, and often makes a biopsy unnecessary - especially since the pituitary gland is in a difficult area to reach and near a number of critical structures, such as the optic chiasm. Since many pituitary adenomas can be treated without surgery, by using medications or radiation, the issue of accessing this area of the body for biopsy may be irrelevant.

How are pituitary adenomas staged?

There is no official or widely used staging system for pituitary adenomas. In general, pituitary adenomas are classified as either
macroadenomas (>10mm; can extend outside the bony structure around the pituitary gland) or microadenomas (≤10mm), and by whether they are secreting (adenomas that produce hormones, also called functional) or non-secreting (adenomas that do not produce hormones, also called non-functional).

What are the treatments for pituitary adenomas?

**Surgery**

The most common therapy for pituitary adenomas is surgical resection. For non-secreting macroadenomas, surgery removes excess tissue and relieves pressure from the adenoma on surrounding tissues. For hormone secreting adenomas, surgery often results in a rapid drop in the excessive hormone production.

Surgery for pituitary tumors can be performed in several different ways. The most common approach is the transsphenoidal approach. In this procedure, an incision is made on the inside of the upper lip just above the teeth, or along the septum of the nose. The pituitary gland is accessed by cutting through the bond of the sphenoid sinus, which lies behind the nose and just in front of the pituitary gland. For microadenomas, this procedure has high overall cure rates with few complications. Occasionally, this surgery can lead to decreased hormone production from the pituitary gland, leaks of cerebral spinal fluid leading to meningitis, and possible loss of vision. These complications are rare and occur in less than 1% of transsphenoidal surgeries performed by an experienced neurosurgeon. The transsphenoidal approach is less optimal for larger tumors, particularly macroadenomas that are very fibrous or extend too far towards the back of the head.

Recently, more pituitary surgeries have been performed endoscopically. Endoscopic surgery is performed by using a fiberoptic camera (the endoscope) to access the pituitary fossa (usually through the nostril in a transsphenoidal approach). Small instruments are passed through the small hole made by the endoscope and used to remove the pituitary adenoma. This procedure works well for small tumors and has the advantage of being less invasive than a transsphenoidal surgery, with a quicker patient recovery time and a low complication rate. However, this procedure may not be appropriate for larger tumors or tumors that are not in the appropriate position.

For larger tumors with a large amount of extension beyond the normal pituitary gland, a craniotomy can be performed. A craniotomy requires the neurosurgeon to cut through the bones of the skull to access the pituitary gland. Although it may be the only type of surgery possible in some cases, there is a higher risk of neurologic complications and a longer recovery time for the patient as compared to the other surgeries.

With any surgery to the pituitary gland, the development of central diabetes insipidus is fairly common. In diabetes insipidus, the pituitary gland does not produce enough anti-diuretic hormone (ADH), which leads to excessive loss of water in the urine. In most cases of post-operative diabetes insipidus, the problem goes away by itself after one to two weeks. Occasionally, however, this problem can be permanent. Treatment requires taking replacement ADH (also known as vasopressin), usually as a nasal spray.

**Radiation**

Radiation therapy can also be used in the treatment of pituitary adenomas, though it is not typically used as the first line of treatment. Radiation comes in the form of high energy x-rays that are delivered to the area(s) of the cancer. These x-rays are similar to those used for a chest x-ray, only a much higher amount of energy. The high energy of x-rays in radiation therapy results in damage to the DNA of cells, causing the tumor cells to die. Although the overall control of pituitary tumors with radiation therapy is high, radiation does not remove the pressure that macroadenomas can exert on surrounding structures as surgery does, and hormone levels fall more slowly after radiation therapy than they do after surgery. In most cases, radiation therapy is reserved for patients who have disease left behind after surgical resection, for patients who have their pituitary adenoma come back after surgery, for patients whose adenomas are in a location such that surgical resection would carry a high rate of complications, or in patients who are not medically operable.

Standard radiation (also called conventional radiotherapy) for pituitary adenomas is given daily, Monday through Friday, usually for 5 to 6 weeks. The radiation treatments themselves are short, lasting only a few minutes. Like diagnostic x-rays, radiation treatments cannot be seen, heard, or felt, and they do not hurt. Generally, the side effects of treatment are limited to the areas being treated. Most commonly, standard radiation treatment for pituitary adenomas can result in loss of hair and fatigue. Because the pituitary gland sits very close to the optic nerves and optic chiasm, there is a risk that radiation treatments can
cause loss of vision, although this is unusual in the hands of a skilled radiation oncologist. Compared to surgery, patients receiving radiation can experience hypopituitarism, where the pituitary has decreased production of one or more of the hormones that it usually releases. If this occurs, these hormones can be replaced in the form of medication. Finally, although the risk is low, radiation for pituitary tumors may cause cancers to form in the radiation field years after the radiation has been given.

**Stereotactic Radiosurgery**

Stereotactic radiosurgery is a way of delivering radiation therapy to brain tumors in a very precise way. This method of radiation treats a tumor with large doses of radiation over a few days, or even in a single treatment, rather than spreading the treatment out over a number of weeks, as is done with standard radiation therapy. When performed in other parts of the brain, this technique can deliver high doses of radiation to a specific area of the brain while reducing the amount of radiation that is delivered to normal, healthy brain tissue. Stereotactic radiosurgery has been tried in pituitary adenomas, and compared to standard radiation therapy, it results in more rapid decrease in hormone levels of secreting adenomas. However, because higher doses are delivered with each treatment, a higher rate of complications has been seen with stereotactic radiosurgery, particularly with regards to damage to the optic nerves and the optic chiasm. For this reason, stereotactic radiosurgery is not often used to treat pituitary adenomas. Occasionally, stereotactic radiosurgery can be used in situations where a pituitary adenoma has recurred after previous treatment.

**Treatment with Medications**

For some pituitary adenomas that secrete hormones (functional adenomas), treatment with medication rather than surgery or radiation can be effective, and is often the first treatment tried for these types of adenomas. For pituitary adenomas that produce the hormone prolactin, the medications most commonly used are bromocriptine (Parlodel) and cabergoline (Dostinex). Lisuride and pergolide mesylate have also been used with some success. These medications are similar to a chemical produced in the brain called dopamine which normally prevents the pituitary gland from producing prolactin until it is needed. The result is reduced prolactin production in the pituitary adenoma. This can actually lead to shrinkage of the tumor in the majority of patients. The rate at which these tumors shrink in response to medical therapy can vary greatly, taking anywhere from days to months. If the medication is stopped, the adenoma will resume producing prolactin and can grow again. Therefore, medical therapy as the only treatment for a prolactin-secreting pituitary adenoma requires lifelong treatment. Approximately 10% to 20% of patients taking bromocriptine experience side effects from treatment. These can include nausea, vomiting, dizziness, low blood pressure, and headaches.

Pituitary adenomas that produce growth hormone can be treated with drugs such as octreotide, lanreotide, pasirotide (somatostatin analogs) or pegvisomant (growth hormone antagonist).

**What are the treatment options for malignant pituitary carcinoma (cancer)?**

In general, treatment with a combination of surgery and radiation therapy is used for pituitary carcinoma. These are rare cancers, and unfortunately the ultimate outcome with either of these modalities is often poor, especially in the setting of disease that has spread to other part of the central nervous system (metastasized). Chemotherapy has been tried, but has demonstrated little benefit. Temzolimide has been shown to have some benefit with aggressive pituitary tumors or carcinomas. It is occasionally used to help palliate symptoms from pituitary carcinoma that has metastasized.

**Clinical Trials**

Clinical trials are designed to determine the value of specific treatments. Trials are often designed to treat a certain stage of cancer, either as the first form of treatment offered, or as an option for treatment after other treatments have failed to work. They can be used to evaluate medications or treatments to prevent cancer, detect it earlier, or help manage side effects. Clinical trials are extremely important in furthering our knowledge of this disease. It is through clinical trials that we know what we do today, and many exciting new therapies are currently being tested. Talk to your provider about participating in clinical trials in your area. You can also explore currently open clinical trials using the [OncoLink Clinical Trials Matching Service](https://www.oncolink.org/clinicaltrials).

**Follow Up Care**

Shortly after treatment for functional (secreting) pituitary adenomas, blood will be drawn to measure hormone levels in the body.
If the hormone levels have returned to normal after therapy, the main follow-up will be repeat blood draws, measuring for hormone levels every 3-6 months, for several years after treatment. An MRI of the head may also be performed as part of follow-up care for these tumors. For patients who are taking medication to treat a functional pituitary adenoma, follow-up visits to the doctor and blood draws may be even more frequent. In the case of non-functional (non-secreting) adenomas and pituitary carcinomas, follow-up MRIs of the head will be obtained for the first few years.

The side effects of treatment, particularly radiation therapy, may take years to develop, and it is not unusual for new side effects, such as decreased hormone production from the pituitary, to develop several years after treatment. Therefore, it is important to continue regular follow-up with your doctors after treatment. If side effects such as hypopituitarism do develop, you will need to take medications to replace these hormones.