

Prolactinoma - A Conclusive Guide

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Abstract: Prolactinoma is a benign tumour (adenoma) that is: a non- cancerous tumour of the pituitary gland which results in, excessive production of a hormone called Prolactin. The major effect of prolactinoma is decreased levels of some sex hormones — oestrogen in women and testosterone in men. It is the most common type of functioning pituitary tumour in the general population, making up about 40 percent of all pituitary tumours. Although prolactinoma is not life-threatening, it can cause vision difficulties, infertility, and other problems (further elaborated). Prolactinomas come in various sizes, but the vast majority is less than 10mm (3/8 inch) in diameter. These are called microprolactinomas. The rarer, large tumours greater than 10 mm in size are called macroprolactinomas. Prolactinomas can occur in both men and women. The symptoms produced by a prolactinoma depend on the sex of the patient and the size of the tumour. The majority of prolactinomas are less than 1 cm in size. The increase in number of prolactin-producing cells leads to excess production of the hormone prolactin.

Keywords: Adenoma, Pituitary tumor, Prolactin, Hormone

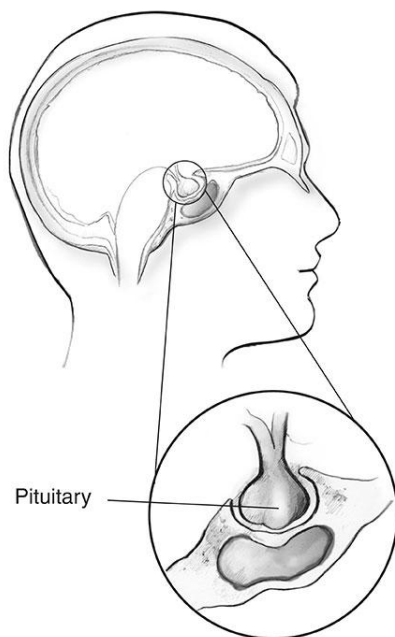


Figure 1: Location of prolactinoma diagrammatically

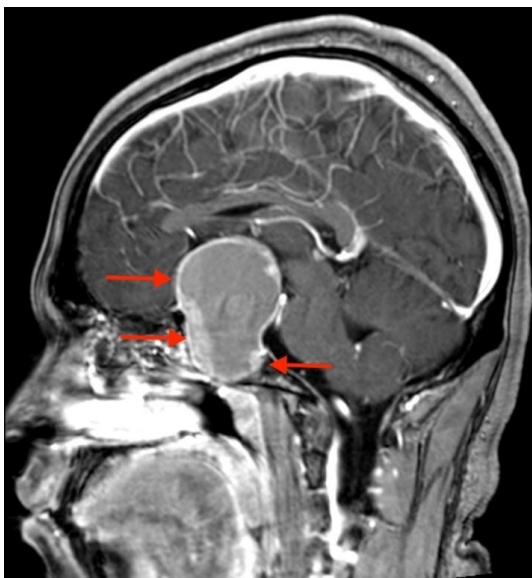


Figure 1.2: MRI image of a prolactinoma

Underlined words: to be further explained.

- a) **Benign tumour:** a tumour is a mass or collection of cells in a specific part of the body. There are two main types of tumours:

Benign: tumours that lack the ability to either invade neighbouring tissue or **metastasize (spread throughout the body)**. When removed, benign tumours usually do not grow back. They usually have a slower growth rate than malignant tumours and the tumour cells are usually more **differentiated (cells have more normal features)**. They are typically surrounded by an outer surface (fibrous sheath of connective tissue) or stay contained within the epithelium. Although they are relatively harmless, they still produce negative health effects. The growth of benign tumours produces a **mass effect (a growing chunk of cells that pushes on a neighbouring tissue)** that may cause nerve damage, reduction of blood flow to an area of the body (*ischaemia*), tissue death (*necrosis*) and organ damage. The health effects of the tumour may be more prominent if the tumour is within an enclosed space such as the cranium, respiratory tract, sinus or inside bones. Tumours of endocrine tissues may overproduce certain hormones, as in the case of prolactinoma. The causes of such tumours are usually unknown, but the growth of a benign tumour might be linked to:

- Environmental toxins, such as exposure to radiation
- Genetics
- Diet
- Stress
- Local trauma or injury
- Inflammation or infection

Surgery is a common type of treatment for benign tumours. The goal is to remove the tumour without damaging surrounding tissues. Other types of treatment may include medication or radiation.

Malignant tumours: the tumour is made of cancer cells, and it can invade nearby tissues. Some cancer cells can move

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into the bloodstream or lymph nodes, where they can spread to other tissues within the body-this is called metastasis. These cells have abnormal chromosomes and DNA characterized by large, dark nuclei; may have abnormal shape. Cancer can occur anywhere in the body including the breast, intestines, lungs, reproductive organs, blood, and skin. They usually grow rapidly and often invade **basal membrane (thin sheets of specialized extracellular matrix)** that surrounds nearby healthy tissue. Removal methods are often tedious with variable success rate depending on the type of cancer, cancer stage, the kind of treatment, age, any other prevailing diseases etc. the good news is that the rate of survival in recent years has seen a betterment. These treatments include surgery, radiation, chemotherapy, and immunotherapy medications. The cancer may recur on the same site as the initial tumour-or a different site-even after treatment.

- **Adenoma:** There are many different types of benign tumours that arise from different structures in the body. Adenomas are benign tumours starting in the epithelial tissue of a gland or gland-like structure. The epithelial tissue is the thin layer of tissue covering organs, glands, and other structures. Benign tumours are very diverse; they may be asymptomatic or may cause specific symptoms, depending on their **anatomic location (terms used to describe location are based on a body positioned in what is called the standard anatomical position)** and tissue type. They grow outward, producing large, rounded masses which can cause what is known as a "mass effect". This growth can cause compression of local tissues or organs, leading to many effects, such as blockage of ducts, reduced blood flow (ischaemia), tissue death (necrosis) and nerve pain or damage. If needed, adenomas can often be removed with surgery. Although not common, this type of tumour can become malignant. In the colon, less than 1 out of every 10 adenomas become cancerous.
- **Hormone:** Hormones are your body's chemical messengers. They travel in your bloodstream to tissues or organs. Endocrine glands, which are special groups of cells, make hormones. They perform long distance cell signalling.
- **Pituitary gland:** also known as the *hypophysis*, is an endocrine gland, it is a small pea-sized gland that is referred to as the body's 'master gland' because it controls the activity of most other hormone-secreting glands. It sits in the *sella turcica* ('Turkish saddle'), **a bony hollow in the base of the skull, underneath the brain and behind the bridge of the nose.** The pituitary gland has two main parts, the **anterior pituitary gland (is the front lobe of the gland that regulates several physiological processes including stress, growth, reproduction, and lactation)** and the **posterior pituitary gland (it releases Vasopressin. This is also called antidiuretic hormone. It helps your body conserve water and prevent dehydration.**

Oxytocin. This hormone stimulates the release of breast milk. It also stimulates contractions of the uterus during labour). The gland is attached to a part of the brain (the

hypothalamus) that controls its activity. The anterior pituitary gland is connected to the brain by short blood vessels. The posterior pituitary gland is part of the brain and it secretes hormones directly into the bloodstream under the command of the brain. In general, the pituitary gland detects the body's needs and sends signals to different organs and glands throughout the body to regulate their function and maintain an appropriate environment. It secretes a variety of hormones into the bloodstream which act as messengers to transmit information from the pituitary gland to distant cells, regulating their activity. The anterior pituitary gland produces the following hormones and releases them into the bloodstream (important for prolactinoma understanding):

- 1) *Adrenocorticotropic* hormone, which stimulates the adrenal glands to secrete steroid hormones, principally cortisol. Cortisol plays an important role in helping you to: Respond to stress.
 - 2) Growth hormone, which regulates growth, metabolism, and body composition.
 - 3) Luteinising hormone (LH) and follicle stimulating hormone (FSH), also known as gonadotrophins (sex hormones). They act on the ovaries or testes to stimulate sex hormone production, and egg and sperm maturity.
 - 4) **Prolactin, which stimulates milk production.**
 - 5) Thyroid stimulating hormone, which stimulates the thyroid gland to secrete thyroid hormones.
- **Prolactin:** is produced by the pituitary gland in the brain in the front portion of the pituitary gland in your brain, as well as in the uterus, brain, breasts, prostate, adipose tissue, skin, and immune cells. It is also known as PRL or lactogenic hormone. Prolactin is mainly used to help women produce milk after childbirth. It is important for both male and female reproductive health. The specific function of prolactin in men is not well-known. However, prolactin levels have been used to measure sexual satisfaction in both men and women. It also regulates behaviour, the immune system, metabolism, reproductive systems, and many different bodily fluids. This makes it a crucial hormone for overall health and well-being. Production of prolactin is controlled by two main hormones: dopamine and oestrogen. These hormones send a message to the pituitary gland primarily indicating whether to begin or cease the production of prolactin. Dopamine restrains the production of prolactin, while oestrogen increases it.

Citation of artwork and tables:

Fig.1.1.

Fig.1.2.

Fig.1.3.

Fig.1.4.

TABLE 1

D) What triggers Prolactinoma?

Most pituitary tumours develop on their own. The cause of these tumours is unknown. In some cases, genetic factors may play a role. For example, the inherited disorder multiple endocrine **neoplasia type 1 (is a hereditary condition associated with tumours of the endocrine glands. It is also known as MEN1; it was originally known as Wermer syndrome. The most common tumours seen in**

MEN1 involve the parathyroid gland (four small glands of the endocrine system which regulate the calcium in our bodies. Parathyroid glands are in the neck behind the thyroid where they continuously monitor and regulate blood calcium levels.), islet cells of the pancreas (regulates glucose metabolism), and pituitary gland.) increases the risk for prolactinomas. Some suspected causes of increase in prolactin concentration in blood include:

• **Hypothyroidism-**

A condition in which the thyroid gland does not produce enough thyroid hormone. Hypothyroidism's deficiency of thyroid hormones can disrupt such things as heart rate, body temperature and all aspects of metabolism.

Primary hypothyroidism (thyroid hormone deficiency) can cause hyperprolactinemia (is a condition in which a person has higher-than-normal levels of the hormone prolactin in the blood.) and galactorrhoea (is lactation in any men or in women who are not breastfeeding. It is generally due to a prolactin-secreting pituitary adenoma.) because increased levels of thyroid-releasing hormone increase secretion of prolactin as well as thyroid-stimulating hormone (TSH).

• **Kidney disease (renal failure)-**

Prolactin levels may rise in circulation because of renal insufficiency due to impaired renal clearance of prolactin. So, prolactin may remain in high concentrations in blood streams.

• **Breast stimulation**

Nipple stimulation and pregnancy are physiologic causes of increased prolactin secretion to support the needs of lactation for a new-born child.

• **Other pituitary and non-pituitary tumours** in arising in or near the pituitary may block the flow of dopamine (neurotransmitter that plays a part in controlling the movements a person makes, as well as their emotional responses) from the brain to the prolactin-secreting cells leading to hyperprolactinemia (higher-than-normal levels of the hormone prolactin in the blood) this may be associated with hypogonadotropic (results from gonadal failure due to abnormal pituitary gonadotropin levels may result from either absent or inadequate hypothalamic GnRH secretion or failure of pituitary gonadotropin secretion) and hypogonadism (means diminished functional activity of the gonads—the testes or the ovaries—that may result in diminished production of sex hormones) probably through inhibition of gonadotrophin-releasing hormone (GnRH) release or action on the pituitary gonadotrophs (basophilic cells of the anterior pituitary gland specialized to secrete gonadotropins in response to elevation in intracellular calcium concentration).

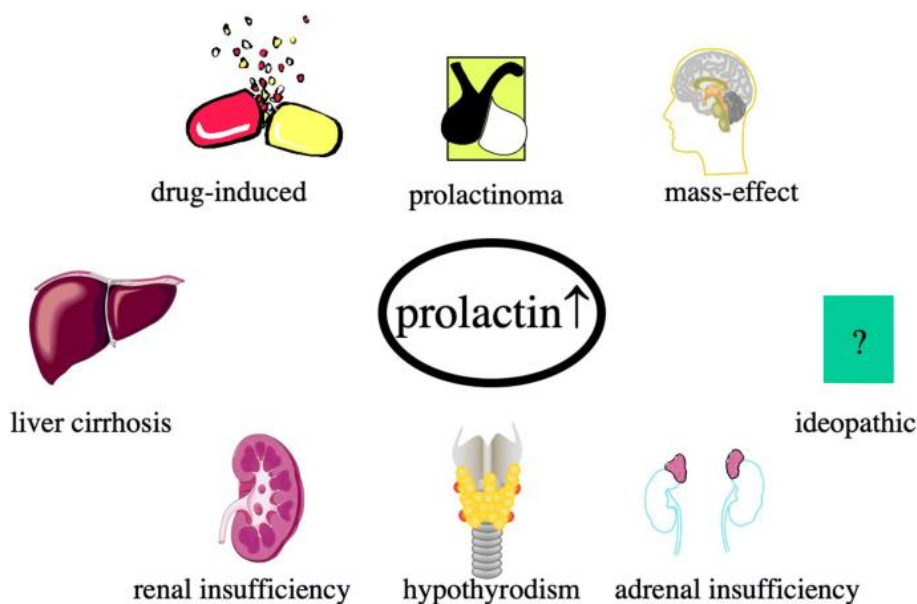


Figure 1.3: What increases blood prolactin level

II) Statistical data about the frequency of prolactinoma:

Prolactinomas are the **most common form of pituitary gland associated with tumours excess hormone production**. About 1 in 10,000 people have a prolactinoma. It can occur in both sexes and at any age, but it is more common in women aged 20-50 years. Usually, prolactinomas affect premenopausal women and present with typical symptoms of menstrual disturbance and/or galactorrhoea. Before 2006, few data was available about the prevalence of pituitary adenomas in the clinical setting. The first study about the prevalence of clinically relevant

pituitary adenomas was conducted in the Liège area of Belgium in 2006. Three distinct districts (rural, suburban, and urban) with a total of 71,972 inhabitants were studied and a pituitary adenoma prevalence of 1 case/1,064 of the population was reported. Of these cases, 66.2% were prolactinomas, of which 80% were microprolactinomas (< 10 mm diameter) occurring in females. These results were confirmed in different geographical settings thereafter. In 2009 in Switzerland, Fontana and Gaillard [5] found 44 adenomas out of 54,607 inhabitants (prevalence of 1/1,241), of which 73% were women. Once again, prolactinomas predominated (56% of adenomas).

Subsequently in the United Kingdom, Fernandez et al. found 63 cases of pituitary adenomas in a population of 81, 149 (prevalence 1/1, 289), of which 57% were prolactinomas. Prolactinomas were the more frequent subtype in people under 60 years of age, while non-functioning adenomas were more frequent in those aged > 60 years of age. Other data from Finland and Malta found similar results and the same proportions of prolactinomas. In Sweden, the prevalence was estimated at 1/2, 688 inhabitants. Although this confirmed the increased frequency of PA in the general population, these results were lower than other reports. They

also found a lower proportion of prolactinomas (32%) and a higher proportion of non-functioning pituitary adenomas (54%). This imbalance may be the consequence of the criteria used for considering prolactinomas (prolactin levels > 3 times the upper limit of normal). The lower prevalence may be also due to a lack of data from general practitioners, as it was a registry-based study. Moreover, they reported a higher prevalence of macroadenomas (65%) versus microadenomas (33%). In contrast, the pituitary adenoma prevalence in Iceland in 2012 was the highest yet reported (1/865), with 40% being prolactinomas.

Table 1: Characteristics of patients with clinically active pituitary tumours in the study population

Patient no.	District	Sex	Age at diagnosis (yr)	Duration prediagnosis (months)	Biochemical diagnosis	Max. tumor diameter (mm)
Prolactinomas						
1	I	M	19	12	Increased PRL, +TRH test	20
2	I	F	33	5	Increased PRL, +TRH test	3.5
3	I	M	61	36	Increased PRL, +TRH test	20
4	I	F	42	36	Increased PRL, +TRH test	15
5	I	M	48	N/A	Increased PRL	27
6	I	F	47	24	Increased PRL, +TRH test	6
7	I	F	21	24	Increased PRL, ± TRH test	6
8	I	F	50	N/A	Increased PRL	4
9	II	M	38	90	Increased PRL, +TRH test	7
10	II	F	33	18	Increased PRL	N/A
11	II	F	23	60	Increased PRL, +TRH test	8
12	II	F	24	54	Increased PRL, +TRH test	7.5
13	II	F	36	24	Increased PRL, +TRH test	5
14	II	F	28	42	Increased PRL, +TRH test	6
15	II	F	51	18	Increased PRL, +TRH test	9
16	II	F	24	36	Increased PRL, +TRH test	6
17	II	M	12	12	Increased PRL, +TRH test	8
18	II	F	32	6	Increased PRL, +TRH test	9
19	II	F	53	N/A	Increased PRL, +TRH test	N/A
20	II	M	31	N/A	Increased PRL, +TRH test	5
21	II	F	35	144	Increased PRL, +TRH test	10
22	II	F	28	12	Increased PRL, +TRH test	4
23	II	M	39	1	Increased PRL, +TRH test	20
24	II	F	54	N/A	Increased PRL	35
25	II	F	52	6	Increased PRL, +TRH test	25
26	II	M	54		Increased PRL	5
27	II	F	42	N/A	Increased PRL	N/A
28	II	F	42	N/A	Increased PRL	4
29	II	F	21	12	Increased PRL	5
30	II	F	45	N/A	Increased PRL	4
31	II	F	40	12	Increased PRL, +TRH test	7
32	III	F	23	72	Increased PRL, +TRH test	20
33	III	F	26	12	Increased PRL, +TRH test	5
34	III	F	32	180	Increased PRL, +TRH test	N/A
35	III	F	27	6	Increased PRL, +TRH test	9
36	III	F	40	216	Increased PRL, +TRH test	N/A
37	III	F	26	1	Increased PRL, +TRH test	20
38	III	F	28	36	Increased PRL, +TRH test	5
39	III	F	45	120	Increased PRL, +TRH test	3
40	III	F	15	N/A	Increased PRL, +TRH test	5
41	III	M	30	12	Increased PRL, +TRH test	5
42	III	F	30	6	Increased PRL, +TRH test	4
43	III	F	37	18	Increased PRL, +TRH test	5
44	III	F	35	N/A	Increased PRL	3
45	III	F	25	12	Increased PRL, +TRH test	2
Somatotropinomas						
46	I	M	35	12	Increased IGF-I, GH, +OGTT	11
47	I	M	47	180	Increased GH, IGF-I, +OGTT	13
48	I	M	60	300	Increased GH, IGF-I	36
49	II	M	19	60	Increased GH, PRL, TSH, +OGTT	15

50	II	M	32	72	Increased GH, IGF-I, +OGTT	30
51	III	F	63	20	Increased GH, +OGTT	14
52	III	F	17	36	Increased GH, +OGTT	N/A
53	III	F	56	60	Increased GH, IGF-I, +OGTT	28
54	III	M	65	48	Increased GH, IGF-I, +OGTT	15
Nonsecreting adenomas						
55	I	M	50	12	Low LH/FSH/GH, +ITT	15
56	I	F	77	24	Low LH/FSH, +TRH/LHRH test	35
57	I	M	76	4	Low LH, low Tes	20
58	II	F	42	24	No pituitary hormone abnormality	5
59	III	M	49	4	Panhypopituitarism, +TRH/LHRH test	19
60	III	M	69	36	High LH/FSH	23
61	III	M	86	1	Low LH, low IGF-I	50
62	III	M	61	12	Low Tes/IGF-I, +ITT	35
63	III	M	62	24	Low Tes	14
64	III	F	41	120	Low LH/FSH, low Est	10
Cushing's disease						
65	I	F	55	120	Increased ACTH, + including 24-h dexamethasone suppression test	5
66	I	F	30	N/A	Increased ACTH, + 24 h urinary cortisol	5
67	II	F	37	24	Increased ACTH, + 24 h urinary cortisol	N/A
68	III	F	36	24	Increased cortisol, + 24 h urinary cortisol, + dexamethasone suppression test	12

III) Symptoms

High levels of prolactin in the blood can cause various symptoms. The symptoms differ slightly between men, women, and children. High prolactin levels in the blood. Less commonly, large prolactinomas can cause compression of surrounding structures. But women who are taking sex hormones—in birth control pills or hormone replacement therapy—may not experience these changes. The same is true for women who have reached menopause and no longer have periods. Among these women, and among men, a lack of clear signs and symptoms may lead to a delayed diagnosis.

a) Women may have:

- Irregular periods or no periods.
- Reduced fertility.
- Reduced sex drive.
- Breast tenderness
- Milk leaking from the breasts (known as galactorrhoea). The milk may leak out by itself or may only show when the breast is squeezed. (Note: leakage of milk from the breasts is normal towards the end of pregnancy, with recent childbirth, if breast-feeding and for some time after finishing breast-feeding.)
- Increased growth of hair on the face or body.
- Painful intercourse due to vaginal dryness
- Acne and excessive body
- Pregnancy complications. During a normal pregnancy, the production of oestrogen increases. If you are pregnant and have a large prolactinoma, these high levels of oestrogen may cause tumour growth and associated signs and symptoms, such as headaches and changes in vision.

b) Men may have:

- Reduced fertility.
- Difficulty having an erection (erectile dysfunction).
- Reduced sex drive (libido).
- Low energy levels
- Breast enlargement (called gynaecomastia).

- Very rarely, leakage of milk from the breasts.

c) Children and teenagers may have:

- Reduced growth.
- Delayed puberty.
- Prolactinomas which are large may press on the brain or nearby nerves (the nearest nerves are the optic nerves which go to the eye). Some prolactinomas can get bigger during pregnancy.

d) Larger prolactinomas may cause symptoms such as:

- Headache-It has long been considered that headache is related to tumour size and Dural stretch.
- Eye symptoms-you may get reduced vision or double vision. The early changes can easily go unnoticed because they affect the peripheral vision-that is, the edges of your vision to the extreme left and right. This means that you may see less of what you around but can still see well if you focus on something directly. This is due to compression, by the tumour, of the optic nerve.
- Low bone density-(osteoporosis). Too much prolactin can reduce production of the hormones oestrogen and testosterone, resulting in decreased bone density and an increased risk of osteoporosis.
- Reduction of other hormone production by the pituitary gland because of tumour pressure. With larger prolactinomas, pressure on the normal pituitary gland can lead to lower levels of other hormones controlled by the pituitary, including thyroid hormones and cortisol (a stress-response hormone).
- Loss of interest in sexual activity

IV) How to diagnose prolactinoma?

The diagnosis may be suspected from the symptoms. Women tend to be diagnosed earlier than men because a change in the woman's periods is an early symptom and is easily noticed. Some prolactinomas are diagnosed by chance if you have tests for another reason. If a prolactinoma is suspected, you may be offered several tests.

a) Blood tests:

The first test for women is a pregnancy test-prolactin goes up in pregnancy, and occasionally an undiagnosed pregnancy can be mistaken for a prolactinoma. A blood sample can check the level of prolactin in the blood. A very high prolactin level usually means that a prolactinoma is present. However, there are other causes of raised prolactin levels. For example, some medicines may cause high prolactin levels. These include:

- The anti-sickness medicines metoclopramide and domperidone.
- Antidepressants of the selective serotonin reuptake inhibitor (SSRI) type.
- Some medicines used to treat schizophrenia or bipolar disorder.

Other blood tests may be done at the same time. It is important to test the thyroid gland and to check kidney function, as both these can affect prolactin levels. Further tests may be needed to see if the tumour is causing a lack of other hormones made by the pituitary gland.

b) Eye tests:

Eye tests will assess if the tumour is pressing on the optic nerve-this includes a test of visual fields.

c) Scans:

A magnetic resonance imaging (MRI) scan or a computed tomography (CT) scan can show the size of the tumour. A bone density scan may be advised for some patients, to check whether they are at risk of osteoporosis, which is a possible complication.

V) Treatment for prolactinoma

Oral medications often can decrease the production of prolactin and eliminate symptoms. Medications may also shrink the tumour. However, long-term treatment with medications is generally necessary. Doctors use drugs known as dopamine agonists to treat prolactinoma. These drugs mimic the effects of dopamine — the brain chemical that normally controls prolactin production.

Treating the prolactinoma usually improves fertility, so can help you become pregnant. *Bromocriptine* (Cycloset, Parlodel) and *cabergoline* is thought to be the safest of the dopamine agonists for pregnancy because it is the most tried and tested one.

These drugs decrease prolactin production and may shrink the tumour in most people with prolactinoma. Many women have had babies after taking bromocriptine. Goals in the treatment of prolactinoma include:

- Return the production of prolactin to normal levels.
- Restore normal pituitary gland function.
- Reduce the size of the pituitary tumour.
- Eliminate any signs or symptoms from tumour pressure, such as headaches or vision problems. Nausea and vomiting, nasal stuffiness, headache, and drowsiness are common side effects of these medications. However, these side effects often can be minimized if your doctor

starts you with a very low dose of medication and gradually increases the dose.

There have been rare cases of heart valve damage with cabergoline, but it's usually in people taking much higher doses for Parkinson's disease. Some people may develop compulsive behaviours, such as gambling, while taking these medications. If medication shrinks the tumour significantly and your prolactin level remains normal for two years, you may be able to taper off the medication with your doctor's guidance. However, recurrence is common. Don't stop taking your medication without your doctor's approval.

Surgery may be an option if medication does not work, is not wanted, or for larger prolactinomas.

The type of surgery you have will depend largely on the size and extent of your tumour:

- Nasal surgery. Most people who need surgery have a procedure in which the tumour is removed through the nasal cavity. It's called *transsphenoidal surgery*. Complication rates are low because no other areas of the brain are touched during surgery, and this surgery leaves no visible scars.
- Transcranial surgery. If your tumour is large or has spread to nearby brain tissue, you may need this procedure, also known as a craniotomy. The surgeon removes the tumour through the upper part of the skull. The outcome of surgery depends on the size and location of the tumour and your prolactin levels before surgery, as well as the skill of the surgeon. The higher the prolactin level, the slimmer the chance that prolactin production will return to normal after surgery.

Surgery corrects the prolactin level in most people with small pituitary tumours. However, many pituitary tumours come back within five years of surgery. For people with larger tumours that can only be partially removed, drug therapy often can return the prolactin level to a normal range after surgery.

Transsphenoidal surgery:

Endoscopic surgery is performed through the nose to remove tumours from the pituitary gland and skull base. In this minimally invasive surgery, the surgeon works through the nostrils with a tiny endoscope camera and light to remove tumours with long instruments. Pituitary tumours can cause hormone problems and vision loss. Tumour removal often reverses vision problems and restores normal hormone balance. Transsphenoidal literally means "through the sphenoid sinus." It is a surgery performed through the nose and sphenoid sinus to remove pituitary tumours. Transsphenoidal surgery can be performed with an endoscope, microscope, or both. It is often a team effort between neurosurgeons and ear, nose, and throat (ENT) surgeons. A traditional microscope technique uses a skin incision under the upper lip and removal of a large portion of the nasal septum so that the surgeon can directly see the sphenoid sinus area.

A minimally invasive technique, called endoscopic endonasal surgery, uses a small incision at the back of the

nasal cavity and causes little disruption of the nasal tissues. The ENT surgeon works through the nostrils with a tiny camera and light called an endoscope.

Radiation is for people who do not respond to medication and are not candidates for surgery; radiation therapy may be an option.

Because doctors are not sure what causes prolactinoma, it's not possible to prevent the condition.

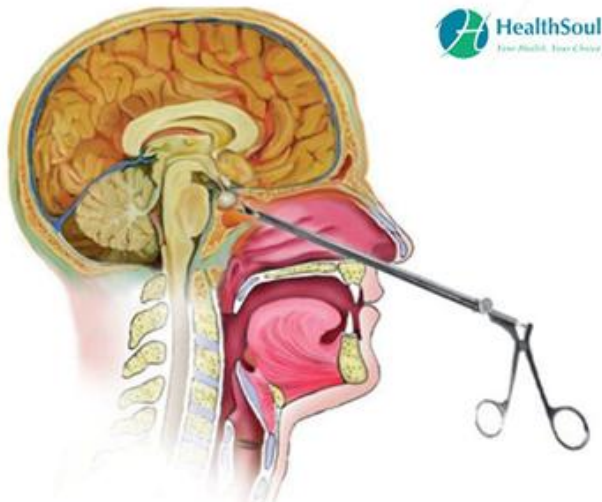


Figure 1.4: Surgical removal of a prolactinoma

In many cases, prolactinoma tumours are treated with medications to regulate hormones and shrink tumours. In those cases, the tumour never fully goes away. Other times, surgery may be used to remove the tumour. This may be done through the nasal cavity or by opening the skull. However, even if a tumour is removed, it is estimated that 20 to 50% of tumours return, most commonly within five years after treatment. Because of this, it is important to talk to your doctor about finding the most effective combination of treatments for you.

Conclusion

Prolactinoma is not a deadly tumour, it is quite common and treatable although, chances of reoccurrence are quite possible. This adenomas cause is till unknown which is why is future research are quite possible in this field. The author hypothesises that this adenoma is caused due to genetic mutation possibly as a result of an unhealthy lifestyle or a certain harmful compound consumed in diet that affects the cell activity of endocrine cells.

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Artwork and table citations

Fig 1.1. *PROLACTINOMA DIAGRAM.* Heer Gajjar. https://www.niddk.nih.gov/-/media/Images/Health-Information/Endocrine-Diseases/Pituitary_Gland.jpg

Fig 1.2. *PROLACTINOMA DIAGRAM.* Heer Gajjar. https://www.niddk.nih.gov/-/media/Images/Health-Information/Endocrine-Diseases/Pituitary_Gland.jpg

Fig 1.3. *CAUSES.* Heer Gajjar. https://media.springernature.com/lw685/springer-static/image/art%3A10.1007%2F11102-019-01024-z/MediaObjects/11102_2019_1024_Fig3_HTML.png

Fig 1.4. *CAUSES.* Heer Gajjar. https://media.springernature.com/lw685/springer-static/image/art%3A10.1007%2F11102-019-01024-z/MediaObjects/11102_2019_1024_Fig3_HTML.png

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