HYPERPROLACTINEMIA

Hyperprolactinaemia, High Level Of Prolactin

The presence of abnormally high levels of prolactin in the blood.

Diagnosis  Male & Female

Related Diagnoses:
- Erectile dysfunction
- Polycystic ovary syndrome
- Anovulation
- Thyroid disorders
- Premature ovarian failure
- Hypogonadism
- Testicular failure
- Luteinised unruptured follicle syndrome

About Hyperprolactinemia

Hyperprolactinaemia or hyperprolactinemia (HP) is the presence of abnormally high levels of prolactin in the blood. This hormone is made by the pituitary gland, which is located at the base of the brain. Normal levels are less than 500 mIU/L [20 ng/mL or ug/L] for women, and less than 450 mIU/L for men. In young women, hyperprolactinemia is probably one of the most common endocrine disorders related to pituitary function.

Prolactin is a peptide hormone that is primarily associated with lactation and plays a vital role in breast development during pregnancy. Hyperprolactinaemia may cause galactorrhea (production and spontaneous flow of breast milk) and disruptions in the normal menstrual period in women and hypogonadism, infertility and erectile dysfunction in men.

Hyperprolactinemia is a regular indicator of impending or existing thyroid hormone deficiency or hypothyroidism (Hashimoto’s disease) which in most cases results from antithyroglobulin and/or antimicrosomal antibodies that attack thyroid hormone producing glands, substituting them with connective tissue.

Almost half of worldwide cases, where the woman has such thyroid antibodies in her blood (regardless of whether or not they have concomitant hormonal or clinical evidence of thyroid deficiency) she will also have increased natural killer cells activity(NKa).

When this issue occurs embryo implantation will be probably disturbed and the woman will frequently present with incapacity to conceive (“infertility”), unexplained IVF failure, or with recurrent pregnancy loss (RPL).

HP is also a part of mental stress or normal body changes during pregnancy and breastfeeding. It can also be caused by diseases affecting the hypothalamus and pituitary gland or disruption of the normal regulation of prolactin levels by drugs, medicinal herbs and heavy metals. In many cases may be also the result of disease of other organs such as the liver, kidneys, ovaries and thyroid.

Prolactin secretion in the pituitary is normally suppressed by the brain chemical dopamine (Pic. 1). 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 the major tranquillizers (phenothiazines), trifluoperazine (Stelazine), and haloperidol (Haldol); antipsychotic medications, such as risperidone and quietaamine; metoclopramide (Reglan), domperidone, cisapride used to treat gastro-oesophageal reflux; medication-induced nausea (such as cancer drugs); and, less often, alpha-methyldopa and reserpine, used to control hypertension; and estrogens and TRH. The sleep drug ramelteon (Rozerem) also increases the risk of hyperprolactinaemia. A benzodiazepine analog, etizolam, can also increase the risk of hyperprolactinaemia.

Often, the cause of hyperprolactinaemia is a prolactin-producing tumour in the pituitary gland, called a prolactinoma. This tumour is mostly benign (adenomas), meaning not invasive (invasive tumours with multiple
recurrences are “atypical adenomas”), and not metastatic. It is more common in women than men. Rarely, children and adolescents develop prolactinomas. Other brain tumours may also cause the pituitary gland to make too much prolactin. A pituitary adenoma with a diameter of less than 1 cm is defined as “microadenoma”.

Magnetic resonance imaging (MRI) is the most sensitive test for detecting pituitary tumours and determining their size. MRI scans may be repeated periodically to assess tumour progression and the effects of therapy. Computed Tomography (CT scan) also gives an image of the pituitary, but it is less sensitive than the MRI. In addition to assessing the size of the pituitary tumour, doctors 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 tumour, the doctor may request an eye exam with measurement of visual fields. The hormone prolactin is downregulated by dopamine and is upregulated by oestrogen. A falsely-high measurement may occur due to the presence of the biologically-inactive macroprolactin in the serum. This can show up as high prolactin in some types of tests, but is asymptomatic.

In general, treatment of hyperprolactinemia, is accepted as necessary. Medications in the form of dopamine agonists (such as cabergoline, bromocriptine (often preferred when pregnancy is possible), and less frequently lisuride are the first line of treatment, with surgery and radiotherapy reserved for refractory and medication-intolerant patients. The objectives of therapy are to improve the symptoms associated with high PRL (prolactin) levels and to reduce the size of a pituitary tumour.

Associated diseases

- amenorrhoea
- galactorrhoea
- Hashimoto’s disease (the thyroid gland is attacked by a variety of cell- and antibody-mediated immune processes)
- prolactinomas
- kidney failure
- granulomatous diseases of the pituitary gland

Complications

Possible complications of hyperprolactinaemia are especially related to tumor size and the physiologic effects of the condition. These include blindness, hemorrhage, diabetes, osteoporosis, and infertility.

Risk factors

- prolactinoma
- pituitary tumors
- hypothyroidism
- sarcoidosis
- chronic renal failure
- polycystic ovary syndrome
- stress
- certain medications, including commonly prescribed antidepressants, anti-psychotics, and blood pressure medications

Impact on fertility

High prolactin levels are associated with anovulation or may cause directly or indirectly infertility. In young women, hyperprolactinemia is probably one of the most common endocrine disorders related to pituitary function.

Prolactin negatively modulates the secretion of pituitary hormones responsible for gonadal function, including luteinizing hormone and follicle-stimulating hormone. Clinically significant hyperprolactinemia may result in hypogonadism, infertility, and galactorrhoea, or in some cases it may remain asymptomatic for a long period.

Women who are not pregnant and are not breastfeeding should have lower levels of basal PRL (typically 10–28 µg/L in women and 5–10 µg/L in men are defined as “normal levels”) If a non-pregnant woman has abnormally high levels of PRL, it may cause her difficulty in becoming pregnant. It is considered as the most frequent cause of anovulatory sterility, although spontaneous pregnancy may occur occasionally.
Prevention

Preventive measures are unknown for hyperprolactinaemia.

Symptoms

In women, a high blood level of prolactin often causes hypoestrogenism with anovulatory infertility and a decrease in menstruation. In some women, menstruation may disappear altogether (amenorrhea). In others, menstruation 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) and breast pain, especially when prolactin levels begin to rise for the first time, as the hormone promotes tissue changes in the breast. Intercourse may become difficult or painful because of vaginal dryness.

In men, the most common symptoms of hyperprolactinaemia are decreased libido, sexual dysfunction erectile dysfunction, infertility, and gynecomastia. Because men have no reliable indicator such as menstruation to signal a problem, many men with hyperprolactinaemia being caused by a pituitary adenoma may delay going to the doctor until they have headaches or eye problems caused by the enlarged pituitary pressing against the adjacent optic chiasm. 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.

Therapies

Self therapy

Vitex agnus-castus

Vitex agnus-castus is one of the few temperate-zone species of Vitex, which is on the whole a genus of tropical and sub-tropical flowering plants. Vitex agnus-castus extract is used to alleviate symptoms of various gynecological problems and can be tried in cases of mild hyperprolactinaemia.

Conventional medicine

Pharmacotherapy

The two most commonly prescribed drugs in the treatment of hyperprolactinemia are bromocriptine and cabergoline. Both medications are dopamine receptor agonists and share many characteristics and adverse effects, such as headache, nausea and vomiting, among others, though frequency and severity of adverse effects appears to be less in cabergoline compared to bromocriptine. Previous concerns about valvular heart disease with the use of these agents have largely been disproved by more recent reports. Frequency of dosing may also affect treatment decisions as cabergoline is dosed twice weekly, whereas bromocriptine is given daily. However, cabergoline costs at least twice as much as bromocriptine and was not found to be superior in other outcomes. Though both drugs have been found to be safe in pregnancy, the number of reports studying bromocriptine in pregnancy far exceeds that of cabergoline in pregnancy.

A large body of moderate quality evidence from observational studies supports the use of dopamine agonists to normalize prolactin levels and resolve the symptoms related to mass effect and elevated prolactin levels. The large treatment effect of dopamine agonists, the potential dose response effect, biological plausibility, temporality between treatment and effect, consistency across studies, settings and methods, and coherence (consistency across agents within the same class), strongly support the effectiveness of these treatment agents in reducing prolactin levels and improving symptoms. In addition, the recurrence of hyperprolactinemia after withdrawal of dopamine agonists strengthens the inference about causality (that is, challenge-rechallenge phenomenon). Clinicians using these medications are well aware of potential adverse effects that sometimes limit use, which include nausea, vomiting, psychosis and dyskinesia, among others.
Surgical therapy

Surgery should 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 present). If medical therapy is only partially successful, this therapy should continue, possibly combined with surgery or radiation treatment.

If hyperprolactinemia is causing of a tumor on the pituitary gland, so the results of surgery depend a great deal on tumor size and prolactin level. The higher the prolactin level the lower the chance of normalizing serum prolactin. In the best medical centers, surgery corrects prolactin levels in 80% of patients with a serum prolactin less than 250 ng/ml. Depending on the size of the tumor and how much of it is removed, studies show that 20 to 50% will recur, usually within five years.

Other therapies

Radiation

Rarely, if medicines and surgery have not been effective, radiation is used to shrink the tumor, which causes hyperprolactinemia.

Assisted reproduction

In vitro fertilization may be a treatment option when other fertility treatments have failed or are unavailable.

IVF and related techniques are called assisted reproductive technology (ART) techniques that generally start with stimulating the ovaries to increase egg production. Most fertility medications are agents that stimulate the development of follicles in the ovary. Examples are gonadotropins and gonadotropin releasing hormone.

After stimulation, the physician surgically extracts one or more eggs from the ovary, and unites them with sperm in a laboratory setting, with the intent of producing one or more embryos. Fertilization takes place outside the body, and the fertilized egg is reinserted into the woman's reproductive tract, in a procedure called embryo transfer. Infertile couples may also resort to egg donation or embryo donation when the female partner cannot have genetic children because her own eggs cannot generate a viable pregnancy.

Surrogacy via a gestational carrier is also an option when a patient's medical condition prevents a safe pregnancy, when a patient has ovaries but no uterus due to congenital absence or previous surgical removal, and where a patient has no ovaries and is also unable to carry a pregnancy to full term.

The rate of success for IVF is correlated with a woman’s age. More than 40 percent of women under 35 succeed in giving birth following IVF, but the rate drops to a little over 10 percent in women over 40.

Find more about related issues

Diagnoses

Erectile dysfunction
The inability (that lasts more than 6 months) to develop or maintain an erection of the penis during sexual activity. Learn more at: www.fertilitypedia.org/therapy/diag/erectile-dysfunction

Polycystic ovary syndrome
A condition in which a woman has an imbalance of female sex hormones. This may lead to changes in the menstrual cycle, cysts in the ovaries, trouble g
Learn more at: www.fertilitypedia.org/therapy/diag/polycystic-ovary-syndrome
Anovulation
Failure of the ovaries to release an oocyte over a period of time generally exceeding 3 months.
Learn more at: www.fertilitypedia.org/therapy/diag/anovulation

Thyroid disorders
A medical condition impairing the function of the thyroid.
Learn more at: www.fertilitypedia.org/therapy/diag/thyroid-disorders

Premature ovarian failure
The loss of function of the ovaries before age 40.
Learn more at: www.fertilitypedia.org/therapy/diag/premature-ovarian-failure

Hypogonadism
A medical term which describes a diminished functional activity of the gonads – the testes and ovaries.
Learn more at: www.fertilitypedia.org/therapy/diag/hypogonadism

Testicular failure
The inability of the testicles to produce sperm or testosterone.
Learn more at: www.fertilitypedia.org/therapy/diag/testicular-failure

Luteinised unruptured follicle syndrome
The luteinisation of ovulatory follicle without a release of an oocyte.
Learn more at: www.fertilitypedia.org/therapy/diag/luteinised-unruptured-follicle-syndrome

❤️ Organs

Hypothalamus
A region of the forebrain that regulates body temperature, some metabolic processes and governs the autonomic nervous system.
Learn more at: www.fertilitypedia.org/edu/organs/hypothalamus

Ovary
The ovum-producing organs of the internal female reproductive system
Learn more at: www.fertilitypedia.org/edu/organs/ovary

Pituitary gland
An endocrine gland, about the size of a pea, whose secretions control the other endocrine glands and influence growth, metabolism, and maturation.
Learn more at: www.fertilitypedia.org/edu/organs/pituitary-gland

Thyroid gland
One of the largest endocrine glands in the body, controls rate of use of energy sources, protein synthesis, and body’s sensitivity to other hormones.
Learn more at: www.fertilitypedia.org/edu/organs/thyroid-gland

🌞 Reproductive cells

Oocyte
A female germ cell involved in reproduction.
Learn more at: www.fertilitypedia.org/edu/reproductive-cells/oocyte

📺 Biological control
Estriol
A dominant estrogen during pregnancy, and is secreted mainly by the placenta.
Learn more at: www.fertilitypedia.org/edu/biological-control/estriol

Estrogen
The primary female sex hormone responsible for the development and regulation of the female reproductive system and secondary sex characteristics.
Learn more at: www.fertilitypedia.org/edu/biological-control/estrogen

Follicle-stimulating hormone
FSH is a hormone secreted by the anterior pituitary gland. It regulates the development, growth, pubertal matur and reproductive functions of the body.
Learn more at: www.fertilitypedia.org/edu/biological-control/follicle-stimulating-hormone

Gonadotropin-releasing hormone
A releasing hormone responsible for the release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the anterior pituitary.
Learn more at: www.fertilitypedia.org/edu/biological-control/gonadotropin-releasing-hormone

Reproductive functions

Oogenesis
The process of the maturation of the female gametes through the meiotic division.
Learn more at: www.fertilitypedia.org/edu/reproductive-functions/oogenesis

Risk factors

High level of prolactin
The presence of abnormally high levels of prolactin in the blood.
Learn more at: www.fertilitypedia.org/therapy/rf/high-level-of-prolactin

Low level of estrogen
A diminished level of blood estrogen level.
Learn more at: www.fertilitypedia.org/therapy/rf/low-level-of-estrogen

Low level of FSH
A condition with low serum follicle-stimulating hormone (FSH) concentration.
Learn more at: www.fertilitypedia.org/therapy/rf/low-level-of-fsh

Low level of LH
A serum luteinizing hormone (LH) levels under normal serum concentration for gender and age.
Learn more at: www.fertilitypedia.org/therapy/rf/low-level-of-lh

Symptoms

Absence of menstrual periods
The absence of a menstrual period in a woman of reproductive age.
Learn more at: www.fertilitypedia.org/edu/symptoms/absence-of-menstrual-periods-3

Absence of ovulation
An anovulatory cycle is a menstrual cycle during which the ovaries do not release an oocyte.
Learn more at: www.fertilitypedia.org/edu/symptoms/absence-of-ovulation-3
Breast pain
A medical condition most frequently related to females.
Learn more at: www.fertilitypedia.org/edu/symptoms/breast-pain

Elevated level of prolactin
The presence of abnormally high levels of prolactin in the blood.
Learn more at: www.fertilitypedia.org/edu/symptoms/elevated-level-of-prolactin

Gynecomastia
A disorder of the endocrine system in which there is a non-cancerous swelling of the breast tissue in boys or men.
Learn more at: www.fertilitypedia.org/edu/symptoms/gynecomastia

Inability to have or maintain an erection
The inability to develop or maintain an erection of the penis during sexual activity in humans.
Learn more at: www.fertilitypedia.org/edu/symptoms/inability-to-have-or-maintain-an-erection

Infertility
The failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.
Learn more at: www.fertilitypedia.org/edu/symptoms/infertility

Infrequent menstruation
The medical term for infrequent, often light menstrual periods (intervals exceeding 35 days).
Learn more at: www.fertilitypedia.org/edu/symptoms/infrequent-menstruation-1

Irregular menstruation
Irregular menstruation is a menstrual disorder whose manifestations include irregular cycle lengths as well as metrorrhagia.
Learn more at: www.fertilitypedia.org/edu/symptoms/irregular-menstruation

Lowered libido
The absence of sexual appetite.
Learn more at: www.fertilitypedia.org/edu/symptoms/lowered-libido

Painful sexual intercourse
The painful feelings during sexual intercourse.
Learn more at: www.fertilitypedia.org/edu/symptoms/painful-sexual-intercourse

Vaginal dryness
Decreased or missing lubrication of vagina.
Learn more at: www.fertilitypedia.org/edu/symptoms/vaginal-dryness

Therapies

Egg donation
Process by which a woman donates eggs for purposes of assisted reproduction or biomedical research.
Learn more at: www.fertilitypedia.org/edu/therapies/egg-donation

ICSI
A micromanipulative fertilization technique in which a single sperm is injected directly into an egg.
Learn more at: www.fertilitypedia.org/edu/therapies/icsi

Sperm donation
The procedure in which a man (sperm donor) provides his sperm for fertility treatment.
Learn more at: www.fertilitypedia.org/edu/therapies/sperm-donation
**Standard IVF**
A process in which an egg is fertilised by sperm outside the body: in vitro. Own or donated gametes may be used. Learn more at: [www.fertilitypedia.org/edu/therAPIes/standard-IVF](http://www.fertilitypedia.org/edu/therAPIes/standard-IVF)

**Prolactin regulation**
Pic. 1: Regulation of prolactin secretion by hypothalamus with feed back mechanisms.

![Prolactin regulation diagram](image)

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