

HYPERPROLACTINEMIA

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The upper normal value for serum prolactin is approximately 20 ng/ml

PHYSIOLOGIC CAUSES

1) Pregnancy

Serum prolactin increases throughout pregnancy, reaching a peak at delivery. The mean value at term was 207 ng/mL, but the range was from 35 to 600 ng/mL (35 to 600 mcg/L SI units). The probable cause of the hyperprolactinemia is the increasing serum estradiol concentrations during pregnancy. By six weeks after delivery, estradiol secretion has decreased, and the basal serum prolactin concentration is usually normal, even when the mother is breastfeeding.

2) Nipple stimulation during breastfeeding

- Increases serum prolactin concentrations.
- In nonlactating females and males, nipple stimulation, breast imaging (mammography, ultrasound) , or breast examination does not increase prolactin secretion.

3) Stress

Stress of any kind, physical or psychological, can cause an increase in the serum prolactin concentration. The values rarely exceed 40 ng/ml.

4) Meals

Meals may stimulate prolactin secretion slightly. So Fasting blood sample

PATHOLOGIC CAUSES

1) Lactotroph adenomas (prolactinomas)

- Are benign tumors of the lactotroph cell.
- In women between the ages of 20 and 40 years.
- Serum prolactin concentrations tend to vary with adenoma size. Adenomas <1 cm in diameter (microadenoma) are typically associated with serum prolactin values below 200 ng/mL, those approximately 1.0 to 2.0 cm in diameter with values between 200 and 1000 ng/mL, and those greater than 2.0 cm in diameter with values above 1000 ng/mL.

2) Decreased dopaminergic inhibition of prolactin secretion

- Several conditions interfere with normal dopamine inhibition of prolactin secretion. These include damage to the dopaminergic neurons of the hypothalamus, pituitary stalk section, or drugs that block dopamine receptors on lactotroph cells.

Any disease in or near the hypothalamus or pituitary that interferes with the secretion of dopamine or its delivery to the pituitary can cause hyperprolactinemia...tumours, trauma

- Drug -induced hyperprolactinemia

- Serum prolactin concentrations are typically in the 25 to 100 ng/mL range.
- Antipsychotics / Metoclopramide and domperidone are gastric motility drugs / The antihypertensive drug methyldopa.

3) Hypothyroidism

- Hypothyroidism predisposes to hyperprolactinemia. However, basal serum prolactin concentrations are normal in most hypothyroid patients.
- The mechanism of hyperprolactinemia in hypothyroidism is not known.
- The values return to normal when the hypothyroidism is corrected.

4) Decreased clearance of prolactin : chronic renal failure and macroprolactinemia

- Macroprolactinemia
- Aggregates of prolactin and antibodies (in particular, antiprolactin autoantibodies) in the blood.
- These complexes are immunologically detectable but not biologically active, so they appear to cause no clinical abnormality.

5) Idiopathic hyperprolactinemia

CLINICAL PRESENTATION

Hyperprolactinemia causes typical symptoms in premenopausal females and in males, but not in postmenopausal females.

Premenopausal females

Hyperprolactinemia in premenopausal females causes hypogonadism, with symptoms that include **infertility, oligomenorrhea, or amenorrhea** and less often **galactorrhea**.

1) Menstrual cycle dysfunction

- The mechanism appears to involve inhibition of luteinizing hormone (LH), and perhaps follicle-stimulating hormone (FSH) secretion, via inhibition of the release of gonadotropin-releasing hormone (GnRH). As a result, serum gonadotropin concentrations are normal or low.
- Mild degrees of hyperprolactinemia, eg, serum prolactin values of 20 to 50 ng/mL: may cause only insufficient progesterone secretion and, therefore, a short luteal phase of the menstrual cycle. Mild hyperprolactinemia can cause infertility even when there is no abnormality of the menstrual cycle.
- Moderate degrees of hyperprolactinemia, eg, serum prolactin values of 50 to 100 ng/mL, cause either amenorrhea or oligomenorrhea.
- A serum prolactin concentration greater than 100 ng/mL is typically associated with overt hypogonadism, subnormal estradiol secretion, and its consequences, including amenorrhea, hot flashes, and vaginal dryness.

2) Galactorrhea

Hyperprolactinemia in premenopausal females can also cause galactorrhea, but most premenopausal females who have hyperprolactinemia do not have galactorrhea. Many females who have galactorrhea have normal serum prolactin concentrations.

3) Bone density

Females with amenorrhea secondary to hyperprolactinemia have a lower spine and forearm bone mineral density compared with normal females or females with hyperprolactinemia and normal menses. Restoration of menses following therapy results in an increase in bone density, although it may not return to normal.

Postmenopausal females

Postmenopausal females, by definition, are already hypogonadal, and hyperprolactinemia does not change that situation. Because postmenopausal females are also markedly hypoestrogenemic, galactorrhea is rare. Hyperprolactinemia in these females is recognized only in the relatively unusual situation when a lactotroph adenoma becomes so large as to cause headaches or impair vision.

Males

Hyperprolactinemia in males also causes hypogonadotropic hypogonadism, which is manifested by decreased libido, erectile dysfunction, infertility, gynecomastia, decreased muscle mass, decreased body hair, osteoporosis, or rarely, galactorrhea.

Laboratory/imaging tests

- Serum prolactin.
- Studies should be performed to test for hypopituitarism, primary hypothyroidism, and renal insufficiency. (FSH, LH, TSH, CREATININE)
- Magnetic resonance imaging (MRI) of the pituitary
 - Should be performed in a patient with any degree of hyperprolactinemia to look for a mass lesion in the hypothalamic-pituitary region, unless the patient is taking a medication known to cause hyperprolactinemia or has marked renal impairment.
 - If the MRI shows a normal hypothalamic-pituitary region and there are no obvious causes of hyperprolactinemia, the diagnosis is idiopathic hyperprolactinemia.

Management

Dopamine agonists

- These drugs **decrease serum prolactin concentrations** and **decrease the size of most lactotroph adenomas**.
- Cabergoline or Bromocriptine..... cabergoline is the first choice because of its efficacy and favorable side-effect profile.
- Course of clinical response :
 - The fall in serum prolactin typically occurs within the first two to three weeks of therapy.
 - The decrease in adenoma size can be detected by imaging within six weeks after initiation of treatment.
 - Vision usually begins to improve within days after the initiation of treatment.
 - Following the decrease in serum prolactin and adenoma size in patients with macroadenomas, visual and pituitary function often return to normal. There is recovery of menses and fertility in women and of testosterone secretion, sperm count, and erectile function in men.
- Duration of treatment for 24 months (at least one year).
- Dopamine agonists should be stopped in women who become pregnant.

Transsphenoidal surgery

Postoperative radiation therapy

Radiation is primarily used to prevent regrowth of residual tumor in a patient with a very large macroadenoma after transsphenoidal debulking of lactotroph adenomas that are resistant to cabergoline.