

## Prolactin

### WHAT IS PROLACTIN?

Prolactin is a hormone produced in the pituitary gland and various other sites elsewhere in the body, including the brain, placenta, uterus, mammary gland, and lymphocytes of the immune system. Prolactin was named based on its function of promoting milk production (lactation), but it is now known to also have over 300 other functions in the body (1).

### PURPOSE OF A PROLACTIN TEST

A prolactin test is beneficial for the evaluation of females with abnormal nipple discharge, painful breasts, irregular or absent menstrual periods, or difficulties getting pregnant. In males, prolactin tests can help in the evaluation of men with suspected pituitary gland issues, reduced sex drive, enlarged breast tissue and nipple discharge, low testosterone, or erectile dysfunction. Prolactin tests are also used to monitor the effectiveness of therapy for prolactin-producing tumors.

### ROLES OF PROLACTIN

Prolactin has many roles that are important for reproduction. It is best known for the effects on the mammary gland, which include stimulating the growth and development of the mammary gland (mammogenesis), synthesis of milk (lactogenesis), and maintenance of milk secretion (galactopoiesis) (2). Prolactin influences luteal function with abnormal prolactin levels affecting the normal luteal phase of the menstrual cycle (3), as well as the normal production of estradiol and progesterone (4).

Prolactin is produced in skin and hair follicles, playing important roles in the regulation of keratin expression, promotion of hair growth, and control of epithelial stem cell function (5). Prolactin is also important for normal bone growth, as elevated levels are associated with decreased bone mineral density and increased risk of vertebral fractures (6). In addition, numerous links have been reported between prolactin, the environment, and psychological stress, illustrating a role for prolactin in the stress response (7).

Prolactin also plays roles in the regulation of the immune system, osmotic balance, angiogenesis, metabolic homeostasis (including body weight control), fat tissue formation, pancreatic function, and maternal behaviour (8).

### CONTROL OF PROLACTIN

The main regulator of prolactin is dopamine, a hormone produced by the hypothalamus. Dopamine is known as the “feel-good messenger”. It inhibits prolactin production, resulting in reduced prolactin secretion when there are higher levels of dopamine (2).

Estrogen also controls prolactin production by stimulating the production and secretion of prolactin from the pituitary gland. This is what occurs during pregnancy, as estrogen levels increase significantly; hence increasing the levels of prolactin which are required for the production of breast milk (lactation) (2). Other hormones that control prolactin levels include thyrotropin-releasing hormone, oxytocin, and anti-diuretic hormone (9).

### HYPERPROLACTINEMIA

Hyperprolactinemia is the term to describe when circulating prolactin levels are chronically increased to levels higher than the reference population. It is usually defined as fasting levels of above 20 ng/mL in men and above 25 ng/mL in women at least two hours after waking up (10). Physiological hyperprolactinemia is usually mild or moderate,

with the most common causes being pregnancy (prolactin rises to ~200-500 ng/mL) and lactation (10). Various medications can also increase prolactin levels, including antipsychotics, antidepressants and opiates. Common causes of pathological hyperprolactinemia include prolactinomas (benign pituitary tumours), reduced thyroid activity, and renal failure (8).

Hyperprolactinaemia is a common cause of amenorrhoea (absence of menstruation) and is one of the most prevalent endocrine causes of female infertility. It can also lead to galactorrhea (milky nipple discharge), decreased libido, and decreased bone mass (10).

### HYPOPROLACTINEMIA

Low level of prolactin (hypoprolactinemia) is very rare. It can be caused by genetic changes that lead to abnormal lactotroph cell development, destruction of pituitary tissue (through tumour, surgery, infection, or inflammation), or specific medications (8). Most reported cases have been in women with an absence of lactation (breast milk production) after delivery. Aside from an absence of lactation, hypoprolactinemia has no reported clinical consequence (11).

### TEST PROCEDURE

Correct specimen collection and handling is required for optimal assay performance. Sample should be collected in the morning after overnight fasting.

This test requires a blood sample from a finger prick. All supplies for sample collection are provided in this kit. First wash and dry hands. Warm hands aid in blood collection. Clean the finger prick site with the alcohol swab and allow to air dry. Use the provided lancet to puncture the skin in one quick, continuous and deliberate stroke. Wipe away the first drop of blood. Massage hand and finger to increase blood flow to the puncture site. Angle arm and hand downwards to facilitate blood collection on the fingertip. Drip blood onto the blood collection card or into the microtainer tube.

Avoid squeezing or ‘milking’ the finger excessively. If blood flow stops, perform a second skin puncture on another finger, if more blood is required. Do not touch the fingertip.

Dispose of all sharps safely and return sample to the laboratory in the provided prepaid return shipping envelope.

Upon receipt at the laboratory, the blood sample is analyzed by the fully automated Alinity i Prolactin chemiluminescent microparticle immunoassay on the Alinity ci series analyzer. This assay measures prolactin levels by binding to monoclonal anti-prolactin coated microparticles. The amount of prolactin in the blood sample is measured in relative light units by a chemiluminescent reaction.

### SPECIAL INSTRUCTIONS

Diurnal variations in prolactin levels occur, with higher levels in the afternoon than the morning; hence specimen collection is preferred in the morning after overnight fasting.

If an elevated prolactin level is detected, it is recommended that a second blood sample is collected and analyzed before diagnosis of hyperprolactinemia.

## TEST INTERPRETATION

This assay will provide accurate prolactin values for the tested specimen. This value is to be used in conjunction with other clinical and laboratory information for analyses of women's health and fertility.

## DISCLAIMERS/LIMITATIONS

These results should be interpreted in conjunction with other laboratory and clinical information.

Assay interference may occur in specimens from individuals routinely exposed to animals or to animal serum products, or in individuals who have received preparations of mouse monoclonal antibodies for diagnosis or therapy. Additional clinical or diagnostic information may be required for these specimens.

Additional testing is recommended if prolactin results are inconsistent with clinical evidence.

Certain medications (e.g., birth control pills and high blood pressure medicines), recent emotional stress or strenuous exercise, sleeping issues, nipple stimulation, cocaine use, and a recent test using a radioactive substance (e.g., bone scan) may affect prolactin test results.

Additional testing may be required for patients with elevated prolactin levels, as prolactin may exist in alternate structural forms (e.g. macroprolactin), which may exhibit variable levels of physiological activity.

If an elevated prolactin level is detected, it is recommended that a second blood sample is collected and analyzed before diagnosis of hyperprolactinemia.

Correct specimen collection and handling is required for optimal assay performance. The assay is unaffected ( $\leq 10\%$  interference) by hemoglobin (500 mg/dL), bilirubin (20 mg/dL), triglycerides (3000 mg/dL), and protein (12 g/dL).

## REFERENCES

- (1) Bole-Feysot C, et al. (1998). Prolactin (PRL) and its receptor: actions, signal transduction pathways and phenotypes observed in PRL receptor knockout mice. *Endocr Rev*, 19(3), 225-68.
- (2) Freeman ME, et al. (2000). Prolactin: Structure, Function, and Regulation of Secretion. *Physiol Rev*, 80(4), 1523-1631.
- (3) Adashi EY & Resnick CE. (1987). Prolactin as an inhibitor of granulosa cell luteinization: implications for hyperprolactinemia-associated luteal phase dysfunction. *Fertil Steril*, 48(1), 131-9.
- (4) Lee MS, et al. (1986). Effects of prolactin on steroidogenesis by human luteinized granulosa cells. *Fertil Steril*, 46(1), 32-6.
- (5) Langan EA, et al. (2010). Prolactin: an emerging force along the cutaneous-endocrine axis. *Trends Endocrinol Metab*, 21(9), 569-77.
- (6) Klibanski A, et al. (1980). Decreased bone density in hyperprolactinemic women. *N Engl J Med*, 303(26), 1511-4.
- (7) Sobrinho LG. (2003). Prolactin, Psychological Stress and Environment in Humans: Adaptation and Maladaptation. *Pituitary*, 6, 35-39.
- (8) Bernard V, Young J & Binart N. (2019). Prolactin — a pleiotropic factor in health and disease. *Nat Rev Endocrinol*, 15, 356-365.
- (9) Prolactin. You and Your Hormones. Society for Endocrinology, 2018.
- (10) Majundar A & Mangal NS. (2013). Hyperprolactinemia. *J Hum Reprod Sci*, 6(3), 168-175.
- (11) Kauppila A, et al. (1987). Isolated Prolactin Deficiency in a Woman with Puerperal Alactogenesis. *J Clin Endocrinol Metab*, 64(2), 309-312.