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The hormones secreted by the hypothalamus and the pituitary are all Peptides or low-molecular-weight proteins that act by binding to specific Receptor sites on their target tissues. The hormones of the anterior pituitary are regulated by neuropeptides that are called either “releasing” or “inhibiting” factors or hormones. These are produced in cell bodies in the hypothalamus, and they reach the cells of the pituitary by the hypophyseal portal system.

**Adrenocorticotropic hormone (corticotropin)**: Corticotropin-releasing hormone (CRH) is responsible for the synthesis and release of the peptide pro-opiomelanocortin by the pituitary . *Adrenocorticotropic hormone* (ACTH), or *corticotropin*  is a product of the posttranslational processing of this precursor polypeptide. Normally, ACTH is released from the pituitary in pulses with an overriding diurnal rhythm, with the ighest concentration occurring at approximately 6 AM and the lowest in the late evening. Stress stimulates its secretion, whereas cortisol acting via negative feedback suppresses its release. The target organ of ACTH is the adrenal cortex, where it binds to specific receptors on the cell surfaces. The occupied receptors activate G protein-coupled processes to increase cyclic adenosine monophosphate (cAMP), which in turn stimulates synthesis and release of the adrenocorticosteroids and the adrenal androgens.

**Uses:**

* As a diagnostic tool for differentiating between primary adrenal insufficiency (Addison disease, associated with adrenal atrophy) and secondary adrenal insufficiency (caused by the inadequate secretion of ACTH by the pituitary).
* multiple sclerosis
* Infantile spasm (West syndrome).

**Adverse effects:** osteoporosis, hypertension, peripheral edema, hypokalemia, emotional disturbances, and increased risk of infection.

**Growth hormone (somatotropin)**: Somatotropin is a large polypeptide that is released by the anterior pituitary in response to growth hormone (GH)-releasing hormone produced by the hypothalamus Secretion of GH is inhibited by another pituitary hormone, somatostatin. GH is released in a pulsatile manner, with the highest levels occurring during sleep. With increasing age, GH secretion decreases, being accompanied by a decrease in lean muscle mass. Somatotropin influences a wide variety of biochemical processes; for example, through stimulation of protein synthetic processes, cell proliferation and bone growth are promoted. Increased formation of hydroxyproline from proline boosts cartilage synthesis. Synthetic human GH is produced using recombinant DNA technology and is called *somatropin*.

Although many physiologic effects of GH are exerted directly at its targets, others are mediated through the somatomedins—insulin-like growth factors I and II (IGF-I and IGF-II). [Note: In acromegaly (a syndrome of excess growth hormone), IGF-I levels are consistently high, reflecting elevated GH.]

**Uses:**

* Treatment of GH deficiency or growth failure in children.
* Growth failure due to Prader-Willi syndrome
* Management of AIDS wasting syndrome
* Short bowel syndrome
* GH replacement in adults with confirmed GH deficiency
* improve cognitive function and may be useful in the treatment of patients with cognitive impairment

Note: *Somatropin* should not be used in pediatric patients with closed epiphyses. It should also be avoided in patients with increased intracranial pressure, diabetic retinopathy, and obese patients with Prader-Willi syndrome.

Stimulators of growth hormone (GH) secretion include:

* peptide hormones
	+ GHRH (somatocrinin) through binding to the growth hormone-releasing hormone receptor (GHRHR)
	+ ghrelin through binding to growth hormone secretagogue receptors ([GHSR](https://en.wikipedia.org/wiki/Growth_hormone_secretagogue_receptor))
* sex hormones
	+ increased androgen secretion during puberty (in males from testis and in females from adrenal cortex)
	+ estrogen
* [clonidine](https://en.wikipedia.org/wiki/Clonidine) and L-DOPA by stimulating GHRH release
* [α4β2 nicotinic agonists](https://en.wikipedia.org/wiki/Alpha-4_beta-2_nicotinic_receptor#Agonists), including nicotine, which also act synergistically with [clonidine](https://en.wikipedia.org/wiki/Clonidine%22%20%5Co%20%22Clonidine).
* [hypoglycemia](https://en.wikipedia.org/wiki/Hypoglycemia), [arginine](https://en.wikipedia.org/wiki/Arginine%22%20%5Co%20%22Arginine) and [propranolol](https://en.wikipedia.org/wiki/Propranolol%22%20%5Co%20%22Propranolol) by inhibiting [somatostatin](https://en.wikipedia.org/wiki/Somatostatin%22%20%5Co%20%22Somatostatin) release
* deep sleep
* niacin as nicotinic acid (Vitamin B3)
* fasting
* vigorous exercise

Inhibitors of GH secretion include:

* GHIH (somatostatin) from the periventricular nucleus
* circulating concentrations of GH and [IGF-1](https://en.wikipedia.org/wiki/IGF-1) (negative feedback on the pituitary and [hypothalamus](https://en.wikipedia.org/wiki/Hypothalamus))
* hyperglycemia
* glucocorticoids
* dihydrotestosterone

**Function**

In addition to increasing height in children and adolescents, growth hormone has many other effects on the body:

* Increases calcium retention, and strengthens and increases the mineralization of bone
* Increases muscle mass through [sarcomere](https://en.wikipedia.org/wiki/Sarcomere%22%20%5Co%20%22Sarcomere) hypertrophy
* Promotes lipolysis
* Increases protein synthesis
* Stimulates the growth of all internal organs excluding the brain
* Plays a role in homeostasis
* Reduces liver uptake of glucose
* Promotes [gluconeogenesis](https://en.wikipedia.org/wiki/Gluconeogenesis%22%20%5Co%20%22Gluconeogenesis) in the liver
* Contributes to the maintenance and function of pancreatic islets
* Stimulates the immune system
* Increases deiodination of T4 to T3

**Somatostatin (Growth hormone–inhibiting hormone)**: somatostatin binds to distinct receptors, SSTR2 and SSTR5, which suppress GH and thyroid-stimulating hormone release. somatostatin is a small polypeptide that is also found in neurons throughout the body as well as in the intestine and pancreas. Somatostatin therefore has a number of actions. For example, it not only inhibits the release of GH but, also, that of insulin, glucagon, and gastrin.

**Octreotide**is a synthetic octapeptide analog of somatostatin. Its half-life is longer than that of the natural compound, and a depot form is also available. The injectable solution and the depot formulation suppress GH and IGF-I for 12 hours and 6 weeks, respectively. They have found use in the treatment of acromegaly caused by hormone-secreting tumors and in secretory diarrhea associated with tumors producing vasoactive intestinal peptide (VIPomas).

Since octreotide resembles somatostatin in physiological activities, it can:

* inhibit secretion of many hormones, such as gastrin, cholecystokinin, glucagon, growth hormone, insulin, [secretin](https://en.wikipedia.org/wiki/Secretin%22%20%5Co%20%22Secretin), pancreatic polypeptide, [TSH](https://en.wikipedia.org/wiki/Thyroid-stimulating_hormone), and vasoactive intestinal peptide,
* reduce secretion of fluids by the intestine and [pancreas](https://en.wikipedia.org/wiki/Pancreas),
* reduce gastrointestinal motility and inhibit contraction of the gallbladder,
* inhibit the action of certain hormones from the anterior pituitary,
* cause vasoconstriction in the blood vessels, and
* reduce portal vessel pressures in bleeding varices.

It has also been shown to produce [analgesic](https://en.wikipedia.org/wiki/Analgesic) effects, most probably acting as a partial agonist at the mu opioid receptor.

**pegvisomant** is an antagonist at the GH receptor used in the treatment of refractory acromegaly . Pegvisomant blocks the action of growth hormone at the growth hormone receptor to reduce the production of IGF-1. IGF-1 is responsible for most of the symptoms of acromegaly, and normalising its levels may control the symptoms.Long-term treatment studies with pegvisomant as a monotherapy have shown it be safe. Recent studies have shown the potential of using pegvisomant as an anti-tumor treatment for certain types of cancers, in combination with other treatments

**Gonadotropin-releasing hormone (luteinizing hormone–releasing hormone)**: also called *gonadorelin* is a decapeptide obtained from the hypothalamus. Pulsatile secretion of GnRH is essential for the release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the pituitary, whereas continuous administration inhibits gonadotropin release. synthetic analogs, such as *leuprolide* , *goserelin,nafarelin*  and *histrelin*  actas agonists at GnRH receptors. These are effective in sup- pressing production of the gonadal hormones when administered continuously and, thus, are effective in the treatment of prostatic cancer, endometriosis, and precocious puberty.

**Gonadotropins** ( **Human menopausal gonadotropin, folliclestimulating**

**hormone, and human chorionic gonadotropin**): The gonadotropins are glycoproteins that are produced in the anterior pituitary. The regulation of gonadal steroid hormones depends on these agents. They find use in the treatment of infertility in men and women.

Menotropins : (human menopausal gonadotropins,or hMG) obtained from the urine of postmenopausal women and contain FSH and luteinizing hormone (LH).

Urofollitropin is FSH obtained from postmenopausal women and is devoid of LH.

Follitropin alpha and follitropin beta are human FSH products manufactured using recombinant DNA technology. All of these hormones are injected via the IM or subcutaneous route. Injection of hMG or FSH over a period of 5 to 12 days causes ovarian follicular growth and maturation, and with subsequent injection of hCG, ovulation occurs. In men who are lacking gonadotropins, treatment with hCG causes external sexual maturation, and with the subsequent injection of hMG or follitropin, spermatogenesis occurs.

**Prolactin:** is a peptide hormone similar in structure to GH, and is also secreted by the anterior pituitary. Its secretion is inhibited by dopamine acting. Its primary function is to stimulate and maintain lactation. In addition, it decreases sexual drive and reproductive function.

On the other hand, hyperprolactinemia, which is associated with galactorrhea and hypogonadism, is usually treated with D2-receptor agonists, such as *bromocriptine* and *cabergoline*. Both of these agents also find use in the treatment of pituitary microadenomas, macroprolactinomas, and hyperprolactinemia. Among their adverse effects are nausea, headache, and sometimes, psychiatric problems.

**Note:** Prolactin also acts in a cytokine-like manner and as an important regulator of the immune system. It has important cell cycle-related functions as a growth-, differentiating- and anti-apoptotic factor.

Thyrotropin-releasing factor(thyrotropin-releasing hormone) has a stimulatory effect on prolactin release.

Prolactin provides the body with sexual gratification after sexual acts: The hormone counteracts the effect of dopamine, which is linked to sexual arousal. This is thought to cause the sexual refractory period. Elevated levels of prolactin decrease the levels of sex hormones estrogen in women and testosterone in men via suppressesion of GnRH secretion. Physiologic levels of prolactin in males enhance luteinizing hormone-receptors in Leydig cells, resulting in testosterone secretion, which leads to spermatogenesis. Levels can rise after exercise, high-protein meals, sexual intercourse, breast examination minor surgical procedures, following epileptic seizures[[](https://en.wikipedia.org/wiki/Prolactin#cite_note-Mellors-25) or due to physical or emotional stress. Prolactin levels may be of some use in distinguishing epileptic seizures from psychogenic non-epileptic seizures. The serum prolactin level usually rises following an epileptic seizure. The D2 receptor is involved in the regulation of prolactin secretion, and agonists of the receptor such as bromocriptine and cabergoline decrease prolactin levels while antagonists of the receptor such as domperidone, metoclopramide, haloperidol, risperidone, and sulpiride increase prolactin levels. D2 receptor antagonists like domperidone, metoclopramide, and sulpiride are used as galactogogues to increase prolatin secretion and induce lactation in humans.

**HORMONES OF THE POSTERIOR PITUITARY**

In contrast to the hormones of the anterior lobe of the pituitary, those of the posterior lobe, *vasopressin* and *oxytocin*, are not regulated by releasing hormones. Instead, they are synthesized in the hypothalamus, transported to the posterior pituitary, and released in response to specific physiologic signals, such as high plasma osmolarity or parturition.

**Oxytocin :** originally extracted from animal posterior pituitaries, is now chemically synthesized. Its only use is in obstetrics, where it is employed to stimulate uterine contraction to induce or reinforce

labor. [Note: The sensitivity of the uterus to *oxytocin* increases with the duration of pregnancy when it is under estrogenic dominance.] To induce labor, the drug is administered intravenously. *Oxytocin* causes

milk ejection by contracting the myoepithelial cells around the mammary alveoli. Although toxicities are uncommon when the drug is used properly, hypertension, uterine rupture, water retention, and fetal death have been reported. Its antidiuretic and pressor activities are very much lower than those of *vasopressin*.

Estrogen has been found to increase the secretion of oxytocin and to increase the expression of its receptor, the oxytocin receptor, in the brain. In women, a single dose of estradiol has been found to be sufficient to increase circulating oxytocin concentrations. Endogenous oxytocin concentrations in the brain have been found to be as much as 1000-fold higher than peripheral levels. Outside the brain, oxytocin-containing cells have been identified in several diverse tissues, including in females in the corpus luteum  and the placenta, in males in the testicles' interstitial cells of Leydig, the retina, the adrenal medulla, the thymus and the pancreas. The finding of significant amounts of this classically "neurohypophysial" hormone outside the central nervous system raises many questions regarding its possible importance in these different tissues.

### Physiological effects of oxytocin

### Milk ejection reflex/Letdown reflex: In lactating (breastfeeding) mothers

### Uterine contraction: Important for cervical dilation

### High doses can result in hyponatremia.

### Promoting cardiomyocyte differentiation.

### Indirectly inhibits release of adrenocorticotropic hormone and cortisol

* Switch in the action of neurotransmitter GABA from excitatory to inhibitory on fetal cortical neurons.
* Oxytocin has been implicated in the etiology of autism
* Maternal behavior: This is higher in mothers after they interact with unfamiliar children rather than their own
* Oxytocin can increase positive attitudes, such as bonding, toward individuals with similar characteristics Oxytocin is typically remembered for the effect it has on prosocial behaviors, such as its role in facilitating trust and attachment between individuals.
* Nasally administered oxytocin has been reported to reduce fear, possibly by inhibiting the amygdale
* Oxytocin produces antidepressant-like effects by modulation of a different target, perhaps the vasopressin V1A receptor, Sildenafil  evoked oxytocin release from the pituitary gland causing oxytocin-dependent antidepressant-like effects
* Romantic attachment: high levels of plasma oxytocin have been correlated with romantic attachment. Oxytocin may aid romantically attached couples by decreasing their feelings of anxiety when they are separated
* Increases in plasma oxytocin at orgasm in both men and women
* Oxytocin affects social distance between adult males and females and may be responsible at least in part for romantic attraction and subsequent monogamous pair bonding.
* Oxytocin is also thought to modulate inflammation by decreasing certain cytokines. Thus, the increased release in oxytocin following positive social interactions has the potential to improve wound healing.
* Drug interaction Impact on effects of alcohol and other drugs: According to several studies in animals, oxytocin inhibits the development of tolerance to various addictive drugs (opiates, cocaine, alcohol), and reduces withdrawal symptoms. MDMA (ecstasy) may increase feelings of love, empathy, and connection to others by stimulating oxytocin activity primarily via activation of serotonin [5-HT1A receptors](https://en.wikipedia.org/wiki/5-HT1A_receptor), if initial studies in animals apply to humans. The [anxiolytic](https://en.wikipedia.org/wiki/Anxiolytic%22%20%5Co%20%22Anxiolytic) [Buspar](https://en.wikipedia.org/wiki/Buspar%22%20%5Co%20%22Buspar) (buspirone) may produce some of its effects via 5-HT1A receptor-induced oxytocin stimulation as well.
* Addiction vulnerability Endogenous oxytocin can also impact on drug effects and susceptibility to develop Substance use disorder. Endogenous oxytocin concentrations can directly impact on drug effects. Additionally, bilateral interactions with numerous systems, including the dopamine system, Hypothalamic–pituitary–adrenal axis and immune system, can impact on development of dependence. The status of the endogenous oxytocin system might enhance or reduce susceptibility to addiction through its interaction with these systems.

**Atosiban** is a competitive vasopressin/oxytocin receptor antagonist (VOTra). Atosiban inhibits the oxytocin-mediated release of inositol trisphosphate from the myometrial cell membrane. As a result, there is reduced release of intracellular, stored calcium from the sarcoplasmic reticulum of myometrial cells, and reduced influx of Ca2+from the extracellular space through voltage gated channels. In addition, atosiban suppresses oxytocin-mediated release of PGE and PGF from the decidua.

In human pre-term labour, atosiban, at the recommended dosage, antagonises uterine contractions and induces uterine quiescence. The onset of uterus relaxation following atosiban is rapid, uterine contractions being significantly reduced within 10 minutes to achieve stable uterine quiescence.

**Vasopressin** (antidiuretic hormone): is structurally related to oxytocin. Vasopressin has both antidiuretic and vasopressor effects. In the kidney, it binds to the V2 receptor to increase water permeability and reabsorption in the collecting tubules. Thus, the major use of vasopressin is to treat diabetes insipidus. It also finds use in the management of cardiac arrest and in controlling bleeding due to esophageal varices or colonic diverticula. Other effects of vasopressin are mediated by the V1 receptor, which is found in liver, vascular smooth muscle (where it causes constriction), and other tissues. desmopressin which has minimal activity at the V1 receptor, making it largely free of pressor effects. This analog is now preferred for diabetes insipidus and nocturnal enuresis and is longer-acting than vasopressin. Desmopressin is conveniently administered intranasally or orally. However, the nasal formulation is no longer indicated for enuresis due to reports of seizures in children using the nasal spray.