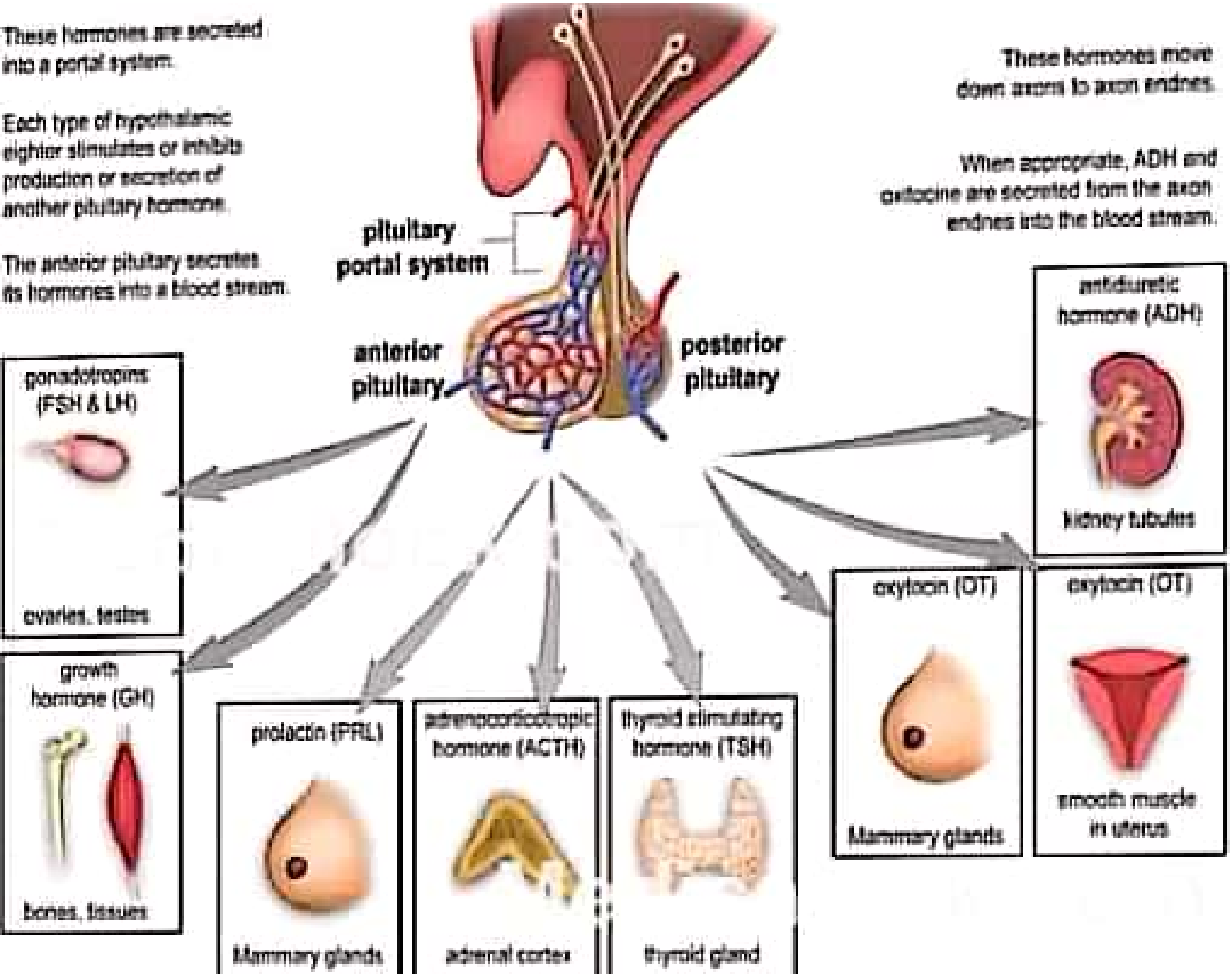


Whenever, the blood level of GH decreases, the GHRH is secreted from the hypothalamus. It in turn causes secretion of GH from pituitary.

Role of ghrelin in the secretion of GH

Ghrelin is a peptide hormone synthesized by epithelial cells in the fundus of stomach. It is also produced in smaller amount in hypothalamus, pituitary, kidney and placenta (Chapter 44). Ghrelin promotes secretion of GH by stimulating somatotropes directly.

■ OTHER HORMONES OF ANTERIOR PITUITARY

Thyroid-stimulating Hormone (TSH)

TSH is necessary for the growth and secretory activity of the thyroid gland. It has many actions on the thyroid gland. Refer Chapter 67 for details of TSH.

Adrenocorticotropic Hormone (ACTH)

ACTH is necessary for the structural integrity and the secretory activity of adrenal cortex. It has other functions also. Refer Chapter 70 for details of ACTH.

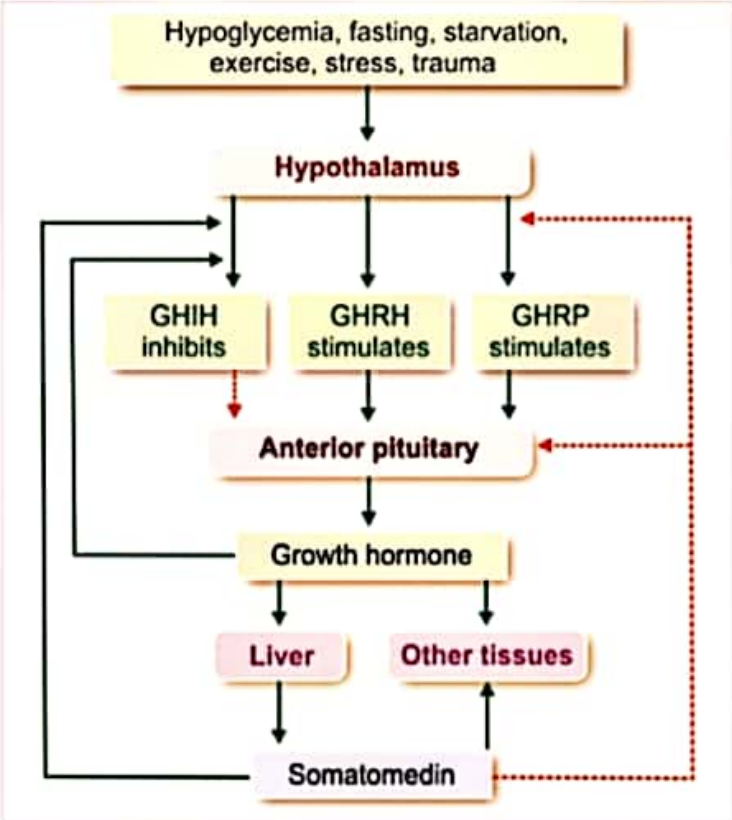


FIGURE 66.3: Regulation of GH secretion. GHIH = Growth hormone-inhibiting hormone, GHRH = Growth hormone-releasing hormone, GHRP = Growth hormone-releasing polypeptide. Growth hormone and somatomedin stimulate hypothalamus to release GHIH . Somatomedin inhibits anterior pituitary directly. Solid green line = Stimulation/secretion, Dashed red line = Inhibition.

Follicle-stimulating Hormone (FSH)

Follicle-stimulating hormone is a glycoprotein made up of one α-subunit and a β-subunit. The α-subunit has 92 amino acids and β-subunit has 118 amino acids. The half-life of FSH is about 3 to 4 hours.

Actions of FSH

In males, FSH acts along with testosterone and accelerates the process of **spermeogenesis** (refer Chapter 74 for details).

In females FSH:

1. Causes the development of **graafian follicle** from primordial follicle
2. Stimulates the theca cells of graafian follicle and causes secretion of estrogen (refer Chapter 79 for details)
3. Promotes the **aromatase activity** in granulosa cells, resulting in conversion of androgens into estrogen (Chapter 80).

Luteinizing Hormone (LH)

LH is a glycoprotein made up of one α-subunit and one β-subunit. The α-subunit has 92 amino acids and β-subunit has 141 amino acids. The half-life of LH is about 60 minutes.

Actions of LH

In males, LH is known as **interstitial cell-stimulating hormone** (ICSH) because it stimulates the interstitial cells of Leydig in testes. This hormone is essential for the secretion of testosterone from Leydig cells (Chapter 74).

In females, LH:

1. Causes maturation of vesicular follicle into graafian follicle along with follicle-stimulating hormone
2. Induces synthesis of androgens from theca cells of growing follicle
3. Is responsible for **ovulation**
4. Is necessary for the formation of corpus luteum
5. Activates the secretory functions of corpus luteum.

Prolactin

Prolactin is a single chain polypeptide with 199 amino acids. Its half-life is about 20 minutes. Prolactin is necessary for the final preparation of mammary glands for the production and secretion of milk.

Prolactin acts directly on the epithelial cells of mammary glands and causes localized **alveolar hyperplasia.** Refer Chapter 87 for details.

■ ANTIDIURETIC HORMONE

Source of Secretion

Antidiuretic hormone (ADH) is secreted mainly by **supraoptic nucleus** of hypothalamus. It is also secreted by **paraventricular nucleus** in small quantity. From here, this hormone is transported to posterior pituitary through the nerve fibers of hypothalamo-hypophyseal tract, by means of axonic flow.

Chemistry and Half-life

Antidiuretic hormone is a polypeptide containing 9 amino acids. Its half-life is 18 to 20 minutes.

Actions

Antidiuretic hormone has two actions:
1.Retention of water
2.Vasopressor action.

1. *Retention of water*

Major function of ADH is retention of water by acting on kidneys. It increases the **facultative reabsorption** of water from distal convoluted tubule and collecting duct in the kidneys (Chapter 52).

In the absence of ADH, the distal convoluted tubule and collecting duct are totally impermeable to water. So, reabsorption of water does not occur in the renal tubules and dilute urine is excreted. This leads to loss of large amount of water through urine. This condition is called **diabetes insipidus** and the excretion of large amount of water is called diuresis.

Mode of action on renal tubules

ADH increases water reabsorption in tubular epithelial membrane by regulating the **water channel proteins** called **aquaporins** through **V2 receptors** (Chapter 52).

2. *Vasopressor action*

In large amount, ADH shows vasoconstrictor action. Particularly, causes constriction of the arteries in all parts of the body. Due to vasoconstriction, the blood pressure increases. ADH acts on blood vessels through V_{1A} receptors.

However, the amount of ADH required to cause the vasopressor effect is greater than the amount required to cause the **antidiuretic effect.**

Regulation of Secretion

ADH secretion depends upon the volume of body fluid and the osmolarity of the body fluids.

Potent stimulants for ADH secretion are:
1. Decrease in the extracellular fluid (ECF) volume
2. Increase in osmolar concentration in the ECF.

Role of osmoreceptors

Osmoreceptors are the receptors which give response to change in the osmolar concentration of the blood. These receptors are situated in the hypothalamus near supraoptic and paraventricular nuclei. When osmolar concentration of blood increases, the osmoreceptors are activated. In turn, the osmoreceptors stimulate the supraoptic and paraventricular nuclei which send motor impulses to posterior pituitary through the nerve fibers and cause release of ADH. ADH causes reabsorption of water from the renal tubules. This increases ECF volume and restores the normal osmolarity.

■ OXYTOCIN

Source of Secretion

Oxytocin is secreted mainly by **paraventricular nucleus** of hypothalamus. It is also secreted by **supraoptic nucleus** in small quantity and it is transported from hypothalamus to posterior pituitary through the nerve fibers of hypothalamo-hypophyseal tract.

In the posterior pituitary, the oxytocin is stored in the nerve endings of hypothalamo-hypophyseal tract. When suitable stimuli reach the posterior pituitary from hypothalamus, oxytocin is released into the blood. Oxytocin is secreted in both males and females.

Chemistry and Half-life

Oxytocin is a polypeptide having 9 amino acids. It has a half-life of about 6 minutes.

Actions in Females

In females, oxytocin acts on mammary glands and uterus.

Action of oxytocin on mammary glands

Oxytocin causes ejection of milk from the mammary glands. Ducts of the mammary glands are lined by myo-epithelial cells. Oxytocin causes contraction of the myo-epithelial cells and flow of milk from alveoli of mammary glands to the exterior through duct system and nipple. The process by which the milk is ejected from alveoli of mammary glands is called milk ejection reflex or milk let-down reflex. It is one of the **neuroendocrine reflexes.**

Milk ejection reflex

Plenty of touch receptors are present on the mammary glands, particularly around the nipple. When the

infant suckles mother nipple, the touch receptors are stimulated. The impulses discharged from touch receptors are carried by the somatic afferent nerve fibers to paraventricular and supraoptic nuclei of hypothalamus.

Now hypothalamus, in turn sends impulses to the posterior pituitary through hypothalamo-hypophyseal tract. Afferent impulses cause release of oxytocin into the blood. When the hormone reaches the mammary gland, it causes contraction of myoepithelial cells, resulting in ejection of milk from mammary glands (Fig. 66.5).

As this reflex is initiated by the nervous factors and completed by the hormonal action, it is called a **neuroendocrine reflex.** During this reflex, large amount of oxytocin is released by **positive feedback mechanism.**

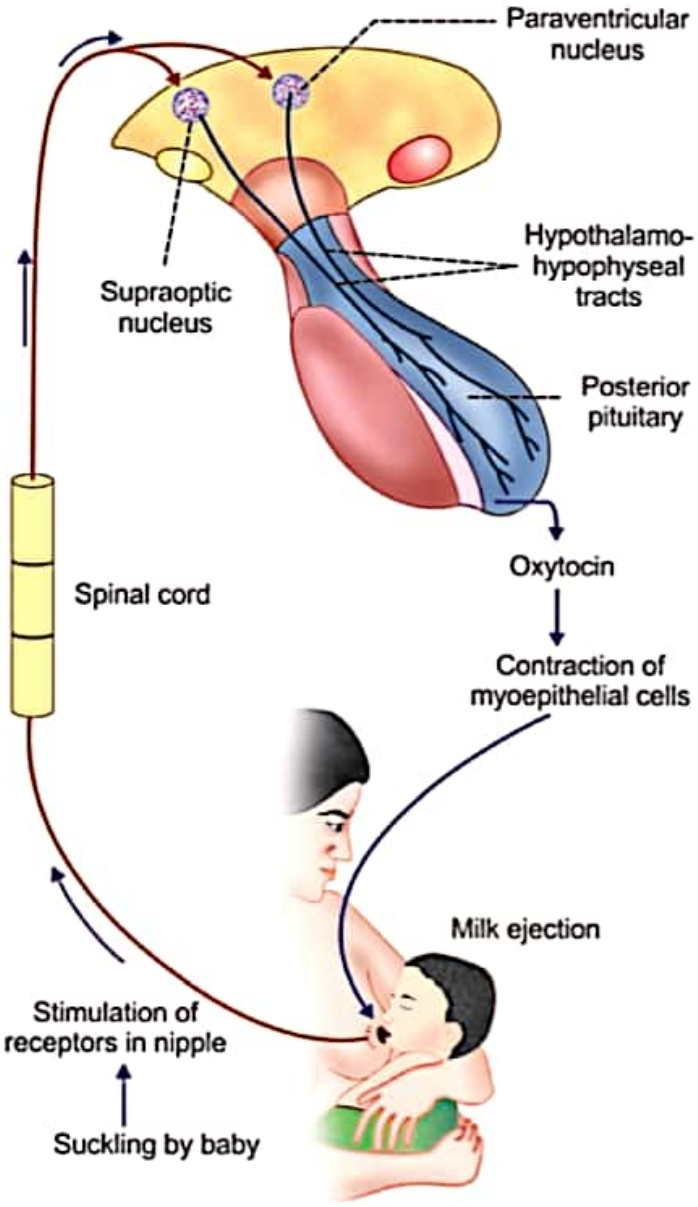


FIGURE 66.5: Milk ejection reflex

Action on uterus

Oxytocin acts on pregnant uterus and also non-pregnant uterus.

On pregnant uterus

Throughout the period of pregnancy, oxytocin secretion is inhibited by estrogen and progesterone. At the end of pregnancy, the secretion of these two hormones decreases suddenly and the secretion of oxytocin increases. Oxytocin causes contraction of uterus and helps in the expulsion of fetus.

During the later stages of pregnancy, the number of receptors for oxytocin increases in the wall of the uterus. Because of this, the uterus becomes more sensitive to oxytocin.

Oxytocin secretion increases during **labor.** At the onset of labor, the cervix dilates and the fetus descends through the birth canal. During the movement of fetus through cervix, the receptors on the cervix are stimulated and start discharging large number of impulses. These impulses are carried to the paraventricular and supraoptic nuclei of hypothalamus by the somatic afferent nerve fibers. Now, these two hypothalamic nuclei secrete large quantity of oxytocin, which enhances labor by causing contraction of uterus (Chapter 84).

Throughout labor, large quantity of oxytocin is released by means of **positive feedback mechanism,** i.e. oxytocin induces contraction of uterus, which in turn causes release of more amount of oxytocin (Fig. 4.5).

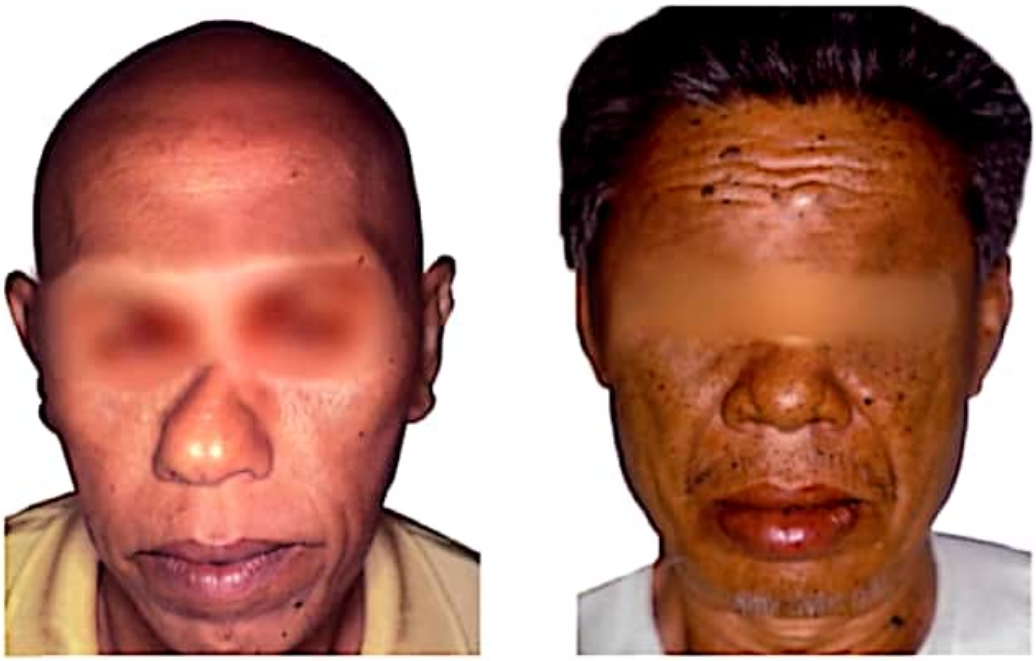
The contraction of uterus during labor is also a neuroendocrine reflex. Oxytocin also stimulates the release of prostaglandins in the placenta. Prostaglandins intensify the uterine contraction induced by oxytocin.

On non-pregnant uterus

The action of oxytocin on non-pregnant uterus is to facilitate the transport of sperms through female genital tract up to the fallopian tube, by producing the uterine contraction during sexual intercourse.

During the sexual intercourse, the receptors in the vagina are stimulated. Vaginal receptors generate the impulses, which are transmitted by somatic afferent nerves to the paraventricular and supraoptic nuclei of hypothalamus. When, these two nuclei are stimulated, oxytocin is released and transported by blood. While reaching the female genital tract, the hormone causes antiperistaltic contractions of uterus towards the fallopian tube. It is also a **neuroendocrine reflex.**

Sensitivity of uterus to oxytocin is accelerated by estrogen and decreased by progesterone.



Gorilla face: Protrution of supraorbital ridges, broad nose, thickened lips and protrution of lower jaw.

Wrinkled forehead, with other features of acromegalic face.

FIGURE 66.6: Acromegaly (*Courtesy:* Prof Mafauzy Mohamad)

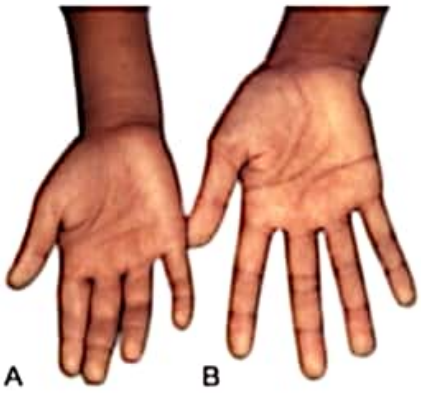


FIGURE 66.7: A. Normal hand; B. Acromegalic hand (*Courtesy:* Prof Mafauzy Mohamad)

in children, before the fusion of epiphysis with shaft of the bones causes gigantism and if hypersecretion of GH is continued even after the fusion of epiphysis, the symptoms of acromegaly also appear.

4. *Cushing Disease*

It is also a rare disease characterized by obesity.

Causes

Cushing disease develops by basophilic adenoma of adenohypophysis. It increases the secretion of adrenocorticotropic hormone, which in turn stimulates the adrenal cortex to release cortisol. Cushing disease also develops by hyperplasia or tumor of adrenal cortex.

Usually, the disorder due to the pituitary cause is called **Cushing disease** and when it is due to the adrenal cause, it is called **Cushing syndrome.**

Details of this condition are given in Chapter 70.

■ HYPOACTIVITY OF ANTERIOR PITUITARY

1. *Dwarfism*

Dwarfism is a pituitary disorder in children, characterized by the stunted growth.

Causes

Reduction in GH secretion in infancy or early childhood causes dwarfism. It occurs because of the following reasons:

i. Tumor of chromophobes: It is a non-functioning tumor, which compresses and destroys the normal cells secreting GH. It is the most common cause for hyposecretion of GH, leading to dwarfism
ii. Deficiency of GH-releasing hormone secreted by hypothalamus
iii. Deficiency of somatomedin C
iv. Atrophy or degeneration of acidophilic cells in the anterior pituitary
iv. **Panhypopituitarism:** In this condition, there is reduction in the secretion of all the hormones of anterior pituitary gland. This type of dwarfism is associated with other symptoms due to the deficiency of other anterior pituitary hormones.

Signs and symptoms

i. Primary symptom of hypopituitarism in children is the stunted skeletal growth. The maximum height of anterior pituitary dwarf at the adult age is only about 3 feet
ii. But the proportions of different parts of the body are almost normal. Only the head becomes slightly larger in relation to the body
iii. Pituitary dwarfs do not show any deformity and their mental activity is normal with no mental retardation
iv. Reproductive function is not affected, if there is only GH deficiency. However, during panhypopituitarism, the dwarfs do not obtain puberty due to the deficiency of gonadotropic hormones.

Laron dwarfism

Laron dwarfism is a genetic disorder. It is also called **GH insensitivity.** It occurs due to the presence of abnormal growth hormone **secretagogue** (GHS) receptors in liver. GHS receptors become abnormal because of the mutation of genes for the receptors.

GH secretion is normal or high. But the hormone cannot stimulate growth because of the abnormal GHS receptors. So, dwarfism occurs.

Psychogenic dwarfism

Dwarfism occurs if the child is exposed to extreme emotional deprivation or stress. The short stature is because of deficiency of GH. This type of dwarfism is called psychogenic dwarfism, **psychosocial dwarfism** or **stress dwarfism.**

Dwarfism in dystrophia adiposogenitalis

Dystrophia adiposogenitalis or **Fröhlich syndrome** is a pituitary disorder (see below). Dwarfism occurs if it develops in children.

Dwarfism in panhypopituitarism

Panhypopituitarism is the pituitary disorder due to reduction in secretion of all anterior pituitary hormones. These dwarfs do not attain puberty.

2. *Acromicria*

Acromicria is a rare disease in adults characterized by the atrophy of the extremities of the body.

ii. Atrophy or degeneration of acidophilic cells in the anterior pituitary
iii. Tumor of chromophobes: It is a non-functioning tumor, which compresses and destroys the normal cells secreting the GH. This is the most common cause for hyposecretion of GH leading to acromicria
iv. Panhypopituitarism: In this condition, there is a reduction in secretion of all the hormones of anterior pituitary gland. Acromicria is associated with other symptoms due to the deficiency of other anterior pituitary hormones.

Signs and symptoms

i. Atrophy and thinning of extremities of the body, (hands and feet) are the major symptoms in acromicria
ii. Acromicria is mostly associated with hypothyroidism
iii. Hyposecretion of adrenocortical hormones also is common in acromicria
iv. The person becomes lethargic and obese
v. There is loss of sexual functions.

3. *Simmond Disease*

Simmond disease is a rare pituitary disease. It is also called **pituitary cachexia.**

Causes

It occurs mostly in panhypopituitarism, i.e. hyposecretion of all the anterior pituitary hormones due to the atrophy or degeneration of anterior pituitary.

Symptoms

i. A major feature of Simmond disease is the rapidly developing **senile decay.** Thus, a 30-years-old person looks like a 60-years-old person. The senile decay is mainly due to deficiency of hormones from target glands of anterior pituitary, i.e. the thyroid gland, adrenal cortex and the gonads
ii. There is loss of hair over the body and loss of teeth
iii. Skin on face becomes dry and wrinkled. So, there is a shrunken appearance of facial features. It is the most common feature of this disease.

■ HYPERACTIVITY OF POSTERIOR PITUITARY

■ INTRODUCTION

Human beings have four parathyroid glands, which are situated on the posterior surface of upper and lower poles of thyroid gland (Fig. 68.1). Parathyroid glands are very small in size, measuring about 6 mm long, 3 mm wide and 2 mm thick, with dark brown color.

Histology

Each parathyroid gland is made up of **chief cells** and **oxyphil cells.** Chief cells secrete parathormone. Oxyphil cells are the degenerated chief cells and their function is known. However, these cells may secrete parathormone during pathological condition called **parathyroid adenoma.** The number of oxyphil cells increases after puberty.

■ PARATHORMONE

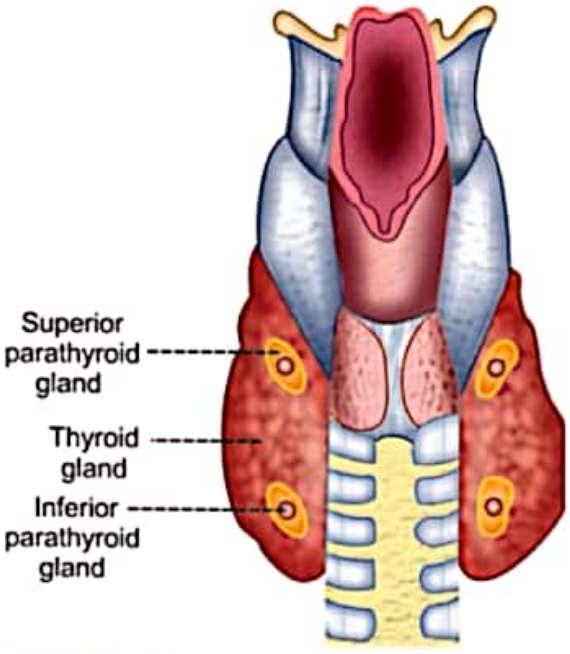
Parathormone secreted by parathyroid gland is essential for the maintenance of blood calcium level within a very narrow critical level. Maintenance of blood calcium level is necessary because calcium is an important inorganic ion for many physiological functions (see below).

Source of Secretion

Parathormone (PTH) is secreted by the chief cells of the parathyroid glands.

Chemistry

Parathormone is protein in nature, having 84 amino acids. Its molecular weight is 9,500.



Half-life and Plasma Level

Parathormone has a half-life of 10 minutes. Normal plasma level of PTH is about 1.5 to 5.5 ng/dL.

Synthesis

Parathormone is synthesized from the precursor called **prepro-PTH** containing 115 amino acids. First, the prepro-PTH enters the endoplasmic reticulum of chief cells of parathyroid glands. There it is converted into a prohormone called **pro-PTH,** which contains 96 amino acids. Pro-PTH enters the Golgi apparatus, where it is converted into PTH.

Metabolism

Sixty to seventy percent of PTH is degraded by **Kupffer cells** of liver, by means of proteolysis. Degradation of about 20% to 30% PTH occurs in kidneys and to a lesser extent in other organs.

■ ACTIONS OF PARATHORMONE

PTH plays an important role in maintaining blood calcium level. It also controls blood phosphate level.

■ ACTIONS OF PARATHORMONE ON BLOOD CALCIUM LEVEL

Primary action of PTH is to maintain the blood calcium level within the critical range of 9 to 11 mg/dL. The blood calcium level has to be maintained critically because, it is very important for many of the activities in the body.

PTH maintains blood calcium level by acting on:

1. Bones
2. Kidney
3. Gastrointestinal tract.

1. On Bone

Parathormone enhances the resorption of calcium from the bones **(osteoclastic activity)** by acting on **osteoblasts** and **osteoclasts** of the bone.

Resorption of calcium from bones occurs in two phases:

i. Rapid phase
ii. Slow phase.

Rapid phase

Rapid phase occurs within minutes after the release of PTH from parathyroid glands. Immediately after reaching the bone, PTH gets attached with the receptors on the cell membrane of osteoblasts and osteocytes. The

the calcium pump mechanism, so that calcium ions move out of these bone cells and enter the blood at a faster rate.

Slow phase

Slow phase of calcium resorption from bone is due to the activation of osteoclasts by PTH. When osteoclasts are activated, some substances such as proteolytic enzymes, citric acid and lactic acid are released from lysosomes of these cells. All these substances digest or dissolve the organic matrix of the bone, releasing the calcium ions. The calcium ions slowly enter the blood.

PTH increases calcium resorption from bone by stimulating the proliferation of osteoclasts also.

2. *On Kidney*

PTH increases the reabsorption of calcium from the renal tubules along with magnesium ions and hydrogen ions. It increases calcium reabsorption mainly from distal convoluted tubule and proximal part of collecting duct.

PTH also increases the formation of **1,25-dihydroxycholecalciferol** (activated form of vitamin D) from 25-hydroxycholecalciferol in kidneys (see below).

3. *On Gastrointestinal Tract*

PTH increases the absorption of calcium ions from the GI tract indirectly. It increases the formation of 1,25-dihydroxycholecalciferol in the kidneys. This vitamin, in turn increases the absorption of calcium from GI tract.

Thus, the activated vitamin D is very essential for the absorption of calcium from the GI tract. And PTH is essential for the formation of activated vitamin D.

Role of PTH in the activation of vitamin D

Vitamin D is very essential for calcium absorption from the GI tract. But vitamin D itself is not an active substance. Instead, vitamin D has to be converted into 1, 25-dihydroxycholecalciferol in the liver and kidney in the presence of PTH. The 1,25-dihydroxycholecalciferol is the active product.

Activation of vitamin D

There are various forms of vitamin D. But, the most important one is vitamin D3. It is also known as cholecalciferol. Vitamin D3 is synthesized in the skin from 7-dehydrocholesterol, by the action of **ultraviolet rays** from the **sunlight.** It is also obtained from dietary sources.

The activation of vitamin D3 occurs in two steps (Fig. 68.2).

First step

Cholecalciferol (vitamin D3) is converted into 25-hydroxycholecalciferol in the liver. This process is limited and is inhibited by 25-hydroxycholecalciferol itself by feedback mechanism. This inhibition is essential for two reasons:

i. Regulation of the amount of active vitamin D
ii. Storage of vitamin D for months together.

If vitamin D3 is converted into 25-hydroxycholecalciferol, it remains in the body only for 2 to 5 days. But vitamin D3 is stored in liver for several months.

Second step

25-hydroxycholecalciferol is converted into 1,25-dihydroxycholecalciferol **(calcitriol)** in kidney. It is the active form of vitamin D3. This step needs the presence of PTH.

Role of Calcium Ion in Regulating 1, 25-Dihydroxycholecalciferol

When blood calcium level increases, it inhibits the formation of 1,25-dihydroxycholecalciferol. The mechanism involved in the inhibition of the formation of 1,25-dihydroxycholecalciferol is as follows:

i. Increase in calcium ion concentration directly suppresses the conversion of 25-hydroxycholecalciferol into 1,25-dihydroxycholecalciferol. This effect is very mild

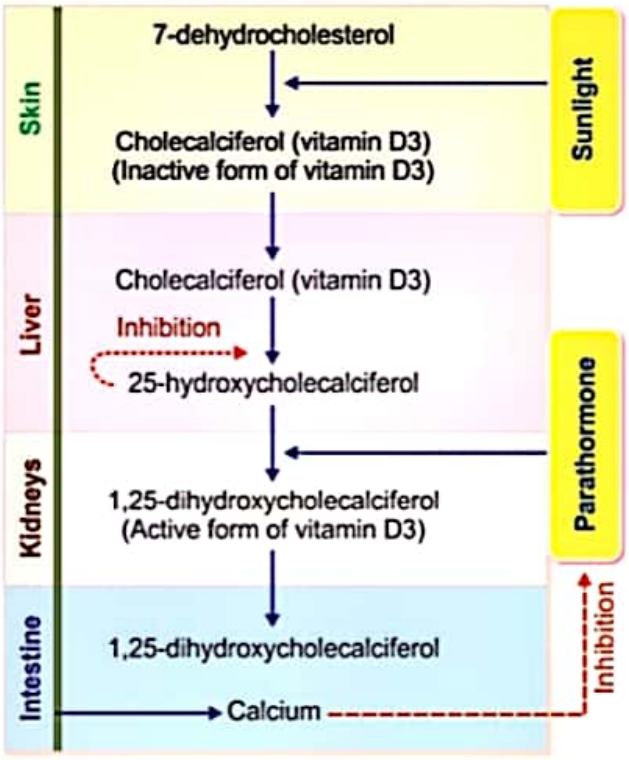


FIGURE 68.2: Schematic diagram showing activation of vitamin D

ii. Increase in calcium ion concentration decreases the PTH secretion, which in turn suppresses the conversion of 25-hydroxycholecalciferol into 1,25-dihydroxycholecalciferol.

This regulates the calcium ion concentration of plasma itself indirectly, i.e. when the PTH synthesis is inhibited, the conversion of 25-hydroxycholecalciferol into 1,25-hydroxycholecalciferol is also inhibited. Lack of 1,25-dihydroxycholecalciferol, decreases the absorption of calcium ions from the intestine, from the bones and from the renal tubules as well. This makes the calcium level in the plasma to fall back to normal.

Actions of 1, 25-Dihydroxycholecalciferol

1. It increases the absorption of calcium from the intestine, by increasing the formation of calcium-binding proteins in the intestinal epithelial cells. These proteins act as carrier proteins for facilitated diffusion, by which the calcium ions are transported. The proteins remain in the cells for several weeks after 1,25-dihydroxycholecalciferol has been removed from the body, thus causing a prolonged effect on calcium absorption
2. It increases the synthesis of calcium-induced ATPase in the intestinal epithelium
3. It increases the synthesis of alkaline phophatase in the intestinal epithelium
4. It increases the absorption of phosphate from intestine along with calcium.

■ ACTIONS OF PARATHORMONE ON BLOOD PHOSPHATE LEVEL

PTH decreases blood level of phosphate by increasing its urinary excretion. It also acts on bone and GI tract.

1. *On Bone*

Along with calcium resorption, PTH also increases phosphate absorption from the bones.

2. *On Kidney*

Phosphaturic action

It is the effect of PTH by which phosphate is excreted through urine. PTH increases phosphate excretion by inhibiting reabsorption of phosphate from renal tubules. It acts mainly on proximal convoluted tubule.

3. *On Gastrointestinal Tract*

Parathormone increases the absorption of phosphate from GI tract through calcitriol.

Sequence of events

i. PTH converts 25-hydroxycholecalciferol into 1,25-dihydroxycholecalciferol (calcitriol: active form of vitamin D3) in kidney
ii. Calcitriol increases the synthesis of calcium induced ATPase in the intestinal epithelium
iii. ATPase increases the synthesis of alkaline phophatase
iv. Alkaline phosphatase increases the absorption of phosphate from intestine along with calcium.

■ MODE OF ACTION OF PARATHORMONE

Parathormone Receptors

Parathormone receptors (PTH receptors) are of three types, PTHR1, PTHR2 and PTHR3, which are G protein-coupled receptors. PTHR1 is physiologically more important than the other two types. PTHR1 mediates the actions of PTH and **PTH-related protein** (see below). Role of PTHR2 and PTHR3 is not known clearly.

On the target cells, PTH binds with PTHR1 which is coupled to G protein and forms hormone-receptor complex. Hormone-receptor complex causes formation of cAMP, which acts as a second messenger for the hormone.

■ REGULATION OF PARATHORMONE SECRETION

Blood level of calcium is the main factor regulating the secretion of PTH. Blood phosphate level also regulates PTH secretion.

Blood Level of Calcium

Parathormone secretion is inversely proportional to blood calcium level. Increase in blood calcium level decreases PTH secretion.

Conditions when PTH secretion decreases are:

1. Excess quantities of calcium in the diet
2. Increased vitamin D in the diet
3. Increased resorption of calcium from the bones, caused by some other factors such as bone diseases.

On the other hand, decrease in calcium ion concentration of blood increases PTH secretion, as in the case of rickets, pregnancy and in lactation.

Blood Level of Phosphate

PTH secretion is directly proportional to blood phosphate level. Whenever the blood level of phosphate increases,

Progesterone Functions

- Conversion of uterus to secretory gland readying it for implantation
- Formation of cervical plug
- Inhibition of myometrial contraction
- Inhibition of prostaglandin synthesis from uterus
- Development of alveolus and lobule in breast
- Inhibit lactose synthesis

- Effect on Fallopian tubes: secretory activities are increased for nutrition of the fertilized ovum.
- Effect on Uterus: promotes secretory activities of the endometrium to prepare the uterus for the implantation of the fertilized ovum.
- Effect on Cervix: increases the thickness of cervical mucosa inhibiting transport of sperm into uterus.
- Effect on mammary glands: increases the secretory function of the breasts.
- Effect on Hypothalamus: inhibits release of LH.
- Thermogenesis: increases body temperature after ovulation.

4. Estrogens

Physiological Role:

1. Development of genital tract and breast.
2. Secondary sex characters. Menstrual cycle
3. During follicular phase it cause endometrium to grow
4. Metabolic effects:
   - Increase bone mass and prevent bone resorption.
   - Increase blood glucose.
   - Increase serum TGs and decrease cholesterol.
   - Salt and water retention.
5. Increase blood coagulation and platelet adhesiveness.