University of Al- Ameed - College of Dentistry
Professor Dr. Basim Zwain
Lectures on Medical Physiology

Lectures 14-16

ENDOCRINE PHYSIOLOGY

Endocrine system

Glands are endocrine and exocrine. Exocrine glands have ducts. Endocrine glands are ductless. They secrete hormones into surrounding tissue vascular or lymphatic fluid. Examples of endocrine glands are: pituitary, thyroid, parathyroid, adrenal, pineal and thymus glands. Some organs have endocrine tissue as well as exocrine tissue like pancreas, gonads and hypothalamus.

Hormones are chemical substances secreted by cells into extracellular fluids that regulate metabolic function of other cells in the body (increase or decrease rates of normal cellular activity).

Types of hormones:

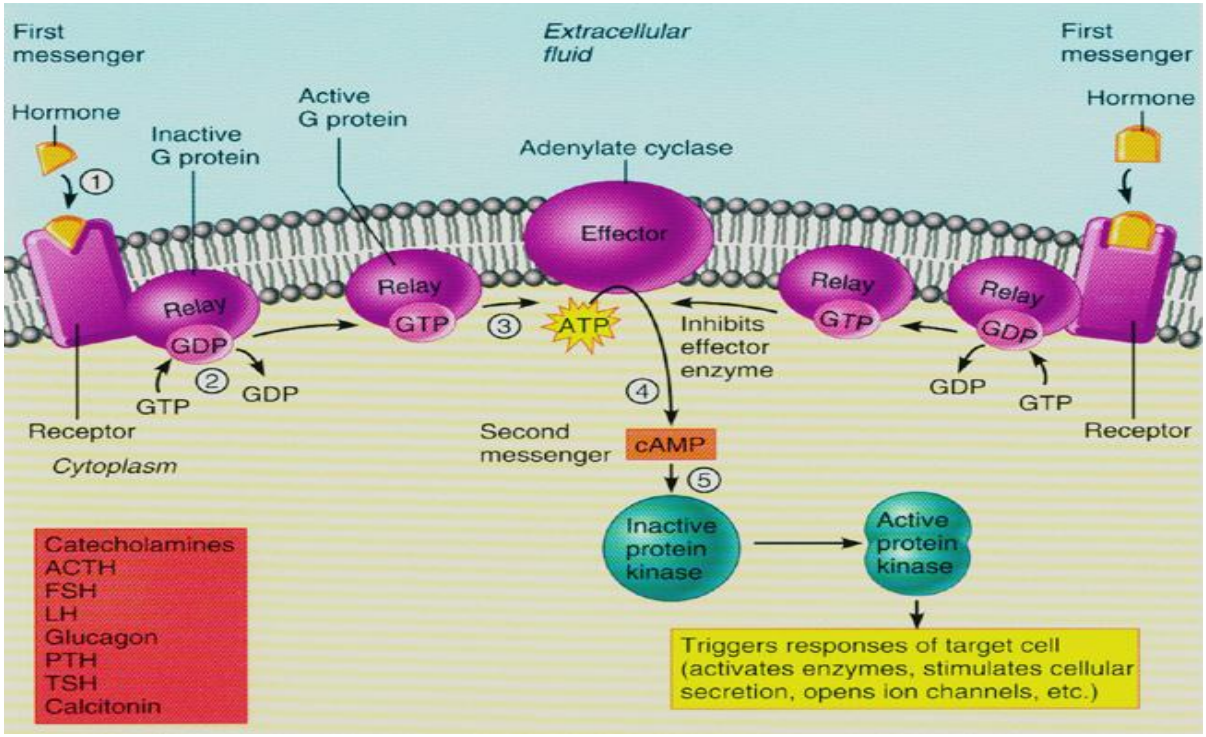
a. Amino acid-based hormones (Most hormones)
b. Steroid hormones (gonadal and adrenocortical hormones)

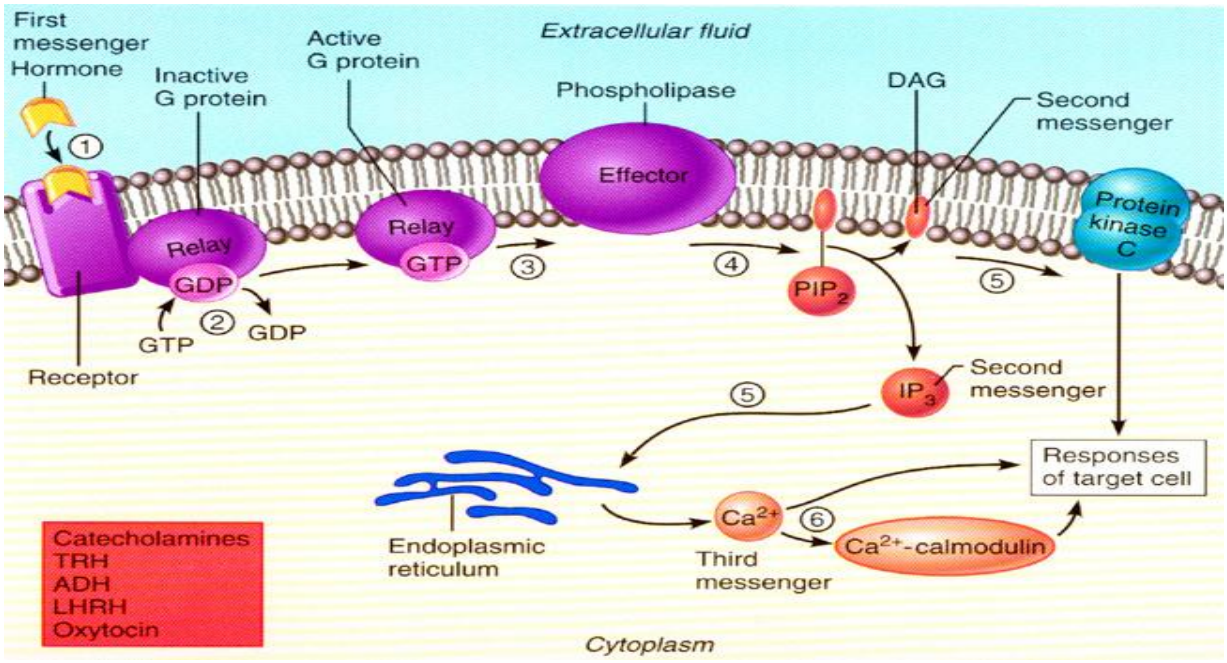
Hormonal effects:

a. Alter plasma membrane permeability
b. Alter protein or regulatory molecule synthesis
c. Activate or inactivate enzyme
d. Induction of secretory activity
e. Stimulate mitosis

Mechanisms of hormonal actions:

a. G-protein linked receptor: activation of intracellular 2nd messengers which is mechanism of amino acid hormones.

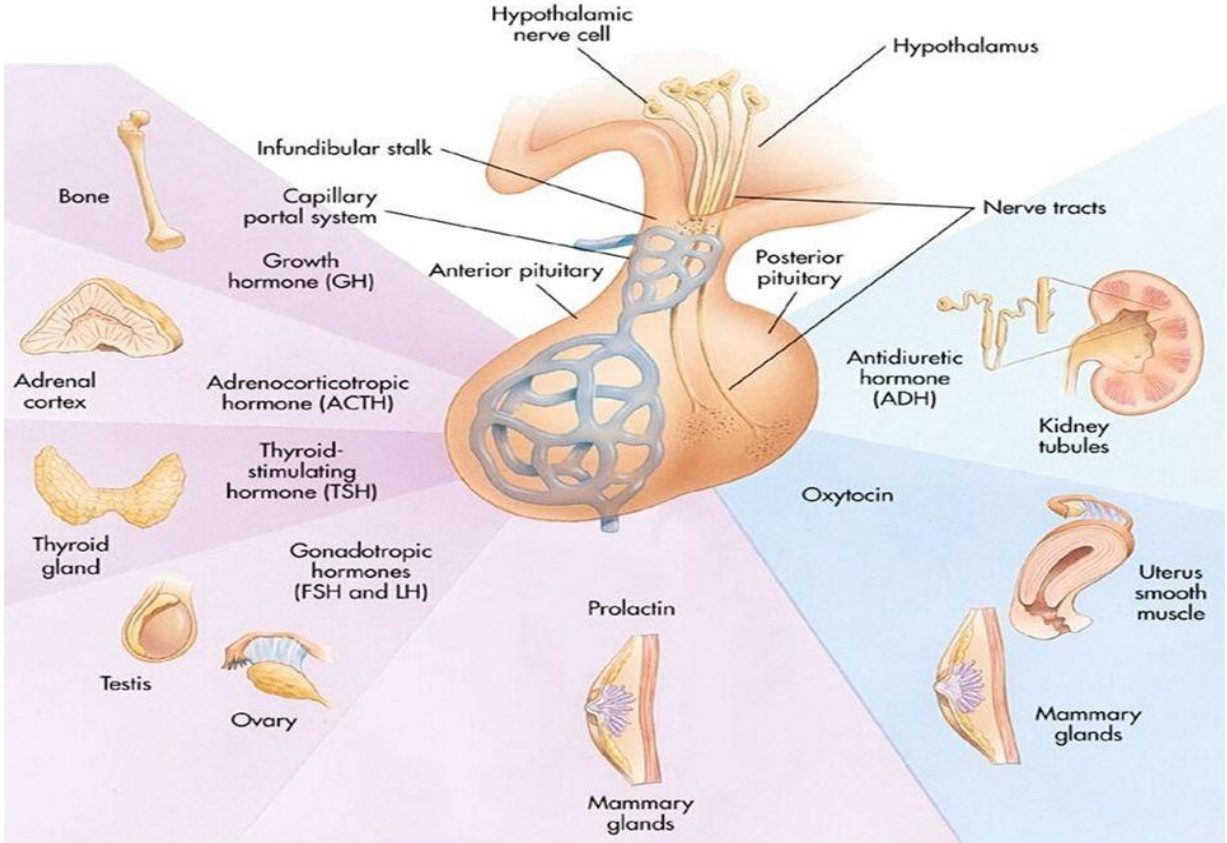




b. Direct gene activation which is the mechanism of steroid hormones and thyroid hormones. Steroid hormones are lipid soluble and thyroid hormones are small peptides so they pass through plasma membrane

Hypothalamus – pituitary hormones

Two lobes of pituitary gland. Anterior lobe is adenohyophysis. Posterior lobe is neurohypophysis which is an outgrowth of the hypothalamus.



There is only vascular connection via hypophyseal portal veins which carry releasing and inhibiting hormones secreted by hypothalamus to anterior pituitary gland in order to regulate the activity of secretory cells in anterior pituitary.

Anterior pituitary hormones

Anterior pituitary is referred to as the Master gland. It secretes six hormones as well as a number of other active molecules. Four of these hormones are *the tropic hormones* which regulate secretory activity of other endocrine glands:

a. TSH—thyroid-stimulating hormone
b. ACTH—adrenocorticotropic hormone
c. FSH—follicle-stimulating hormone
d. LH—lutenizing hormone

The other two hormones *have neuroendocrine targets* which are:

a. PRL—Prolactin
b. GH—growth hormone

Growth hormone (GH)

GH stimulates most cells in the body to grow and divide but the major targets are bones and muscles. GH is anabolic hormone which promotes metabolism. Regulation of GH secretion is by hypothalamic hormones (negative feedback) where it is **stimulated by somatocrinin** (GHRH growth hormone releasing hormone) and **inhibited by somatostatin** (GHIH growth hormone inhibiting hormone).

Abnormalities of GH secretion

Adolescent hypersecretion: gigantism (excessive proportional growth)
Adult hypersecretion: acromegaly (tissues grow disproportionately)
Adult hyposecretion: little effect but
Adolescent hyposecretion results in pituitary dwarfism

Prolaction

It stimulates milk production. Its secretion is controlled by PRH and PIH (serotonin and dopamine).

The levels of prolactin parallel those of estrogen.

Thyroid-stimulating hormone (TSH)

TSH stimulates normal growth and activity of thyroid gland. It is controlled by hypothalamic TRH (thyrotropin releasing hormone). Thyroid hormones signal hypothalamus and anterior pituitary to stop TRH and TSH respectively. GHIH also inhibits TRH.

Hyposecretion of TSH:

- In childhood: Cretinism
- In adulthood: Myxedema

Hypersecretion of TSH:

- Grave's disease

Adrenocorticotropic hormone (ACTH)

ACTH stimulates adrenal cortex to release corticosteroid hormones. There is a feedback inhibition where rising glucocorticoids inhibit CRH secretion.

Hypersecretion of ACTH:

- Cushing syndrome

Hyposecretion of ACTH:

- Hypoadrenalism

Gonadotropins: FSH and LH

They regulate gonads. FSH stimulates gamete production. LH promotes production of gonadal hormones. FSH and LH work in concert to cause follicle to mature. In females; LH causes egg to be extruded from follicle. In males; LH stimulates interstitial cells of the testes to produce testosterone.

LH and FSH release is controlled by the hypothalamic GnRH (gonadotropin-releasing hormone). Negative feedback inhibition regulates FSH and LH release (testosterone, estrogen, inhibin)

Hypersecretion of gonadotropins:

1- Hypersecretion of FSH: Kleinfelter's syndrome

2- Hypersecretion of LH: Turner syndrome

Posterior pituitary hormones

1- ADH (antidiuretic hormone)

It prevents urine production. Hypothalamus has osmoreceptors and ADH is released from hypothalamus in response to increased solute concentration. ADH causes kidney tubules to reabsorb more water. At high doses, causes vasoconstriction (increases systolic blood pressure).

Hypersecretion of ADH:

- Syndrome of inappropriate antidiuretic hormone (SIADH)

Hyposecretion of ADH:

- Diabetes insipidus

2- Oxytocin (OXT)

It stimulates smooth muscle contraction. The number of its receptors increases during pregnancy. Afferent impulses as uterus stretches during pregnancy signals release of oxytocin during late stages of pregnancy resulting in hormonal trigger for milk ejection (positive feedback mechanism)

Hypersecretion of Oxytocin (OXT):

- Prostatic hyperplasia

Hyposecretion of Oxytocin (OXT):

- Depression

Hormones from other endocrine glands:

Thyroid hormones (TH): T3 and T4

Follicle cells produce thyroglobin and lumen stores colloid (thyroglobin in association with iodine). T2, T3 and T4 are iodinated thyroglobins. The metabolically active hormones are thyroxine (T4) and triiodothyronine (T3). Thyroxine (T4) is produced by thyroid gland while triiodothyronine (T3) is formed at target tissue when T4 is converted into T3. They increase metabolism in most tissues by stimulating glucose oxidation. They increase adrenergic receptors in blood vessels and regulates tissue growth and development.

Thyroid disorders:

- Hypothyroidism
- Hypothyroidism in infants (Cretinism)
- Hyperthyroidism (thyrotoxicosis)

Other thyroid hormones: Calcitonin

Calcitonin is produced by parafollicular cells. It lowers blood Ca^{++} levels. It inhibits calcium release from bones by osteoclast activity and stimulates Ca^{++} uptake and incorporation. Calcium in the blood acts as signal for calcitonin release

Hypersecretion of calcitonin:

- Hypocalcemia

Hyposecretion of calcitonin:

- Hypercalcemia

Parathyroid hormones PTH

PTH (or called parathormone) is secreted by chief cells of parathyroid glands. It stimulates osteoclast activity, releases Ca^{++} and phosphates to the blood. It also enhances Ca^{++} reabsorption and phosphates secretion by kidney tubules. It increases Ca^{++} absorption by intestine and it stimulates kidney conversion of vitamin D into active form.

Hypersecretion of PTH:

- Hyperparathyroidism: hypercalcemia

Hyposecretion of PTH:

- Hypoparathyroidism: hypocalcemia

Adrenocortical hormones

Adrenal glands represent two endocrine glands; adrenal medulla and cortex. They are involved in response to stressful conditions. Adrenal cortex secretes corticosteroids which are synthesized from cholesterol. Corticosteroids are: mineralocorticoids, glucocorticoids and gonadocorticoids.

A. Mineralocorticoids:

They regulate electrolyte concentrations in extracellular fluid. Aldosterone is the most abundant mineralocorticoid. It reduces excretion of sodium from the body and stimulates reabsortion of sodium in the distal tubule of kidney.

Hypersecretion of aldosterone:

- Primary aldosteronism (due to adrenal tumors).

Hyposecretion of aldosterone:

- Addison's disease

B. Glucocorticoids:

They influence metabolism and mediate response to stress. They are: cortisol (hydroctisone), cortisone and corticosterone. Only cortisol is secreted in significant amounts. If there is no stress: cortisol inhibit CRH and ACTH. In stress: Sympathetic nervous system triggers CRH release.

Hypersecretion of cortisol:

- Cushing syndrome

Hyposecretion of cortisol:

- Addison's disease

C. Gonadocorticoids (Sex hormones):

Primarily androgens: androstenedione converted to testosterone and dihydro-testosterone with small amounts of estrogens. Adrenal cortex secretes very small amounts of sex hormones with possible role in onset of puberty.

Adrenal medulla
It is composed of chromaffin cells which secrete epinephrine and norepinephrine. This is the initial response to stress mediated by sympathetic NS. Activation of adrenal medulla and associated release of catecholamines (EPI and NE) prolongs sympathetic response resulting in elevated BP and HR, mobilization of glucose and shunt blood from GIT.

Hyposecretion of adrenal medulla: No significant effect
Hypersecretion of adrenal medulla:
- Tumor of chromaffin cells called pheochromocytoma (uncontrolled sympathetic system activity)

Pancreatic hormones
Pancreas is both endocrine and exocrine organ. Exocrine secretions are the pancreatic juice enzymes to the pancreatic duct. Endocrine secretions are insulin, glucagon, somatostatin and pancretic peptide (PP). Beta cells of pancreas produce insulin which is hypoglycemic hormone. Alpha cells produce glucagon.
Hypersecretion of insulin:
- Hyperinsulinism: (hypoglycemia)
Hyposecretion of insulin:
- Diabetes mellitus (DM) is hyposecretion or hypoactivity of insulin: (hypoglycemia)
Hypersecretion of glucagon:
- Hyperglucagonemia: Glucagonoma syndrome (hypoglycemia)
Hyposecretion of glucagon:
- glucagon deficiency (hyperglycemia)

Testosterone:
It is formed by the interstitial cells of Leydig which lie in adult testes. In general, testosterone is responsible for the distinguishing characteristics of the masculine body. It affects the distribution of body hair. It also decreases the growth of hair on the top of the head. It causes typical adult masculine voice. It increases the thickness of the skin over the entire body. It increases the ruggedness of the subcutaneous tissues (acne). It increases musculature. Testosterone also increases the total quantity of bone matrix and causes calcium retention. It greatly increases the strength of the bony skeleton for load-bearing. It can increase basal metabolic rate. It also increases the number of RBC per cubic millimeter.

Estrogen & progesterone
They are secreted by ovaries in response to FSH and LH. Estrogen regulates mestrual cycle. Progesterone functions mainly to prepare the uterus for pregnancy and the breasts for lactation.
Disturbances in testosterone, estrogen or progesterone results in disturbance in sexual function and mood.

Summarized hormones' properties

Hormone	secreted by	targets at	results in	hyper-secretion	hypo-secretion	What stimulates its release?	What inhibits its release?
Growth hormone (GH)	Anterior pituitary	Bone, muscle, all body cells	Growth, division	1- In adolescence, causes gigantism 2- In adulthood, causes acromegaly	Dwarfism	Hypothalamic hormone somatocrinin (growth hormone releasing hormone GHRH)	Hypothalamic hormone somatostatin (growth hormone inhibiting hormone GHIH)
Prolactin PRL	Anterior pituitary	Breast	Production of milk	hyperprolactinemia	Rare	Prolactin releasing factors (VIP, serotonin)	Prolactin inhibitory factors (dopamine)
Thyroid-stimulating hormone (TSH)	Anterior pituitary	Thyroid gland	Stimulates growth and activity of thyroid (production of thyroxin: T3 and T4)	1- In childhood: cretinism 2- In adulthood: myxedema	Graves disease	Hypothalamic thyrotropin releasing hormone (TRH)	Thyroid hormones (T3, T4), (also somatostatin inhibits TRH)
Adreno-cortico-tropic-hormone (ACTH)	Anterior pituitary	Adrenal cortex	stimulates secretion of glucocorticoid steroid hormones from adrenal cortex	Cushing syndrome	Adrenal insufficiency (hypoadrenalism)	Hypothalamic corticotropin-releasing-hormone (CRH)	Adrenal cortical cortisol inhibits CRH and ACTH
Gonadotropins: Follicle-stimulating hormone (FSH) and (luteinizing hormone (LH)	Anterior pituitary		FSH: Stimulates gamete production LH: Promotes production of gonadal hormones	Hyper-gonadotrophic-hypo-gonadism (Klinefelter's syndrome in men and Turner syndrome in female)	hypogonadotrophic-hypogonadism (Kallman's syndrome)	Hypothalamic gonadotropin-releasing-hormone (GnRH)	Gonadal testosterone, estrogen, progesterone, inhibin
Antidiuretic hormone (ADH)	Posterior pituitary	Renal tubules	Water reabsorption	Syndrome of inappropriate antidiuretic hormone (SIADH)	Diabetes insipidus	Hyperosmolarity (high Na^+ concentration)	Hypo-osmolarity, alcohol ingestion

Oxytocin (OXT)	Posterior pituitary	Breast, uterus	Milk secretion, childbirth	Prostatic hyperplasia	Depression	Milk ejection, childbirth are also stimuli (positive feedback)	Catecholamines, stress
Calcitonin	Thyroid gland: Para-follicular cells	Bone, kidney tubules	Decreases blood Ca^{++} concentration	Hypocalcemia	Hypercalcemia	High blood Ca^{++}	Low blood Ca^{++}
Thyroxin (T4) and T3	Thyroid gland: Follicle cells	Many body cells	Regulation of metabolism and growth	Thyrotoxicosis (hyper-thyroidism)	Hypothyroidism	TSH	Lack of TSH
Para-thormone PTH	Para-thyroid glands (chief cells)	Bone, kidney tubules, intestine	Increases blood Ca^{++} concentration	Hyper-para-thyroidism	Hypo-para-thyroidism (very rare)	Low blood Ca^{++}	High blood Ca^{++}
Aldosterone (steroids)	Adrenal cortex: Zona glomerulosa	Kidney tubules, colon	Increases blood Na^{+} and decreases K^{+} concentration	Primary hyper-aldosteronism	Addison's disease	ACTH, Angiotensin-II, hyperkalemia (high blood K^{+}), hyponatremia (low blood Na+) and low blood pressure	Lack of angiotensin-II, hypokalemia (low blood K^{+}), hypernatremia (high blood Na+) and high blood pressure
Gluco-corticoids: Cortisol (steroids)	Adrenal cortex: Zona fasciculata	Many body organs	Regulation of glucose metabolism and immune, mtabolic, developmental, arousal and cognition effects and body fluid homeostasis	Cushing syndrome	Adrenal insufficiency (Addison's disease	ACTH, Stress	Lack of ACTH
Epinephrine and nor epinephrine	Adrenal medulla	Heart, blood vessels & others	Increases heart rate, blood pressure, blood glucose, break down of fat...	Pheochromocytoma (tumor of adrenal medulla), hypertension	No known effects	Increased sympathetic activity, stress.	Lower sympathetic activity

Insulin	Pancreas: Beta cells	Muscle, fat and liver cells	Decreases blood glucose, enhances glucose absorption into muscle and fat cells, inhibits breakdown of glycogen, promotes oxidation of glucose for ATP production, synthesis and storage of glycogen, conversion of glucose to fat	Hyperinsulinism, hypoglycemia (low blood glucose)	Diabetes mellitus, ketoacidosis	High blood glucose	Low blood glucose
Glucagon	Pancreas: alpha cells	Muscle, fat and liver cells	Breakdown of glycogen to glucose (glycogeno-lysis), synthesis of glucose from lactic acid, fatty acids and amino acids (gluco-neogenesis), Release of glucose from liver	Hyper-glucagonemia (Glucagonoma Syndrome)	Glucagon deficiency	Low blood glucose	High blood glucose
Testosterone	Testes: Leydig cells	Male genitalia, muscle, skin, bone marrow and other tissues	Spermatogenesis, secondary male sexual characteristics, erythropoiesis ...	Infertility and (in female): Hirsutism, deep voice, vrilism, heavy muscularity, acne...	Lack of male characteristics, mood disturbance	Luteinizing hormone (LH)	Lack of luteinizing hormone
Estrogen	Ovaries: Granulosa and corpus luteum	Female genitalia, breasts, uterus, skin, and others	Menstrual cycle, secondary female characteristics	Menstrual disturbances, mood disturbance, ...	Menstrual disturbances, mood disturbance,	Luteinizing hormone (LH)	Lack of luteinizing hormone
Progesterone	Ovaries: Corpus luteum	Uterus, breasts	Prepare the uterus for fertilization and breasts for milk production	Increased risk for developing breast cancer.	Disturbed menstruation, miscarriage	Luteinizing hormone (LH), human chorionic gonadotrophin HCG	Lack of luteinizing hormone or HCG