KARPAGAM ACADEMY OF HIGHER EDUCATION

(Deemed University Established Under Section 3 of UGC Act 1956)
Coimbatore - 641021.
(For the candidates admitted from 2015 onwards)
DEPARTMENT OF BIOCHEMISTRY

SUBJECT : HORMONES: BIOCHEMISTRY AND FUNCTION
SEMESTER : III
SUBJECT CODE : 16BCU303 **CLASS :** II B.Sc.(BC)

Programme outcome: Demonstrate the major hormones released from the hypothalamus, pituitary, and target gland/organ that are clinically important in regard to thyroid, adrenal, and reproductive function and to impart the students to acquire knowledge related to the major hormones released from the hypothalamus, pituitary, and target gland/organ that are clinically important in regard to thyroid, adrenal, and reproductive function

Unit 1-Introduction to hormones and receptors

Functions of hormones and their regulation. Chemical signaling - endocrine, paracrine, autocrine, intracrine and neuroendocrine mechanisms. Chemical classification of hormones, transport of hormones in the circulation and their half-lives. Hormone therapy. General introduction to Endocrine methodology. Hormone receptors - extracellular and intracellular. Receptor - hormone binding, Scatchard analysis. G protein coupled receptors, G proteins

Unit 2- Mechanisms of hormonal actions

Second messengers - cAMP, cGMP, IP3, DAG, Ca^{2+}, NO. Effector systems - adenylate cyclase, guanylate cyclase, PDE, PLC. Protein kinases (PKA, PKB, PKC, PKG). Growth factor signaling, PDGF, EGF, IGF-II, and erythropoietin. Receptor tyrosine kinases - EGF, insulin, erythropoietin receptor; ras - MAP kinase cascade, JAK - STAT pathway. Steroid hormone/ thyroid hormone receptor mediated gene regulation. Receptor regulation and cross talk.

Unit 3-Hypothalamic, pituitary and thyroid hormones

Hypothalamic - pituitary axis. Study the physiological and biochemical actions of hypothalamic hormones, pituitary hormones - GH, prolactin, TSH, LH, FSH, POMC peptide family, oxytocin and vasopressin, feedback regulation cycle. Endocrine disorders - gigantism, acromegaly, dwarfs, pigmies and diabetes insipidus. Thyroid gland. Biosynthesis of thyroid hormone and its

regulation; its physiological and biochemical action. Pathophysiology - Goiter, Graves disease, cretinism, myxedema, Hashimato's disease.

Unit 4- PTH, calcitonin and gastrointestinal hormones

PTH, Vitamin D and calcitonin. Mechanism of Ca^{2+} regulation and pathways involving bone, skin, liver, gut and kidneys. Pathophysiology - rickets, osteomalacia, osteoporosis.

Regulation of release of insulin, glucagon, gastrin, secretin, CCK, GIP, adipolectin, leptin and ghrelin. Summary of hormone metabolite control of GI function. Physiological and biochemical action. Pathophysiology - diabetes type I and type II.

Unit 5-Adrenal and gonadal hormones

Aldosterone, renin angiotensin system, cortisol, epinephrine and norepinephrine. Fight or flight response, stress response. Pathophysiology – Addison's disease, Conn's syndrome, Cushing syndrome.Male and female sex hormones. Interplay of hormones during reproductive cycle, pregnancy, parturition and lactation. Hormone based contraception.

REFERENCES

Nelson, D.L. and Cox, M.M., (2013). Lehninger: Principles of Biochemistry 6th ed., W.H. Freeman & Company (NewYork), ISBN:13: 978-1-4641-0962-1 / ISBN:10-14641-0962-1.

Widmaier, E.P., Raff, H., and Strang, K.T., (2008). Vander's Human Physiology 11th ed.,. McGraw Hill International Publications, ISBN: 978-0-07-128366-3.

Hadley, M.C., and Levine, J.E., (2007). Endocrinology 6th ed., Pearson Education (New Delhi), Inc. ISBN: 978-81-317-2610-5.

Cooper, G.M., and Hausman, R.E., (2009). The Cell: A Molecular Approach 5th Ed. ASM Press & Sunderland, (Washington DC), Sinauer Associates. (MA). ISBN:978-0-87893-300-6.

KARPAGAM UNIVERSITY
DEPARTMENT OF BIOCHEMISTRY & BIOINFORMATICS
II B.Sc., BIOCHEMISTRY
Third Semester
HORMONES: BIOCHEMISTRY AND FUNCTION (16BCU303)
LECTURE PLAN

S.No	Duration of period	Topics covered	Books referred	Page No	Web page referred
		UNIT-I			
1	1	Syllabi discussion			
2	1	Hormones-Introduction	T1	490	
3	1	Classification of Hormones	T1	490-491	
4	1	Chemical Structure and Synthesis of hormones	T2	827-828; 886-888	
5	1	Hormones and homeostasis	T1	315	
6	1	Classes of second messengers	T2	890-892	
7	1	Hormone secretion	T1	493	
8	1	Transport and clearance of hormones			
9	1	Hormones and behaviour	T1	528	
10	1	Feed back control of hormonal secretion			
11	1	Mechanisms of hormonal actions	T1	491-493	
12	1	Hormone receptors	T3	509-510	
13	1	Revision of Unit I			
14	1	Possible questions discussion			
Total	**14**				
		Unit- II			
1	1	Hypothalamic hormones	T3	522-523	
2	1	Pituitary hormones	T1	493	
3	1	Anatomy of pituitary gland	T4	129,131,135	
4	1	Pathophysiology of hypothalmus	T3	523	
5	1	Neurophysis	T3	530	
6	1	Adenohypophysis hormone synthesis			
7	1	Adenohypophysis disorders			
8	1	Mechanism of action of oxytocin	T1	498	
9	1	Mechanism of action of vasopressin	T3	530-532	
10	1	Growth hormones	T1	494	
11	1	Somatomedin	T3	595	
12	1	Pathophysiology	T2	526-530	
13	1	Revision of Unit II			
14	1	Possible questions discussion			
Total	**14**				
		Unit III			
1	1	Introduction to thyroid gland	T1	498	
2	1	Synthesis and chemistry of thyroid hormones	T1	498-499	
3	1	Physiological roles of thyroid hormones	T1	498-504	

4	1	Pathophysiology of thyroid hormones			
5	1	Synthesis of parathyroid hormone	T1	505-507	
6	1	Control of calcium homeostasis	T1	507	
7	1	Melanotropic hormones	T1	452	
		Synthesis of melatonin			
		Chemistry of melatonin			
		Mechanism of action of pineal hormones			
8	1	Pathophysiology of pineal gland	T2	387-395	
9	1	Revision of Unit III			
10	1	Possible questions discussion			
Total	**10**				
		Unit IV			
1	1	Introduction to pancreas	T1	509-510	
2	1	Synthesis of insulin			
3	1	Synthesis of glucagons	T1	515	
4	1	Synthesis of somatostatin			
5	1	Mechansim of action of pancreatic hormones	T1	507-515	
6	1	Physiological role of pancreatic hormones	T1	524-525	
7	1	Chemistry and functions of neurohormones			
8	1	Synthesis of adrenal cortical hormones			
9	1	Physiological role of adrenal hormones	T1	515-524	
10	1	Chemistry of adrenal hormones			
11	1	Pathophysiology of adrenal hormones			
12	1	Revision of Unit IV			
13	1	Possible questions discussion			
Total	**13**				
		Unit V			
1	1	Introduction to gonadal hormones	T1	525-526	
2	1	Syntheis of male reproductive hormones	T1	526	
3	1	Mechanism of action of testosterone			
4	1	Syntheis of female reproductive hormones	T1	528-531	
5	1	Mechanism of action of estradiol	T1	528	
6	1	Pathophysiology of male and female reproductive hormones	R1 1736-1768		
		Endocrinology of pregnancy			
7	2	Endocrinology of parturition	T3: 505-507		
8		Endocrinology of lactation	T1: 135-148		
		Causes for human infertility			
		Treatments for infertility			
9	1	Revision of Unit V			
Total	**9**				
Grand Total	**60**				

References

T1: Chatterjea MN, Shinde R (2006) Textbook of medical biochemistry, Jaypee Brothers Medical Publishers Pvt Ltd

T2: Nelson DL, Cox MM (2007) Lehninger textbook of biochemistry 4th ed WH Freeman and Co, New York

T3: Murray RK, Gramner DK, Mayes PA and Rowell (2003). Harper's Illustrative biochemistry, 27th ed. Mc GrawHill company, London

T4: Larsen PR, Kronenberg HM, Meimed S, Polonsky KS (2003) Williams textbook of endocrinology, 10th Ed saunders, Philadelphia

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UNIT I - COURSE MATERIAL

Unit 1 Introduction to hormones and receptors

Functions of hormones and their regulation. Chemical signaling - endocrine, paracrine, autocrine, intracrine and neuroendocrine mechanisms. Chemical classification of hormones, transport of hormones in the circulation and their half-lives. Hormone therapy. General introduction to Endocrine methodology. Hormone receptors - extracellular and intracellular. Receptor - hormone binding, Scatchard analysis. G protein coupled receptors, G proteins

Hormones- Definition

Substances that provide the chemical basis for ommunication between cells are called "hormones." This word, coined by Bayliss and Starling, was originally used to describe the products of ductless glands released into the general circulation in order to respond to changes in homeostasis. "Hormone" has taken on a broader usage in recent years. Sometimes hormones are released into portal (closed) circulatory systems and have local actions. The word "paracrine" is used to describe the release of locally acting substances. This word also describes local hormone action as the diffusion of gastrin acts on neighboring cells. Hormonal substances released by an animal that influence responses in another animal are referred to as "pheromones."

Classification of hormones

Chemical structure and synthesis of hormones

FUNCTIONS OF HORMONES

Endocrine gland	Hormone	Main tissues acted on by hormone	Main function of hormones
Hypothalamus	Thyrotrophin releasing hormone (TRH)	Anterior pituitary	Stimulates release of thyroid stimulating hormone (TSH) from the anterior pituitary
	Somatostatin	Anterior pituitary	Inhibitory hormone that prevents release of hormones such as growth hormone from the anterior pituitary
	Gonadotrophin releasing hormone (GnRH)	Anterior pituitary	Stimulates release of follicle stimulating hormone (FSH) and luteinising hormone (LH) from the anterior pituitary
	Corticotrophin releasing hormone (CRH)	Anterior pituitary	Stimulates adrenocorticotrophic hormone (ACTH) release from the anterior pituitary
	Growth Hormone Releasing Hormone (GHRH)	Anterior pituitary	Stimulates release of growth hormone (GH) form the anterior pituitary
Anterior pituitary	Thyroid stimulating hormone (TSH)	Thyroid gland	Stimulates release of thyroxine and tri-iodothyronine from the thyroid gland
	Luteinising hormone (LH)	Ovary/Testis	Females: promotes ovulation of the egg and stimulates oestrogen and progesterone production Males: promotes testosterone release from the testis
	Follicle stimulating hormone (FSH)	Ovary/Testis	Females: promotes development of eggs and follicles in the ovary prior to ovulationMales: promotes production of testosterone from testis
	Growth Hormone (GH)	Bones, cartilage, muscle, fat, liver, heart	Acts to promote growth of bones and organs
	Prolactin (PRL)	Breasts, brain	Stimulates milk production in the breasts and plays a role in sexual behaviour
	Adrenocortico-trophic hormone (ACTH)	Adrenal glands	Stimulates the adrenal glands to produce mainly cortisol
Posterior pituitary	Vasopressin (anti-diuretic hormone, ADH)	Kidney, blood vessels, blood components	Acts to maintain blood pressure by causing the kidney to retain fluid and by constricting blood vessels
	Oxytocin	Uterus, milk ducts of breasts	Causes ejection of milk from the milk ducts and causes constriction of the uterus during labour
Thyroid gland	Thyroxine (T4)	Most tissues	Acts to regulate the body's metabolic rate
	Tri-iodothyronine (T3)	Most tissues	Acts to regulate the body's metabolic rate
Parathyroid glands	Parathyroid hormone (PTH)	Kidney, Bone cells	Increases blood calcium levels in the blood when they are low
	Calcitonin	Kidney, Bone cells	Decreases blood calcium levels when they are high

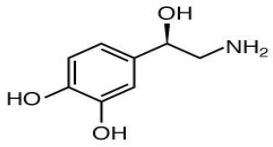
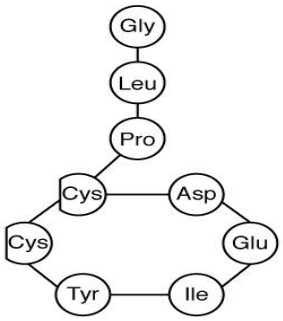
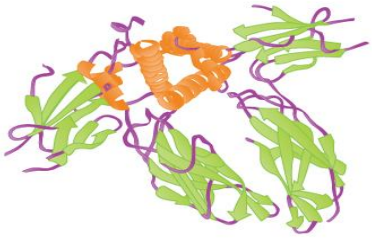
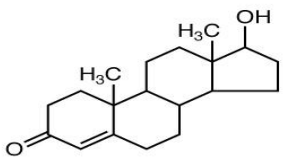
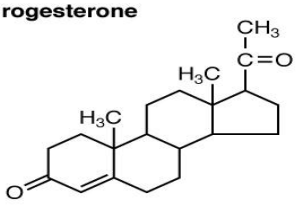
Adrenal cortex	**Cortisol**	Most tissues	Involved in a huge array of physiological functions including blood pressure regulation, immune system functioning and blood glucose regulation
	Aldosterone	Kidney	Acts to maintain blood pressure by causing salt and water retention
	Androgens	Most tissues	Steroid hormones that promote development of male characteristics. Physiological function unclear
Adrenal medulla	**Adrenaline and noradrenaline (the catecholamines)**	Most tissues	Involved in many physiological systems including blood pressure regulation, gastrointestinal movement and patency of the airways
Pancreas	**Insulin**	Muscle, fat tissue	Acts to lower blood glucose levels
	Glucagon	Liver	Acts to raise blood glucose levels
	Somatostatin	Pancreas	Acts to inhibit glucagon and insulin release
Ovary	**Oestrogens**	Breast, Uterus, Internal and external genitalia	Acts to promote development of female primary and secondary sexual characteristics. Important role in preparing the uterus for implantation of embryo
	Progesterone	BreastUterus	Affects female sexual characteristics and important in the maintenance of pregnancy
Testis	**Testosterone**	Sexual organs	Promotes the development of male sexual characteristics including sperm development
Stomach	**Gastrin**	Stomach	Promotes acid secretion in the stomach
	Serotonin (5-HT)	Stomach	Causes constriction of the stomach muscles
Duodenum and jejunum	**Secretin**	Stomach, Liver	Inhibits secretions from the stomach and increases bile production
	Cholecystokinin (CCK)	Liver, Pancreas	Stimulates release of bile from the gall bladder and causes the pancreas to release digestive enzymes
Kidney	**Erythropoietin**	Bone marrow	Stimulates red blood cell development in the bone marrow
Heart	**Atrial natiuretic factor (ANF)**	Kidney	Lowers blood pressure by promoting salt and water loss
Skin	**Vitamin D**	Small intestine, Kidney, Bone cells	Stimulates the uptake of calcium in the small intestine, retention of calcium and release of calcium from bone stores

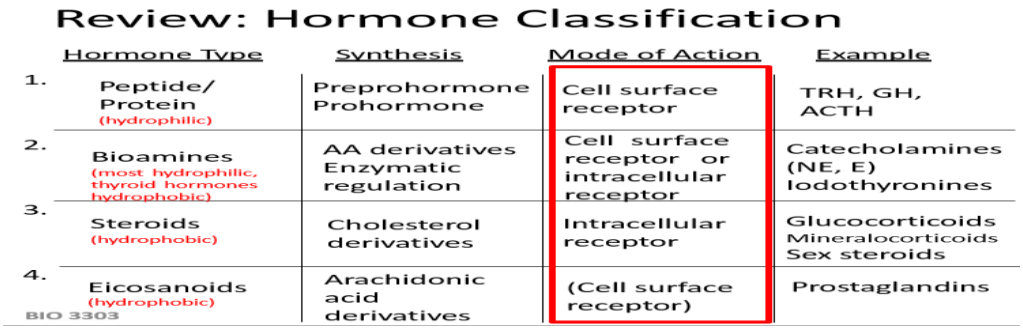
Intracrine refers to a hormone that acts inside a cell, regulating intracellular events. Steroid hormones act through intracellular (mostly nuclear) receptors and, thus, may be considered to be intracrines. In contrast, peptide or protein hormones, in general, act as endocrines, **autocrines**, or **paracrines** by binding to their receptors present on the cell surface. Several peptide/protein hormones or their isoforms also act inside the cell through different mechanisms. These peptide/protein hormones, which have intracellular functions, are also called intracrines. The term 'intracrine' is thought to have been coined to represent peptide/protein hormones that also have intracellular actions.

The biological effects produced by intracellular actions are referred as intracrine effects, whereas those produced by binding to cell surface receptors are called endocrine, autocrine, or paracrine effects, depending on the origin of the hormone. The intracrine effect of some of the peptide/protein hormones are similar to their endocrine, autocrine, or paracrine effects; however, these effects are different for some other hormones.

Intracrine can also refer to a hormone acting within the cell that synthesizes it.

Chemical Classification of Hormones

Hormone Class	Components	Example(s)
Amine Hormone	Amino acids with modified groups (e.g. norepinephrine's carboxyl group is replaced with a benzene ring)	**Norepinephrine** 
Peptide Hormone	Short chains of linked amino acids	**Oxytocin** 
Protein Hormone	Long chains of linked amino acids	**Human Growth Hormone** 
Steroid Hormones	Derived from the lipid cholesterol	**Testosterone**  **Progesterone** 



Review: Hormone Classification

	Hormone Type	Synthesis	Mode of Action	Example
1.	Peptide/ Protein (hydrophilic)	Preprohormone Prohormone	Cell surface receptor	TRH, GH, ACTH
2.	Bioamines (most hydrophilic, thyroid hormones hydrophobic)	AA derivatives Enzymatic regulation	Cell surface receptor or intracellular receptor	Catecholamines (NE, E) Iodothyronines
3.	Steroids (hydrophobic)	Cholesterol derivatives	Intracellular receptor	Glucocorticoids Mineralocorticoids Sex steroids
4.	Eicosanoids (hydrophobic)	Arachidonic acid derivatives	(Cell surface receptor)	Prostaglandins

BIO 3303

Protein and peptide hormones are synthesized on the rough end of the endoplasmic reticulum of the different endocrine cells, in the same fashion as most other proteins. They are usually synthesized first as larger proteins that are not biologically active (preprohormones) and are cleaved to form smaller prohormones in the endoplasmic reticulum. These are then transferred to the Golgi apparatus for packaging into secretory vesicles. In this process, enzymes in the vesicles cleave the prohormones to produce smaller, biologically active hormones and inactive fragments. The vesicles are stored within the cytoplasm, and many are bound to the cell membrane until their secretion is needed. Secretion of the hormones (as well as the inactive fragments) occurs when the secretory vesicles fuse with the cell membrane and the granular contents are extruded into the interstitial fluid or directly into the blood stream by exocytosis.

n many cases, the stimulus for exocytosis is an increase in cytosolic calcium concentration caused by depolarization of the plasma membrane. In other instances, stimulation of an endocrine cell surface receptor causes increased cyclic adenosine monophosphate (cAMP) and subsequently activation of protein kinases that initiate secretion of the hormone. The peptide hormones are water soluble, allowing them to enter the circulatory system easily, where they are carried to their target tissues.

Steroid Hormones Are Usually Synthesized from Cholesterol and Are Not Stored. The chemical structure of steroid hormones is similar to that of cholesterol, and in most instances they are synthesized from cholesterol itself.

Hormones and homeostasis

Hormones regulate various homeostasis, such as glucose homeostasis and calcium homeostasis. Homeostasis is maintained by the endocrine system which secretes hormones—steroids, peptides and amines

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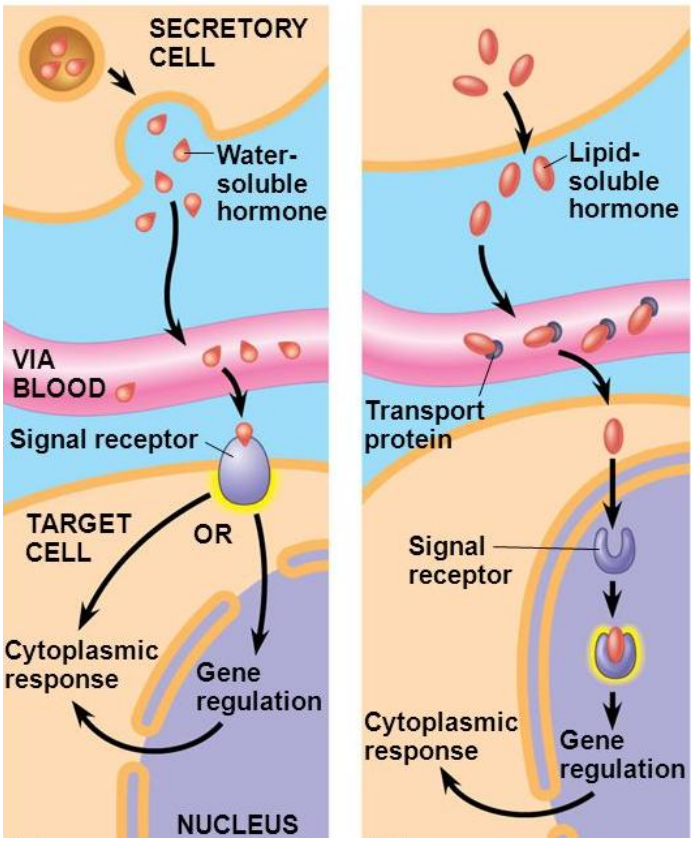


Hormonal secretion and transport

HORMONAL CLEARANCE

Hormone clearance is the process of lowering hormone levels in the blood through two mechanisms: decreased secretion of a hormone and/or increased degradation of a hormone. Hormones can be broken down by their target cells by the enzymes that remove them from receptors, are degradated in the blood (another factor with the shorter half life), or circulate to the liver and are broken down. All three of these steps leads to excretion from the body via bile (steroid hormones) or via urine by the kidneys.

CONTROL OF HORMONAL SECRETION

Up and Down Regulation

Cells can increase and decrease their sensitivity to cells by regulating the number of their receptors. Remember that receptors are proteins and are manufactured by the cell itself, so a cell can increase and decrease the amount of receptors within its plasma membrane. If a cell increases the number of receptors then we call it up regulation; and if the cell decreases the number of receptors we call it down regulation.

Up regulation is used by cells to increase their sensitivity to a specific hormone. Up regulation occurs when a cell produces more receptors, the cell decreases its degradation of receptors or by activating already present recpetors. Cells typically up regulate when the concentration of a hormone is very little. If there is a lower concentration of a hormone in the blood stream and the cell increases the number of receptors, it increases the chances of interacting with that hormone (sensitivity). Hormones themselves can also cause cells to up regulate.

Down regulation is when a cell decreases its sensitivity to a hormone by decreasing the amount of available receptors.

MECHANISM OF HORMONE ACTION

RECEPTORS

A hormone receptor is a receptor molecule that binds to a specific hormone. Hormone receptors are a wide family of proteins made up of receptors for thyroid and steroid hormones, retinoids and Vitamin D, and a variety of other receptors for various ligands, such as fatty acids and prostaglandins.

There are two main classes of hormone receptors. Receptors for peptide hormones tend to be cell surface receptors built into the plasma membrane of cells and are thus referred to as trans membrane receptors. An example of this is insulin

Receptors for steroid hormones are usually found within the cytoplasm and are referred to as intracellular or nuclear receptors, such as testosterone. Upon hormone binding, the receptor can initiate multiple signaling pathways which ultimately lead to changes in the behavior of the target cells.

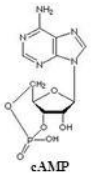
SECOND MESSENGERS

Second messengers are intracellular signaling molecules released by the cell to trigger physiological changes such as proliferation, differentiation, migration, survival, and apoptosis. Secondary messengers are therefore one of the initiating components of intracellular signal transduction cascades. Examples of second messenger molecules include cyclic AMP, cyclic GMP, inositol trisphosphate, diacylglycerol, and calcium. The cell releases second messenger molecules in response to exposure to extracellular signaling molecules—the first messengers

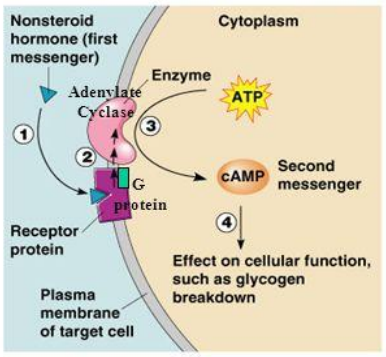
Two Mechanisms of Hormone Action

Non-steroid hormone action

1. Hormone binds to a membrane **receptor**; does not enter cell
2. Sets off a reaction where a **G protein** with bound GTP activates adenylate cyclase enzyme.
3. **Adenylate cyclase** produces cyclic AMP (second messenger) by converting ATP --> **cAMP**
5. cAMP, in turn, **activates phosphorylating activation proteins (protein kinases)** that trigger additional intracellular changes (enzyme activation, secretion, ion channel changes) to promote a specific response



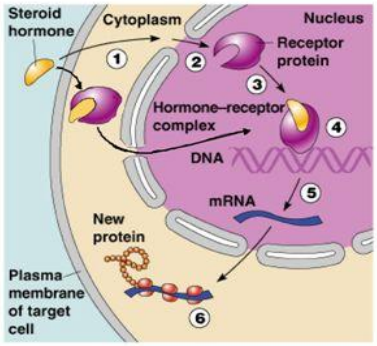
(A few peptide hormones activate Ca^{+2} release via second messengers in the PIP_2 calcium signaling system).



(b) Nonsteroid hormone action

Steroid hormone action

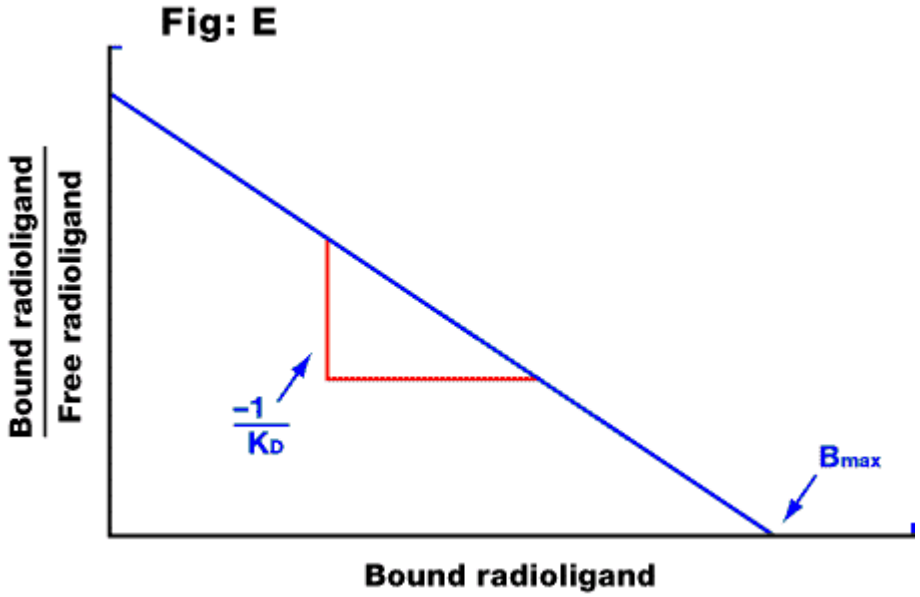
1. Diffuses through the plasma membrane of target cells
2. Enters the nucleus or binds to cytoplasmic receptor
3. Binds to a specific protein within the nucleus if not already bound
4. Binds to specific sites on the cell's DNA
5. Activates genes that result in synthesis of new proteins



(a) Steroid hormone action

The Scatchard plot is a graphical method of analyzing equilibrium ligand binding data. It is used to determine the number of ligand-binding sites on a receptor, whether these sites show cooperative interactions, whether more than one class of site exists, and the respective affinities of each site. The experimental parameters used for a Scatchard plot are the free ligand concentration [L] and the average number of ligand molecules bound to a receptor, n, at a particular ligand concentration at equilibrium.

Fig: E



Application of Scatchard Plot

To assess the number of ligand binding sites in the receptor

To determine the IC50, ED50 of the drugs

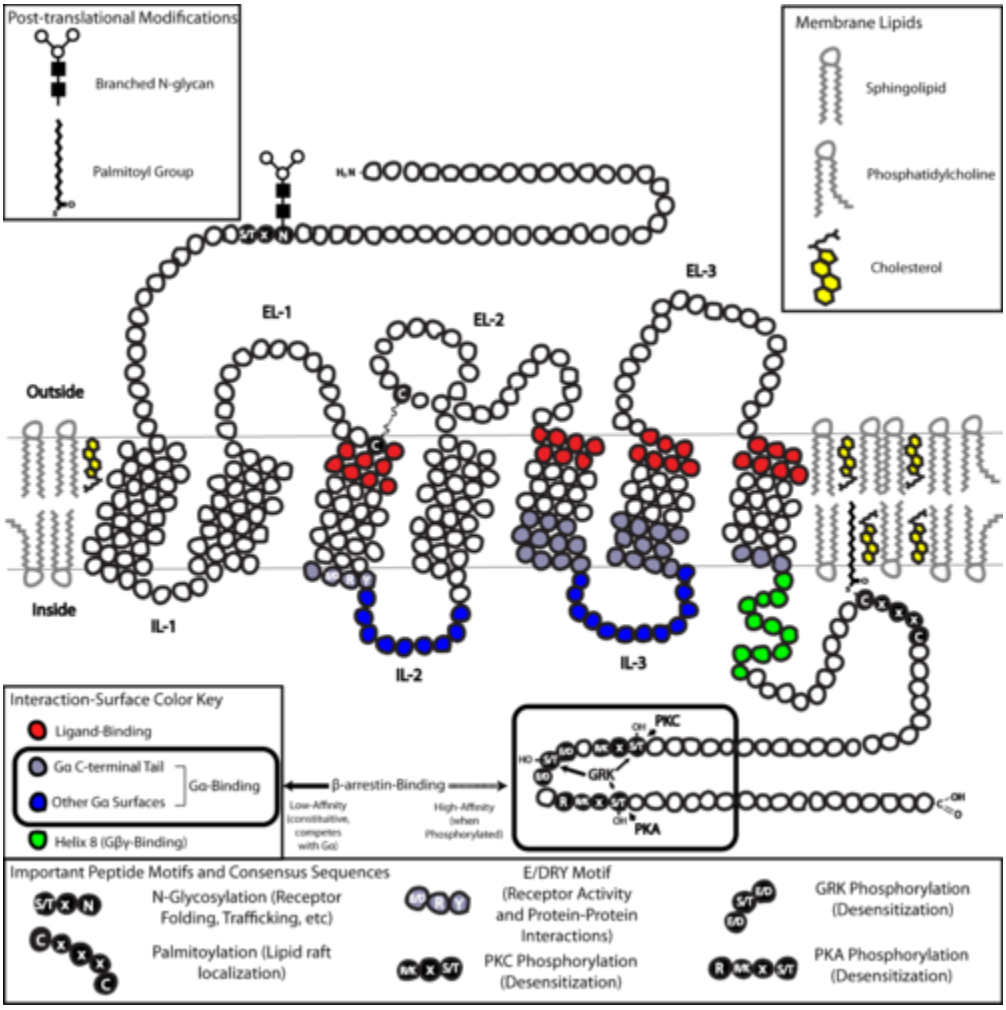
G proteins, also known as guanine nucleotide-binding proteins, are a family of proteins that act as molecular switches inside cells, and are involved in transmitting signals from a variety of stimuli outside a cell to its interior. Their activity is regulated by factors that control their ability to bind to and hydrolyze guanosine triphosphate (GTP) to guanosine diphosphate (GDP). When they are bound to GTP, they are 'on', and, when they are bound to GDP, they are 'off'. G proteins belong to the larger group of enzymes called GTPases.

There are two classes of G proteins. The first function as monomeric small GTPases, while the second function as heterotrimeric G protein complexes. The latter class of complexes is made up of alpha (α), beta (β) and gamma (γ) subunits

G protein–coupled receptors (GPCRs) which are also known as seven-(pass)-transmembrane domain receptors, 7TM receptors, heptahelical receptors, serpentine receptor, and G protein–linked receptors (GPLR), constitute a large protein family of receptors that detect molecules outside the cell and activate internal signal transduction pathways and, ultimately, cellular

responses. Coupling with G proteins, they are called seven-transmembrane receptors because they pass through the cell membrane seven times.

G protein–coupled receptors are found only in eukaryotes, including yeast, choanoflagellates, and animals. The ligands that bind and activate these receptors include light-sensitive compounds, odors, pheromones, hormones, and neurotransmitters, and vary in size from small molecules to peptides to large proteins. G protein–coupled receptors are involved in many diseases, and are also the target of approximately 34% of all modern medicinal drugs.



There are two principal signal transduction pathways involving the G protein–coupled receptors:

* cAMP signal pathway
* phosphatidylinositol signal pathway

When a ligand binds to the GPCR it causes a conformational change in the GPCR, which allows it to act as a guanine nucleotide exchange factor (GEF). The GPCR can then activate an associated G protein by exchanging the GDP bound to the G protein for a GTP. The G protein's α subunit, together with the bound GTP, can then dissociate from the β and γ subunits to further affect intracellular signaling proteins or target functional proteins directly depending on the α subunit type (Gαs, Gαi/o, Gαq/11, α12/13)

The cAMP-dependent pathway is used as a signal transduction pathway for many hormones including:

ADH – Promotes water retention by the kidneys (created by the V2 Cells of Posterior Pituitary)

GHRH – Stimulates the synthesis and release of GH (Somatotroph Cells of Anterior Pituitary)

GHIH – Inhibits the synthesis and release of GH (Somatotroph Cells of Anterior Pituitary)

CRH – Stimulates the synthesis and release of ACTH (Anterior Pituitary)

ACTH – Stimulates the synthesis and release of Cortisol (zona fasiculata of adrenal cortex in adrenals

TSH – Stimulates the synthesis and release of a majority of T4 (Thyroid Gland)

LH – Stimulates follicular maturation and ovulation in women; or testosterone production and spermatogenesis in men

FSH – Stimulates follicular development in women; or spermatogenesis in men

PTH – Increases blood calcium levels. This is accomplished via the Parathyroid hormone 1 receptor (PTH1) in the kidneys and bones, or via the Parathyroid hormone 2 receptor (PTH2) in the central nervous system and brain, as well as the bones and kidneys.

Calcitonin – Decreases blood calcium levels (via the calcitonin receptor in the intestines, bones, kidneys, and brain)

Glucagon – Stimulates glycogen breakdown in the liver

hCG – Promotes cellular differentiation, and is potentially involved in apoptosis

Epinephrine – released by the adrenal medulla during the fasting state, when body is under metabolic duress. It stimulates glycogenolysis, in addition to the actions of glucagon.

Unit 1

1	Ghrelin is a	hypothalamic hormone	pituitary hormone	gastrointestinal hormone	gonadal hormone	gastrointestinal hormone
2	Which of the following is not secreted by insulin?	Bicarbonate	Biphosphate	insulin	glucagon	Biphosphate
	Median eminence is present in	Anterior pituitary	Posterior pituitary gland	Bone	Hypothalamus	Hypothalamus
3	Cretinism is	Congenital hypothyroidism	acquired infection	iodine deficiency in adults	reduced thyroid levels in aged p	Congenital hypothyroidism
4	Increased levels of BMR is observed in	hyperthyroidism	hypothyroidism	hyperprolactinemia	hypoparathyroidemia	hyperthyroidism
5	Decreased levels of BMR is observed in	hyperthyroidism	hypothyroidism	hyperprolactinemia	hypoparathyroidemia	hypothyroidism
6	Which of these is not secreted from the Anterior Hypohysi	Thyroid Stimulating Hormone	Adrenocorticotrophin Hormon	Oxytocin	Follicular Stimulating Hormon	Oxytocin
7	Diabetes Insipidus is due to deficiency of	Atrial Natriuretic Peptide	Vasopressin	Aldosterone	Insulin	Vasopressin
8	Excess prolactin causes:	Acromegaly	Gynaecomastia	Dwarfism	Anaemia	Gynaecomastia
9	Which of the following signs strongly support a diagnosis	Carpopedal Spasm	Bitemporal Hemianopsia	Chvostek's Sign	Tremor	Bitemporal Hemianopsia
10	ADH is secreted by the	Hypothalamus	Posterior lobe of the pituitary	Intermediate Lobe of the pituita	Anterior lobe of the pituitary	Posterior lobe of the pituitary
11	ADH has it greatest influence on the kidneys at	Cortex	Distal convoluted tubule	Medulla	Proximal convoluted tubule	Medulla
12	TSH stimulation in the thyroid causes	Decreased blood flow	Decrease in gland size	Increased in follicular epitheliu	Increase in colloid	Increased in follicular epithelium
13	Which type of gland secretes hormones directly into the bl	endocrine gland	exocrine gland	serous gland	target gland	endocrine gland
14	Down regulation of receptors cannot occur by	Inactivation of receptor molecules	Inactivation of intracellular pro	Sequestration of receptors inside cell	Increased mRNA expression	Increased mRNA expression
15	Dopa decarboxylase is inhibited by	epinephrine	nor-epinephrine	alpha methyldopa	proline	alpha methyldopa
16	Renal clearance of Hormones involves	Metabolic destruction by tissues/ target cells.	Binding with the tissues	Excretion by liver into bile	Excretion by kidneys into urine	Excretion by kidneys into urine
17	Testosterone is a	protein hormone	steroid hormones	peptide hormone	lipid	steroid hormones
18	Thyroid hormone is	a protein	peptide hormone	steroid hormone	amino acid derivative	amino acid derivative
19	Cyclic AMP acts as the second messenger for	ADH	Glucagon	Calcitonin	ADH, glucagaon and calcitonir	ADH, glucagaon and calcitonin
20	Cylic AMP acts as the second messenger for all of the foll	oxytocin	TSH	ACTH	FSH	oxytocin
21	Cyclic GMP acts as the second messenger for	Nerve growth factor	Atrial naturietic factor	epinephrine	nor-epinephrine	Atrial naturietic factor
22	Some hormones produce their intracellular effects by activ	Phospholipase A	Phospholipase B	Phospholipase C	Phospholipase D	Phospholipase C
23	G protein acts as	Hormone carriers	Hormone receptors	Second messengers	Signal transducers	Signal transducers
24	G proteins have a nucleotide-binding site for	ADP/ATP	GDP/GTP	CDP/CTP	UDP/UTP	GDP/GTP
25	Protein kinase C is activated by	cAMP	cGMP	diacylglycerol	innositol triphosphate	diacylglycerol
26	Secretion of growth hormone is inhibited by	somatomedin C	somatostatin	feed back inhibition	gene expression	somatostatin
27	Number of aminoacid in human growth hormone is	51	84	191	198	191
28	The number of aminoacid residues in prolactin is	51	84	191	198	198
29	Which of the following is not a neurotransmitter	acetylcholine	cyclic AMP	noradrenaline	dopamine	cyclic AMP
30	Phosphorylase catalyze	addition of phosphate group	removal of phosphate group	lysis of phosphagen	lysis of phosphorus	addition of phosphate group
31	Phosphatase	addition of phosphate group	removal of phosphate group	lysis of phosphagen	lysis of phosphorus	removal of phosphate group
32	G-proteins are	monomer	dimer	trimer	tetramer	trimer
33	Steroid hormones have receptors in	inner cell membrane	outer cell membrane	mitochondria	cytosol	cytosol
34	Steroid hormone receptors are found in association with	albumin	globulin	heat shock proteins	cold shock proteins	heat shock proteins
35	Heat shock proteins are referred as	transducer	chaperon	operon	cameron	chaperon
36	cAMP activates	Protein kinase A	Protein kinase B	protein kinase C	protein kinase D	Protein kinase A
37	How many catalytic subunits does PK-A have?	1	2	3	4	2
38	How many regulatory subunits does PK-A have?	1	2	3	4	2
39	Activation of PK-A is by	dissociation of catalytic unit	association of catalytic unit	disintegration of catalytic unit	degradation of catalytic unit	dissociation of catalytic unit
40	Cholera is caused by activation of	A protein	B Protein	G Protein	H Protein	G Protein
41	Cholera is caused by	ADP ribosylation of G Protein	ATP ribosylation of H protein	UTP proteolysis	fungal infection	ADP ribosylation of G Protein
42	Insulin receptor is present in	cell membrane	cytosol	nucleus	insulin do not have receptor	cell membrane
43	Bronze diabetes is due to	increased iron level	decreased irol level	increased copper level	increased sodium level	increased iron level
44	Increased iron level is referred as	anemia	hemochromatosis	leukemia	polycythemia	hemochromatosis
45	Calcium acts as	a hormone	enzyme	Second messengers	membrane	Second messengers
46	Which organalle stores calcium	Nucleus	Endoplasmic reticulum	Golgi bodies	lysosomes	Endoplasmic reticulum
47	What are mitogens?	agents cause cell differentiation	agents cause cell proliferation	agents cause apoptosis	agents cause necrosis	agents cause cell proliferation
48	Programmed cell death is	Necrosis	Phagocytosis	Apoptosis	Senescence	Apoptosis
49	Transcription is	synthesis of RNA from DNA	synthesis of DNA from RNA	synthesis of DNA from carbohy	synthesis of protein from RNA	synthesis of RNA from DNA
50	Protein synthesis occurs in	Rough endoplasmic reticulum	Smooth endoplasmic reticulum	lysosomes	peroxisomes	Rough endoplasmic reticulum
51	Steroidogenesis occurs in	Rough endoplasmic reticulum	Smooth endoplasmic reticulum	lysosomes	peroxisomes	Smooth endoplasmic reticulum
52	Which of the following is potent androgen	Testosterone	Progesterone	dihydrotestosterone	pregnenalone	dihydrotestosterone
53	Which of the following is potent estrogen	estrone	estradiol	estriol	progesterone	estradiol
54	Conversion of testosterone to estradiol is catalyzed by	11 hydroxylase	21 hydroxylase	aromatase	5 alpha reductase	aromatase
55	Conversion of testosterone to DHT is catalyzed by	11 hydroxylase	21 hydroxylase	aromatase	5 alpha reductase	5 alpha reductase
56	Aromatase is regulated by ____in females	LH	testosterone	FSH	benzene	FSH
57	In females aromatase is expressed in	thecal cells	granulosa cells	Leydig cells	Sertoli cells	granulosa cells
58	In females androgens are produced in	thecal cells	granulosa cells	Leydig cells	Sertoli cells	thecal cells
59	In females receptors for LH are present in	granulosa cells	Leydig cells	thecal cells	Sertoli cells	thecal cells
60	In females receptors for FSH are present in	thecal cells	granulosa cells	Leydig cells	Sertoli cells	granulosa cells

KARPAGAM ACADEMY OF HIGHER EDUCATION
(Deemed University Established Under Section 3 of UGC Act 1956)
Coimbatore - 641021.
(For the candidates admitted from 2015 onwards)
DEPARTMENT OF BIOCHEMISTRY

SUBJECT : HORMONES: BIOCHEMISTRY AND FUNCTION
SEMESTER : III
SUBJECT CODE : 16BCU303 CLASS : II B.Sc.BC

Unit II-Mechanisms of hormonal actions

Second messengers - cAMP, cGMP, IP3, DAG, Ca^{2+}, NO. Effector systems - adenylate cyclase, guanylate cyclase, PDE, PLC. Protein kinases (PKA, PKB, PKC, PKG). Growth factor signaling, PDGF, EGF, IGF-II, and erythropoietin. Receptor tyrosine kinases - EGF, insulin, erythropoietin receptor; ras - MAP kinase cascade, JAK - STAT pathway. Steroid hormone/ thyroid hormone receptor mediated gene regulation. Receptor regulation and cross talk.

Second messengers are intracellular signaling molecules released by the cell to trigger physiological changes such as proliferation, differentiation, migration, survival, and apoptosis. Secondary messengers are therefore one of the initiating components of intracellular signal transduction cascades. **Examples of second messenger molecules include cyclic AMP, cyclic GMP, inositol trisphosphate, diacylglycerol, and calcium.** The cell releases second messenger molecules in response to exposure to extracellular signaling molecules—the first messengers. First messengers are extracellular factors, often hormones or neurotransmitters, such as epinephrine, growth hormone, and serotonin. Because peptide hormones and neurotransmitters typically are biochemically hydrophilic molecules, these first messengers may not physically cross the phospholipid bilayer to initiate changes within the cell directly—unlike steroid hormones, which usually do. This functional limitation necessitates the cell to devise signal transduction mechanisms to transduce first messenger into second messengers, so that the extracellular signal may be propagated intracellularly. An important feature of the second messenger signaling system is that second messengers may be coupled downstream to multi-cyclic kinase cascades to greatly amplify the strength of the original first messenger signal.

Types

There are **three basic types** of secondary messenger molecules:

Hydrophobic molecules: water-insoluble molecules such as diacylglycerol, and phosphatidylinositols, which are membrane-associated and diffuse from the plasma membrane into the intermembrane space where they can reach and regulate membrane-associated effector proteins

Hydrophilic molecules: water-soluble molecules, such as cAMP, cGMP, IP3, and Ca2+, that are located within the cytosol

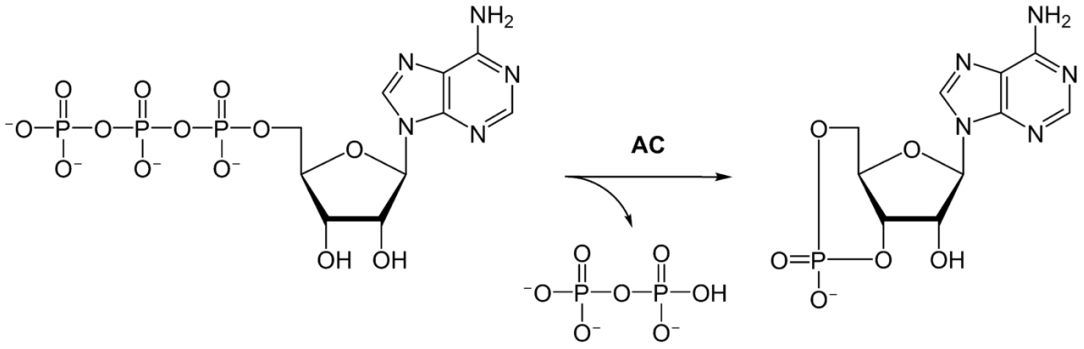
Gases: nitric oxide (NO), carbon monoxide (CO) and hydrogen sulfide (H2S) which can diffuse both through cytosol and across cellular membranes.

	cAMP System	Phosphoinositol system	Arachidonic acid system	cGMP System	Tyrosine kinase system
First Messenger: Neurotransmitters (Receptor)	Epinephrine (α2, β1, β2) Acetylcholine (M2)	Epinephrine (α1) Acetylcholine (M1, M3)	Histamine (Histamine receptor)	-	-
First Messenger: Hormones	ACTH, ANP, CRH, CT, FSH, Glucagon, hCG, LH, MSH, PTH, TSH	AGT, GnRH, GHRH, Oxytocin, TRH	-	ANP, Nitric oxide	INS, IGF, PDGF
Signal Transducer	GPCR/G_s (β1, β2), G_i (α2, M2)	GPCR/G_q	Unknown G-protein	-	RTK
Primary effector	Adenylyl cyclase	Phospholipase C	Phospholipase A	guanylate cyclase	RasGEF (Grb2-Sos)
Second messenger	cAMP (cyclic adenosine monophosphate)	IP3; DAG; Ca2+	Arachidonic acid	cGMP	Ras.GTP (Small G Protein)
Secondary effector	protein kinase A	PKC; CaM	5-Lipoxygenase, 12-Lipoxygenase, cycloxygenase	protein kinase G	MAP3K (c-Raf)

Adenylyl cyclase (EC 4.6.1.1, also commonly known as adenyl cyclase and adenylate cyclase, abbreviated AC) is an enzyme with key regulatory roles in essentially all cells. It is the most polyphyletic known enzyme: six distinct classes have been described, all catalyzing the same reaction but representing unrelated gene families with no known sequence or structural homology. The best known class of adenylyl cyclases is class III or AC-III (Roman numerals are used for classes). AC-III occurs widely in eukaryotes and has important roles in many human tissues.

All classes of adenylyl cyclases catalyse the conversion of adenosine triphosphate (ATP) to 3',5'-cyclic AMP (cAMP) and pyrophosphate. Magnesium ions are generally required and appears to be closely involved in the enzymatic mechanism. The cAMP produced by AC then serves as a regulatory signal via specific cAMP-binding proteins, either transcription factors, enzymes (e.g., cAMP-dependent kinases), or ion transporters.

Conversion of ATP to cAMP by Adenylate Cyclase:



Guanylate cyclase (EC 4.6.1.2, also known as guanyl cyclase, guanylyl cyclase, or GC) is a lyase enzyme. Guanylate cyclase is often part of the G protein signaling cascade that is activated by low intracellular calcium levels and inhibited by high intracellular calcium levels. In response to calcium levels, guanylate cyclase synthesizes cGMP from GTP. cGMP keeps cGMP-gated channels open, allowing for the entry of calcium into the cell. Like cAMP, cGMP is an important second messenger that internalizes the message carried by intercellular messengers such as peptide hormones and NO, and can also function as an autocrine signal. Depending on cell type, it can drive adaptive/developmental changes requiring protein synthesis. In smooth muscle, cGMP is the signal for relaxation, and is coupled to many homeostatic mechanisms including regulation of vasodilaton, vocal tone, insulin secretion, and peristalsis. Once formed, cGMP can be degraded by **phosphodiesterases**, which themselves are under different forms of regulation, depending on the tissue.

Guanylate cyclase is found in the retina (RETGC) and modulates phototransduction in rods and cones. It is part of the calcium negative feedback system that is activated in response to the hyperpolarization of the photoreceptors by light. This causes less intracellular calcium, which stimulates guanylate cyclase-activating proteins (GCAPs). Studies have shown that cGMP synthesis in cones is about 5-10 times higher than it is in rods, which may play an important role in modulating cone adaption to light.

Guanylate cyclase 2C (GC-C) is an enzyme expressed mainly in intestinal neurons. Activation of GC-C amplifies the excitatory cell response that is modulated by glutamate and acetylcholine receptors. GC-C, while known mainly for its secretory regulation in the intestinal epithelium, is also expressed in the brain.

Phospholipase C (PLC) is a class of membrane-associated enzymes that cleave phospholipids just before the phosphate group (see figure). It is most commonly taken to be synonymous with the human forms of this enzyme, which play an important role in eukaryotic cell physiology, in particular signal transduction pathways. There are thirteen kinds of mammalian phospholipase C

that are classified into six isotypes (β, γ, δ, ε, ζ, η) according to structure. Each PLC has unique and overlapping controls over expression and subcellular distribution. Activators of each PLC vary, but typically include heterotrimeric G protein subunits, protein tyrosine kinases, small G proteins, Ca2+, and phospholipids

Activation

Receptors that activate this pathway are mainly G protein-coupled receptors coupled to the Gαq subunit, including:

5-HT2 serotonergic receptors
α1 (Alpha-1) adrenergic receptors
Calcitonin receptors
H1 histamine receptors
Metabotropic glutamate receptors, Group I
M1, M3, and M5 muscarinic receptors
Thyroid-Releasing Hormone receptor in anterior pituitary gland

Biological Function:

PLC cleaves the phospholipid phosphatidylinositol 4,5-bisphosphate (PIP2) into diacyl glycerol (DAG) and inositol 1,4,5-trisphosphate (IP3). Thus PLC has a profound impact on the depletion of PIP2, which acts as a membrane anchor or allosteric regulator. PIP2 also acts as the substrate for synthesis of the rarer lipid phosphatidylinositol 3,4,5-trisphosphate (PIP3), which is responsible for signaling in multiple reactions. Therefore, PIP2 depletion by the PLC reaction is critical to the regulation of local PIP2 concentrations both in the plasma membrane and the nuclear membrane.

The two products of the PLC catalyzed reaction, DAG and IP3, are important second messengers that control diverse cellular processes and are substrates for synthesis of other important signaling molecules. When PIP2 is cleaved, DAG remains bound to the membrane, and IP3 is released as a soluble structure into the cytosol. IP3 then diffuses through the cytosol to bind to IP3 receptors, particularly calcium channels in the smooth endoplasmic reticulum (ER). This causes the cytosolic concentration of calcium to increase, causing a cascade of intracellular changes and activity. In addition, calcium and DAG together work to activate protein kinase C, which goes on to phosphorylate other molecules, leading to altered cellular activity.

Protein Kinase

A protein kinase is a kinase enzyme that modifies other proteins by chemically adding phosphate groups to them (phosphorylation). Phosphorylation usually results in a functional change of the target protein (substrate) by changing enzyme activity, cellular location, or association with other proteins

Protein Kinase A

In cell biology, protein kinase A (PKA is a family of enzymes whose activity is dependent on cellular levels of cyclic AMP (cAMP). PKA is also known as cAMP-dependent protein kinase (EC 2.7.11.11). Protein kinase A has several functions in the cell, including regulation of glycogen, sugar, and lipid metabolism.

Below is a list of the steps involved in PKA activation:

Cytosolic cAMP increases
Two cAMP molecules bind to each PKA regulatory subunit
The regulatory subunits move out of the active sites of the catalytic subunits and the R2C2 complex dissociates
The free catalytic subunits interact with proteins to phosphorylate Ser or Thr residues.

Protein kinase C, commonly abbreviated to PKC (EC 2.7.11.13), is a family of protein kinase enzymes that are involved in controlling the function of other proteins through the phosphorylation of hydroxyl groups of serine and threonine amino acid residues on these proteins, or a member of this family. PKC enzymes in turn are activated by signals such as increases in the concentration of diacylglycerol (DAG) or calcium ions (Ca2+).

Upon activation, protein kinase C enzymes are translocated to the plasma membrane by RACK proteins (membrane-bound receptor for activated protein kinase C proteins). The protein kinase C enzymes are known for their long-term activation: They remain activated after the original activation signal or the Ca2+-wave is gone. It is presumed that this is achieved by the production of diacylglycerol from phosphatidylinositol by a phospholipase; fatty acids may also play a role in long-term activation.

cGMP-dependent protein kinase or **Protein Kinase G (PKG)** is a serine/threonine-specific protein kinase that is activated by cGMP. It phosphorylates a number of biologically important targets and is implicated in the regulation of smooth muscle relaxation, platelet function, sperm metabolism, cell division, and nucleic acid synthesis.

The PKG-I and PKG-II are homodimers of two identical subunits (~75 kDa and ~85 kDa, respectively) and share common structural features.

Each subunit is composed of three functional domains:

(1) an N-terminal domain that mediates homodimerization, suppression of the kinase activity in the absence of cGMP, and interactions with other proteins including protein substrates
(2) a regulatory domain that contains two non-identical cGMP-binding sites
(3) a kinase domain that catalyzes the phosphate transfer from ATP to the hydroxyl group of a serine/threonine side chain of the target protein

Binding of cGMP to the regulatory domain induces a conformational change which stops the inhibition of the catalytic core by the N-terminus and allows the phosphorylation of substrate

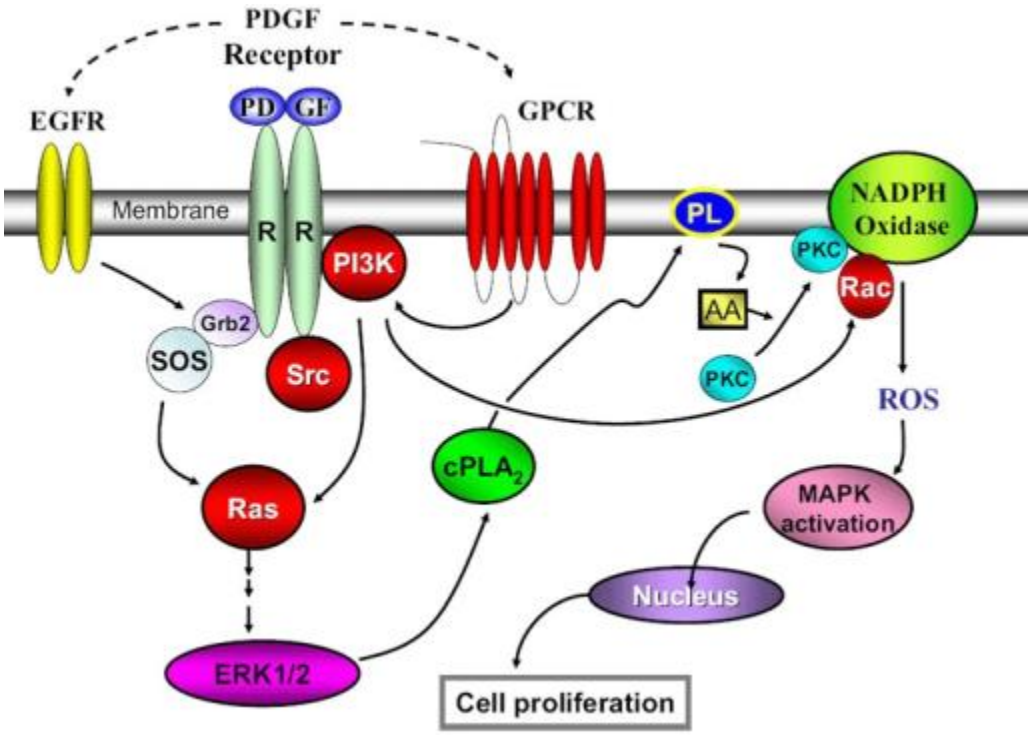
proteins. Whereas PKG-I is predominantly localized in the cytoplasm, PKG-II is anchored to the plasma membrane by N-terminal myristoylation.

Specifically, in smooth muscle tissue, PKG promotes the opening of calcium-activated potassium channels, leading to cell hyperpolarization and relaxation, and blocks agonist activity of phospholipase C, reducing liberation of stored calcium ions by inositol triphosphate.

Platelet-derived growth factor receptors (PDGF-R) are cell surface tyrosine kinase receptors for members of the platelet-derived growth factor (PDGF) family. PDGF subunits -A and -B are important factors regulating cell proliferation, cellular differentiation, cell growth, development and many diseases including cancer. There are two forms of the PDGF-R, alpha and beta each encoded by a different gene. Depending on which growth factor is bound, PDGF-R homo- or heterodimerizes.

The PDGF family consists of PDGF-A, -B, -C and -D, which form either homo- or heterodimers (PDGF-AA, -AB, -BB, -CC, -DD). The four PDGFs are inactive in their monomeric forms. The PDGFs bind to the protein tyrosine kinase receptors PDGF receptor-α and -β. These two receptor isoforms dimerize upon binding the PDGF dimer, leading to three possible receptor combinations, namely -αα, -ββ and -αβ. The extracellular region of the receptor consists of five immunoglobulin-like domains while the intracellular part is a tyrosine kinase domain. The ligand-binding sites of the receptors are located to the three first immunoglobulin-like domains. PDGF-CC specifically interacts with PDGFR-αα and -αβ, but not with -ββ, and thereby resembles PDGF-AB. PDGF-DD binds to PDGFR-ββ with high affinity, and to PDGFR-αβ to a markedly lower extent and is therefore regarded as PDGFR-ββ specific. PDGF-AA binds only to PDGFR-αα, while PDGF-BB is the only PDGF that can bind all three receptor combinations with high affinity.

Dimerization is a prerequisite for the activation of the kinase. Kinase activation is visualized as tyrosine phosphorylation of the receptor molecules, which occurs between the dimerized receptor molecules (transphosphorylation). In conjunction with dimerization and kinase activation, the receptor molecules undergo conformational changes, which allow a basal kinase activity to phosphorylate a critical tyrosine residue, thereby "unlocking" the kinase, leading to full enzymatic activity directed toward other tyrosine residues in the receptor molecules as well as other substrates for the kinase. Expression of both receptors and each of the four PDGFs is under independent control, giving the PDGF/PDGFR system a high flexibility. Different cell types vary greatly in the ratio of PDGF isoforms and PDGFRs expressed. Different external stimuli such as inflammation, embryonic development or differentiation modulate cellular receptor expression

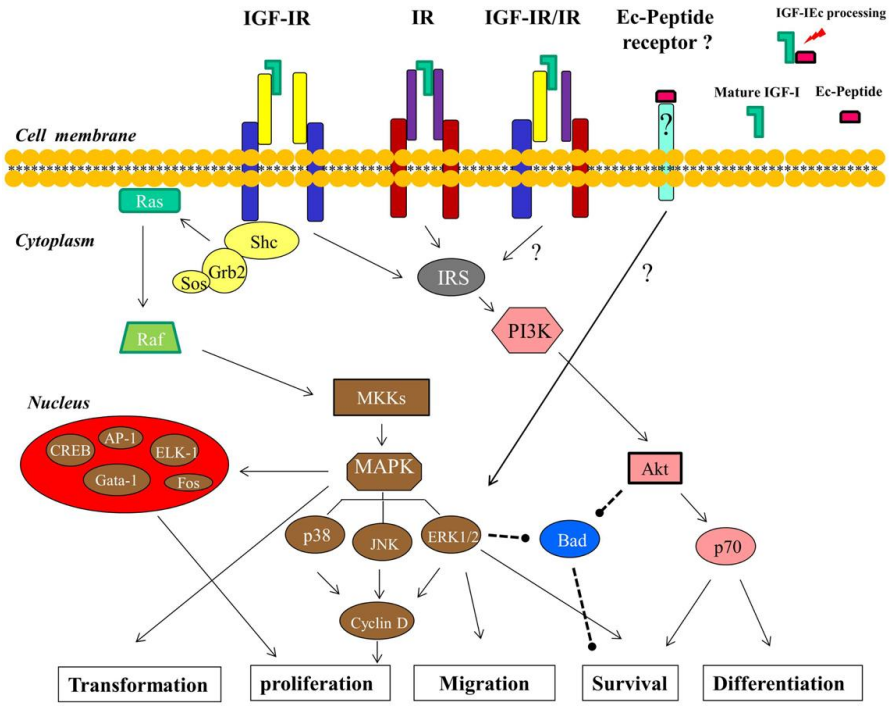


Insulin like growth factor

The insulin-like growth factors (IGFs) are proteins with high sequence similarity to insulin. IGFs are part of a complex system that cells use to communicate with their physiologic environment. This complex system (often referred to as the IGF "axis") consists of two cell-surface receptors (IGF1R and IGF2R), two ligands (Insulin-like growth factor 1 (IGF-1) and Insulin-like growth factor 2 (IGF-2)), a family of six high-affinity IGF-binding proteins (IGFBP-1 to IGFBP-6), as well as associated IGFBP degrading enzymes, referred to collectively as proteases.

IGF Receptor

The IGFs are known to bind the IGF-1 receptor, the insulin receptor, the IGF-2 receptor, the insulin-related receptor and possibly other receptors. The IGF-1 receptor is the "physiological" receptor—IGF-1 binds to it at significantly higher affinity than it binds the insulin receptor. Like the insulin receptor, the IGF-1 receptor is a receptor tyrosine kinase—meaning the receptor signals by causing the addition of a phosphate molecule on particular tyrosines. The IGF-2 receptor only binds IGF-2 and acts as a "clearance receptor"—it activates no intracellular signaling pathways, functioning only as an IGF-2 sequestering agent and preventing IGF-2 signaling.



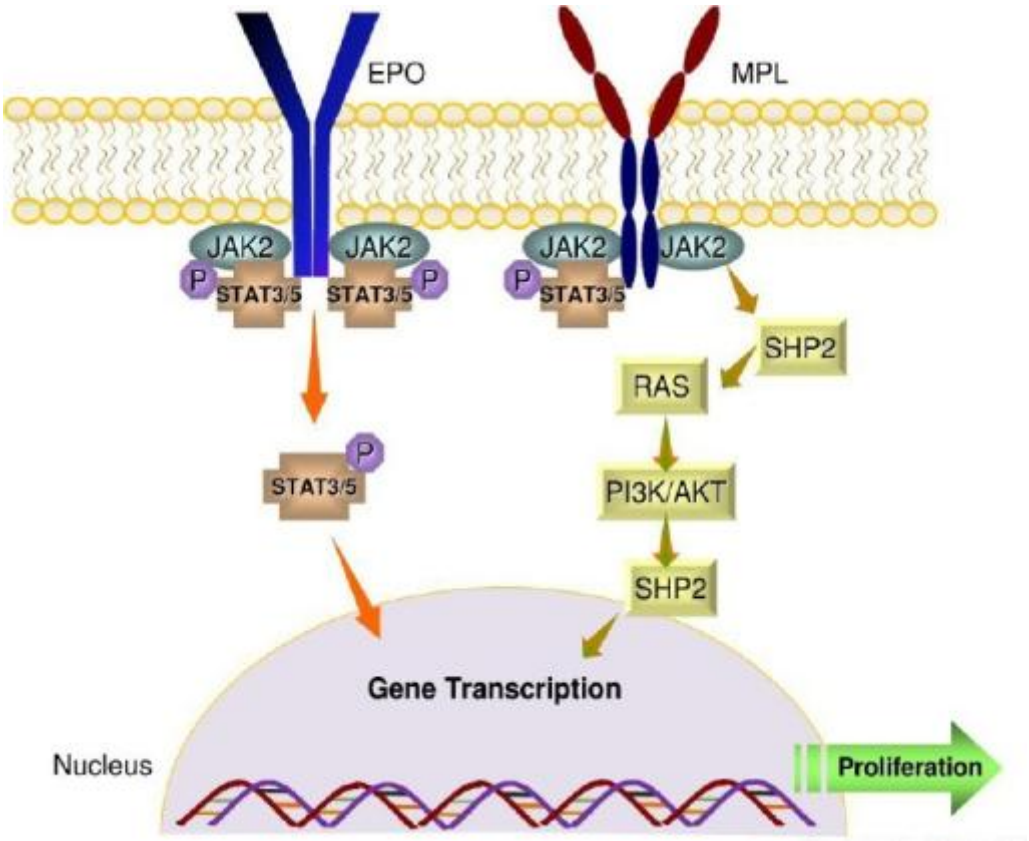
Erythropoietin

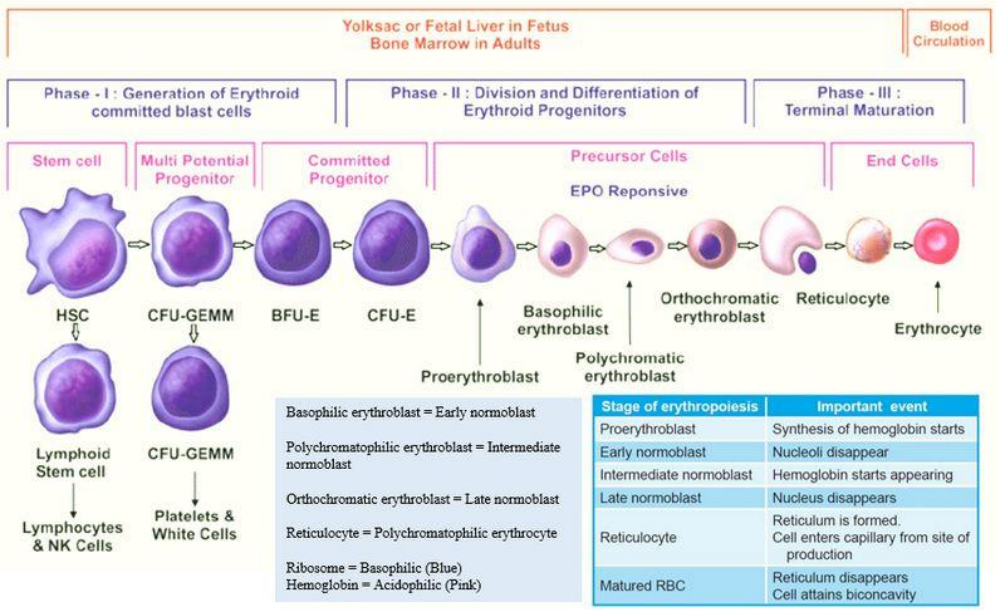
Erythropoietin (EPO), also known as hematopoietin or hemopoietin, is a glycoprotein cytokine secreted by the kidney in response to cellular hypoxia; it stimulates red blood cell production (erythropoiesis) in the bone marrow. Low levels of EPO (around 10 mU/mL) are constantly secreted sufficient to compensate for normal red blood cell turnover. Common causes of cellular hypoxia resulting in elevated levels of EPO (up to 10 000 mU/mL) include any anemia, and hypoxemia due to chronic lung disease.

Function:

Erythropoietin is an essential hormone for red blood cell production. Without it, definitive erythropoiesis does not take place. Under hypoxic conditions, the kidney will produce and secrete erythropoietin to increase the production of red blood cells by targeting CFU-E, proerythroblast and basophilic erythroblast subsets in the differentiation. Erythropoietin has its primary effect on red blood cell progenitors and precursors (which are found in the bone marrow in humans) by promoting their survival through protecting these cells from apoptosis, or cell death.

Erythropoietin is the primary erythropoietic factor that cooperates with various other growth factors (e.g., IL-3, IL-6, glucocorticoids, and SCF) involved in the development of erythroid lineage from multipotent progenitors. The burst-forming unit-erythroid (BFU-E) cells start erythropoietin receptor expression and are sensitive to erythropoietin. Subsequent stage, the colony-forming unit-erythroid (CFU-E), expresses maximal erythropoietin receptor density and is completely dependent on erythropoietin for further differentiation. Precursors of red cells, the proerythroblasts and basophilic erythroblasts also express erythropoietin receptor and are therefore affected by it.





Stage of erythropoiesis	Important event
Proerythroblast	Synthesis of hemoglobin starts
Early normoblast	Nucleoli disappear
Intermediate normoblast	Hemoglobin starts appearing
Late normoblast	Nucleus disappears
Reticulocyte	Reticulum is formed. Cell enters capillary from site of production
Matured RBC	Reticulum disappears Cell attains biconcavity

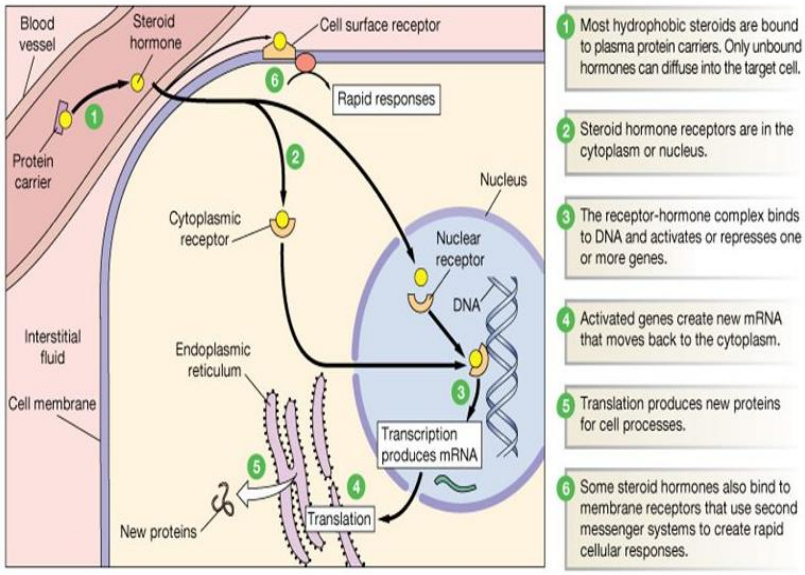
Steroid Hormones

A steroid hormone is a steroid that acts as a hormone. Steroid hormones can be grouped into two classes: corticosteroids (typically made in the adrenal cortex, hence cortico-) and sex steroids (typically made in the gonads or placenta). Within those two classes are five types according to the receptors to which they bind: glucocorticoids, mineralocorticoids (corticosteroids), androgens, estrogens, and progestogens (sex steroids). Vitamin D derivatives are a sixth closely related hormone system with homologous receptors. They have some of the characteristics of true steroids as receptor ligands.

Steroid hormones help control metabolism, inflammation, immune functions, salt and water balance, development of sexual characteristics, and the ability to withstand illness and injury. The term steroid describes both hormones produced by the body and artificially produced medications that duplicate the action for the naturally occurring steroids..

Mechanism of Action

There are many different mechanisms through which steroid hormones affect their target cells. All of these different pathways can be classified as having either a genomic effect, or a non-genomic effect. Genomic pathways are slow and result in altering transcription levels of certain proteins in the cell; non-genomic pathways are much faster.



The first identified mechanisms of steroid hormone action were the genomic effects. In this pathway, the free hormones first pass through the cell membrane because they are fat soluble. In the cytoplasm, the steroid may or may not undergo an enzyme-mediated alteration such as reduction, hydroxylation, or aromatization. Then the steroid binds to a specific steroid hormone receptor, also known as a nuclear receptor, which is a large metalloprotein. Upon steroid binding, many kinds of steroid receptors dimerize: two receptor subunits join together to form one

functional DNA-binding unit that can enter the cell nucleus. Once in the nucleus, the steroid-receptor ligand complex binds to specific DNA sequences and induces transcription of its target genes.

Unit 2

1	Precursor of ACTH is	Cholesterol	Pregnenalone	progesterone	pro-opiomelanocortin	pro-opiomelanocortin
2	ACTH is a polypeptide made up of_____aminoacids	39	41	51	84	39
	Hormones produces by pituitary are referred as	releasing hormones	stimulating hormones	inhibiting hormones	they do not have specific name	stimulating hormones
3	Posterior pituitary produces	TRH	oxytocin	vasopressin	oxytocin and vasopressin	oxytocin and vasopressin
4	Anterior pituitary is referred as	Neurohypophysis	Adenohypophysis	Hypothalamic neurons	Hypothalamic nephrons	Adenohypophysis
5	Growth hormone releasing hormone is secreted from	Anterior pituitary	Posterior pituitary gland	Bone	Hypothalamus	Hypothalamus
6	Gonadotropin releasing hormone is secreted from	Anterior pituitary	Posterior pituitary gland	Bone	Hypothalamus	Hypothalamus
7	Thyrotropin releasing hormone is secreted from	Anterior pituitary	Posterior pituitary gland	Bone	Hypothalamus	Hypothalamus
8	Agonists	increase hormone actions	decrease hormone actions	do not increase or decrease horn	at times increase and at times de	increase hormone actions
9	Antagonists	increase hormone actions	decrease hormone actions	do not increase or decrease horn	at times increase and at times de	decrease hormone actions
10	TRH is release from	Paraventricular nucleus	Supraoptic nucleus	suprachiasmatic nucleus	Arcuate nucleus	Paraventricular nucleus
11	GHRH is released from	Paraventricular nucleus	Supraoptic nucleus	suprachiasmatic nucleus	Arcuate nucleus	Arcuate nucleus
12	Vasopressin and oxytocin are released from	Paraventricular nucleus	Supraoptic nucleus	suprachiasmatic nucleus	Arcuate nucleus	Supraoptic nucleus
13	GnRH is released from	Paraventricular nucleus	Supraoptic nucleus	Medial preoptic nucleus	Arcuate nucleus	Medial preoptic nucleus
14	Synthesis of glucocorticoids are regulated by	TRH	ACTH	vasopressin	oxytocin	ACTH
15	The carboxylterminal aminoacid of GnRH is	amidated	phosphorylated	sulfated	sialyated	amidated
16	GnRH is a	dipeptide	nonapeptide	decapeptide	tripeptide	decapeptide
17	Deficiency of GnRH receptor results in	Kallmann syndrome	adenomatosis	autoimmunity	no obvious disease	Kallmann syndrome
18	Postive estrogen feedback results in	FSH inhibition	FSH activation	LH surge	GnRH inhibition	LH surge
19	TRH is a	dipeptide	nonapeptide	decapeptide	tripeptide	tripeptide
20	Administration of TRH causes the release of _____from anterior pituitary in addition to TSH	LH	FSH	PRL	opiods	PRL
21	LH, FSH, TSH and hCG are	glycoproteins	steroid hormones	glycolipids	hypothalamic hormones	glycoproteins
22	LH, FSH, TSH and hCG	have same alpha subunit	have same beta subunit	do not have same alpha subunit	do not have any similarity	have same alpha subunit
23	LH receptors are	single transmembrane	cytosolic	nuclear	seven transmembrane	seven transmembrane
24	FSH receptors are present in	Leydig cells	Sertoli cells	parietal cells	oxyntic cells	Sertoli cells
25	CRH is released from	pituitary	adrenal medulla	hypothalamus	adrenal cortex	hypothalamus
26	CRH receptors are present in	thyrotrophs	somatotrophs	corticotrophs	gonadotrophs	corticotrophs
27	which is the primary hormonal regulator of the body's stress response	TRH	LH	CRH	FSH	CRH
28	dopamine is synthesized from	alanine	tyrosine	tryptophan	cysteine	tyrosine
29	dexamethasone suprresion test is used for the diagnosis	diabetes mellitus	addison disease	cushing syndrome	cancer	cushing syndrome
30	Acromegaly is due to	increased secretion of growth ho	decreased secretion of growth ho	increased secretion of thyroid ho	decreased secretion of thyroid h	increased secretion of growth ho
31	Decreased secretion of growth hormone causes	cretinism	autism	dwarfism	acromegaly	dwarfism
32	lactotropes are	acidophilic cells	basophilic cells	neutrophilic cells	not responsible for any secretion	acidophilic cells
33	Human FSH has ____aminoacids	100	210	500	32	210
34	Vasopressin deficiency results in	diabetes mellitus	diabetes insipidus	increased water retention	increased fatty acid synthesis	diabetes insipidus
35	Vasopressin deficiency results in	reduced production of GLUT2	reduced production of GLUT4	reduced production of aquaporin	increased production of GLUT2	reduced production of aquaporin
36	Aquaporin is a	membrane bound protein	cytosolic protein	nuclear protein	fatty acid derivative	membrane bound protein
37	Aquaporin	stimulates muscle contraction	stimulates muscle relaxation	stimulates water retention	inhibits water retention	stimulates water retention
38	Vasopressin is a	decapeptide	hexapeptide	nonapeptide	tripeptide	nonapeptide
39	AVP is	arginine vasopressin	alanine vasopressin	anterior vasopressin	anti-vasopressin	arginine vasopressin
40	polydipsia is	increased hunger	decreased hunger	increased thirst for water	decreased thirst for water	increased thirst for water
41	Polyurea is	increased excretion of urea in ur	increased urination	decreased urination	increased synthesis of urea	increased urination
42	Mellitus refers to	sweet	sour	salt	tasteless	sweet
43	Insipidus refers to	sweet	sour	salt	tasteless	tasteless
44	hyponatremia refers to	increased chloride levels	decreased sodium levels	increased sodium levels	decreased potassium levels	decreased sodium levels
45	hypokalemia refers to	increased chloride levels	decreased sodium levels	increased sodium levels	decreased potassium levels	decreased potassium levels
46	Excess prolactin causes:	Acromegaly	Gynaecomastia	dwarfism	anemia	Gynaecomastia
47	In relation to Calcium, phosphorus	Increases in serum concentration	decreases in serum concentration	Linked to Magnesium	Linked to albumin	decreases in serum concentration
48	Severe hypothyroidism characterized by dry, puffy skin, somnolence, slow mentation, and hoarseness is known as	hypoparathryroidsim	myxedema	pheochromocytoma	rickets	myxedema
49	Adrenal hemorrhage and insufficiency due to Neisseria meningitidis is called _____.	Addison disease	Cushing syndrome	Conn's disease	WaterhouseFriderichsen syndrome	WaterhouseFriderichsen syndrome
50	Hypothalamus is a part of	midbrain	forebrain	hindbrain	future brain	forebrain
51	Release of corticotrophin releasing factor is controlled by nervous stimulation of hypothalamus as a result of	stress	heat and cold	pain	stess, heat, cold and pain	stess, heat, cold and pain
52	Hormone that controls release of thyrotrophin releasing factor from hypothalamus is	oxytocin	thyroxine	estrogen	testosterone	thyroxine
53	Displacement of set point in hypothalamus is due to	pathogens	pyrogens	receptors	effectors	pyrogens
54	What is the name of the stalk that connects the hypothalamus to the pituitary	cerebral cortex	anterior	corpus callosum	infundibulum	infundibulum
55	Adrenaline is	produced by the adrenal cortex	also called epinephrine	released when parasympathetic	not an hormone	also called epinephrine
56	Drinking can be induced by	electrical stimulation of the post	osmotic stimulation of supraopti	lesions of the paraventricular nu	neuronal lesions of preoptic nuc	neuronal lesions of preoptic nucl
57	Lesion in which of the following structure leads to Kluver-bucy syndrome	Amygdala	hippocampus	hypothalamus	temporal lobe	Amygdala
58	Neurogenic diabetes insipidus is due to	low levels of vasopressin synthe	low levels of vasopressin recept	low levels of insulin	high levels of insulin	low levels of vasopressin synthes
59	panhypopituitarism refers to	increased secretion of pituitary h	decreased secretion of pancreatic	decreased secretion of pituitary	increased secretion of pancreatic	decreased secretion of pituitary h
60	Oxytocin is required for	glucose maintenance	calcium maintenance	labour	blood pressure regulation	labour

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Unit 3

1	In relation to Calcium, phosphorus	Increases in serum concentratio	Decreases in serum concentrati	Linked to Magnesium	Linked to albumin	Decreases in serum concentrati
2	Long term management of hypercalcemia does not include	Bisphosphonates	Hydration	Calcitonin	Loop diuretics	Calcitonin
	Severe hypothyroidism characterized by dry, puffy skin, somnolence, s	hypoparathryroidsim	myxedema	pheochromocytoma	rickets	myxedema
3	Measurement of T3, T4 and TSH is collectively known as	TFTs	BMP	LFTs	CMP	TFTs
4	Which of the following is a hypoglycemic medication?	Avandia	Ceftin	Lipitor	Prevacid	Avandia
5	Overactivity of the thyroid gland is called	Addison disease	Cushing syndrome	hyperthyroidism	hypothyroidism	hyperthyroidism
6	Which of the following is a complication of diabetes mellitus?	gastropharesis	exophthalmos	hirsutism	moon facies	gastropharesis
7	Graves disease is also known as	hypothyroidism	parathymia	hyperinsulinism	toxic goiter	toxic goiter
8	Enlargement of the thyroid gland is called	bruit	goiter	moon facies	thyroiditis	goiter
9	What is a possible diagnosis for a middleage woman with thinning hai	hyperthyroidism	hypochondria	hypoparathyroidism	hypothyroidism	hypothyroidism
10	All the following statements about TSH are true except	It is a glycoprotein	It is made up of α and β-subunits	Receptor recognition involves both the subunits	Its β-subunit is identical with those of FSH and LH	Its β-subunit is identical with those of FSH and LH
11	An enzyme required for the synthesis of thyroid hormones is	Iodinase	Thyroxine synthetase	Thyroperoxidase	3 beta hydroxy dehydrogenase	Thyroperoxidase
12	In thyroxine, tyrosine residues are iodinated at positions	1 and 3	2 and 4	3 and 5	4 and 6	3 and 5
13	Thyroid gland takes up circulating iodine	By simple diffusion	by facilitated diffusion	by active transport	in exchange for chloride	by active transport
14	Receptors for thyroid hormones are present	On the cell membrane	across the cell membrane	inside the cell	in association with G proteins	inside the cell
15	Binding of tyrosine to the receptors results in	Activation of adenylate cyclase	Activation of guanylate cyclase	activation of G protein	increases transcription	increases transcription
16	The most powerful thyroid hormone is	reverse T3	T3	T4	DIT	T3
17	Melatonin is synthesised in	Hypothalamus	Posterior pituitary gland	Pineal body	Melanocytes	Pineal body
18	Melatonin is synthesised from	tryptophan	alanine	tyrosine	phenylalanine	tryptophan
19	Secretion of insulin- like growth factor is promoted by	insulin	glucagon	growth hormone	somatostatin	growth hormone
20	Vasoconstrictor effect of ADH is mediated by	cAMP	cGMP	protein kinase C	angiotensin II	protein kinase C
21	Serotonin is synthesized from	serine	alanine	aspartic acid	tryptophan	tryptophan
22	Histidine is converted into histamine by	carboxylation	decarboxylation	methylation	hydroxylation	decarboxylation
23	A hormone used for detection of pregnancy is	estrogen	androgens	chorionic gonadotropin	oxytocin	chorionic gonadotropin
24	Placenta secretes all of the following except	FSH	Progesterone	Estradiol	chorionic gonadotropin	FSH
25	The number of aminoacid in calcitonin	9	51	32	84	32
26	parathyroid hormone is synthesized in	Chief cells of parathyroid glands	Oxyphil cells of parathyroid glands	Para follicular cells of thyroid glands	Follicular cells of thyroid gland	Chief cells of parathyroid glands
27	Biological activity of gastrin is present in the	Four N- terminal aminoacids	Four C- terminal aminoacids	Five N- terminal aminoacids	Five C- terminal aminoacids	Four C- terminal aminoacids
28	All the following may occur in hyperthyroidism except	Increased appetite	loss of weight	increased thyroid hormone	low BMR	low BMR
29	Half life of PTH is	5 hrs	50 hrs	5 mins	50 mins	5 mins
30	What is the normal level of fasting glucose in mg/dl	30-50	70-100	125-140	140-180	70-100
31	What is the normal level of calcium	9-12mg/dl	20-30 mg/dl	45-70 mg/dl	80-100 mg/dl	9-12 mg/dl
32	Which hormone primarily increases calcium levels in serum?	calcitonin	parathyroid hormone	insulin	glucagon	parathyroid hormone
33	Which hormone primarily decreases calcium levels in serum?	calcitonin	parathyroid hormone	insulin	glucagon	calcitonin
34	Acetylcholine gated ion channel allows the passage of	anions	uncharged ions	cations	it does not transport any ions	cations
35	Melatonin levels are higher at	morning	afternoon	evening	midnight	midnight
36	5-hydroxytryptamine is	melatonin	melanin	acetylcholine	serotonin	serotonin
37	5-Methoxy, N-Acetyltryptamine	melatonin	melanin	acetylcholine	serotonin	melatonin
38	Melatonin is a _____hormone	hydrophilic	hydrophobic	lipophilic	lipophobic	lipophilic
39	Melatonin is required for	calcium homeostasis	emergency management	sleep	stress development	emergency management
40	Which of the following is required for thyroid hormone biosynthesis?	H2O2	hydroxyl ion	nitric oxide	sulfur	H2O2
41	Conversion of t4 to t3 is catalyzed by	dehydrogenases	dehydrolases	deiodinases	dephosphorylase	deiodinases
42	Which of the following is not controlled by TSH?	sodium iodide symporter	thyroglobulin	water retention	thyroperoxidase	water retention
43	How much amount(%) of total iodine in the body is present in thyroid?	5	25	66	80	80
44	Which of the following drug cause hypothyroidism?	streptazotocin	alloxan	propylthiouracil	potassium permanganate	propylthiouracil
45	Propylthiouracil is a inhibitor of?	pepsin	renin	deiodinases	amylases	deiodinases
46	How many types of deiodinases are available?	1	2	3	4	3
47	thyroid binding globulin is a	protein	glycoprotein	lipid	glycolipid	glycoprotein
48	Sialylation of TBG	increases the half life	decreases the half life	did not interfere with half life	increase its synthesis	increases the half life
49	Half life od desialylated TBG	5 min	15 min	15 hrs	3 days	15 min
50	Fully sialylated TBG has a half life of	5 min	15 min	15 hrs	3 days	3 days
51	Which of the following is not present in thyroid hormone receptor?	DNA binding domain	RNA binding domain	ligand binding domain	amino terminal domain	RNA binding domain
52	What is the half life of thyroxine?	5 min	15 min	8 days	3 days	8 days
53	the receptors for PTH are present in	osteoclast	osteocyte	osteoblast	thyrocyte	osteoblast
54	Principal cells responsible for bone formation is	osteoclast	osteocyte	osteoblast	thyrocyte	osteoblast
55	Principal cells responsible for bone resorption is	osteoclast	osteocyte	osteoblast	thyrocyte	osteoclast
56	Macrophages present in bone are called	osteoclast	osteocyte	osteoblast	thyrocyte	osteoclast
57	Which of the following is the marker of osteoblast	acid phosphatase	alkaline phosphatase	tartrate resistant acid phosphata	tartrate sensitive acid phosphat	alkaline phosphatase
58	Which of the following is the marker of osteoclast	acid phosphatase	alkaline phosphatase	tartrate resistant acid phosphata	tartrate sensitive acid phosphat	tartrate resistant acid phosphata
59	Production of autoantibodies against TSH receptor causes	goitre	toxic nodule	grave's disease	resistance to thyroid hormone	grave's disease
60	1 alpha hydroxylation for the biosynthesis of active vitamin D occurs i	skin	kidney	intestine	brain	kidney

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KARPAGAM ACADEMY OF HIGHER EDUCATION
(Deemed University Established Under Section 3 of UGC Act 1956)
Coimbatore - 641021.
(For the candidates admitted from 2015 onwards)
DEPARTMENT OF BIOCHEMISTRY

SUBJECT : HORMONES: BIOCHEMISTRY AND FUNCTION
SEMESTER : III
SUBJECT CODE : 16BCU303 CLASS : II B.Sc.BC

UNIT III - COURSE MATERIAL

Unit 3-Hypothalamic, pituitary and thyroid hormones

Hypothalamic - pituitary axis. Study the physiological and biochemical actions of hypothalamic hormones, pituitary hormones - GH, prolactin, TSH, LH, FSH, POMC peptide family, oxytocin and vasopressin, feedback regulation cycle. Endocrine disorders - gigantism, acromegaly, dwarfs, pigmies and diabetes insipidus. Thyroid gland. Biosynthesis of thyroid hormone and its regulation; its physiological and biochemical action. Pathophysiology - Goiter, Graves disease, cretinism, myxedema, Hashimato's disease.

Hypothalamic - pituitary axis.

The hypothalamus can be considered the coordinating center of the endocrine system. It consolidates signals derived from upper cortical inputs, autonomic function, environmental cues such as light and temperature, and peripheral endocrine feedback. In turn, the hypothalamus delivers precise signals to the pituitary gland, which then releases hormones that influence most endocrine systems in the body. Specifically, the hypothalamic-pituitary axis directly affects the functions of the thyroid gland, the adrenal gland, and the gonads, as well as influencing growth, milk production, and water balance. The anatomy and unique blood supply of the hypothalamic-pituitary axis are essential to its function. The hypothalamic hormones are small peptides that are generally active only at the relatively high concentrations achieved in the pituitary portal blood system. Their small size and lack of known binding proteins results in rapid degradation and very low concentrations in the peripheral circulation.

The anterior pituitary

The anterior pituitary contains a number of secretory cells that release hormones, the main ones being:

* adrenocorticotrophic hormone (ACTH)
* thyroid stimulating hormone (TSH)
* growth hormone (GH)
* follicle stimulating hormone (FSH)
* luteinising hormone (LH)
* prolactin (PRL)

Anterior pituitary hormone	Hypothalamic releasing hormone	Stimulatory or inhibitory	Stimuli for activation of the system
Adrenocorticotrophic hormone (ACTH)	Corticotrophin releasing hormone (CRH)	Stimulatory	Stress (e.g. pain, fever, hypoglycaemia, low BP)
	Vasopressin	Stimulatory	
Thyroid stimulating hormone (TSH)	Thyrotrophin releasing hormone (TRH)	Stimulatory	Rhythmic activity in the hypothalamus
Follicle stimulating hormone (FSH) and Luteinising hormone (LH)	Gonadotrophin releasing hormone (GnRH)	Stimulatory	Rhythmic activity in the hypothalamus
Growth hormone (GH)	Growth hormone releasing hormone (GHRH)	Stimulatory	Exercise, stress, hypoglycaemia, arginine administration, high amino acid levels
	Somatostatin	Inhibitory	
Prolactin (PRL)	Dopamine	Inhibitory	Sleep, stress, suckling stimulus
	Thyrotrophin releasing hormone (TRH)	Stimulatory	

These hormones are released in response to stimulation by the appropriate releasing hormones. These are peptide hormones secreted by nerve cells in the hypothalamus. They travel through the portal system of vessels in the pituitary stalk to the secretory cells of the anterior pituitary. There,

they cause the production and release of pituitary hormones into the bloodstream. For Growth Hormone and Prolactin there are also hypothalamic inhibitory hormones which stop their release, providing a control mechanism.

For all the anterior pituitary hormones (except Prolactin), negative feedback plays a major role in controlling their release. The pituitary hormones have an inhibitory effect on the stimulatory hypothalamic releasing hormones. In addition, most of the pituitary hormones induce the production of other hormones from their target tissues. These hormones have an inhibitory effect on the pituitary and the hypothalamus, thereby preventing uncontrolled release of the pituitary hormones.

S.No.	Type of cell	Hormone secreted	Percentage of type of cell
1.	Somatotropes	human growth hormone (hGH)	30-40%
2.	Corticotropes	adrenocorticotropin (ACTH)	20%
3.	Thyrotropes	thyroid stimulating hormone (TSH)	3-5%
4.	Gonadotropes	gonadotropic hormone i.e., both luteinizing hormone (LH) and follicle stimulating hormone (FSH)	3-5%
5.	Lactotropes	prolactin (PRL)	3-5%

Hormones secreted from the pituitary gland help control the following body processes:

* Growth
* Blood pressure
* Uterine contractions during childbirth (Parturition)
* Breast milk production
* Sex organ functions in both males and females
* Thyroid gland function
* The conversion of food into energy (metabolism)
* Water and osmolarity regulation in the body
* Water balance via the control of reabsorption of water by the kidneys
* Temperature regulation
* Pain relief

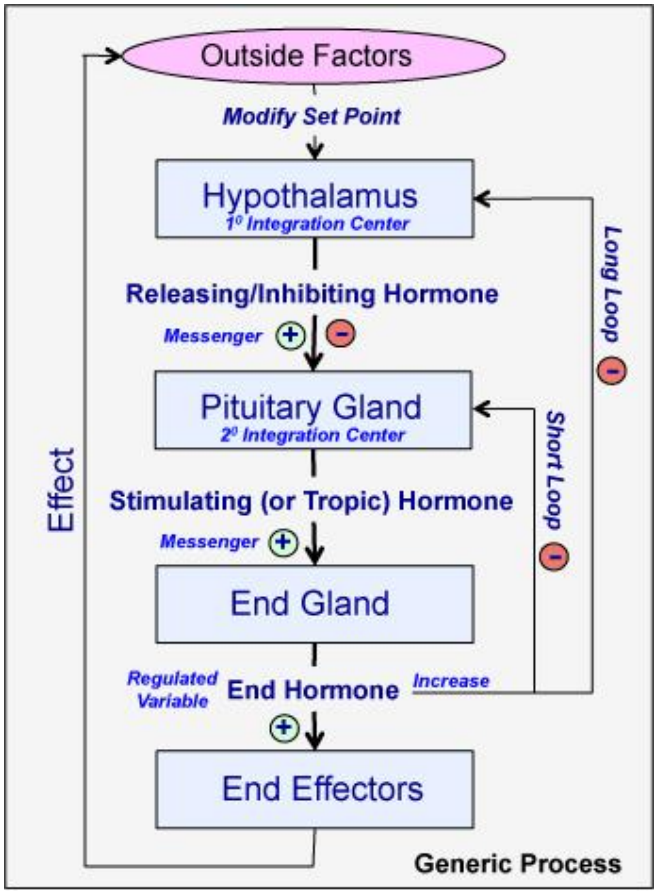
Some of the diseases involving the pituitary gland are:

* Central diabetes insipidus caused by a deficiency of vasopressin.
* Gigantism and acromegaly caused by an excess of growth hormone in childhood and adult respectively.
* Hypothyroidism caused by a deficiency of thyroid-stimulating hormone.
* Hyperpituitarism, the increased (hyper) secretion of one or more of the hormones normally produced by the pituitary gland.
* Hypopituitarism, the decreased (hypo) secretion of one or more of the hormones normally produced by the pituitary gland.
* Panhypopituitarism a decreased secretion of most of the pituitary hormones.
* Pituitary tumours.
* Pituitary adenomas, noncancerous tumors that occur in the pituitary gland.

Feedback Regulation

One distinctive feature of hormones whose secretion is regulated through the hypothalamus and pituitary is that they regulate their own secretion through negative feedback inhibition. What this means is that a hormone from a peripheral gland, for example, cortisol, binds to its receptor on cells in the hypothalamus and adenohypophysis, and has the effect of inhibiting secretion of tropic hormones: in this case, CRH (corticotropin releasing hormone) and ACTH (adrenocorticotropic hormone). Less CRH secretion leads to less ACTH secretion, which leads to less stimulation of cortisol secretion by cells of the zona fasciculata of the adrenal cortex.

The usefulness of negative feedback inhibition is that it works to keep hormone levels within a particular appropriate physiological range. Consider a case where one adrenal gland is damaged. This will cause decreased secretion of cortisol, and there will be a decrease in the degree of negative feedback inhibition on the hypothalamus and anterior pituitary. The reduced negative feedback inhibition means that more CRH and ACTH will be secreted. More ACTH will stimulate the remaining adrenal tissue to grow and to secrete more cortisol. This will have the effect of bringing cortisol back up towards its normal daily level of secretion.



Endocrine Disorders

Acromegaly is a disorder that results from excess growth hormone (GH) after the growth plates have closed. The initial symptom is typically enlargement of the hands and feet. There may also be enlargement of the forehead, jaw, and nose. Other symptoms may include joint pain, thicker skin, deepening of the voice, headaches, and problems with vision. Complications of the disease may include type 2 diabetes, sleep apnea, and high blood pressure.

Acromegaly is typically due to the pituitary gland producing too much growth hormone. In more than 95% of cases the excess production is due to a benign tumor, known as a pituitary adenoma. The condition is not inherited from a person's parents. Rarely acromegaly is due to tumors in other parts of the body. Diagnosis is by measuring growth hormone after a person has drunk glucose or by measuring insulin-like growth factor I in the blood. After diagnosis, medical imaging of the pituitary is carried out to look for an adenoma. If excess growth hormone is produced during childhood the result is **gigantism**.

Signs and symptoms

Features that result from high level of GH or expanding tumor include:

* Soft tissue swelling visibly resulting in enlargement of the hands, feet, nose, lips and ears, and a general thickening of the skin
* Soft tissue swelling of internal organs, notably the heart with attendant weakening of its muscularity, and the kidneys, also the vocal cords resulting in a characteristic thick, deep voice and slowing of speech
* Generalized expansion of the skull at the fontanelle
* Pronounced brow protrusion, often with ocular distension (frontal bossing)
* Pronounced lower jaw protrusion (prognathism) with attendant macroglossia (enlargement of the tongue) and teeth spacing
* Hypertrichosis, hyperpigmentation and hyperhidrosis may occur in these patients.[9]:499
* Acrochordon (skin tags)
* Carpal tunnel syndrome

Complications

* Severe headache
* Arthritis and carpal tunnel syndrome
* Enlarged heart
* Liver fibrosis and bile duct hyperplasia.
* Hypertension
* Diabetes mellitus (excess of GH leads to insulin resistance)
* Heart failure
* Kidney failure

Treatment

There is no known cure for acromegaly. The goals of treatment are to reduce GH production to normal levels, to relieve the pressure that the growing pituitary tumor exerts on the surrounding brain areas, to preserve normal pituitary function, and to reverse or ameliorate the symptoms of acromegaly. Currently, treatment options include surgical removal of the tumor, drug therapy, and radiation therapy of the pituitary.

Pygmies and Dwarfs

A **pygmy** is a member of an ethnic group whose average height is unusually short; anthropologists define pygmy as a member of any group where adult men are on average less than 150 cm (4 feet 11 inches) tall. A member of a slightly taller group is termed "pygmoid".

Dwarfism, also known as short stature, occurs when an organism is extremely small. In humans, it is sometimes defined as an adult height of less than 4 feet 10 inches (58 in; 147 cm), regardless of sex, although some individuals with dwarfism are slightly taller. Disproportionate dwarfism is characterized by either short limbs or a short torso. In cases of proportionate dwarfism, both the limbs and torso are unusually small. Normal intelligence and lifespan are usual.

Causes:

Dwarfism can result from myriad medical conditions, each with its own separate symptoms and causes. Extreme shortness in humans with proportional body parts usually has a hormonal cause, such as growth-hormone deficiency, once called pituitary dwarfism. Two disorders, achondroplasia and growth hormone deficiency, are responsible for the majority of human dwarfism cases.

Diabetes Insipidus

Diabetes insipidus (DI) is a condition characterized by large amounts of dilute urine and increased thirst. The amount of urine produced can be nearly 20 liters per day. Reduction of fluid has little effect on the concentration of the urine. Complications may include dehydration or seizures.

There are four types of DI, each with a different set of causes. Central DI (CDI) is due to a lack of the hormone vasopressin (antidiuretic hormone). This can be due to damage to the hypothalamus or pituitary gland or genetics. Nephrogenic diabetes insipidus (NDI) occurs when the kidneys do not respond properly to vasopressin. Dipsogenic DI is due to abnormal thirst mechanisms in the hypothalamus while gestational DI occurs only during pregnancy. Diagnosis is often based on urine tests, blood tests, and the fluid deprivation test. Diabetes mellitus is a

separate condition with an unrelated mechanism, though both can result in the production of large amounts of urine.

Treatment involves drinking sufficient fluids to prevent dehydration. Other treatments depend on the type. In central and gestational disease treated is with desmopressin. Nephrogenic disease may be treated by addressing the underlying cause or the use of a thiazide, aspirin, or ibuprofen.

Thyroid Gland

The thyroid gland, or simply the thyroid, is an endocrine gland in the neck, consisting of two lobes connected by an isthmus. It is found at the front of the neck, below the Adam's apple. The thyroid gland secretes thyroid hormones, which primarily influence the metabolic rate and protein synthesis. The hormones also have many other effects including those on development. The thyroid hormones triiodothyronine (T3) and thyroxine (T4) are created from iodine and tyrosine. The thyroid also produces the hormone calcitonin, which plays a role in calcium homeostasis.

Biosynthesis of thyroid hormone

The thyroid hormones are created from thyroglobulin. This is a protein within the follicular space that is originally created within the rough endoplasmic reticulum of follicular cells and then transported into the follicular space. Thyroglobulin contains 123 units of tyrosine, which reacts with iodine within the follicular space.

Iodine is essential for the production of the thyroid hormones. Iodine (I0) travels in the blood as iodide (I−), which is taken up into the follicular cells by a sodium-iodide symporter. This is an ion channel on the cell membrane which in the same action transports two sodium ions and an iodide ion into the cell. Iodide then travels from within the cell into the follicular space, through the action of pendrin, an iodide-chloride antiporter. In the follicular space, the iodide is then oxidized to iodine. This makes it more reactive, and the iodine is attached to the active tyrosine units in thyroglobulin by the enzyme thyroid peroxidase. This forms the precursors of thyroid hormones monoiodotyrosine (MIT), and diiodotyrosine (DIT).

When the follicular cells are stimulated by thyroid-stimulating hormone, the follicular cells reabsorb thyroglobulin from the follicular space. The iodinated tyrosines are cleaved, forming the thyroid hormones T4, T3, DIT, MIT, and traces of reverse triiodothyronine. T3 and T4 are released into the blood. The hormones secreted from the gland are about 80–90% T4 and about 10–20% T3. Deiodinase enzymes in peripheral tissues remove the iodine from MIT and DIT and convert T4 to T3 and RT3. This is a major source of both RT3 (95%) and T3 (87%) in peripheral tissues.

Regulation

The production of thyroxine and triiodothyronine is primarily regulated by thyroid-stimulating hormone (TSH), released by the anterior pituitary gland. TSH release in turn is stimulated by thyrotropin releasing hormone (TRH), released in a pulsatile manner from the hypothalamus. The thyroid hormones provide negative feedback to the thyrotropes TSH and TRH: when the thyroid hormones are high, TSH production is suppressed. This negative feedback also occurs when levels of TSH are high, causing TRH production to be suppressed

Functions of thyroid hormone

Diagram explaining the relationship between the thyroid hormones T3 and T4, thyroid stimulating hormone (TSH), and thyrotropin releasing hormone (TRH)

The primary function of the thyroid is the production of the iodine-containing thyroid hormones, triiodothyronine (T3) and thyroxine (T4) and the peptide hormone calcitonin. T3 is so named because it contains three atoms of iodine per molecule and T4 contains four atoms of iodine per molecule. The thyroid hormones have a wide range of effects on the human body.

These include:

Metabolic. The thyroid hormones increase the basal metabolic rate and have effects on almost all body tissues. Appetite, the absorption of substances, and gut motility are all influenced by thyroid hormones. They increase the absorption in the gut, generation, uptake by cells, and breakdown of glucose. They stimulate the breakdown of fats, and increase the number of free fatty acids. Despite increasing free fatty acids, thyroid hormones decrease cholesterol levels, perhaps by increasing the rate of secretion of cholesterol in bile.

Cardiovascular. The hormones increase the rate and strength of the heartbeat. They increase the rate of breathing, intake and consumption of oxygen, and increase the activity of mitochondria. Combined, these factors increase blood flow and the body's temperature.

Developmental. Thyroid hormones are important for normal development. They increase the growth rate of young people, and cells of the developing brain are a major target for the thyroid hormones T3 and T4. Thyroid hormones play a particularly crucial role in brain maturation during fetal development.

The thyroid hormones also play a role in maintaining normal sexual function, sleep, and thought patterns. Increased levels are associated with increased speed of thought generation but decreased focus. Sexual function, including libido and the maintenance of a normal menstrual cycle, are influenced by thyroid hormones.

After secretion, only a very small proportion of the thyroid hormones travel freely in the blood. Most are bound to thyroxine-binding globulin (about 70%), transthyretin (10%), and albumin (15%).[29] Only the 0.03% of T4 and 0.3% of T3 traveling freely has hormonal activity. In addition, up to 85% of the T3 in blood is produced following conversion from T4 by iodothyronine deiodinases in organs around the body.

Thyroid hormones act by crossing the cell membrane and binding to intracellular nuclear thyroid hormone receptors TR-α1,TR-α2,TR-β1 and TR-β2, which bind with hormone response elements and transcription factors to modulate DNA transcription. In addition to these actions on DNA, the thyroid hormones also act within the cell membrane or within cytoplasm via reactions with enzymes, including calcium ATPase, adenylyl cyclase, and glucose transporter.

Disorders of thyroid gland

Cretinism and Myxodema

Cretinism is a condition of severely stunted physical and mental growth owing to untreated congenital deficiency of thyroid hormone (congenital hypothyroidism) usually owing to maternal hypothyroidism.

Around the world, the most common cause of congenital hypothyroidism is iodine deficiency. Cretinism is therefore most probably due to a diet deficient in iodine. It has affected many people worldwide and continues to be a major public health problem in many countries. Iodine is an essential trace element, necessary primarily for the synthesis of thyroid hormones. Iodine deficiency is the most common preventable cause of brain damage worldwide. Although iodine is found in many foods, it is not universally present in all soils in adequate amounts. Most iodine, in iodide form, is in the oceans where the iodide ions oxidize to elemental iodine, which then enters the atmosphere and falls to earth as rain, introducing iodine to soils. Earth deficient in iodine is most common inland and in mountainous areas and areas of frequent flooding, but can also occur in coastal regions owing to past glaciation, and leaching by snow, water and heavy rainfall, which removes iodine from the soil. Plants and animals grown in iodine deficient soils are correspondingly deficient. Populations living in those areas without outside food sources are most at risk of iodine deficiency disease.

Treatment

Sporadic and genetic cretinism results from abnormal development or growth of the foetal thyroid gland. This type of cretinism has been almost completely eliminated in developed countries by early diagnosis by newborn screening schemes followed by lifelong treatment with thyroxine (T4).

Thyroxine must be dosed as tablets only, even to newborns, as the liquid oral suspensions and compounded forms cannot be depended on for reliable dosing. In the case of dosing infants, the T4 tablets are generally crushed and mixed with breast milk, formula milk or water. If the medication is mixed with formulas containing iron or soya products, larger doses may be required, as these substances may alter the absorption of thyroid hormone from the gut. Frequent monitoring (every 2–3 weeks during the first months of life) is recommended to ensure that infants with congenital hypothyroidism remain within the high end of normal range, or euthyroid.

Comparison between Cretinism and Myxedema:

	Cretinism	**Myxedema**
Definition	It is a condition arising from a deficiency of thyroid hormone, which is characterized by dwarfism and mental retardation.	It is a disease resulting from the under-activity of the thyroid gland, which is characterized by puffy eyes, face, hands and mental sluggishness.
Cause	It is caused due to low levels of iodine in the body.	It is caused due to low levels of thyroid hormone in the blood.
Symptoms	It includes: • Fatigue • Lethargy • Mental impairment • Depression • Cold intolerance • Hoarseness • Dry skin • Weight gain	It includes: • Swelling of skin • Hair loss • Mental impairment • Bone maturity delay • Slow thoughts and reflexes. • Thickened skin • Protruding stomach
Treatment	An increase in an iodine filled diet helps preventing cretinism.	It can be managed by treating the underlying cause of the disease, i.e hypothyroidism.
Hypothyroidism	It is neonatal hypothyroidism.	It is adult hypothyroidism.

Hashimoto Thyroiditis

Hashimoto's thyroiditis, also known as chronic lymphocytic thyroiditis and Hashimoto's disease, is an autoimmune disease in which the thyroid gland is gradually destroyed. Early on there may be no symptoms. Over time the thyroid may enlarge forming a painless goiter. Some people eventually develop hypothyroidism with its accompanying weight gain, feeling tired,

constipation, depression, and general pains. Hashimoto's thyroiditis is thought to be due to a combination of genetic and environmental factors. Risk factors include a family history of the condition and having another autoimmune disease. Diagnosis is confirmed with blood tests for TSH, T4, and antithyroid antibodies.

Unit IV

1	Half life of insulin is	5 hrs	50 hrs	5 mins	50 mins	5 mins
2	pyro glu-his-prolinamide is	TRH	CRH	ACTH	PTH	TRH
	gamma glutamylcysteinyl glycine is	TRH	Glutathione	PTH	ACTH	Glutathione
3	α – cells of Islets of langerhans secrete	Insulin	Glucagon	Somatostatin	cholecystokinin	glucagon
4	Insulin is secreted by following cells of Islets of langerhans	alpha	beta	gamma	delta	beta
5	Insulin is made up of	A single polypeptide chain having 51 amino acid residues	A single polypeptide chain having 84 amino acid residues	A chain having 21 and β chain having 30 aminoacid residues	A chain having 30 and β chain having 21 aminoacid residues	A chain having 21 and β chain having 30 aminoacid residues
6	The number of amino acid residues in pre-proinsulin is	51	84	109	119	109
7	Daily secretion of insulin is about	10-20mg	20-40 mg	10-20 units	40-50 units	40-50 units
8	Crystallisation of insulin occurs in the presence of	Chromium	Copper	Zinc	Calcium	Zinc
9	Insulin receptor are decreased in number in	Obesity	Starvation	hyperinsulinism	Kwashiorkar	Obesity
10	Insulin binding sites are present on the	α – subunit of insulin receptor	β- subunit of insulin receptor	δ - subunit of insulin receptor	α and β subunit of insulin recep	α – subunit of insulin receptor
11	α – subunits of insulin receptor are present	Out side the cell membrane	In the cell membrane	Across the cell membrane	In the cytosol	Out side the cell membrane
12	β - subunits of insulin receptor are present	Out side the cell membrane	In the cell membrane	Across the cell membrane	In the cytosol	Across the cell membrane
13	In the insulin receptor tyrosine kinase domain is present in	α – subunit	β – subunit	γ– subunit	δ– subunit	β – subunit
14	Binding of insulin to its receptor activates	Adenylate cyclase	Guanylate cyclase	Phospholipase C	Tyrosine kinase	Tyrosine kinase
15	Insulin receptor is made up of	One α and one β subunit	Two α and two β subunit	Two α, two β and two γ-	One α and β one γ and a	Two α and two β subunit
16	Insulin is required for the active uptake of glucose by most of the c	Muscle cells	Renal tubular cells	Adipocytes	liver cells	liver cells
17	Insulin decreases	Glycogenesis	Glucolysis	Glyconeogenesis	Tubular reabsorption of glucose	Glyconeogenesis
18	Insulin increases	Glycogenesis	Gluconeogenesis	Lipolysis	Blood sugar	Glycogenesis
19	Insulin increases	Protein synthesis	Fatty acid synthesis	Glycogen synthesis	All of the above	All of the above
20	Insulin decrease the synthesis of	Hexokinase	Glucokinase	PEP carboxykinase	Glycogen synthetase	PEP carboxykinase
21	Diabetes mellitus can occur due to all of the following except	Deficient insulin secretion	Tumor of β – cells	Decrease in number of insulin re	Formation of insulin an	Formation of insulin ant
22	Hypoglycemic coma can occur	In untreated diabetes mellitus	In starvation	After overdose of oral hypoglyca	After overdose in insulin	After overdose in insulin
23	Second messenger for glucogon is	Cyclic AMP	Diacylglycerol	Cycle GMP	Inositol tri phosphate	Cyclic AMP
24	Number of amino acid residues in glucagon	29	34	51	84	29
25	Glucagon secretion increase	After a carbohydrate rich meal	After a fat rich meal	When blood glucose is high	When blood glucose is low	When blood glucose is low
26	The main effect of glucagons is to increase	Glycolysis in muscles	Glycogenolysis in muscles	Glycogenolysis in liver	Glycogenesis in liver	Glycogenolysis in liver
27	Insulin shock is characterized by	severe hypoglycemia caused by a	severe hyperglycemia	too little insulin in the bloodstr	an allergic reaction to insulin	severe hypoglycemia caused by a
28	Cortisol is secreted from	Zona Fasiculata	Zona Reticularis	Zona Glomerulus	Anterior Hypophysis	Zona Fasiculata
29	Which gland secretes DHEA and cortisol?	pituitary	adrenal	parathyroid	pineal	adrenal
30	Which of the following is a measure of blood sugar after 4 or mor	fasting glucose	glucose tolerance test	microalbumin test	thyroid function test	fasting glucose
31	Elevated glucose levels, especially in obese persons, may be due t	diabetic acidosis	glucose intolerance	insulin resistance	insulin shock	insulin resistance
32	Chronic excretion of large amounts of urine of low specific gravity	diabetes innocens	diabetes insipidus	diabetes intermittens	diabetes mellitus	diabetes insipidus
33	Potassium, sodium, and chloride are	catecholamines	electrolytes	enzymes	steroids	electrolytes
34	Enlargement of the bones of the hands, feet, and face due to overpr	acromegaly	Cushing syndrome	polydactyly	Addison disease	acromegaly
35	An enzyme involved in catabolism of catecholamines is	Dopa decarboxylase	Aromatic aminoacids decarbox	Monoamine oxidase	Catechol oxidase	Monoamine oxidase
36	Epinephrine decreases	Glycogenolysis	Glycogenolysis	Gluconeogenesis	Lipolysis	Glycogenolysis
37	Epinephrine increases all of the following except	Glycogenenolysis in musles	Glycogenolysis	Gluconeogenesis	Glucagan secretion	Gluconeogenesis
38	Which test is used to evaluate blood glucose levels over the previc	methemoglobin	Creactive protein	hemoglobin A1c	prolactin	hemoglobin A1c
39	Insulin is produced in the	gallbladder	kidney	liver	pancreas	pancreas
40	Who discovered insulin?	Banting	Watson	Crick	Sanger	Banting
41	Insulin is first discovered in	cats	elephant	dogs	rats	dogs
42	Which is the first protein to be sequenced?	albumin	globulin	insulin	TSH	insulin
43	overproduction of cortisol results in	Addison disease	Cushing syndrome	HIV	SCID	Cushing syndrome
44	Decreased production of cortisol causes	Addison disease	Cushing syndrome	HIV	SCID	Addison disease
45	which enzyme converts tyrosine to DOPA?	tyrosine dehydrogenase	tyrosinase	tyrosine hydroxylase	tyrosine hydrolase	tyrosine hydroxylase
46	DOPA is a	neurotransmitter	nephrotransmitter	steroid hormone	doping test procedure	neurotransmitter
47	Suprarenal gland is also known as	thyroid gland	gonadal glands	adrenal gland	heart hormone	adrenal gland
48	Cholecystokinin is a	gastrointestinal hormone	hypothalamic hormone	gonadal hormone	pituitary gland	gastrointestinal hormone
49	Which is called hunger hormone	DOPA	Glucagon	Ghrelin	testosterone	Ghrelin
50	which hormone stimulates the secretionof bicarbonate from pancre	Vasoactive intestinal peptide	Cholecystokinin	Secretin	calcitonin gene related peptide	Secretin
51	Substance P is a	gastrointestinal hormone	hypothalamic hormone	gonadal hormone	pituitary gland	gastrointestinal hormone
52	Somatostatin is a	activating hormone	inhibting hormone	stimulating hormone	steroid hormone	inhibting hormone
53	Somatostatin contains	14 aminoacids	28 aminoacids	cholesterol	fatty acids	14 aminoacids
54	Somatostating is produced from	Hypothalamus	pancreas	both pancreas and hypothalamus	gonads	both pancreas and hypothalamus
55	Somatostatin inhibits	insulin release	growth hormone release	calcium absorption	both insulin and growth hormor	both insulin and growth hormon
56	zona reticularis is present in	Adrenal cortex	adrenal medulla	parathyroid	thyroid	adrenal medulla
57	tumor is adrenal medulla is	ganglioneuroma	pheochromocytoma	addison disease	cretinism	pheochromocytoma
58	a tumor in the nerve cells of the peripheral nervous system	ganglioneuroma	pheochromocytoma	addison disease	cretinism	ganglioneuroma
59	a neuroendocrine tumor of any neural crest tissue of the sympathet	ganglioneuroma	pheochromocytoma	addison disease	neuroblastoma	neuroblastoma
60	adrenal medulla contains	tropic cells	oxyntic cells	chromaffin cells	parietal cells	chromaffin cells

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in overdose of insulin

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KARPAGAM ACADEMY OF HIGHER EDUCATION
(Deemed University Established Under Section 3 of UGC Act 1956)
Coimbatore - 641021.
(For the candidates admitted from 2015 onwards)
DEPARTMENT OF BIOCHEMISTRY

SUBJECT : **HORMONES: BIOCHEMISTRY AND FUNCTION**
SEMESTER : **III**
SUBJECT CODE : **16BCU303** **CLASS** : **II B.Sc.BC**

UNIT IV - COURSE MATERIAL

Unit 4 -PTH, calcitonin and gastrointestinal hormones

PTH, Vitamin D and calcitonin. Mechanism of Ca^{2+} regulation and pathways involving bone, skin, liver, gut and kidneys. Pathophysiology - rickets, osteomalacia, osteoporosis. Regulation of release of insulin, glucagon, gastrin, secretin, CCK, GIP, adipolectin, leptin and ghrelin. Summary of hormone metabolite control of GI function. Physiological and biochemical action. Pathophysiology - diabetes type I and type II.

PTH

Parathyroid hormone (PTH), also called parathormone or parathyrin, is a hormone secreted by the parathyroid glands that is important in bone remodeling, which is an ongoing process in which bone tissue is alternately resorbed and rebuilt over time. PTH is secreted in response to low blood serum calcium (Ca2+) levels. PTH indirectly stimulates osteoclast activity within bone marrow, in an effort to release more ionic calcium (Ca2+) into the blood to elevate serum calcium (Ca2+) levels. The bones act as a (metaphorical) "bank of calcium" from which the body can make "withdrawals" as needed to keep the amount of calcium in the blood at appropriate levels despite the ever-present challenges of metabolism, stress, and nutritional variations. PTH is "a key that unlocks the bank vault" to remove the calcium. In consequence, PTH is vital to health, and health problems that yield too little or too much PTH (such as hypoparathyroidism, hyperparathyroidism, or paraneoplastic syndromes) can wreak havoc in the form of bone disease, hypocalcaemia, and hypercalcaemia.

PTH is secreted by the chief cells of the parathyroid glands as a polypeptide containing 84 amino acids, which is a prohormone; effective hormone-receptor interaction requires solely the 34-N-terminal amino acids. While PTH acts to increase the concentration of ionic calcium (Ca^{2+}) in the blood, calcitonin, a hormone produced by the parafollicular cells (C cells) of the thyroid gland, acts to decrease ionic calcium concentration. PTH essentially acts to increase the concentration of calcium in the blood by acting upon the parathyroid hormone 1 receptor, which is present at high levels in bone and kidney, and the parathyroid hormone 2 receptor, which is present at high levels in the central nervous system, pancreas, testis, and placenta. PTH half-life is approximately 4 minutes. It has a molecular mass of approximately 9500 Da.

Biosynthesis

The formation of parathyroid hormone (PTH) in the parathyroid gland occurs via two successive proteolytic cleavages from larger biosynthetic precursors. The initial product coded for by PTH mRNA is pre-proparathyroid hormone (PreProPTH), a polypeptide of 115 amino acids. Within 1 min of synthesis, the polypeptide, proparathyroid hormone (ProPTH), is formed as a result of the proteolytic removal of the NH2-terminal 25 amino acids from Pre-ProPTH. After a delay of 15-20 min, the NH2-terminal six-amino acid sequence of ProPTH is removed to give PTH of 84 amino acids. To investigate the subcellular sites in the parathyroid cell where the biosynthetic precursors undergo specific proteolytic cleavages, from 15 to 30 min they migrated within secretory vesicles still in the Golgi region and then migrated to mature secretory granules outside the Golgi area. Electrophoretic analyses showed that Pre-ProPTH disappeared rapidly (by 5 min) and that conversion of ProPTH to PTH was first detectable at 15 min and was completed by 30 min. At later times of incubation (30-90 min), autoradiographic grains within the secretion glanules migrated to the periphery of the cell and to the plasma membrane, in correlation with the release of PTH first detected by 30 min. Proteolytic conversion of Pre-ProPTH to ProPTH takes place in the RER and that subsequent conversion of ProPTH to PTH occurs in the Golgi complex.

Vitamin D

Vitamin D refers to a group of fat-soluble secosteroids responsible for increasing intestinal absorption of calcium, magnesium, and phosphate, and multiple other biological effects. In humans, the most important compounds in this group are vitamin D3 (also known as cholecalciferol) and vitamin D2 (ergocalciferol).[1] Cholecalciferol and ergocalciferol can be ingested from the diet and from supplements.[1][2][3] Only a few foods contain vitamin D. The major natural source of the vitamin is synthesis of cholecalciferol in the skin from cholesterol through a chemical reaction that is dependent on sun exposure (specifically UVB radiation). Dietary recommendations typically assume that all of a person's vitamin D is from taken by mouth, as sun exposure in the population is variable and recommendations about the amount of sun exposure that is safe are uncertain in view of the skin cancer risk.

Vitamin D from the diet or skin synthesis is biologically inactive; enzymatic conversion (hydroxylation) in the liver and kidney is required for activation. As vitamin D can be synthesized in adequate amounts by most mammals exposed to sufficient sunlight, it is not an essential dietary factor, and so not technically a vitamin. Instead it could be considered as a hormone, with activation of the vitamin D pro-hormone resulting in the active form, calcitriol, which then produces effects via a nuclear receptor in multiple different locations.

Cholecalciferol is converted in the liver to calcifediol (25-hydroxycholecalciferol); ergocalciferol is converted to 25-hydroxyergocalciferol. These two vitamin D metabolites (called 25-hydroxyvitamin D or 25(OH)D) are measured in serum to determine a person's vitamin D status. Calcifediol is further hydroxylated by the kidneys to form calcitriol (also known as 1,25-dihydroxycholecalciferol), the biologically active form of vitamin D. Calcitriol circulates as a hormone in the blood, having a major role regulating the concentration of calcium and phosphate, and promoting the healthy growth and remodeling of bone. Calcitriol also has other effects, including some on cell growth, neuromuscular and immune functions, and reduction of inflammation.

Vitamin D has a significant role in calcium homeostasis and metabolism. Its discovery was due to effort to find the dietary substance lacking in children with rickets (the childhood form of osteomalacia). Vitamin D supplements are given to treat or to prevent osteomalacia and rickets.

Rickets

Rickets is defective mineralization or calcification of bones before epiphyseal closure in immature mammals due to deficiency or impaired metabolism of vitamin D, phosphorus or calcium, potentially leading to fractures and deformity. Rickets is among the most frequent childhood diseases in many developing countries. The predominant cause is a vitamin D deficiency, but lack of adequate calcium in the diet may also lead to rickets (cases of severe diarrhea and vomiting may be the cause of the deficiency. Although it can occur in adults, the majority of cases occur in children suffering from severe malnutrition, usually resulting from famine or starvation during the early stages of childhood.

Osteomalacia is a similar condition occurring in adults, generally due to a deficiency of vitamin D after epiphyseal closure.

Osteoporosis

Osteoporosis is a disease where increased bone weakness increases the risk of a broken bone. It is the most common reason for a broken bone among the elderly.Bones that commonly break include the vertebrae in the spine, the bones of the forearm, and the hip. Until a broken bone occurs there are typically no symptoms. Bones may weaken to such a degree that a break may

occur with minor stress or spontaneously. Chronic pain and a decreased ability to carry out normal activities may occur following a broken bone. Osteoporosis may be due to lower than normal bone mass and greater than normal bone loss. Bone loss increases after menopause due to lower estrogen levels.

Category	T-score range	% young women
Normal	T-score ≥ −1.0	85%
Osteopenia	−2.5 < T-score < −1.0	14%
Osteoporosis	T-score ≤ −2.5	0.6%
Severe osteoporosis	T-score ≤ −2.5 with fragility fracture	

Gastrointestinal Hormones

The gastrointestinal hormones (or gut hormones) constitute a group of hormones secreted by enteroendocrine cells in the stomach, pancreas, and small intestine that control various functions of the digestive organs. Later studies showed that most of the gut peptides, such as secretin, cholecystokinin or substance P, were found to play a role of neurotransmitters and neuromodulators in the central and peripheral nervous systems.

Enteroendocrine cells do not form glands but are spread throughout the digestive tract. They exert their autocrine and paracrine actions that integrate gastrointestinal function.

Hormone or peptide	**Molecular weight (Da)**	**Number of amino acids**	**Main gut localization**	**Principal physiologic actions**
Gastrin family				
Cholecystokinin	3918	33 (also 385, 59)	Duodenum and jejunum, Enteric nerves	Stimulates gallbladder contraction and intestinal motility; stimulates secretion of pancreatic enzymes, insulin, glucagon, and pancreatic polypeptides; has a role in indicating satiety; the C-terminal 8 amino acid peptide cholecystokinin (CCK)-8 retains full activity
Little gastrin	2098	17	Both forms of	Gastrins stimulate the secretion of

Big gastrin	3839	34	gastrin are found in the gastric antrum and duodenum	gastric acid, pepsinogen, intrinsic factor, and secretin; stimulate intestinal mucosal growth; increase gastric and intestinal motility
Secretin-glucagon family				
Secretin	3056	27	Duodenum and jejunum	Stimulates pancreatic secretion of HCO_3, enzymes and insulin; reduces gastric and duodenal motility, inhibits gastrin release and gastric acid secretion
Vasoactive intestinal polypeptide (VIP)	3326	28	Enteric nerves	Relaxes smooth muscle of gut, blood vessels, and genitourinary system; increases water and electrolyte secretion from pancreas and gut; releases hormones from pancreas, gut, and hypothalamus
Glucose-dependent insulinotropic	4976	42	Duodenum and jejunum	Stimulates insulin release; reduces gastric and intestinal motility; increases fluid and electrolyte secretion from small intestine

Insulin

Insulin (from the Latin, insula meaning island) is a peptide hormone produced by beta cells of the pancreatic islets, and it is considered to be the main anabolic hormone of the body. It regulates the metabolism of carbohydrates, fats and protein by promoting the absorption of, especially, glucose from the blood into fat, liver and skeletal muscle cells. In these tissues the absorbed glucose is converted into either glycogen via glycogenesis or fats (triglycerides) via lipogenesis, or, in the case of the liver, into both. Glucose production and secretion by the liver is strongly inhibited by high concentrations of insulin in the blood. Circulating insulin also affects the synthesis of proteins in a wide variety of tissues. It is therefore an anabolic hormone, promoting the conversion of small molecules in the blood into large molecules inside the cells. Low insulin levels in the blood have the opposite effect by promoting widespread catabolism.

Beta cells are sensitive to glucose concentrations, also known as blood sugar levels. When the glucose level is high, the beta cells secrete insulin into the blood; when glucose levels are low, secretion of insulin is inhibited. Their neighboring alpha cells, by taking their cues from the beta cells secrete glucagon into the blood in the opposite manner: increased secretion when blood glucose is low, and decreased secretion when glucose concentrations are high. Glucagon, through stimulating the liver to release glucose by glycogenolysis and gluconeogenesis, has the opposite effect of insulin. The secretion of insulin and glucagon into the blood in response to the blood glucose concentration is the primary mechanism of glucose homeostasis.

If beta cells are destroyed by an autoimmune reaction, insulin can no longer be synthesized or be secreted into the blood. This results in type 1 diabetes mellitus, which is characterized by abnormally high blood glucose concentrations, and generalized body wasting. In type 2 diabetes mellitus the destruction of beta cells is less pronounced than in type 1 diabetes, and is not due to an autoimmune process. Instead there is an accumulation of amyloid in the pancreatic islets, which likely disrupts their anatomy and physiology. The pathogenesis of type 2 diabetes is not well understood but patients exhibit a reduced population of islet beta-cells, reduced secretory function of islet beta-cells that survive and peripheral tissue insulin resistance Type 2 diabetes is characterized by high rates of glucagon secretion into the blood which are unaffected by, and unresponsive to the concentration of glucose in the blood glucose. Insulin is still secreted into the blood in response to the blood glucose. As a result, the insulin levels, even when the blood sugar level is normal, are much higher than they are in healthy persons. There are a variety of treatment regimens, none of which is entirely satisfactory. When the pancreas's capacity to secrete insulin can no longer keep the blood sugar level within normal bounds, insulin injections are given.

The human insulin protein is composed of 51 amino acids, and has a molecular mass of 5808 Da. It is a dimer of an A-chain and a B-chain, which are linked together by disulfide bonds. Insulin's structure varies slightly between species of animals. Insulin from animal sources differs somewhat in effectiveness (in carbohydrate metabolism effects) from human insulin because of these variations. Porcine insulin is especially close to the human version, and was widely used to treat type 1 diabetics before human insulin could be produced in large quantities by recombinant DNA technologies.

Functions of Insulin

The actions of insulin on the global human metabolism level include:

* Increase of cellular intake of certain substances, most prominently glucose in muscle and adipose tissue (about two-thirds of body cells)
* Increase of DNA replication and protein synthesis via control of amino acid uptake
* Modification of the activity of numerous enzymes.
* The actions of insulin (indirect and direct) on cells include:
* Stimulates the uptake of glucose – Insulin decreases blood glucose concentration by inducing intake of glucose by the cell. This is possible because Insulin causes the insertion of the GLUT4 transporter in the cell membranes of muscle and fat tissues which allows glucose to enter the cell.
* Induce glycogen synthesis – When glucose levels are high, insulin induces the formation of glycogen by the activation of the hexokinase enzyme, which adds a phosphate group in glucose, thus resulting in a molecule that cannot exit the cell. At the same time, insulin inhibits the enzyme glucose-6-phosphatase, which removes the phosphate group. These two enzymes are key for the formation of glycogen. Also, insulin activates the enzymes phosphofructokinase and glycogen synthase which are responsible for glycogen synthesis.
* Increased potassium uptake – forces cells synthesizing glycogen (a very spongy, "wet" substance, that increases the content of intracellular water, and its accompanying K+ ions) to absorb potassium from the extracellular fluids; lack of insulin inhibits absorption. Insulin's increase in cellular potassium uptake lowers potassium levels in blood plasma. This possibly occurs via insulin-induced translocation of the Na+/K+-ATPase to the surface of skeletal muscle cells.
* Decreased gluconeogenesis and glycogenolysis – decreases production of glucose from noncarbohydrate substrates, primarily in the liver (the vast majority of endogenous insulin arriving at the liver never leaves the liver); increase of insulin causes glucose production by the liver from assorted substrates.
* Increased lipid synthesis – insulin forces fat cells to take in blood glucose, which is converted into triglycerides; decrease of insulin causes the reverse.
* Increased esterification of fatty acids – forces adipose tissue to make neutral fats (i.e., triglycerides) from fatty acids; decrease of insulin causes the reverse.
* Decreased lipolysis – forces reduction in conversion of fat cell lipid stores into blood fatty acids and glycerol; decrease of insulin causes the reverse.

* Decreased proteolysis – decreasing the breakdown of protein
* Decreased autophagy – decreased level of degradation of damaged organelles. Postprandial levels inhibit autophagy completely.
* Increased amino acid uptake – forces cells to absorb circulating amino acids; decrease of insulin inhibits absorption.
* Decreased renal sodium excretion.

Diabetes Mellitus

There are several conditions in which insulin disturbance is pathologic:

Diabetes mellitus – general term referring to all states characterized by hyperglycemia

Type 1 DM results from the pancreas's failure to produce enough insulin. This form was previously referred to as "insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes". The cause is autoimmune-mediated destruction of insulin-producing β-cells in the pancreas, resulting in absolute insulin deficiency.

Type 2 DM begins with insulin resistance, a condition in which cells fail to respond to insulin properly. As the disease progresses a lack of insulin may also develop. This form was previously referred to as "non insulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes". The most common cause is excessive body weight and not enough exercise.

Gestational diabetes is the third main form and occurs when pregnant women without a previous history of diabetes develop high blood sugar level

Condition	**2 hour glucose**	**Fasting glucose**	**HbA_{1c}**	
Unit	mmol/l(mg/dl)	mmol/l(mg/dl)	mmol/mol	DCCT %
Normal	<7.8 (<140)	<6.1 (<110)	<42	<6.0
Impaired fasting glycaemia	<7.8 (<140)	≥6.1(≥110) & <7.0(<126)	42-46	6.0–6.4
Impaired glucose tolerance	≥7.8 (≥140)	<7.0 (<126)	42-46	6.0–6.4
Diabetes mellitus	≥11.1 (≥200)	≥7.0 (≥126)	≥48	≥6.5

There is correlation with diet, with sedentary lifestyle, with obesity, with age and with metabolic syndrome. Causality has been demonstrated in multiple model organisms including mice and monkeys; Importantly, non-obese people do get Type 2 diabetes due to diet, sedentary lifestyle and unknown risk factors. It is likely that there is genetic susceptibility to develop Type 2 diabetes under certain environmental conditions

Treatment:

Medications for type 2 diabetes can work in different ways to reduce blood glucose levels. They may:

* increase insulin sensitivity,
* increase glucose excretion,
* decrease absorption of carbohydrates from the digestive tract, or
* work through other mechanisms.

Adiponectin

Adiponectin is a protein hormone that modulates a number of metabolic processes, including glucose regulation and fatty acid oxidation. Adiponectin is secreted from adipose tissue (and also from the placenta in pregnancy into the bloodstream and is very abundant in plasma relative to many hormones. Adiponectin is secreted into the bloodstream where it accounts for approximately 0.01% of all plasma protein at around 5-10 μg/mL (mg/L). In adults, plasma concentrations are higher in females than males, and are reduced in diabetics compared to non-diabetics.

Adiponectin effects:

* glucose flux
* decreased gluconeogenesis
* increased glucose uptake
* lipid catabolism
* β-oxidation
* triglyceride clearance
* protection from endothelial dysfunction (important facet of atherosclerotic formation)

* insulin sensitivity
* weight loss
* control of energy metabolism.
* upregulation of uncoupling proteins
* reduction of TNF-alpha

Unit 5

1	Blood brain barrier can be crossed by	Epinephrine	Dopamine	Dopa	All of the above	Dopa
2	Zona glomerulosa of adrenal cortex synthesis	Glucocorticoids	Mineralocorticoids	Androgen	Estrogen and progesterone	Mineralocorticoids
	Cortisol is a	Glucocorticoid	Mineralocorticoid	Androgen	Estrogen	Glucocorticoid
3	The major mineralocorticoid is	Hydrocortisone	Aldosterone	Aldactone A	Androstenedione	Aldosterone
4	Steroid hormones are synthesized in all of the following except	Testes	Ovaries	Adrenal medulla	Adrenal cortex	Adrenal medulla
5	Steroid hormones are synthesized from	Cholesterol	7- Dehydrocholesterol	Calcitriol	7 – hydroxylcholesterol	Cholesterol
6	The common intermediate in the synthesis of all the steroid hormones is	Pregnelone	17- hydroxyl pregnenolene	Corticosterone	Progesterone	Pregnelone
7	A common intermediate in the synthesis of cortisol and aldosterone is	Progesterone	Testosterone	Estradial	None of the above	Progesterone
8	A common intermediate in the synthesis of estrogens is	Cortisol	Androstenedione	Corticosterone	11 – deoxycorticosteroi	Androstenedione
9	Glucocorticoids are transported in blood	In association with trans	In association with albu	In free form partly	All of the above forms	All of the above forms
10	All the following statements about transcortin are true except	It is synthesized in liver	It transports glucocorticoids	It transports aldosterone	It transports progesterone	It transports aldosterone
11	The secondary messenger for glucocorticoids is	Cyclic AMP	.Cyclic GMP	Inositol triphosphate	No second messenger is	No second messenger is
12	Glucocorticoids increase all of the following except	Gluconeogenesis	Lipolysis in extremities	Synthesis of eicosanoids	Hepatic glycogenesis	Synthesis of eicosanoids
13	Glucocorticoids increase the synthesis of all of the following except	Glucokinase	Glucose – 6-phosphatase	Fructose -1,6, biphosphate	Pyruvate carboxylase	Glucokinase
14	Secretion of glucocorticoids is regulated by all the following except	Hypothalamus	Anterior pituitary	Feed back control by blood gluc	Feed back control by gl	Feed back control by blood gluc
15	Excessive secretion of glucorticoids raises blood glucose by	Decreasing glycogenesis	Increasing glycogenolysis	Increasing glyconeogenesis	Inhibiting HMP shunt	Increasing glyconeogenesis
16	Mineralocorticoids increase the tubular secretion of	Sodium	Potassium	Chloride	bicarbonate	Chloride
17	Mineralocorticoids increase the tubular reabsorption of	Sodium and calcium	Sodium and potassium	Sodium and chloride	Potassium and chloride	Sodium and chloride
18	Seretion of mineral corticoids is increased by	ACTH	Angiotensin	Hypokalaemia	.Hypernatramia	Angiotensin
19	Spironolactone is an antagonist of	Cortisol	Hydrocortisone	Aldosterone	Testosterone	Aldosterone
20	Androgens are synthesized in	Leydig cells in testes	Sertole cells in testes	Seminiferous tubules	Prostate gland	Leydig cells in testes
21	Testosterone is transported in blood by	Transcortin	T	Testosterone estrogen binding g	Albumin	T
22	The metabolites of androgen are	17- Hydroxysteroids	17- Ketosteroids	11 – Hydroxysteroids	11- Ketosteroids	17- Ketosteroids
23	An androgen, which is more powerful than testosterone, is	Androstenedione	Dihydrotestosterone	Androsterone	Epiandrosterone	Dihydrotestosterone
24	Secretion of androgen is increased by	LH	FSH	ACTH	Growth hormone	LH
25	During late pregnancy, the major source of progesterone is	Adrenal cortex	Placenta	Corpus luteum	Graffian follicles	Placenta
26	Progesterone is transported in blood by	Transcortin	Sex hormone binding globulin	Albumin	Testosterone estrogen binding g	Transcortin
27	The major metabolites of progesterone is	Pregnenolene		Pregnanediol		P
28	A hormone used for detection of pregnancy is	Estrogen	Progesterone	Estradiol	Chorionic gonadotropin	Chorionic gonadotropin
29	Which of the following is secreted by the posterior lobe of the pituitary gla	estrogen	oxytocin	progesterone	prolactin	oxytocin
30	In mammals that are seasonal breeders, females are receptive only once a year. This is called	a follicular cycle	an estrous cycle	a menstrual cycle	a luteal cycle	an estrous cycle
31	After sperm are produced, they are delivered first to the	vas deferens	urethra	epididymis	seminal vesicle	epididymis
32	Progesterone is produced by the	corpus luteum	hypothalamus	seminiferous tubules	pituitary gland	corpus luteum
33	Ovulation is caused by the hormone	FSH	Progesterone	Oxytocin	LH	LH
34	What is the name of the vesicle at the tip of a sperm cell that contains enzymes that will help the sperm cell penetrate an egg cell it encounters?	amnion	Chorion	Acrosome	Sertoli cell	Acrosome
35	The lining or inner layer of the uterus is called the	cervix	endometrium	epididymis	Leydig	endometrium
36	What structure is cut and tied off in a vasectomy?	the epididymis	the urethra	the seminiferous tubules	the vas deferens	the vas deferens
37	Testosterone is produced by the	Sertoli cells	Leydig cells	Myocytes	Leukocyte	Leydig cells
38	The hormone testosterone	stimulates cell growth in bone and muscle	is a protein hormone that causes the vocal cords to thicken	decreases activity in the sebaceous glands	is not present in women	stimulates cell growth in bone and muscle
39	LH surge is	not seen in women	seen in women	seen in men	not seen in both sex	seen in women
40	Aromatase is responsile for the production of	Testosterone	Progesterone	Estradiol	Peptide hormone	Estradiol
41	5 alpha reductase produces	Active Testosterone	Progesterone	Estradiol	Peptide hormone	Active Testosterone
42	The periodic shedding of the endometrium is known as	ovulation	oogenesis	the secretory phase	menstruation	menstruation
43	Which hormone is secreted in the urine of pregnant women?	beta hCG	oxytocin	growth hormone	somatotropin	beta hCG
44	LH receptors are primarily present in	Sertoli cells	nurse cells	Leydig cells	islet cells	Leydig cells
45	Which is the marker of Sertoli cells?	Androgen	estrogen	androgen binding protein	estriol	androgen binding protein
46	Placenta secretes all of the following except	FSH	Progesterone	Estrogen	Chorionic gonadotropin	FSH
47	Atrial naturietic factor is produced in	liver	heart	kidney	bone	heart
48	Atrial naturietic factor is produced is a	peptide hormone	steroid hormone	aminoacid	vitamin	peptide hormone
49	Erythropoietin is produced in	liver	heart	kidney	bone	kidney
50	Erythropoietin is	peptide hormone	steroid hormone	aminoacid	vitamin	peptide hormone
51	Calcitriol is the derivative of	vitamin A	vitamin B	vitamin C	vitamin D	vitamin D
52	Angiotensin II contains	10 aminoacids	6 aminoacids	8 aminoacids	23 aminoacids	8 aminoacids
53	Angiotensin I contains	10 aminoacids	6 aminoacids	8 aminoacids	23 aminoacids	10 aminoacids
54	Angiotensin is related to	pepsin	renin	insulin	somatostatin	renin
55	Angiotensin is involved in	reproduction	blood pressure maintenance	calcium homeostasis	it doesnot have any role	blood pressure maintenance
56	B-type naturietic peptide contains	28 aminoacids	29 amino acids	35 aminoacids	33 aminoacids	29 amino acids
57	A-type naturietic peptide contains	28 aminoacids	29 amino acids	35 aminoacids	33 aminoacids	28 amino acids
58	childhood deficiency of calcitriol results in	osteomalacia	rickets	osteopetrosis	anemia	rickets
59	Deficiency of calcitriol in adults causees	osteomalacia	rickets	osteopetrosis	anemia	osteomalacia
60	Renin is a	enzyme	lipid	fatty acid	vitamin	enzyme

required

ose

estosterone binding globulin

regnanediol

KARPAGAM ACADEMY OF HIGHER EDUCATION
(Deemed University Established Under Section 3 of UGC Act 1956)
Coimbatore - 641021.
(For the candidates admitted from 2015 onwards)
DEPARTMENT OF BIOCHEMISTRY

SUBJECT : HORMONES: BIOCHEMISTRY AND FUNCTION
SEMESTER : III
SUBJECT CODE : 16BCU303 CLASS : II B.Sc.BC

UNIT V - COURSE MATERIAL

Unit 5-Adrenal and gonadal hormones

Aldosterone, renin angiotensin system, cortisol, epinephrine and norepinephrine. Fight or flight response, stress response. Pathophysiology – Addison's disease, Conn's syndrome, Cushing syndrome.Male and female sex hormones. Interplay of hormones during reproductive cycle, pregnancy, parturition and lactation. Hormone based contraception.

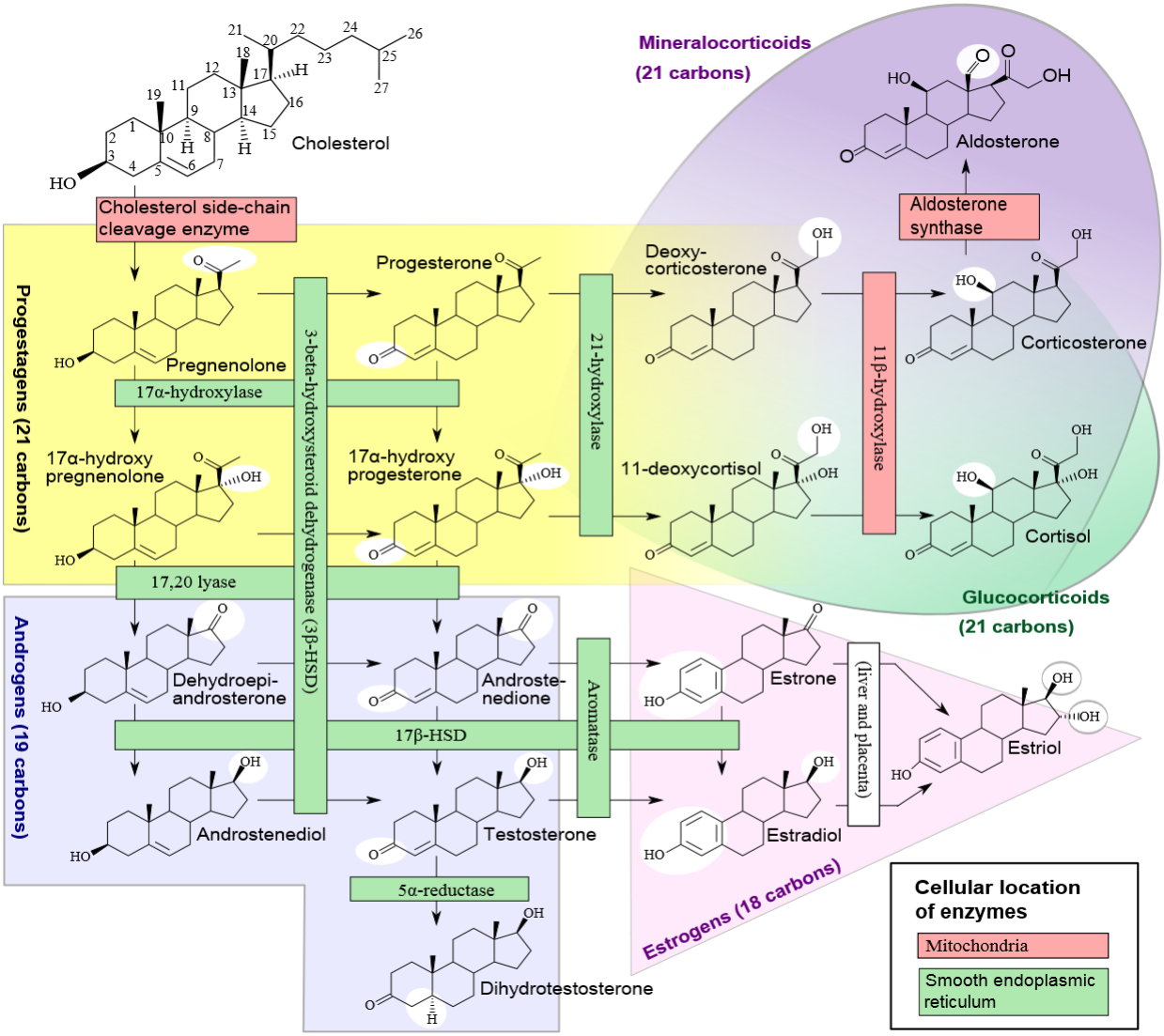
Aldosterone

Aldosterone, the main mineralocorticoid hormone, is a steroid hormone produced by the zona glomerulosa of the adrenal cortex in the adrenal gland. It is essential for sodium conservation in the kidney, salivary glands, sweat glands and colon. It plays a central role in the homeostatic regulation of blood pressure, plasma sodium (Na+), and potassium (K+) levels. It does so mainly by acting on the mineralocorticoid receptors in the distal tubules and collecting ducts of the nephron. It influences the reabsorption of sodium and excretion of potassium (from and into the tubular fluids, respectively) of the kidney, thereby indirectly influencing water retention or loss, blood pressure and blood volume. When dysregulated, aldosterone is pathogenic and contributes to the development and progression of cardiovascular and renal disease. Aldosterone has exactly the opposite function of the atrial natriuretic hormone secreted by the heart.

Aldosterone is part of the renin–angiotensin–aldosterone system. It has a plasma half-life of under 20 minutes. Drugs that interfere with the secretion or action of aldosterone are in use as antihypertensives, like lisinopril, which lowers blood pressure by blocking the angiotensin-converting enzyme (ACE), leading to lower aldosterone secretion. The net effect of these drugs is to reduce sodium and water retention but increase retention of potassium. In other words, these drugs stimulate the excretion of sodium and water in urine, while they block the excretion of potassium.

Another example is spironolactone, a potassium-sparing diuretic of the steroidal spirolactone group, which decreases blood pressure by releasing fluid from the body while retaining potassium.

adrenal cortex; 11β-hydroxylase is found in the zona glomerulosa and zona fasciculata.



The corticosteroids are synthesized from cholesterol within the zona glomerulosa of adrenal cortex. Most steroidogenic reactions are catalysed by enzymes of the cytochrome P450 family. They are located within the mitochondria and require adrenodoxin as a cofactor (except 21-hydroxylase and 17α-hydroxylase).

Aldosterone and corticosterone share the first part of their biosynthetic pathways. The last parts are mediated either by the aldosterone synthase (for aldosterone) or by the 11β-hydroxylase (for

corticosterone). These enzymes are nearly identical (they share 11β-hydroxylation and 18-hydroxylation functions), but aldosterone synthase is also able to perform an 18-oxidation. Moreover, aldosterone synthase is found within the zona glomerulosa at the outer edge of the adrenal cortex; 11β-hydroxylase is found in the zona glomerulosa and zona fasciculata.

Functions

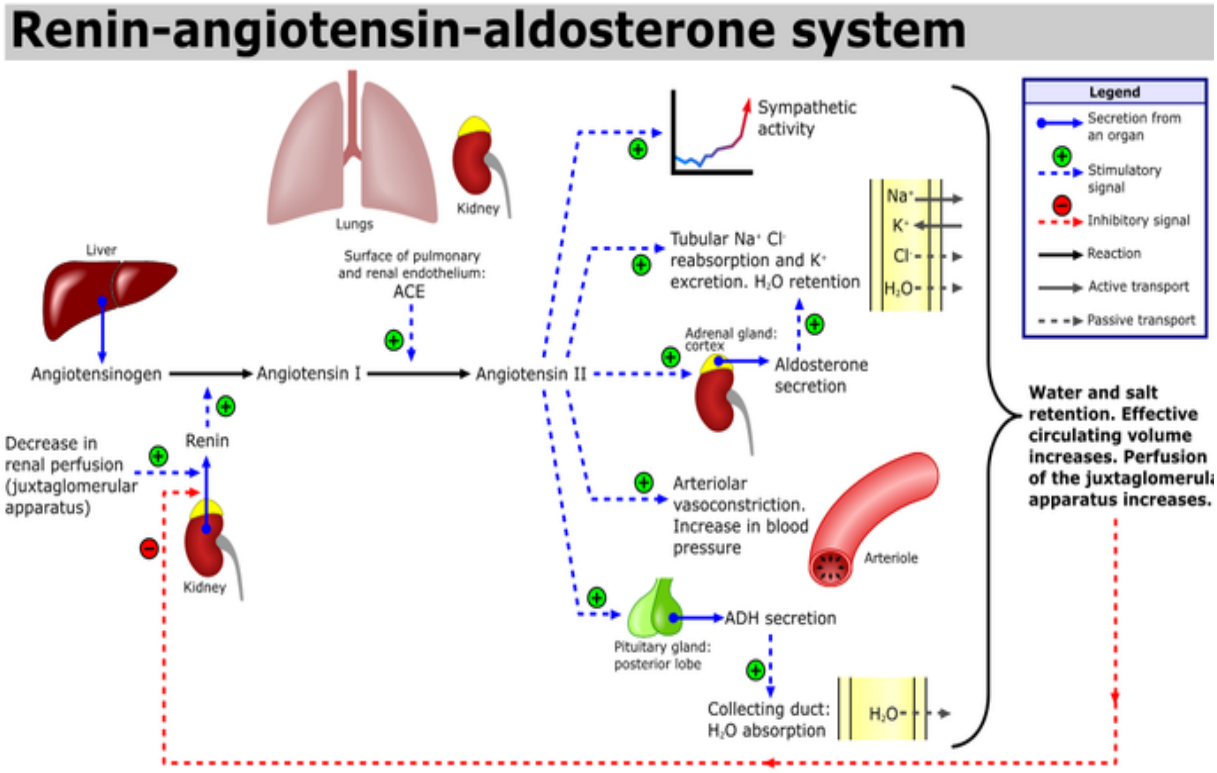
Aldosterone is the primary of several endogenous members of the class of mineralocorticoids in humans. Deoxycorticosterone is another important member of this class. Aldosterone tends to promote Na+ and water retention, and lower plasma K+ concentration by the following mechanisms:

- Acting on the nuclear mineralocorticoid receptors (MR) within the principal cells of the distal tubule and the collecting duct of the kidney nephron, it upregulates and activates the basolateral Na+/K+ pumps, which pumps three sodium ions out of the cell, into the interstitial fluid and two potassium ions into the cell from the interstitial fluid. This creates a concentration gradient which results in reabsorption of sodium (Na+) ions and water (which follows sodium) into the blood, and secreting potassium (K+) ions into the urine (lumen of collecting duct).
- Aldosterone upregulates epithelial sodium channels (ENaCs) in the collecting duct and the colon, increasing apical membrane permeability for Na+ and thus absorption.
- Cl− is reabsorbed in conjunction with sodium cations to maintain the system's electrochemical balance.
- Aldosterone stimulates the secretion of K+ into the tubular lumen.
- Aldosterone stimulates Na+ and water reabsorption from the gut, salivary and sweat glands in exchange for K+.
- Aldosterone stimulates secretion of H+ via the H+/ATPase in the intercalated cells of the cortical collecting tubules
- Aldosterone upregulates expression of NCC in the distal convoluted tubule chronically and its activity acutely.

Renin-Angiotensin System

The renin–angiotensin system (RAS) or the renin–angiotensin–aldosterone system (RAAS) is a hormone system that regulates blood pressure and fluid balance.

When renal blood flow is reduced, juxtaglomerular cells in the kidneys convert the precursor – prorenin, already present in the blood into renin and secrete it directly into the circulation. Plasma renin then carries out the conversion of angiotensinogen, released by the liver, to angiotensin I. Angiotensin I is subsequently converted to angiotensin II by the enzyme angiotensin-converting enzyme (ACE) found in the lungs. Angiotensin II is a potent vasoconstrictive peptide that causes blood vessels to narrow, resulting in increased blood pressure. Angiotensin II also stimulates the secretion of the hormone aldosterone from the adrenal cortex. Aldosterone causes the renal tubules to increase the reabsorption of sodium and water into the blood, while at the same time causing the excretion of potassium (to maintain electrolyte balance). This increases the volume of extracellular fluid in the body, which also increases blood pressure.



Clinical Significance

ACE inhibitors–inhibitors of angiotensin-converting enzyme are often used to reduce the formation of the more potent angiotensin II. Captopril is an example of an ACE inhibitor. ACE cleaves a number of other peptides, and in this capacity is an important regulator of the kinin–kallikrein system, as such blocking ACE can lead to side effects.

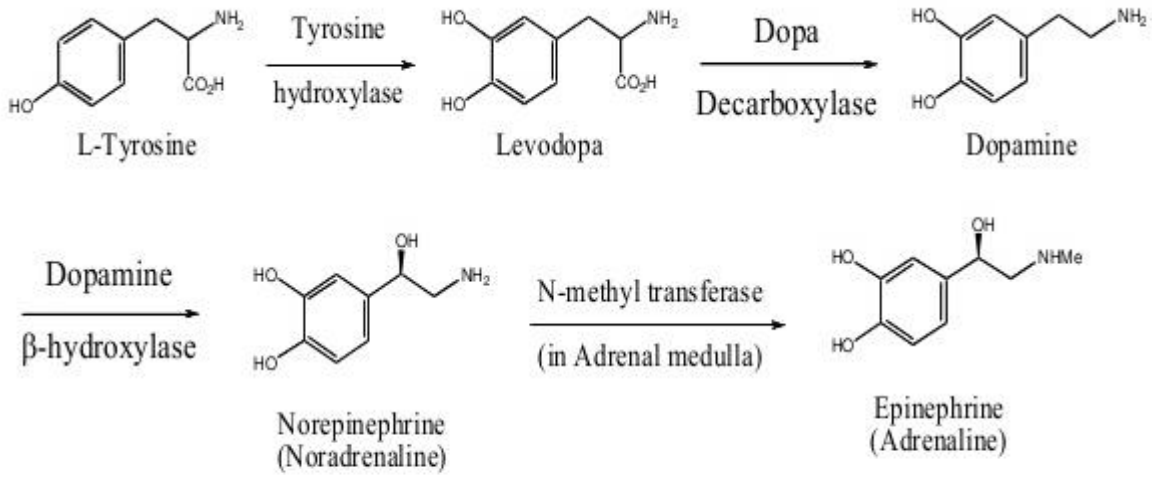
Angiotensin II receptor antagonists, also known as angiotensin receptor blockers, can be used to prevent angiotensin II from acting on its receptors.

Direct renin inhibitors can also be used for hypertension. The drugs that inhibit renin are aliskiren and the investigational remikiren.

Vaccines against angiotensin II, for example CYT006-AngQb, have been investigated

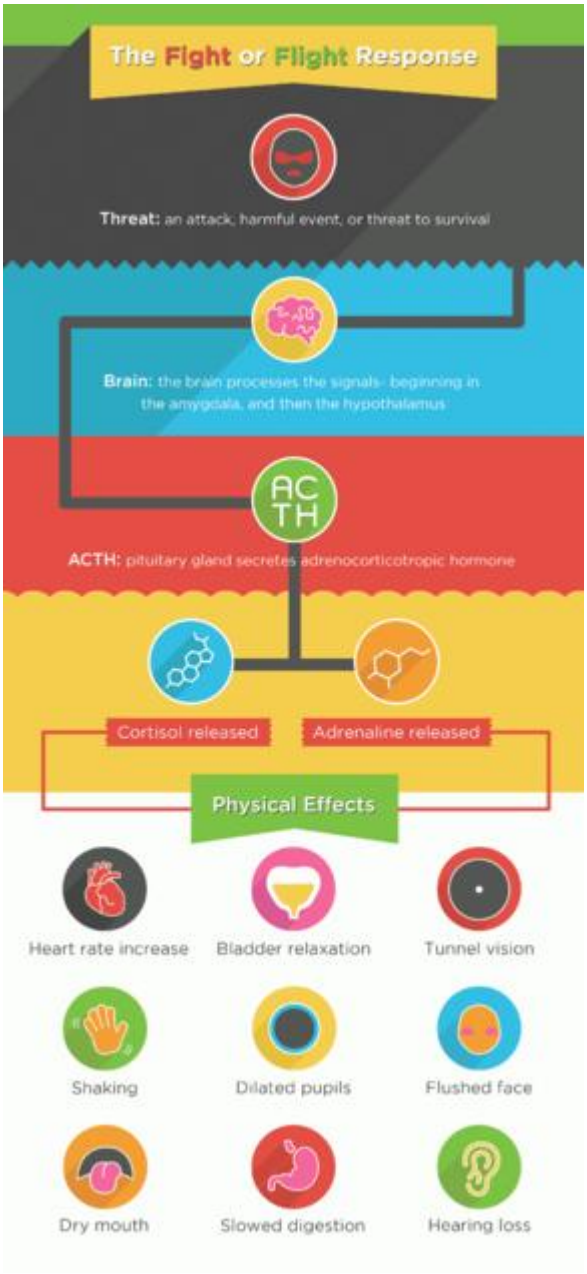
Epinephrine:

Epinephrine, also known as adrenalin or adrenaline, is a hormone, neurotransmitter, and medication. Epinephrine is normally produced by both the adrenal glands and certain neurons. It plays an important role in the fight-or-flight response by increasing blood flow to muscles, output of the heart, pupil dilation, and blood sugar. It does this by binding to alpha and beta receptors.



Fight-or-flight response

The fight-or-flight response (also called hyperarousal, or the acute stress response) is a physiological reaction that occurs in response to a perceived harmful event, attack, or threat to survival. It was first described by Walter Bradford Cannon.His theory states that animals react to threats with a general discharge of the sympathetic nervous system, preparing the animal for fighting or fleeing. More specifically, the adrenal medulla produces a hormonal cascade that results in the secretion of catecholamines, especially norepinephrine and epinephrine. The hormones estrogen, testosterone, and cortisol, as well as the neurotransmitters dopamine and serotonin, also affect how organisms react to stress.



Addison Disease

Addison's disease, also known as primary adrenal insufficiency and hypocortisolism, is a long-term endocrine disorder in which the adrenal glands do not produce enough steroid hormones.

Characteristic symptoms are:

* Sudden penetrating pain in the legs, lower back, or abdomen
* Severe vomiting and diarrhea, resulting in dehydration

* Low blood pressure
* Syncope (loss of consciousness and ability to stand)
* Hypoglycemia (reduced level of blood glucose)
* Confusion, psychosis, slurred speech
* Severe lethargy
* Hyponatremia (low sodium level in the blood)
* Hyperkalemia (elevated potassium level in the blood)
* Hypercalcemia (elevated calcium level in the blood)
* Convulsions
* Fever

Causes:

Causes of adrenal insufficiency can be categorized by the mechanism through which they cause the adrenal glands to produce insufficient cortisol. These are adrenal dysgenesis (the gland has not formed adequately during development), impaired steroidogenesis (the gland is present but is biochemically unable to produce cortisol) or adrenal destruction (disease processes leading to glandular damage.

Treatment

Treatment for Addison's disease involves replacing the missing cortisol, sometimes in the form of hydrocortisone tablets, or prednisone tablets in a dosing regimen that mimics the physiological concentrations of cortisol. Alternatively, one-quarter as much prednisolone may be used for equal glucocorticoid effect as hydrocortisone. Treatment is usually lifelong. In addition, many patients require fludrocortisone as replacement for the missing aldosterone.

Cushing Syndrome

Cushing's syndrome is a collection of signs and symptoms due to prolonged exposure to cortisol.[3][8] Signs and symptoms may include high blood pressure, abdominal obesity but with thin arms and legs, reddish stretch marks, a round red face, a fat lump between the shoulders, weak muscles, weak bones, acne, and fragile skin that heals poorly.[2] Women may have more hair and irregular menstruation.[2] Occasionally there may be changes in mood, headaches, and a chronic feeling of tiredness.[2]

Cushing's syndrome is caused by either excessive cortisol-like medication such as prednisone or a tumor that either produces or results in the production of excessive cortisol by the adrenal glands. Cases due to a pituitary adenoma are known as Cushing's disease. It is the second most common cause of Cushing's syndrome after medication. A number of other tumors may also cause Cushing's. Some of these are associated with inherited disorders such as multiple endocrine neoplasia type 1 and Carney complex.Diagnosis requires a number of steps. The first step is to check the medications a person takes. The second step is to measure levels of cortisol in the urine, saliva or in the blood after taking dexamethasone. If this test is abnormal, the cortisol may be measured late at night. If the cortisol remains high, a blood test for ACTH may be done to determine if the pituitary is involved.

Most cases can be treated and cured. If due to medications, these can often be slowly stopped. If caused by a tumor, it may be treated by a combination of surgery, chemotherapy, and/or radiation.

Signs and symptoms

* Rapid weight gain
* Moodiness, irritability, or depression
* Muscle and bone weakness
* Memory and attention dysfunction
* Osteoporosis
* Diabetes mellitus
* Hypertension
* Immune suppression
* Sleep disturbances
* Menstrual disorders such as amenorrhea in women
* Decreased fertility in men
* Hirsutism
* Baldness

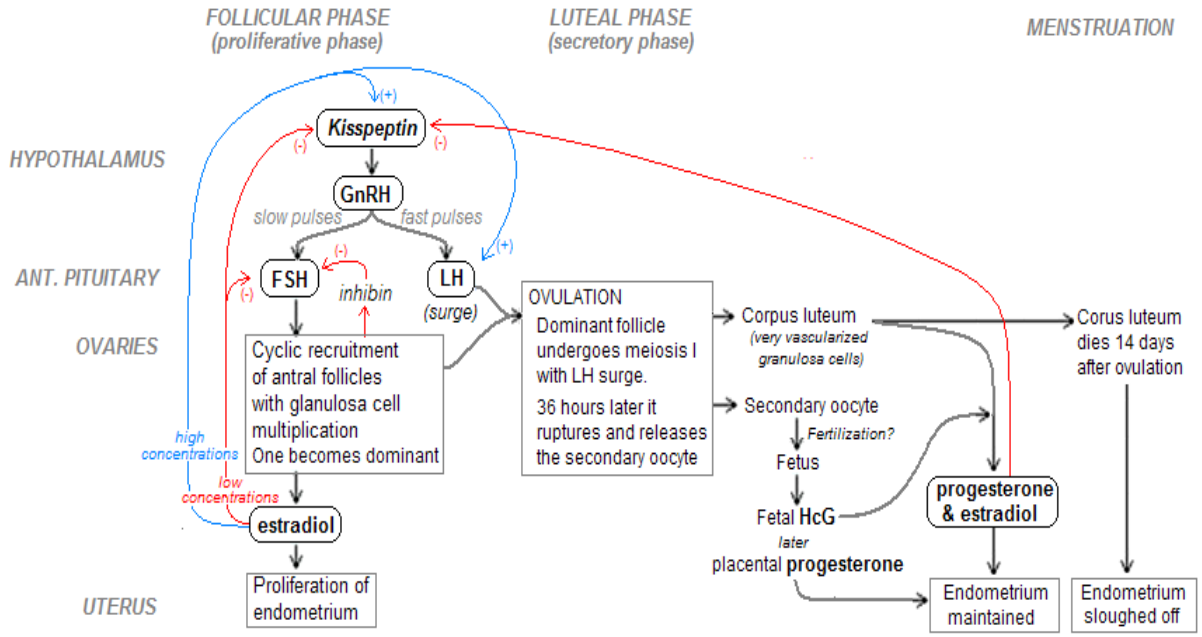
Treatment:

Most Cushing's syndrome cases are caused by corticosteroid medications, such as those used for asthma, arthritis, eczema and other inflammatory conditions. Consequently, most patients are effectively treated by carefully tapering off (and eventually stopping) the medication that causes the symptoms.

If an adrenal adenoma is identified, it may be removed by surgery. An ACTH-secreting corticotrophic pituitary adenoma should be removed after diagnosis. Regardless of the adenoma's location, most patients require steroid replacement postoperatively at least in the interim, as long-term suppression of pituitary ACTH and normal adrenal tissue does not recover immediately. Clearly, if both adrenals are removed, replacement with hydrocortisone or prednisolone is imperative.

Reproductive Cycle

The menstrual cycle can be described by the ovarian or uterine cycle. The ovarian cycle describes changes that occur in the follicles of the ovary whereas the uterine cycle describes changes in the endometrial lining of the uterus. Both cycles can be divided into three phases. The ovarian cycle consists of the follicular phase, ovulation, and the luteal phase whereas the uterine cycle consists of menstruation, proliferative phase, and secretory phase



Disorders

Infrequent or irregular ovulation is called oligoovulation. The absence of ovulation is called anovulation. Normal menstrual flow can occur without ovulation preceding it: an anovulatory cycle. In some cycles, follicular development may start but not be completed; nevertheless, estrogens will be formed and stimulate the uterine lining. Anovulatory flow resulting from a very thick endometrium caused by prolonged, continued high estrogen levels is called estrogen breakthrough bleeding. Anovulatory bleeding triggered by a sudden drop in estrogen levels is called withdrawal bleeding. Anovulatory cycles commonly occur before menopause (perimenopause) and in women with polycystic ovary syndrome.

Very little flow (less than 10 ml) is called hypomenorrhea. Regular cycles with intervals of 21 days or fewer are polymenorrhea; frequent but irregular menstruation is known as metrorrhagia. Sudden heavy flows or amounts greater than 80 ml are termed menorrhagia.

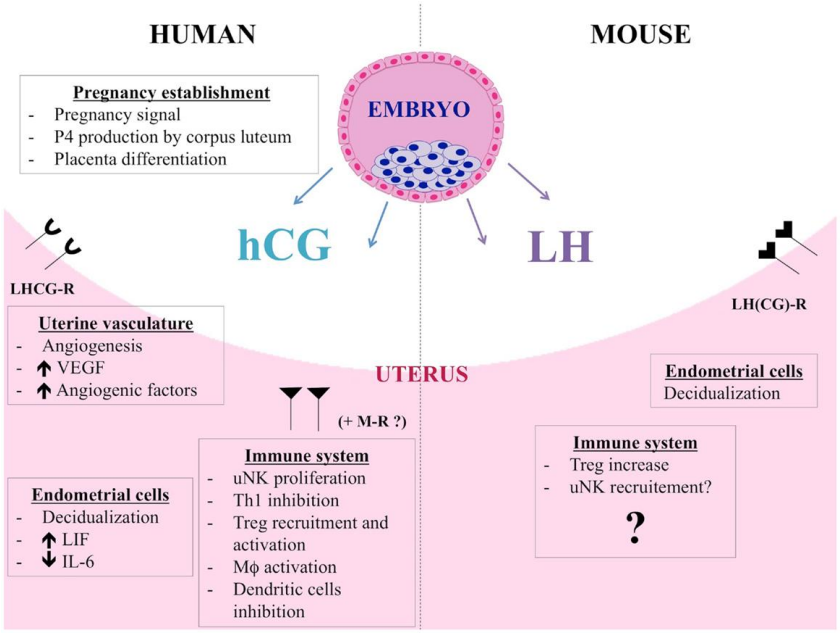
Endocrinology of Pregnancy

The endocrinology of human pregnancy involves endocrine and metabolic changes that result from physiological alterations at the boundary between mother and fetus. Known as the feto-placental unit (FPU), this interface is a major site of protein and steroid hormone production and secretion. Many of the endocrine and metabolic changes that occur during pregnancy can be directly attributed to hormonal signals originating from the FPU. The initiation and maintenance of pregnancy depends primarily on the interactions of neuronal and hormonal factors. Proper timing of these neuro-endocrine events within and between the placental, fetal, and maternal compartments is critical in directing fetal growth and development and in coordinating the timing of parturition. Maternal adaptations to hormonal changes that occur during pregnancy directly affect the development of the fetus and placenta. Gestational adaptations that take place in pregnancy include establishment of a receptive endometrium; implantation and the maintenance of early pregnancy; modification of the maternal system in order to provide adequate nutritional support for the developing fetus; and preparation for parturition and subsequent lactation.

Some of the most significant hormones in pregnancy are:

* Human Chorionic gonadotropin
* oestrogen
* progesterone
* oxytocin
* endorphins

* prolactin



Hormonal Changes During Pregnancy

Hormone	Source	Effect
Human Chorionic Gonadotropin	Placenta	Maintains corpus luteum until week 12
Estrogen/Progesterone	Corpus luteum/ placenta	Stimulate and maintain uterine lining, inhibit FSH and LH, inhibit uterine contractions, and enlarge reproductive organs
Relaxin	Corpus luteum/ placenta	(Possible: Causes pelvic ligaments to relax, widen, and become flexible); inhibits uterine contractions; promotes uterine blood vessel growth
Human Chorionic Somatomammotropin (also Placental Lactogen)	Placenta	Mammary gland development; glucose-sparing effect in mother; weak GH-type effect
Human Chorionic Thyrotropin	Placenta	Increases size/activity of maternal thyroid and parathyroid glands
Aldosterone	Adrenal cortex	Increases fluid retention