M.Sc., Biochemistry **2018-2020**

Semester III

18BCP303 **ENDOCRINOLOGY** **4H-4C**

Instruction hours/week: L:4 T:0 P:0 **Marks:** Internal: **40** External: **60** Total: **100**

End Semester Exam: 3 Hours

Course objectives

- To demonstrate the biosynthesis of various hormones
- To explain the influence of various hormones on the physiological function of the body.

Course outcomes (CO's)

1. Students would understand the synthesis and regulation of hormones biosynthesis
2. Students would understand the physiology of hormone actions and its deficiency/hyperactivity states
3. Students learn the methods to assess hormone functions

Unit I: General Introduction

General Introduction, Hypothalamo-hypophyseal axis, Chemical signaling – endocrine, paracrine, autocrine, intracrine and neuroendocrine mechanisms. Chemical classification of hormones, transport of hormones in the circulation and their half-lives. Hormone receptors – extracellular, transmembrane and intracellular. Receptor – hormone binding, Scatchard analysis, recycling and degradation of receptors. Releasing/release-inhibiting hormones (TRH, GnRH, CRH, GHRH, somatostatin, dopamine), their structure, secretion and regulation.

Unit II: Protein/Peptide hormones

Protein/Peptide hormones, Steroid and Thyroid hormones, GH, prolactin, ACTH, insulin, glucagon, PTH and calcitonin, and glycoprotein hormones (TSH, FSH, LH and hCG) – Structure, synthesis, secretion, regulation, transport and metabolism.

Unit III: Hormones and gonads

Physiological action of hormones in the regulation of spermatogenesis, sperm maturation, oogenesis and menstrual/estrus cycles. Gonadal and adrenal steroidogenesis. Cell-cell communication – Two cell concept. Hormonal control of implantation, gestation, parturition and lactation; hormonal contraception. Semen analysis.

Unit IV: Hormone action

Protein and steroid hormone receptors and their signaling cascades; non-genomic actions; Ras-Raf-MAPK signaling - PI3K signaling. Genomic actions of hormones - thyroid hormone nuclear receptor superfamily. Renin-angiotensin system, atrial natriuretic hormones. Vasopressin and water retention.

Unit V: Investigative techniques in endocrinology

Hormone assays, RIA, IRMA, ELISA, Radio receptor assay, extraction, purification, and quantification of hormone receptors (cell surface, cytosolic and nuclear receptors). Radiolabeling techniques – Radioiodination of peptides, autoradiography. Properties of different types of radioisotopes commonly used in biology, radioactivity, detection and measurement of radioactivity, safely guidelines and disposal procedures.

SUGGESTED READINGS

1. Burtis, C.A., and Edward R. Tietz, E.R., (1999) Textbook of Clinical Chemistry 3rd Edition, WB Saunders Harcourt Brace & Company Asia PTE Ltd., USA.

2. Lehninger, L., Nelson, D.L., and Cox, M.M., (2012). Principles of Biochemistry, WH Freeman and Company, 6th Edition, New York.

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

4. 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.

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

Semester III

18BCP311 **PRACTICAL – V** **4H-2C**

CLINICAL ENZYMES AND IMMUNOLOGY

Instruction hours/week: L:0 T:0 P: 4 **Marks:** Internal: **40** External: **60** Total: **100**

End Semester Exam: 3 Hours

Course objectives

- To understand the principles and diagnostic importance of various clinically important enzymes
- To determine the activity of various clinically important enzymes
- To learn the immunological experiments and understand the antigen – antibody reactions.
- To analyse a case for various diseases like diabetes, cardiac diseases and cancer.

Course outcomes (CO's)

After learning this practicals the students could be able

1. to analyse the biological samples and can be able to interpret the results
2. By doing a case study they will be getting a clear picture of various diseases and their etiology.

ENZYMOLOGY

1. Determination of the activity of the following serum enzymes:
   a. LDH
   b. Acid phosphatase
   c. Alkaline phosphatase
   d. Aspartate amino transferase
   e. Alanine amino transferase
   f. 5' nucleotidase
   g. Sodium potassium ATPase
   h. Ceruloplasmin

IMMUNOLOGY (DEMONSTRATION)

2. Raising of antibodies- single soluble and particulate antigen
3. Immunodiffusion- single radial and double diffusion.
4. Immunoelectrophoresis.
5. Rocket immunoelectrophoresis
6. ELISA
7. Bacterial Agglutination: WIDAL
8. Antibody titration – ELISA

Case study-Report

9. Serum enzyme in liver disease
10. Serum enzyme in cardiac disease
11. Serum enzyme in cancer disease

12. Glucose Tolerance Test

SUGGESTED READINGS

1. Jayaraman, J., (2007). Laboratory Manual in Biochemistry, New Age International Publishers New Delhi.

2. Sadasivam, S., and Manickam, A., (2009). Biochemical Methods, New Age International Publishers, New Delhi.

3. Singh, S.P., (2009). Practical Manual of Biochemistry, CBS Publishers, New Delhi.

4. Talib, V. H., (2003). A Handbook of Medical Laboratory Technology, CBS Publishers, New Delhi.

5. David Wild, (2013). Elsevier; Immuno Assay Hand Book

KARPAGAM ACADEMY OF HIGHER EDUCATION

(Deemed to be University Established Under Section 3 of UGC Act 1956)

Coimbatore – 641 021.

LECTURE PLAN
DEPARTMENT OF BIOCHEMISTRY

STAFF NAME : Dr.M.SRIDHAR MUTHUSAMI

SUBJECT NAME: ENDOCRINOLOGY **SUB.CODE: 18BCP303**

SEMESTER : III **CLASS: II M.Sc (BC)**

Sl. No	Duration of Period	Topics to be Covered	Support material
		Unit I: General Introduction	
1	1	General Introduction, Hypothalamo-hypophyseal axis	
2	1	Chemical signaling – endocrine, paracrine, autocrine, intracrine and neuroendocrine mechanisms	
3	1	Chemical classification of hormones,	
4	1	transport of hormones in the circulation and their half-lives	
5	1	Hormone receptors – extracellular, transmembrane and intracellula	
6	1	Receptor – hormone binding	
7	1	Scatchard analysis, recycling and degradation of receptors	
8	2	Releasing/release-inhibiting hormones (TRH, GnRH, CRH, GHRH, somatostatin, dopamine)	
9	1	Their structure, secretion and regulation	
		Total no of hours planned for UNIT I = 10	
		Unit II: Protein/Peptide hormones	
1	1	Protein/Peptide hormones - Structure, synthesis, secretion, regulation, transport and metabolism.	
2	1	Steroid Hormones	
3	1	Thyroid hormones	
4	1	GH, prolactin and ACTH	
5	1	Insulin and glucagon	

6	1	PTH and calcitonin	
7	1	Glycoprotein hormones –TSH and FSH	
8	1	Glycoprotein hormones - LH and hCG	
		Total no of hours planned for UNIT II = 8	
Unit III: Hormones and gonads			
1	1	Physiological action of hormones in the regulation of spermatogenesis	
2	1	Sperm maturation	
3	1	Oogenesis and menstrual/estrus cycles	
4	1	Gonadal and adrenal steroidogenesis	
5	1	Cell-cell communication – Two cell concept	
6	2	Hormonal control of implantation, gestation, parturition and lactation	
7	1	hormonal contraception	
8	1	Semen analysis	
		Total no of hours planned for UNIT III = 9	
Unit IV: Hormone action			
1	2	Protein and steroid hormone receptors and their signaling cascades	
2	1	Non-genomic actions	
3	1	Ras-Raf-MAPK signaling - PI3K signaling	
4	1	Genomic actions of hormones	
5	1	Hormone nuclear receptor superfamily	
6	1	Renin-angiotensin system	
7	1	Atrial natriuretic hormones	
8	1	Vasopressin and water retention	
		Total no of hours planned for UNIT IV = 9	
Unit V: Investigative techniques in endocrinology			
1	1	Hormone assays, RIA, IRMA	
2	1	ELISA, Radio receptor assay	
3	2	Extraction, purification, and quantification of hormone receptors (cell surface, cytosolic and nuclear receptors)	
4	1	Radiolabeling techniques – Radioiodination of peptides	

5	1	Autoradiography	
6	1	Properties of different types of radioisotopes commonly used in biology	
7	1	Radioactivity, detection and measurement of radioactivity	
8	1	Safely guidelines and disposal procedures	
		Total no of hours planned for UNIT V = 9	
1	1	Revision- All five units summary	
2	1	Previous year End Semester Exam- QP discussion	
3	1	Previous year End Semester Exam- QP discussion	
		Total no of hours planned : 3	
Total no of hours required to complete the course: 48			

SUGGESTED READINGS

1. Burtis, C.A., and Edward R. Tietz, E.R., (1999) Textbook of Clinical Chemistry 3rd Edition, WB Saunders Harcourt Brace & Company Asia PTE Ltd., USA.

2. Lehninger, L., Nelson, D.L., and Cox, M.M., (2012). Principles of Biochemistry, WH Freeman and Company, 6th Edition, New York.

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

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(Deemed University Established Under Section 3 of UGC Act 1956)
Coimbatore - 641021.
(For the candidates admitted from 2018 onwards)
DEPARTMENT OF BIOCHEMISTRY

SUBJECT : **ENDOCRINOLOGY**
SEMESTER : **III**
SUBJECT CODE : **18BCP303** **CLASS** : **M.Sc., Biochemistry**

UNIT I

Unit I: General Introduction

General Introduction, Hypothalamo-hypophyseal axis, Chemical signaling – endocrine, paracrine, autocrine, intracrine and neuroendocrine mechanisms. Chemical classification of hormones, transport of hormones in the circulation and their half-lives. Hormone receptors – extracellular, transmembrane and intracellular. Receptor – hormone binding, Scatchard analysis, recycling and degradation of receptors. Releasing/release-inhibiting hormones (TRH, GnRH, CRH, GHRH, somatostatin, dopamine), their structure, secretion and regulation.

Hormones- Definition

Substances that provide the chemical basis for communication 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."

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%

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.

Classification of hormones

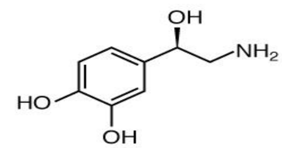
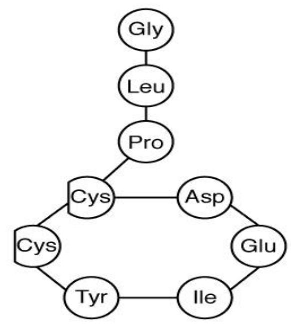
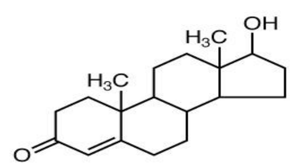
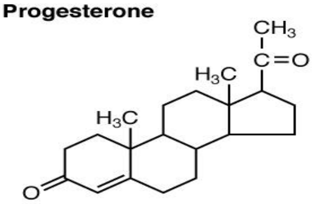
Chemical structure and synthesis of hormones

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

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.

In 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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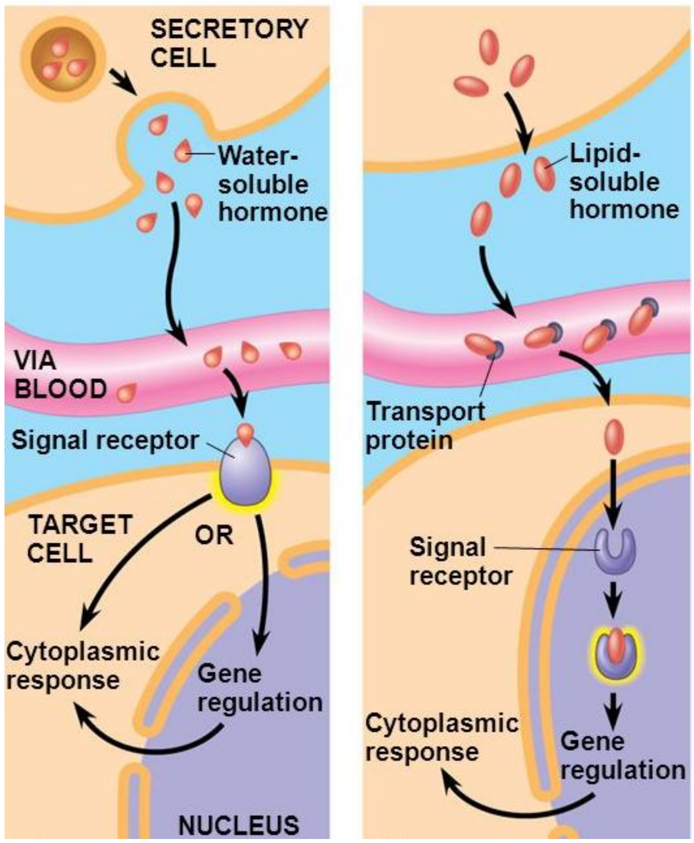


Hormonal secretion and transport

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.

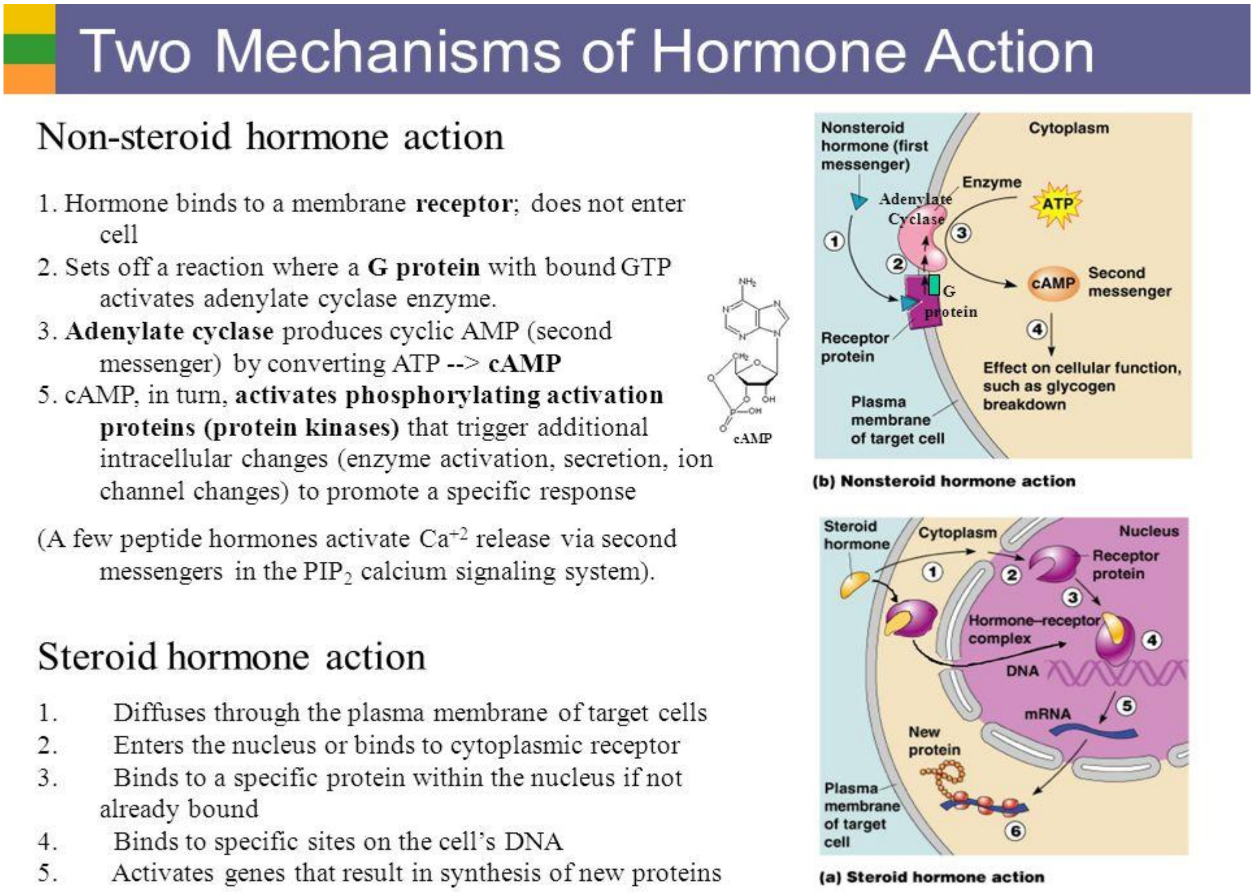
There are two main classes of hormone receptors. Receptors for peptide hormones tend to be cell surface receptors built into the plasma membrane of cells and are thus referred to as trans membrane receptors. An example of this is insulin

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

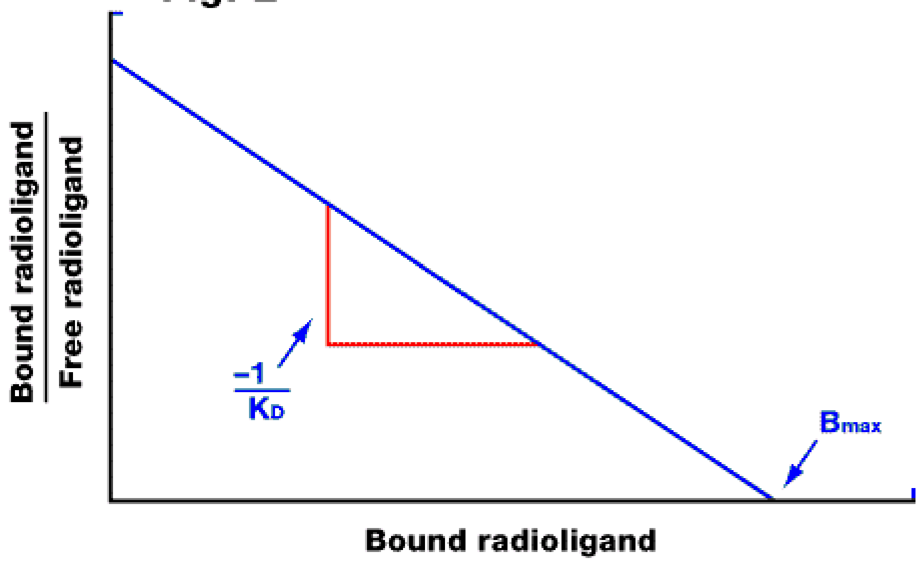
Second messengers are intracellular signaling molecules released by the cell to trigger physiological changes such as proliferation, differentiation, migration, survival, and apoptosis. Secondary messengers are therefore one of the initiating components of intracellular signal transduction cascades. 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



The Scatchard plot

It 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.



Application of Scatchard Plot

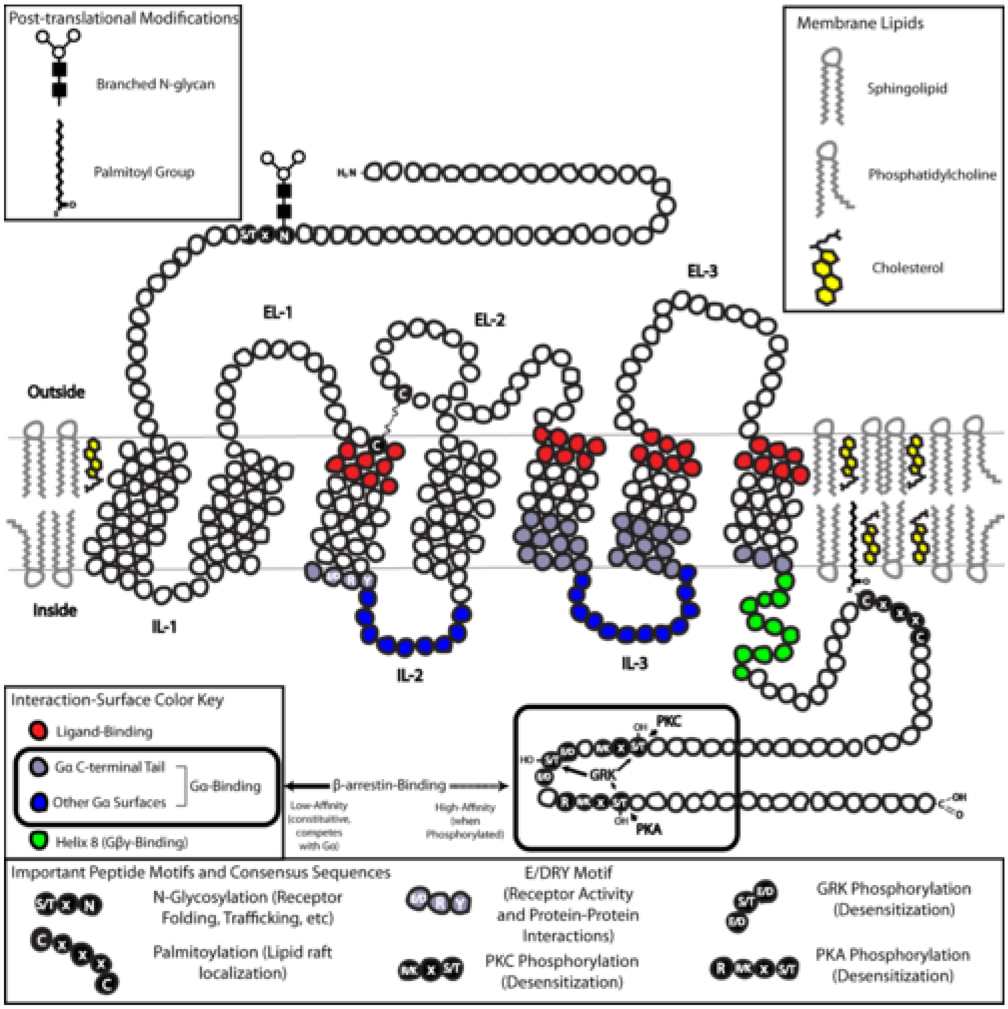
- To assess the number of ligand binding sites in the receptor
- To determine the IC50, ED50 of the drugs

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.

S. No	Question	Opt A	Opt B	Opt C	Opt D	Answer
1	_______ Hormone stimulates leydig cells to secrete testosterone	Scrotum	Epididymis	prostrate gland	cowpers gland	scrotum
2	Acetylcholinesterase is	nodes of Ranvier	dendrites	synapses	Schwann cells	Schwann cells
3	Action potentials	serotonin	dopamine	neuropeptides	norepinephrine	neuropeptides
4	After passing stimulus from receptors to sensory neurons , it passes then to	urea	concentrated urine	uric acid	ammonia	concentrated urine
5	All of the following neurotransmitters are biogenic amines except	axons	dendrites	neuron cell bodies	myelin sheaths	dendrites
6	Autonomic nervous system controls	motor neurons	sensory neurons	associative neurons	relay neurons	motor neurons
7	Autonomic nervous system is further divided into	voluntary movements	reflex actions	semi-voluntary movem	involuntary movements	involuntary movements
8	Between two neurons a microscopic gap exists which is the contact point of neurons called	sleep membrane potent	resting membrane poter	passive membrane pot	dormant membrane potential	resting membrane potential
9	Corpus luteum secretes	Placenta	Pregnancy	Fertilization	Ejaculation	Pregnancy
10	During saltatory conduction, a nerve impulse jumps from one _______________ to another.	neuromuscular junction:	nodes of Ranvier	inhibitory synapses	excitatory synapses	inhibitory synapses
11	Each testis is encased by a white fibrous membrane known as	Spermatogenesis	spermatic cord	spermiation	spermetazoa	spermiation
12	Fertilisation of human ovum is due to	Aldosterone	Testosterone	Coticosterone	Vasopressin	Testosterone
13	For each impulse autonomic nervous system utilizes only	axons	dendrites	cell body	myelin	myelin
14	GABA (gamma aminobutyric acid) is normally found at	dendrites	axon	myelin sheaths	hormones	dendrites
15	Graded potentials may become action potential by	are summable	are amplifiable	result from facilitated (	are all-or-nothing events	are all-or-nothing events
16	Human spermatozoa	Penetration of the ovum	Only one sperm is allow	May occur one week a	Usually occurs at the ampullary –Isth	Penetration of the ovum by the sperm brought about by a lysosomal enzyme present
17	In hydra nervous system is a network of neurons present between the	effectors	motor neurons	associative neurons	Back to receptors	associative neurons
18	In myelinated neurons the impulse jumps from node to node. This is called	node of ranvier	neuron bridges	synapse	gaps	synapse
19	In normal menstrual cycle	Require temperature lov	They are motile even wh	In the absence of fertil	Take about 45 min to pass from the c	Require temperature lower than that of the interior of body for their genesis
20	In sensory neurons, stimuli are received by the	summation	multiplication	hypopolarization	decreasing frequency	summation
21	Interstial cells of Leydig secrete	Prostrate gland	Epidymis	Seminiferous tubules	Ampulla	Seminiferous tubules
22	Leutinizing hormone releasing hormone is secreted in	Thyroxin	Calcitonin	Estrogen	Progesterone	Progesterone
23	Most of the sperms are stored in	Castration	Enuuchism	Frohlich's syndrome	Fibro adenoma	Castration
24	Name the hormone that regulates the water reabsorption in the distal tubule	Spermatogenesis	Cytogenesis	Oogenesis	Embryogenesis	Spermatogenesis
25	Nephrons have extensive blood supply by	cortical nephrons	medullar nephrons	juxtamedullary nephro	cortical and medullar nephrons	juxtamedullary nephrons
26	Nerve impulses are normally carried toward a neuron cell body by the neuron's	neurotransmitter	synapse	node of Ranvier	threshold	synapse
27	Neurons at rest (non-conducting neuron) has electric potential called	ectoderm and mesoderr	ectoderm and endoderm	endoderm and mesode	mesoderm and pericarp	ectoderm and endoderm
28	Neurotransmitters are released from vesicles at the	a neurotransmitter	an enzyme that breaks c	a stimulant that trigger	a hormone	an enzyme that breaks down a neurotransmitter
29	Oxytocin is secreted in	LH	Growth hormone	ACTH	PRL	LH
30	Postsynaptic membranes are most likely to be found on	myelin sheath	synapse	node of Ranvier	dendrite	node of Ranvier
31	Prolactin is secreted by	Vasderferens	Spermatids	Spermatogonia	Sertoli cells	Vasderferens
32	Semen also contains a hormone like substance known as	graffian follicle	zona pellucida	ovulation	ophorous	zona pellucida
33	Somatic nervous system is made up of	four neurons and two ga	two neurons and one ga	one neuron and one ga	one neuron and two ganglions	two neurons and one ganglion
34	Spermatogenesis occurs in	Pituitary gland	Ovaries	Hypothalamus	Adrenal gland	Hypothalamus
35	Sympathetic nervous system is associated with	three parts	two parts	four parts	five parts	two parts
36	The cell membrane of the oocyte is called as	Ovulation	cumulus oophorous	corpus leuteum	theca interna	Ovulation
37	The development of the young within the female reproductive system from the time of conception to childbirth is called	4 phases	3 phases	5 phases	6 phases	4 phases
38	The formation of sperm is known as	Sperm	Ovum	Both	None	Ovum
39	The hormone which is responsible for ovulation,formation of the corpus luteum and the secretion of the luteal hormone progesterone is	Diuretic hormone	Antidiuretic hormone	Lutenizing hormone	Follicle stimulating hormone	Antidiuretic hormone
40	The hormone which stimulus secretion of "Uterine milk" is	Adrenal gland	Posterior pituitary	Anterior pituitary	Parathyroid gland	Posterior pituitary
41	The inner end of nephrons is a cup shaped swelling structure known as	hormonal secretions	fear and rage	skeletal muscles	fight and flight	fight and flight
42	The junction between a neuron and its target cell is called a	cell body	dendrite	cell nucleus	presynaptic membrane	presynaptic membrane
43	The juxtamedullary nephrons are specialized for the production of	renal veins	renal arteries	hepatic arteries	peritoneal veins	renal arteries
44	The male organ for copulation is	Testosterone	Androgens	cumulus oophorus	antaglutins	Androgens
45	The menstrual fluid is normally non clotting because of the presence of	Proliferation	Ovulation	Secretory phase	Menstrual phase	Ovulation
46	The meta estrone phase is otherwise termed as	LH	Aldosterone	Vasopressin	FSH	FSH
47	The midbrain of vertebrates is also called the	cerebrum	forebrain	midbrain	hindbrain	hindbrain
48	The myelin sheath is formed by _______________, which wrap around the axons of some neurons.	maintain proper ionic co	generate the nerve impu	transmit the nerve imp	provide a source of Na+ and K+ by sp	maintain proper ionic concentration gradients across the neuron membrane
49	The nephrons which are arranged along the border of medulla looping deep in inner medulla are called	glomerulus	Bowman's capsule	medulla	cortex	Bowman's capsule

50	The neurotransmitter at neuromuscular junctions is	an unmyelinated, small (	an unmyelinated, large (	a myelinated, small dia	a myelinated, large diameter nerve	an unmyelinated, small diameter nerve
51	The outer surface of the ovary is covered by	Thrombolysin	Proteolysin	Anticoagulin	Fibrinolysin	Fibrinolysin
52	The phenomenon of the release of ovum from the graffian follicle is described as	LH	FSH	Relaxin	Progesterone	Progesterone
53	The primary function of the Graffian follicle is to form	Hypothalamus	Posterior pituitary	Anterior pituitary	Adrenal cortex	Anterior pituitary
54	The progestational phase of the endometrial cycle occur after	Pre-ovulatory phase	Ovulatory phase	Post ovulatory phase	None of the above	Ovulatory phase
55	The release of sperms from the sertoli cells is known as	Penis	Spermetagenisis	Spermetocytes	Spermetazoa	Penis
56	The role of the Na+/K+ pump in the nervous system is to	GABA	serotonin	acetylcholinesterase	acetylcholine	acetylcholine
57	The testes are small ovoid organs lodged in a pouch like structure called as	Tunica albicans	tunica albuginea	tunica degeneratum	septum	tunica albuginea
58	The testicular hormones are known as	Primordial follicles	Ligaments	Mesovaria	prostaglandins	prostagladins
59	When a boy loses his testes prior to puberty it leads to a condition called	Primodial follicle	Hilar connective tissue	Germinal epithelium	Fallopian tubes	Germinal epithelium
60	Which of the following should have the slowest conduction velocity?	medulla	mesencephalon	diencephalon	hypothalamus	mesencephalon

KARPAGAM ACADEMY OF HIGHER EDUCATION

(Deemed University Established Under Section 3 of UGC Act 1956)

Coimbatore - 641021.

(For the candidates admitted from 2018 onwards)

DEPARTMENT OF BIOCHEMISTRY

SUBJECT : **ENDOCRINOLOGY**

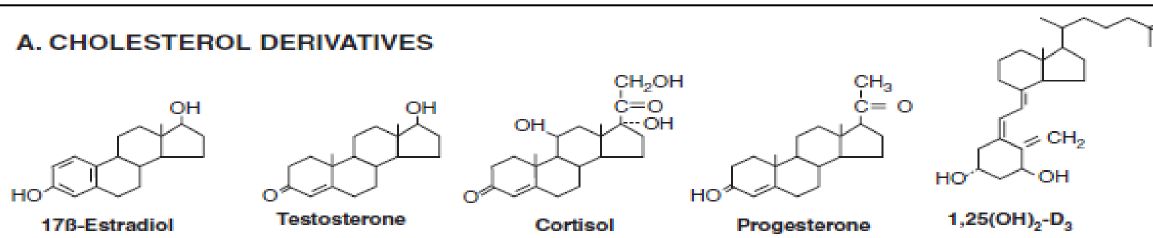
SEMESTER : **III**

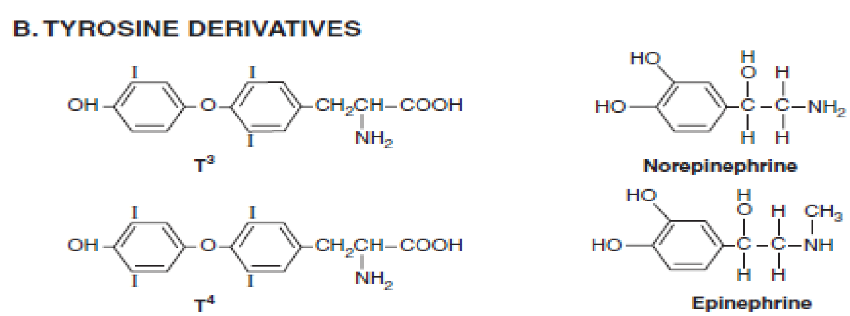
SUBJECT CODE : **18BCP303** **CLASS** : **M.Sc., Biochemistry**

UNIT II

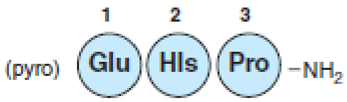
Unit II: Protein/Peptide hormones

Protein/Peptide hormones, Steroid and Thyroid hormones, GH, prolactin, ACTH, insulin, glucagon, PTH and calcitonin, and glycoprotein hormones (TSH, FSH, LH and hCG) – Structure, synthesis, secretion, regulation, transport and metabolism.

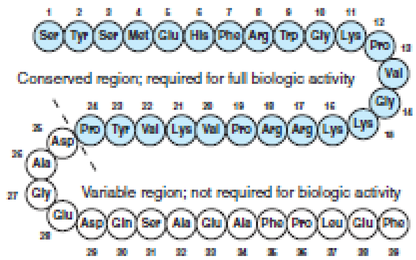




C. PEPTIDES OF VARIOUS SIZES



TRH



Structure of human ACTH.

ACTH

D. GLYCOPROTEINS (TSH, FSH, LH)

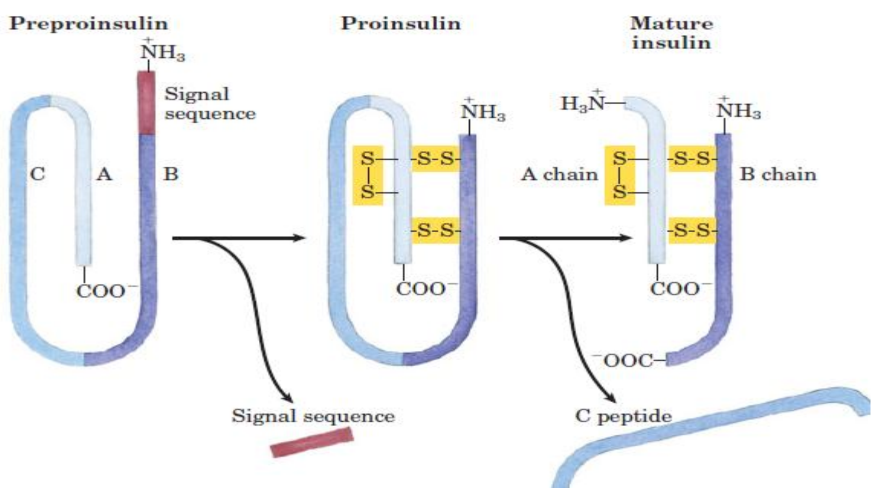
common α subunits
unique β subunits

Peptide Hormones

- Peptide hormones may have from 3 to 200 or more amino acid residues. They include the pancreatic hormones insulin, glucagon, and somatostatin; the parathyroid hormone , calcitonin; and all the hormones of the hypothalamus and pituitary . These hormones are synthesized on ribosomes in the form of longer precursor proteins (prohormones), then packaged into secretory vesicles and proteolytically cleaved to form the active peptides.
- **Insulin** is a small protein (Mr 5,800) with two polypeptide chains, A and B, joined by two disulfide bonds. It is synthesized in the pancreas as an inactive single-chain precursor, preproinsulin, with an amino-terminal"signal sequence" that directs its passage into secretory vesicles.
- Proteolytic removal of the signal sequence and formation of three disulfide bonds produces proinsulin, which is stored in secretory granules in pancreatic cells.
- When blood glucose is elevated sufficientlyto trigger insulin secretion, proinsulin is converted to active insulin by specific proteases, which cleave two peptide bonds to form the mature insulin molecule.
- In some cases, prohormone proteins, rather thanyielding a single peptide hormone, produce several active hormones. Pro-opiomelanocortin (POMC) is a spectacularexample of multiple

hormones encoded by a single gene. The POMC gene encodes a large polypeptide that is progressively carved up into at least nine biologically active peptides.

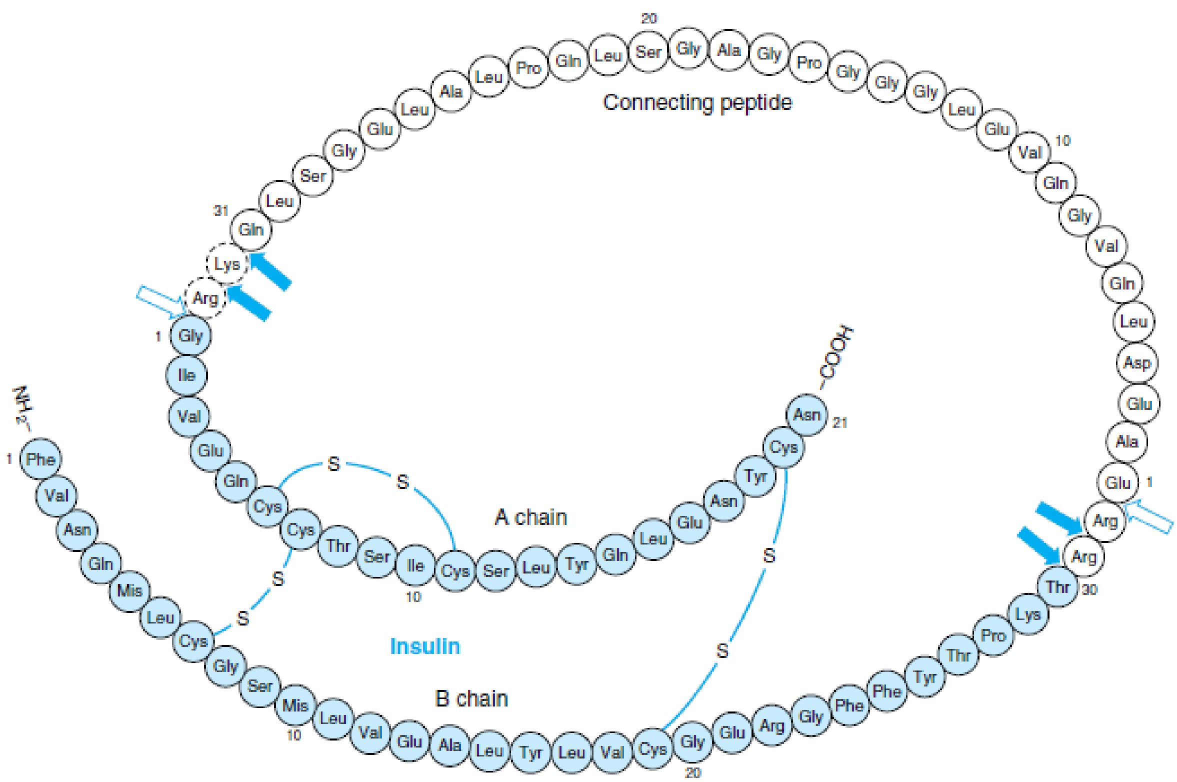
* In many peptide hormones the terminal residues are modified, as in TRH. The concentration of peptide hormones in secretory granules is so high that the vesicle contents are virtually crystalline; when the contents are released by exocytosis, a large amount of hormone is released suddenly.
* The capillaries that serve peptide-producing endocrine glands are fenestrated (and thus permeable to peptides), so the hormone molecules readily enter the bloodstream for transport to target cells elsewhere.
* All peptide hormones act by binding to receptors in the plasma membrane. They cause the generation of a second messenger in the cytosol, which changes the activity of an intracellular enzyme, thereby altering the cell's metabolism.



Insulin Is Synthesized as a Preprohormone & Modified Within the _ Cell

* Insulin has an AB heterodimeric structure with one intrachain (A6–A11) and two interchain disulfide bridges (A7–B7 and A20–B19). The A and B chains could be synthesized in the laboratory, but attempts at a biochemical synthesis of the mature insulin molecule yielded very poor results.

* The reason for this became apparent when it was discovered that insulin is synthesized as a **preprohormone** (molecular weight approximately 11,500), which is the prototype for peptides that are processed from larger precursor molecules.
* The hydrophobic 23-amino-acid pre-, or leader, sequence directs the molecule into the cisternae of the endoplasmic reticulum and then is removed.
* This results in the 9000- W proinsulin molecule, which provides the conformation necessary for the proper and efficient formation of the disulfide bridges. The sequence of proinsulin, starting from the amino terminal, is B chain—connecting (C) peptide—A chain.
* The proinsulin molecule undergoes a series of site-specific peptide cleavages that result in the formation of equimolar amounts of mature insulin and C peptide.



Thyroid hormones:

T_3 & T_4 Illustrate the Diversity in Hormone Synthesis:

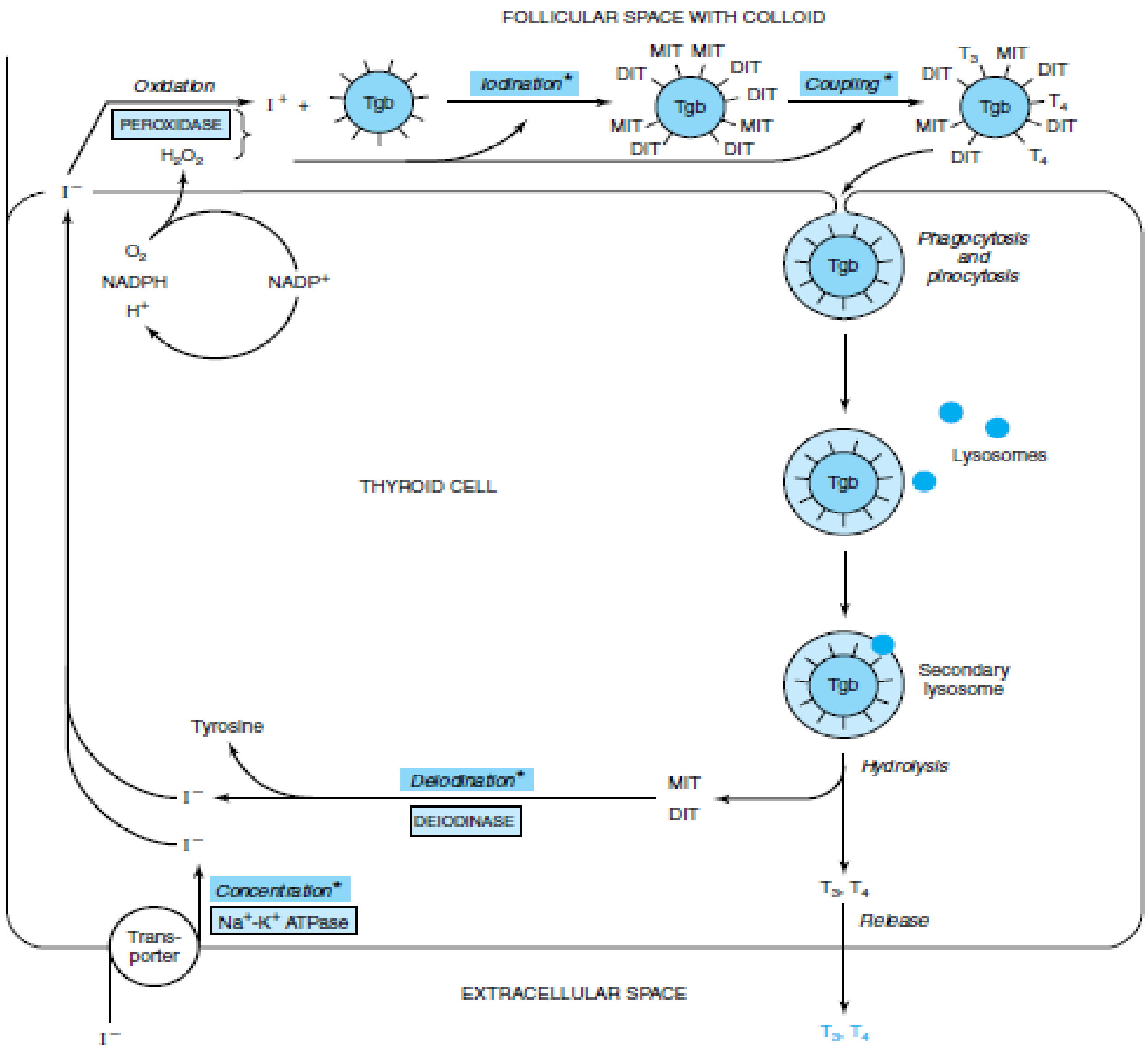
* The formation of **triiodothyronine (T3**) and **tetraiodothyronine (thyroxine; T4**) illustrates many of the principles of diversity discussed in this chapter
* . These hormones require a rare element (iodine) for bioactivity; they are synthesized as part of a very large precursor molecule (thyroglobulin); they are stored in an intracellular reservoir (colloid); and there is peripheral conversion of T4 to T3, which is a much more active hormone.
* The thyroid hormones T3 and T4 are unique in that iodine (as iodide) is an essential component of both. In most parts of the world, iodine is a scarce component of soil, and for that reason there is little in food.
* A complex mechanism has evolved to acquire and retain thiscrucial element and to convert it into a form suitable for incorporation into organic compounds. At the same time, the thyroid must synthesize thyronine from tyrosine, and this synthesis takes place in thyroglobulin.
* **Thyroglobulin** is the precursor of T4 and T3. It is a large iodinated, glycosylated protein with a molecular mass of 660 kDa. Carbohydrate accounts for 8–10% of the weight of thyroglobulin and iodide for about 0.2–1%, depending upon the iodine content in the diet. Thyroglobulin is composed of two large subunits.
* It contains 115 tyrosine residues, each of which is a potential site of iodination. About 70% of the iodide in thyroglobulin exists in the inactive precursors, **monoiodotyrosine (MIT)** and **diiodotyrosine (DIT),** while 30% is in the **iodothyronyl residues,** T4 and T3. When iodine supplies are sufficient, the T4:T3 ratio is about 7:1.
* In **iodine deficiency,** this ratio decreases, as does the DIT:MIT ratio. Thyroglobulin, a large molecule of about 5000 amino acids, provides the conformation required for tyrosyl coupling and iodide organification necessary in the formation of the diaminoacid thyroid hormones.
* It is synthesized in the basal portion of the cell and moves to the lumen, where it is a storage form of T3 and T4 in the colloid; several weeks' supply of these hormones exist in the normal thyroid. Within minutes after stimulation of the thyroid by TSH, colloid reenters the cell and there is a marked increase of phagolysosome activity.

* Various acid proteases and peptidases hydrolyze the thyroglobulin into its constituent amino acids, including T4 and T3, which are discharged from the basal portion of the cell. Thyroglobulin is thus a very large prohormone.

Iodide Metabolism Involves Several Discrete Steps:

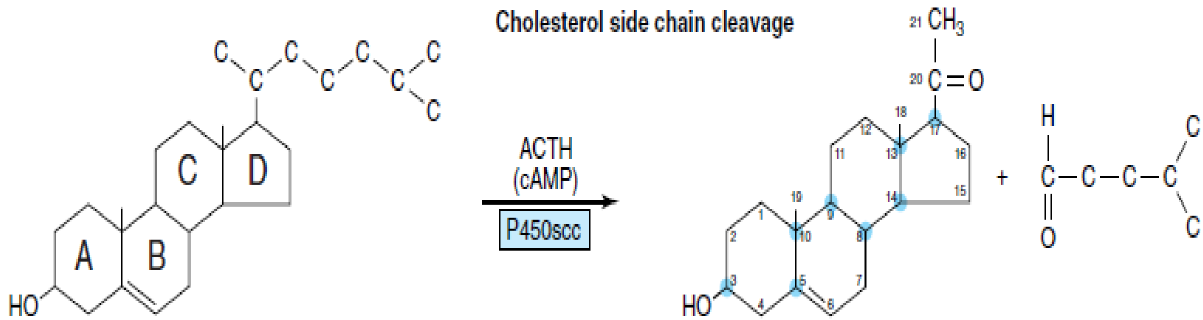
* The thyroid is able to concentrate I− against a strong electrochemical gradient. This is an energy-dependent process and is linked to the Na+-K+ ATPase-dependent thyroidal I− transporter. The ratio of iodide in thyroid to iodide in serum (T:S ratio) is a reflection of the activity of this transporter.
* This ativity is primarily controlled by TSH and ranges from 500:1 in animals chronically stimulated with TSH to 5:1 or less in hypophysectomized animals (no TSH).
* The T:S ratio in humans on a normal iodine diet is about 25:1. The thyroid is the only tissue that can oxidize I− to a higher valence state, an obligatory step in I− organification and thyroid hormone biosynthesis.
* This step involves a heme-containing peroxidase and occurs at the luminal surface of the follicular cell. Thyroperoxidase, a tetrameric protein with a molecular mass of 60 kDa, requires hydrogen peroxide as an oxidizing agent.
* The H2O2 is produced by an NADPH-dependent enzyme resembling cytochrome *c* reductase. A number of compounds inhibit I− oxidation and therefore its subsequent incorporation into MIT and DIT.
* The most important of these are the thiourea drugs. They are used as antithyroid drugs because of their ability to inhibit thyroid hormone biosynthesis at this step. Once iodination occurs, the iodine does not readily leave the thyroid.
* Free tyrosine can be iodinated, but it is not incorporatedinto proteins since no tRNA recognizes iodinated tyrosine. The coupling of two DIT molecules to form T4—or of an MIT and DIT to form T3—occurs within the thyroglobulin molecule.
* A separate coupling enzyme has not been found, and since this is an oxidative process it is assumed that the same thyroperoxidase catalyzes this reaction by stimulating free radical formationof iodotyrosine.

* This hypothesis is supported by the observation that the same drugs which inhibit I− oxidation also inhibit coupling. The formed thyroid hormones remain as integral parts of thyroglobulin until the latter is degraded, as described above.
* A deiodinase removes I− from the inactive monoand diiodothyronine molecules in the thyroid. This mechanism provides a substantial amount of the I− used in T3 and T4 biosynthesis.
* A peripheral deiodinase in target tissues such as pituitary, kidney, and liver selectively removes I− from the 5′ position of T4 to make T3, which is a much more active molecule. In this sense, T4 can be thought of as a prohormone, though it does have some intrinsic activity.



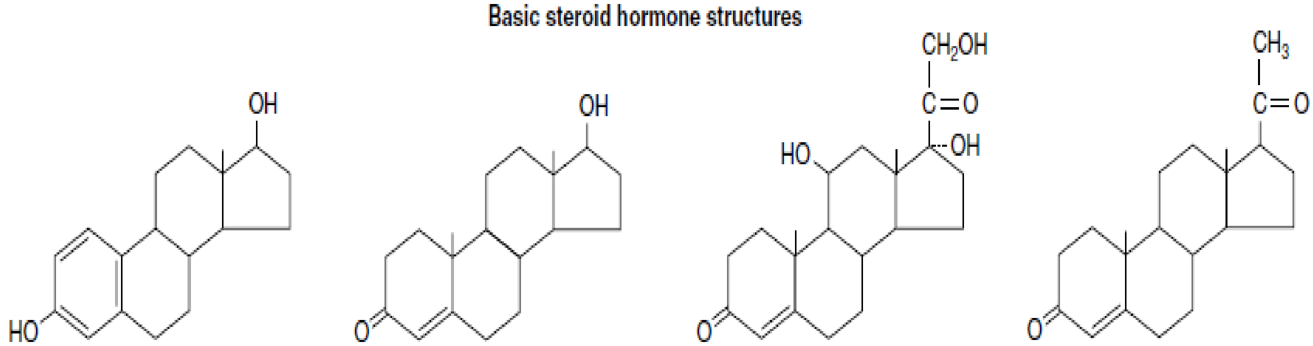
Steroid Hormones:

Cholesterol side chain cleavage



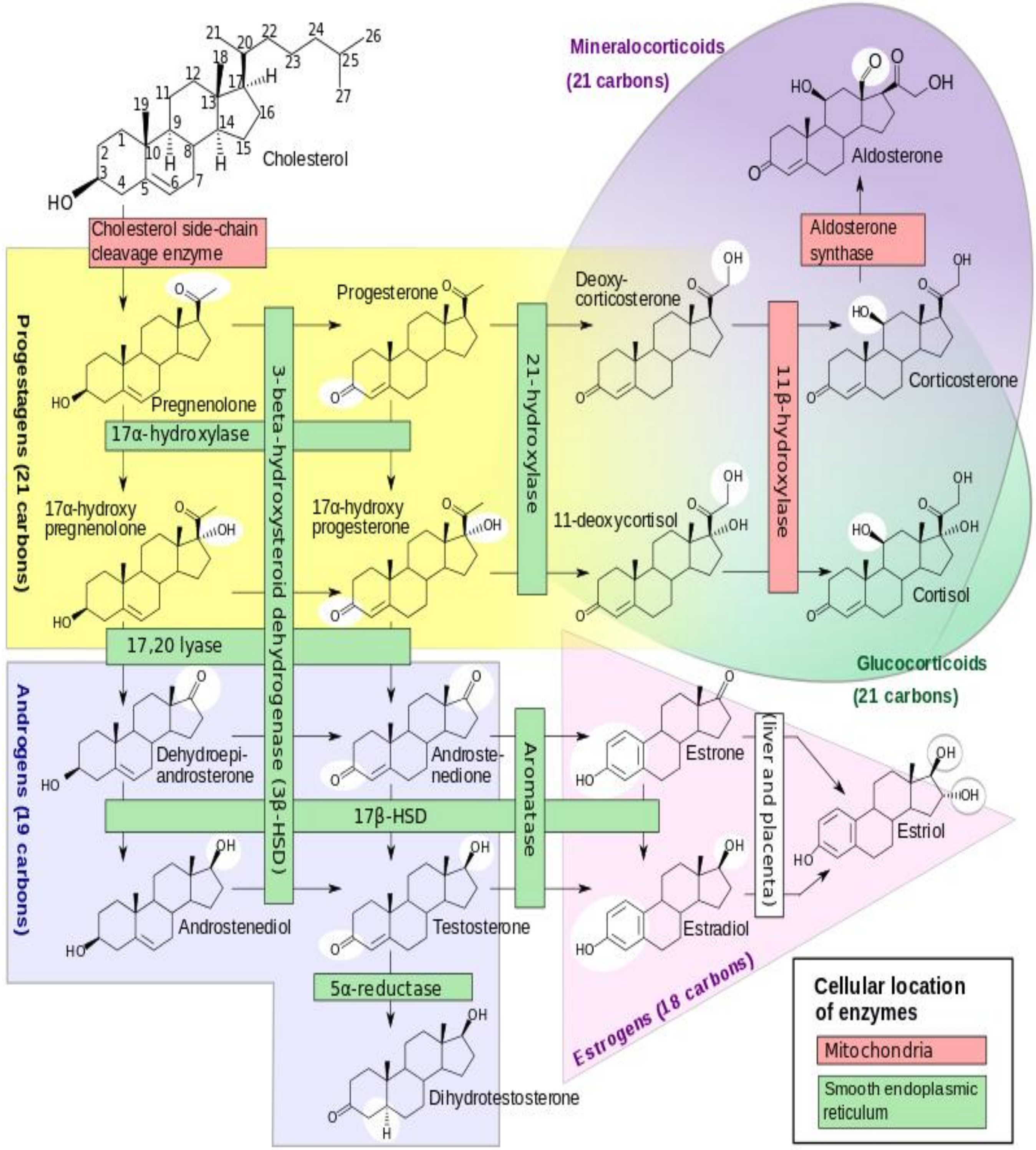
Cholesterol | Pregnenolone + isocaproaldehyde

Basic steroid hormone structures



17β—Estradiol | Testosterone | Cortisol | Progesterone

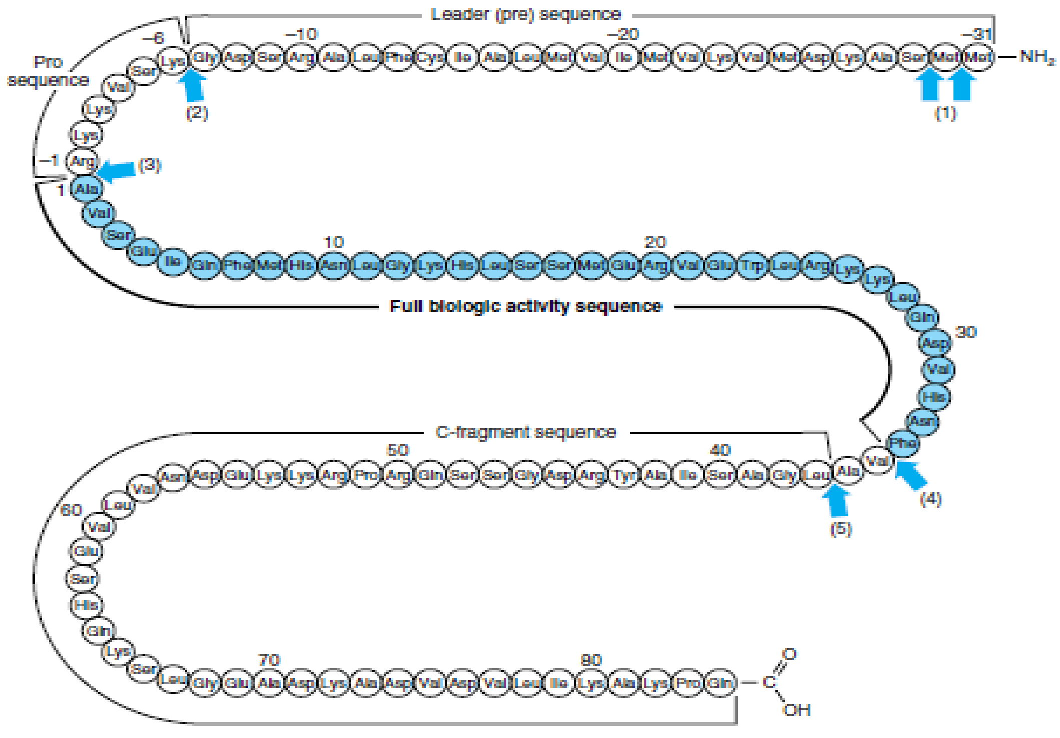
Estrane group (C18) | Androstane group (C19) | Pregnane group (C21)



Cholesterol
Cholesterol side-chain cleavage enzyme
Mineralocorticoids (21 carbons)
Aldosterone
Aldosterone synthase
Progestagens (21 carbons)
Pregnenolone
Progesterone
Deoxy-corticosterone
Corticosterone
17α-hydroxylase
3-beta-hydroxysteroid dehydrogenase (3β-HSD)
21-hydroxylase
11β-hydroxylase
17α-hydroxy pregnenolone
17α-hydroxy progesterone
11-deoxycortisol
Cortisol
17,20 lyase
Glucocorticoids (21 carbons)
Androgens (19 carbons)
Dehydroepi-androsterone
Androste-nedione
Aromatase
Estrone
(liver and placenta)
Estriol
17β-HSD
Androstenediol
Testosterone
Estradiol
Estrogens (18 carbons)
5α-reductase
Dihydrotestosterone
Cellular location of enzymes
Mitochondria
Smooth endoplasmic reticulum

Parathyroid Hormone (PTH):

* The immediate precursor of PTH is **proPTH,** which differs from the native 84-amino-acid hormone by having a highly basic hexapeptide amino terminal extension. The primary gene product and the immediate precursor for proPTH is the 115-amino-acid **preproPTH.**
* This differs from proPTH by having an additional 25- amino-acid amino terminal extension that, in common with the other leader or signal sequences characteristic of secreted proteins, is hydrophobic. The complete structure of preproPTH and the sequences of proPTH and PTH . PTH1–34 has full biologic activity, and the region 25–34 is primarily responsible for receptor binding.
* The biosynthesis of PTH and its subsequent secretion are regulated by the plasma ionized calcium (Ca^{2+}) concentration through a complex process. An acute decrease of Ca^{2+} results in a marked increase of PTH mRNA, and this is followed by an increased rate of PTH synthesis and secretion.
* It was later discovered that this rate of degradation decreases when Ca^{2+} concentrations are low, and it increases when Ca^{2+} concentrations are high. Very specificfragments of PTH are generated during its proteolytic digestion.
* A number of proteolyticenzymes, including cathepsins B and D, have been identified in parathyroid tissue. Cathepsin Bcleaves PTH into two fragments: PTH1–36 and PTH37–84. PTH37–84 is not further degraded; however, PTH1–36 is rapidly and progressively cleaved into diand tripeptides.
* Most of the proteolysis of PTH occurs within the gland, but a number of studies confirm that PTH, once secreted, is proteolytically degraded in other tissues, especially the liver, by similar mechanisms.



Glucagon Opposes the Actions of Insulin:

- Glucagon is the hormone produced by the A cells of the pancreatic islets. Its secretion is stimulated by hypoglycemia.
- In the liver, it stimulates glycogenolysis by activating phosphorylase. Unlike epinephrine, glucagon does not have an effect on muscle phosphorylase.
- Glucagon also enhances gluconeogenesis from amino acids and lactate. In all these actions, glucagon acts via generation of cAMP . Both hepatic glycogenolysis and gluconeogenesis contribute to the **hyperglycemic effect** of glucagon, whose actions oppose those of insulin. Most of the endogenous glucagon (and insulin) is cleared from the circulation by the liver.
- Glucagon causes an increase in blood glucose concentration in several ways. Like epinephrine, it stimulates the net breakdown of liver glycogen by activating glycogen phosphorylase and inactivating glycogen synthase; both effects are the result of phosphorylation of the regulated enzymes, triggered by cAMP.
- Glucagon inhibits glucose breakdown by glycolysis in the liver, and stimulates glucose synthesis by gluconeogenesis. Both effects result from lowering the concentration of fructose 2,6-

bisphosphate, an allosteric inhibitor of the gluconeogenic enzyme fructose 1,6-bisphosphatase (FBPase-1) and an activator of the glycolytic enzyme phosphofructokinase-1.

* Recall that [fructose 2,6-bisphosphate] is ultimately controlled by a cAMP-dependent protein phosphorylation reaction. Glucagon also inhibits the glycolytic enzyme pyruvate kinase (by promoting its cAMP-dependent phosphorylation), thus blocking the conversion of phosphoenolpyruvate to pyruvate and preventing oxidation of pyruvate via the citric acid cycle.
* The resulting accumulation of phosphoenolpyruvate favors gluconeogenesis. This effect is augmented by glucagon's stimulation of the synthesis of the gluconeogenic enzyme PEP carboxykinase.
* By stimulating glycogen breakdown, preventing glycolysis, and promoting gluconeogenesis in hepatocytes, glucagon enables the liver to export glucose, restoring blood glucose to its normal level.

TABLE 23–4 Effects of Glucagon on Blood Glucose: Production and Release of Glucose by the Liver

Metabolic effect	Effect on glucose metabolism	Target enzyme
↑ Glycogen breakdown (liver)	Glycogen ⟶ glucose	↑ Glycogen phosphorylase
↓ Glycogen synthesis (liver)	Less glucose stored as glycogen	↓ Glycogen synthase
↓ Glycolysis (liver)	Less glucose used as fuel in liver	↓ PFK-1
↑ Gluconeogenesis (liver)	Amino acids, Glycerol, Oxaloacetate } ⟶ glucose	↑ FBPase-2 ↓ Pyruvate kinase ↑ PEP carboxykinase
↑ Fatty acid mobilization (adipose tissue)	Less glucose used as fuel by liver, muscle	↑ Hormone-sensitive lipase ↑ PKA (perilipin—P)
↑ Ketogenesis	Provides alternative to glucose as energy source for brain	↓ Acetyl-CoA carboxylase

S. No.	Question	Opt A	Opt B	Opt C	Opt D	Answer
1	A blockage within the heart arteries caused by the death of heart muscle cells is known as:	an embolism	an infarct	an abscess	a trachanter	an infarct
2	All arteries of the body flow:	to the liver	to the brain	away from the lungs	away from the heart	away from the lungs
3	All the following apply to the bicuspid valve except:	it is also called the mitral valve	it is a semilunar valve	it is found on the left side of the heart	it prevents blood from backing into the left atrium	it is a semilunar valve
4	All the following have the ability to regulate blood flow in the body except:	antidiuretic hormone	epinephrine and norepinephrine	chemoreceptors	enzymes from the salivary glands	enzymes from the salivary glands
5	A-V valve on the right side is:	Mitral valve	Tricuspid valve	Aortic valve	Pulmonary valve	Mitral valve
6	Back flow of blood is prevented by valve classified as	Bronchial valve	Lymphatic valve	Atria vale	Thebesian valve	Thebesian valve
7	Blood flowing through a vein tends to:	pulse	flow smoothly	carry oxygen to the body cells	flow at a faster rate than in the artery	flow smoothly
8	Blood returning to the heart from the body organs enters the:	left atrium through the aorta	right atrium through the vena cava	left ventricle by the pulmonary artery	right ventricle by the pulmonary vein	right atrium through the vena cava
9	BP component, which does not show fluctuations:	Systolic pressure	Diastolic pressure	Pulse pressure	Mean pressure	Diastolic pressure
10	Bradycardia in athletes is because:	Increased sympathetic tone	Increased vagal tone	Decreased cardiac output	Low venous return	Increased vagal tone
11	Cardiac index is the ratio of	Cardiac output to the body weight	Cardiac output to the body surface area	Cardiac output to work of heart	Stroke volume to body surface area	Cardiac output to the body surface area
12	Cardiac output is not decreased in	Acute venous dilation	Beriberi	Cardiac tamponade	Myocardial infarction	Beriberi
13	Each small square in ECG paper represents a voltage of:	1 mV	0.1 mV	0.2 mV	0.5 mV	0.1 mV

14	Each small square in EEG paper represents:	0.02 sec	0.04 sec	0.5 sec	1 sec	0.04 sec
15	Fourth heart beat sound is heard in:	Early ventricular diastole	Late ventricular diastole	Early ventricular systole	Late ventricular systole	Late ventricular diastole
16	If the heart’s natural pacemaker fails to fire, then:	no blood would enter the atria	no blood would enter the ventricles	the node on the floor of the right atrium would act as a secondary pacemaker	the node on the floor of the left ventricle would act as a secondary pacemaker	the node on the floor of the right atrium would act as a secondary pacemaker
17	If you decrease a blood vessel's radius in half, by what fraction does the blood flow change?	1/2	1/4	1/8	1/16	1/16
18	Immediately following strenuous and vigorous exercise, which of the following is most likely to occur?	blood will be rapidly diverted to the digestive organs	the skin will be cold and clammy	capillaries of the active muscles will be engorged with blood	blood flow to the kidneys quickly increases	capillaries of the active muscles will be engorged with blood
19	Intercalated disks are found:	between the right side and right side of the heart	between the flaps of the tricuspid valve	where the aorta joins the pulmonary artery	between the cardiac muscle cells	between the cardiac muscle cells
20	Mean blood pressure means	Systolic pressure + diastolic pressure /2	Systolic pressure + diastolic pressure	Systolic pressure + 1/3 pulse pressure	Diastolic pressure + 1/3 pulse pressure	Diastolic pressure + 1/3 pulse pressure
21	Most of the cardiac muscle of the heart is found in the:	endocardium	epicardium	myocardium	pericardium	myocardium
22	Nervous control of the heart can be exerted by:	nerves from the thoracic region of the spinal column	the second and third cranial nerves	by fibers of the sensory somatic system	by fibers of the autonomic nervous system	by fibers of the autonomic nervous system
23	Normal end diastolic volume is:	75 mL	100 mL	110-120 mL	130-150 mL	110-120 mL
24	Normal end systolic volume is:	40-50 mL	50-60 mL	60-70 mL	75-80 mL	40-50 mL
25	Prime contributor of atherosclerosis is	accumulation of monocytes	accumulation of mesophyll	accumulation of albumin	accumulation of cholesterol	accumulation of mesophyll
26	Study of properties of blood flow is classified as	physiology	hemodynamic	hemorheology	cardiology	hemorheology
27	The arteries supplying blood to the tissue of the heart are the:	renal arteries	myocardial arteries	coronary arteries	vena cavae	coronary arteries
28	The blood pressure is measured by an instrument known as a:	electrocardiogram	electroencephalograph	sphygmomanometer	CAT scan machine	sphygmomanometer

29	The bundle of His:	is found in the aorta	is a group of Purkinje fibers	prevents the mitral valve from flapping backward	is a group of arteries that supply the heart	is a group of Purkinje fibers
30	The circulatory pathway that carries blood from the digestive tract towards the liver is termed the:	coronary circuit	cerebral circuit	hepatic portal circuit	pulmonary circuit	hepatic portal circuit
31	The condition called arrhythmia is characterized by:	rapid heart contraction	irregular heart rhythms	mitral valve prolapse	semilunar valve dysfunction	irregular heart rhythms
32	The exchange of gases and nutrients between blood and tissues is a major function of:	arterioles	arteries	capillaries	veins	capillaries
33	The heart’s electrical conduction network found within the ventricular myocardium is termed the:	sinoatrial node	bundle of His/atrioventricular bundle	left and right bundle branches	Purkinje fibers	Purkinje fibers
34	The heart’s natural pacemaker is termed the:	sinoatrial node	bundle of His/atrioventricular bundle	left and right bundle branches	Purkinje fibers	sinoatrial node
35	The hepatic portal vein transports blood:	from the heart to the liver	from the liver to the spleen	from the gastrointsestinal tract to the liver	from the liver to the gastrointerstinal tract	from the gastrointsestinal tract to the liver
36	The interventricular septum and the intra-atrial septum separate the:	chambers of the heart	chambers of the lungs	aorta and pulmonary artery	bicuspid and tricuspid valves	chambers of the heart
37	The lining of the inner walls of the heart’s chambers is termed the:	visceral pericardium	epicardium	myocardium	endocardium	endocardium
38	The only vein in the body that transports oxygen-rich blood is the:	coronary vein	hepatic portal vein	pulmonary vein	aortic vein	pulmonary vein
39	The outermost layer of the heart’s serous pericardium is termed the:	visceral pericardium	parietal pericardium	epicardium	myocardium	parietal pericardium
40	The peak pressure of atrial systole is:	7-8 mm Hg	8-15 mm Hg	15-20 mm Hg	20-25 mm Hg	7-8 mm Hg
41	The pericardium is the double sac membrane that:	encloses the heart	line the aorta	makes up the heart valves	is found only in the capillaries	encloses the heart
42	The PR interval of ECG corresponds to	ventricular repolarization	ventricular repolarization	atrial repolarization and conduction through AV node	repolarization of AV node and bundle of His	atrial repolarization and conduction through AV node

43	The pulse rate of a normal individual averages about:	10 beats per minute	40 beats per minute	50 beats per minute	70 beats per minute	70 beats per minute
44	The semilunar valves prevent blood from flowing backwards:	into the atria	into the ventricles	into the brain	into the liver	into the ventricles
45	The systemic circuit of the cardiovascular system extends:	from the heart to the lungs	from heart to the coronary arteries	from the heart to the body's organs and tissues	from the gastrointestinal tract to the liver	from the heart to the body's organs and tissues
46	The 'T' wave in ECG is above the isoelectric line because of	depolarisation of ventricles	depolarisation of bundle of His	change in the direction of repolarisation from the wave of depolarization of the ventricles	repolarisation of purkinje fibres	change in the direction of repolarisation from the wave of depolarization of the ventricles
47	The term vasoconstriction refers to:	increasing the size of the lumen of the blood vessel	decreasing the size of the lumen of the blood vessel	delivering oxygen and nutrients to the body tissues	delivering waste products to the kidney for excretion	decreasing the size of the lumen of the blood vessel
48	The terms systole and diastole refer to:	sounds from the heart	the major artery and vein from and to the heart	heart contractions and relaxations	rates of heart pulse	heart contractions and relaxations
49	Venous return depends upon	Velocity of blood	Increased mean systemic filling pressure	Cardiac output	Stiffness of vessel	Increased mean systemic filling pressure
50	Ventricular depolarization in ECG is seen as:	P-wave	QRS complex	T-wave	ST segment	QRS complex
51	Which is the most desirable blood pressure (taken as average of 2 consecutive measurements at one point in time)?	180/110mmHg	140/80mmHg	120/80mm	80/60mmHg	120/80mm
52	Which of the following agents helps to increase the Ca storage capacity of the SR in the heart?	dihydropyridines	ryanodine	calsequestrin	acetylcholine	calsequestrin
53	Which of the following applies to the sinoatrial node?	it is a mass of nerve cells	it produces important enzymes	it generates autorhythmic impulses to contract the heart	it contains both bicuspid and tricuspid valves	it generates autorhythmic impulses to contract the heart
54	Which of the following blood vessels has the greatest compliance?	Arteries	Veins	Arterioles	Capillaries	Veins

55	Which of the following is a correct formula for the mean arterial blood pressure?	MAP = CO X SV	MAP = CO X HR	MAP = SV X HR X TPR	MAP = HR X TPR	MAP = SV X HR X TPR
56	Which of the following is usually the dominant pacemaker and fires the fastest?	SA node	AV node	His bundle	Purkinje fibers	SA node
57	Which of the following represents the flow of blood from the heart to the body organs and back to the heart?	venules to capillaries to veins to arteries	arteries to capillaries to veins	capillaries to arterioles to arteries to veins	veins to arteries to capillaries to arterioles	arteries to capillaries to veins
58	Which of the following statements best describes arteries?	all arteries carry oxygenated blood towards the heart	all arteries contain valves to prevent the back-flow of blood	all arteries carry blood away from the heart	only large arteries are lined with endothelium	all arteries carry blood away from the heart
59	Which of these vessels does not have sympathetic control	cerebral	splanchnic	cardiac	cutaneous	cerebral
60	Which tunic of an artery contains endothelium?	tunica interna/intima	tunica media	tunica externa	tunica adventitia	tunica interna/intima

KARPAGAM ACADEMY OF HIGHER EDUCATION
(Deemed University Established Under Section 3 of UGC Act 1956)
Coimbatore - 641021.
(For the candidates admitted from 2018 onwards)
DEPARTMENT OF BIOCHEMISTRY

SUBJECT : ENDOCRINOLOGY
SEMESTER : III
SUBJECT CODE : 18BCP303 CLASS : M.Sc., Biochemistry

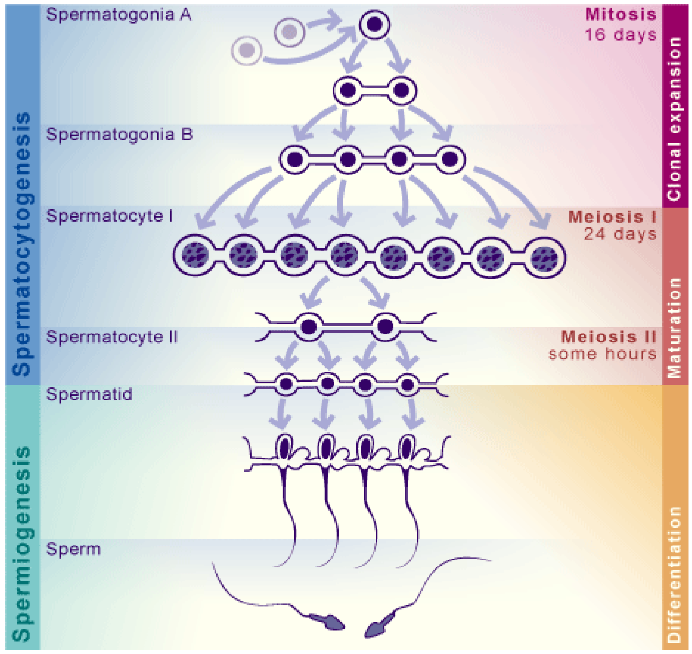
UNIT III

Unit III: Hormones and gonads

Physiological action of hormones in the regulation of spermatogenesis, sperm maturation, oogenesis and menstrual/estrus cycles. Gonadal and adrenal steroidogenesis. Cell-cell communication – Two cell concept. Hormonal control of implantation, gestation, parturition and lactation; hormonal contraception. Semen analysis.

Physiological action of hormones in the regulation of spermatogenesis, sperm maturation:

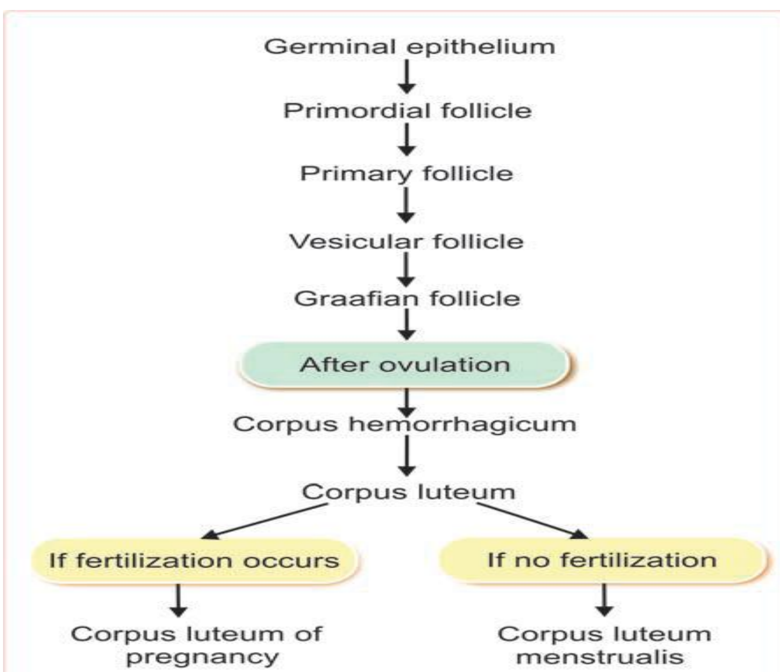
- Spermatogenesis occurs in the seminiferous tubules. The mammalian testes are divided into many lobules, and each lobule contains many tiny seminiferous tubules. Sperm develop in an ordered fashion in these tubules. Cells start to mature on the outside and move inward (towards the lumen) as the become mature sperm.
- Spermatogonia are the most primative cells. They differentiate as primary spermatocyte $\rightarrow$ secondary $\rightarrow$ spermatid $\rightarrow$ sperm are released into lumen. Sertoli cells are supporting cells that stretch from the lumen to the edge of the tubule.
- They nourish the developing sperm. They form a blood-testis barrier to control spermatogenesis (similar to the blood-brain barrier). These cells also inhibit spermatogenesis before puberty and stimulate the process after puberty.
- Spermiogenesis is the maturation process into sperm. The golgi vesicles combine to form an acrosomal vesicle that lies over the nucleus. Its full of enzymes. Centrosomes start to organize microtubules into long flagella Mitochondria start to localize next to the flagella to provide ready energy.
- The nucleus condenses in size and is stabilized by special proteins called protamines. The excess cytoplasm is pinched off as a residual body (no need for organelles and cytoplasmic proteins).



Oogenesis and menstrual/estrus cycles:

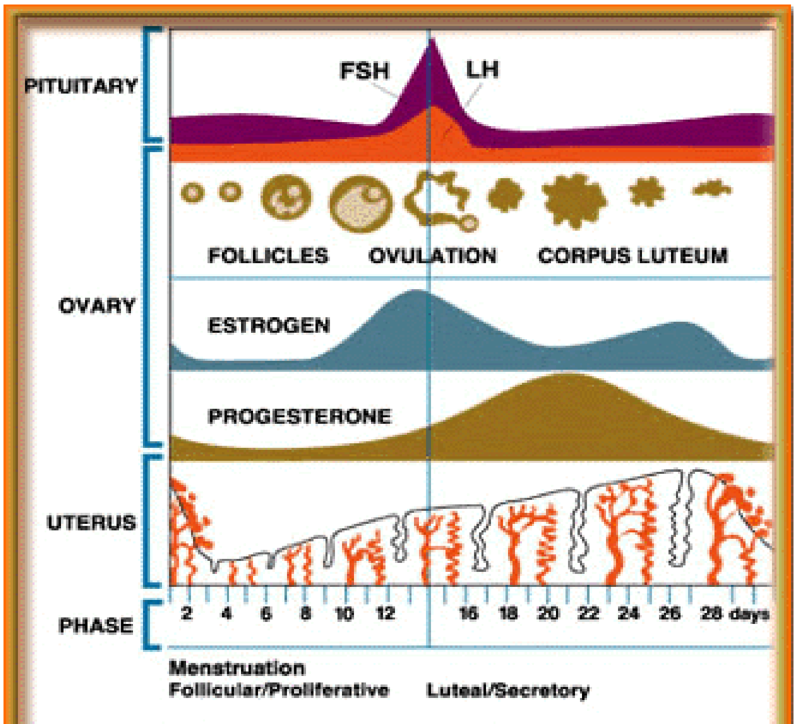
- The process of formation of egg or ovum is called ad Oogenesis.
- This process was done by three steps.

a).Multiplication phase, b).Growth phase and c).Maturation phase



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.



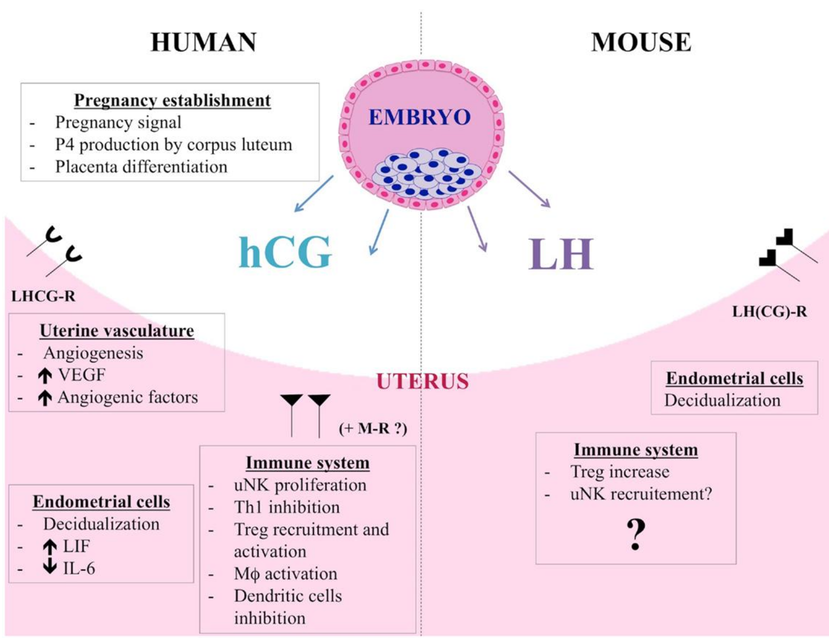
The Hormonal Cycle

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

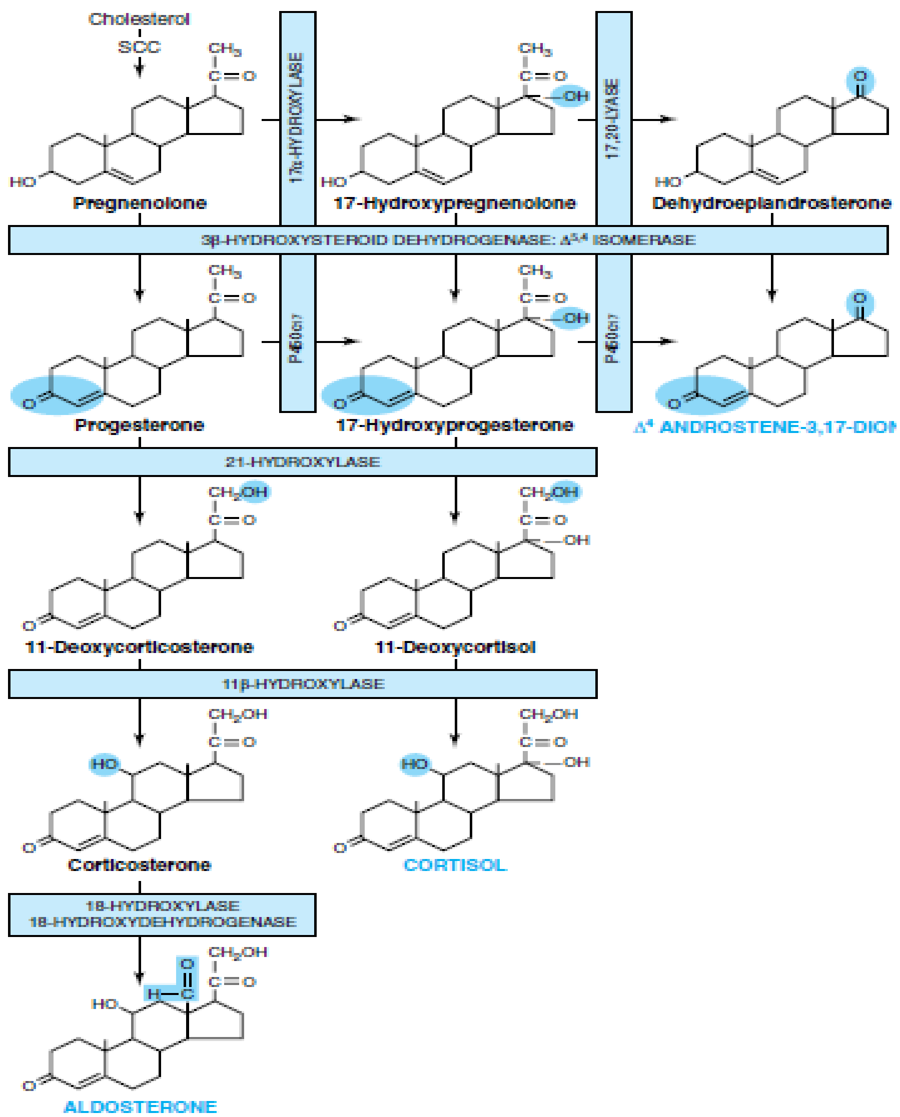
Hormone	Source	Effect
Human Chorionic Gonadotropin	Placenta	Maintains corpus luteum until week 12
Estrogen/Progesterone	Corpus luteum/ placenta	Stimulate and maintain uterine lining, inhibit FSH and LH, inhibit uterine contractions, and enlarge reproductive organs
Relaxin	Corpus luteum/ placenta	(Possible: 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

Adrenal Steroidogenesis

- The adrenal steroid hormones are synthesized from cholesterol. Cholesterol is mostly derived from the plasma, but a small portion is synthesized in situ from acetyl-CoA via mevalonate and squalene. Much of the cholesterol in the adrenal is esterified and stored in cytoplasmic lipid droplets.
- Upon stimulation of the adrenal by ACTH, an esterase is activated, and the free cholesterol formed is transported into the mitochondrion, where a cytochrome P450 side chain cleavage enzyme (P450scc) converts cholesterol to pregnenolone.
- Cleavage of the side chain involves sequential hydroxylations, first at C22 and then at C20, followed by side chain cleavage (removal of the six-carbon fragment isocaproaldehyde) to give the 21-carbon .
- An ACTH-dependent steroidogenic acute regulatory (StAR) protein is essential for the transport of cholesterol to P450scc in the inner mitochondrial membrane. All mammalian steroid hormones are formed from cholesterol via pregnenolone through a series of reactions that occur in either the mitochondria or endoplasmic reticulum of the adrenal cell.
- Hydroxylases that require molecular oxygen and NADPH are essential, and dehydrogenases, an isomerase, and a lyase reaction are also necessary for certain steps.
- There is cellular specificity in adrenal steroidogenesis. For instance, 18- hydroxylase and 19-hydroxysteroid dehydrogenase, which are required for aldosterone synthesis, are

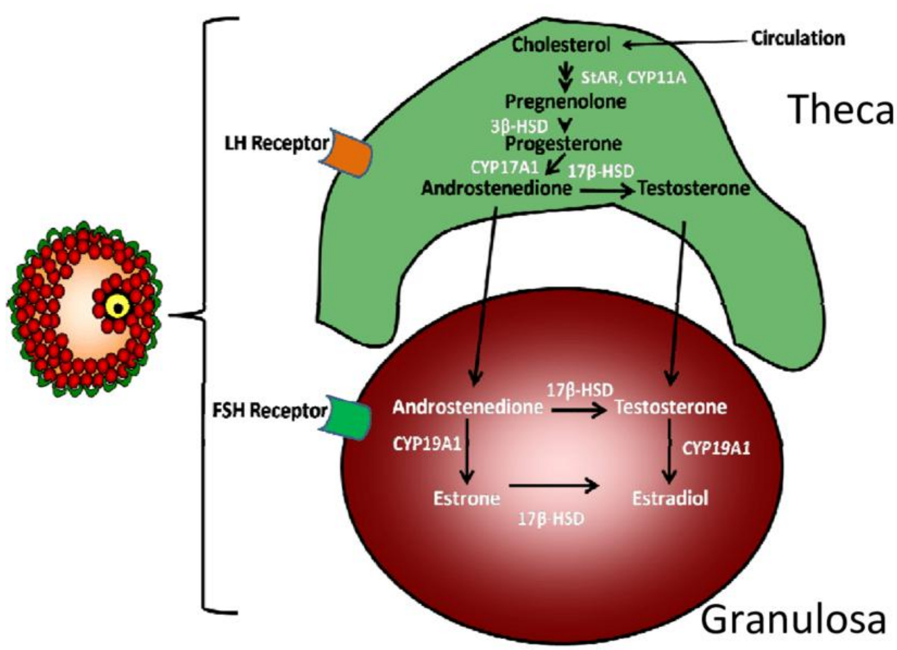
found only in the zona glomerulosa cells (the outer region of the adrenal cortex), so that the biosynthesis of this mineralocorticoid is confined to this region.

- A schematic representation of the pathways involved in the synthesis of the three major classes of adrenal steroids. The enzymes are shown in the rectangular boxes, and the modifications at each step are shaded.



Cell-cell communication – Two cell concept:

- Two cell, two-gonadotropin theory of ovarian steroidogenesis. This theory establishes that ovarian steroids are synthesized from cholesterol through the cooperative interactions of theca and granulosa cells
- . Theca cells (green): luteinizing hormone (LH) binds to luteinizing/chorionic gonadotropin receptor (LH/CGR) on the cell surface and stimulates the expression of the steroidogenic enzymes necessary for androgen production. Cholesterol is mobilized into mitochondria by steroidogenic acute regulatory protein (STAR) where it is converted to pregnenolone by cholesterol sidechain cleavage enzyme (CYP11A1).
- Pregnenolone diffuses into the smooth endoplasmic reticulum and is converted to progesterone by 3β-hydroxysteroid dehydrogenase (HSD3B). Progesterone is then converted to androstenedione by 17α-hydroxylase/17,20desmolase (CYP17A1).
- Granulosa cells (red): follicle-stimulating hormone (FSH) via signaling through follicle-stimulating hormone receptor (FSHR) stimulates the expression of enzymes necessary for estrogen synthesis.
- Androstenedione produced by theca cells diffuses into granulosa cells and is converted to testosterone by the enzyme 17βhydroxysteroid dehydrogenase (HSD17B) or to estrone by aromatase (CYP19A1). CYP19A1 utilizes testosterone to produce 17β-estradiol. However, HSD17B can also produce 17β-estradiol using estrone as a substrate.



Hormonal control of implantation, gestation, parturition and lactation:

Parturition is the end point of a succession of endocrine events involving maternal, fetal and placental interactions. The major hormones involved in the onset and maintenance of human parturition are oestrogens, progesterone, relaxin, oxytocin, prostaglandins, catecholamines, cortisol and β-endorphin. Oestrogens, relaxin and prostaglandins promote cervical ripening; prostaglandins, progesterone, oestrogens and oxytocin regulate myometrial activity. Catecholamines and cortisol help regulate the energetics of uterine contraction, and β-endorphin acts as a pain modulator. The release of β-endorphin (which is substantially reduced by epidural anaesthesia or by analgesics) is a response to the stress of labour and mirrors plasma cortisol levels; that is, plasma β-endorphin levels rise during labour, reach a peak at delivery, then fall to non-pregnant levels within 24–48 hours thereafter.

Lactation is controlled by hormones from several endocrine glands. An undisturbed function of the anterior pituitary, of the adrenals, and of the ovaries is a prerequisite for a normal morphogenesis of the mammary gland. The epithelial ducts proliferative under the combined influence of estrogens, glucocorticoids and growth hormone, whereas the lobuloalveolar development depends on progesterone and prolactin in addition to the fore-mentioned hormones. During pregnancy pituitary prolactin may be substituted by placental lactogen. Milk synthesis begins in the second half of pregnancy. It is supported by prolactin and cortisol, which directly act on enzyme activities and processes of differentiation of the alveolar cells. The sudden surge in the secretion of milk after parturition is most likely due to the rapid decline of the serum levels of progesterone. The ejection of milk from the lactating mammary gland is controlled by a neuroendocrine reflex mechanism. Suckling is the appropriate stimulus for the release of oxytocin from the posterior pituitary. Oxytocin increases intramammary pressure by inducing contraction of the myoepithelial cells and thus aids in expelling the milk from the mammary glands. Maintenance of normal postpartum lactation depends on frequent and intensive suckling. Suckling does not only stimulate the release of oxytocin, but also provokes secretion of prolactin and ACTH. This increase in prolactin caused by suckling guarantees galactopoesis. Influencing secretion of prolactin has been proven to be a useful tool for regulating lactation.

S. No.	Question	Opt A	Opt B	Opt C	Opt D	Answer
1	An increase in the concentration of plasma potassium causes increase in:	release of renin	secretion of aldosterone	secretion of ADH	production of angiotensin II .	secretion of aldosterone
2	Amino acids are almost completely reabsorbed from the glomerular filtrate via active transport in the :	proximal tubule	loop of Henle	distal tubule	collecting duct	proximal tubule
3	Glomerular filtration rate would be increased by :	constriction of the afferent arteriole	a decrease in afferent arteriolar pressure	compression of the renal capsule	a decrease in the concentration of plasma protein	a decrease in the concentration of plasma protein
4	The greatest amount of hydrogen ion secreted by the proximal tubule is associated with :	excretion of potassium ion	excretion of hydrogen ion	reabsorption of calcium ion	reabsorption of bicarbonate ion	reabsorption of bicarbonate ion
5	In controlling the synthesis and secretion of aldosterone , which of the following factors is least important ?	angiotensin II	concentration of plasma Na+	concentration of plasma K+	adrenocorticotropic hormone (ACTH)	adrenocorticotropic hormone (ACTH)
6	Renal correction of acute hyperkalemia will result in :	alkalosis	acidosis	increased secretion of H+	increased secretion of Na+	acidosis
7	Most of the glucose that is filtered through the glomerulus undergoes reabsorption in the :	proximal tubule	descending limp of the loop of Henle	ascending limb of the loop of Henle	distal tubule	proximal tubule

8	Ammonia is an affective important urinary buffer for which of the following reasons :	its production in the kidney decrease during chronic acidosis	the walls of the renal tubules are impermeable to NH3	the walls of the renal tubules are impermeable to NH4	its acid base reaction has a low pKa	the walls of the renal tubules are impermeable to NH4
9	The amount of potassium excreted by the kidney will decreases if :	distal tubular flow increases	circulating aldosterone level increase	dietary intake of potassium increase	Na+ reabsorption by the distal nephron decreases	Na+ reabsorption by the distal nephron decreases
10	In the presence of ADH, The distal nephron is least permeable to :	water	ammonia	urea	sodium	urea
11	Which of the following substances will be more concentrated at the end of the proximal tubule than at the beginning of the proximal tubule ?	glucose	creatinine	sodium	bicarbonate	creatinine
12	When a person is dehydrated, hypotonic fluid will be found in the:	glomerular filtrate	proximal tubule	loop of Henle	distal convoluted tubule	loop of Henle
13	Which one of the following statements about aldosterone is correct?	it produces its effect by activating C-AMP .	it produces its effect by increasing membrane permeability to potassium	it causes an increased reabsorption of hydrogen ion.	it has its main effect on the proximal tubule .	it produces its effect by increasing membrane permeability to potassium
14	The effect of antidiuretic hormone (ADH)	increase the permeability of the distal nephron to water.	increase the excretion of Na+	increase the excretion of water	increase the diameter of the renal artery .	increase the permeability of the distal nephron to water.
15	In the distal tubules, sodium reabsorption is increased directly by increased :	sympathetic nerve stimulation of the kidney .	atrial natriuretic hormone secretion .	antidiuretic hormone secretion .	aldosterone secretion	aldosterone secretion

16	The ability of the kidney to excrete a concentrated urine will increase if :	the permeability of the proximal tubule to water decreases .	the rate of blood flow through the medulla decreases .	the rate of flow through the loop of Henle increases .	the activity of the Na-K pump in the loop of Henle decreases	the rate of blood flow through the medulla decreases .
17	The glomerular filtration rate will increase if :	circulating blood volume increase .	the afferent arteriolar resistance increases .	the efferent arteriolar resistance decreases .	the plasma protein concentration decreases .	the plasma protein concentration decreases .
18	The volume of plasma needed each minute to supply a substance at the rate at which it is excreted in the urine is known as the :	diffusion constant of the substance	clearance of the substance	extraction ratio of the substance	tubular mass of the substance	clearance of the substance
19	An increase in the osmolarity of the extracellular compartment will:	stimulate the volume and osmoreceptors , and inhibit ADH secretion	inhibit the volume and osmoreceptors , and stimulate ADH secretion .	inhibit the volume and osmoreceptors , and inhibit ADH secretion	stimulate the volume and osmoreceptors , and stimulate ADH secretion.	stimulate the volume and osmoreceptors , and stimulate ADH secretion.
20	Select the correct answer about proximal tubules :	K+ is secreted in exchange with the Na+ which is reabsorbed under the effect of	aldosterone	glucose , amino acids & proteins are completely reabsorbed	only 10% of the filtered water is reabsorbed	aldosterone
21	The primary renal site for the secretion of organic ions e.g urate, creatinine is :	proximal tubule	loop of Henle	distal tubule	collecting duct .	proximal tubule
22	Reabsorption of Na+ :	takes place in association with CL- & HCO3 –	occurs only in PT	is under control of parathormone hormone	is a passive process .	takes place in association with CL- & HCO3 –
23	Diamox causes :	water diuresis	hypokalaemia	alkalosis	acidosis	hypokalaemia
24	K+ excretion is markedly influenced by :	aldosterone	amount of Na+ delivered to tubules	rate of tubular secretion of H+	insulin	aldosterone
25	More hydrogen is secreted in :	alkalosis	administration of diamox	hypokalaemia	hyperventilation.	hypokalaemia

26	Major determinants of plasma osmolarity include all the following except:	sodium	hemoglobin	chloride	albumin	hemoglobin
27	The hypothalamus will effect the release of ADH in response to all the following stimuli except :	dehydration	severe hemorrhage	pain , anxiety , or surgical stress	nicotine	nicotine
28	H+ secretion in the distal nephron is enhanced by all the following except :	an increase in the level of plasma aldosterone	an increase in the tubular luminal concentration of poorly reabsorbable anions	hyperkalemia	metabolic acidosis	hyperkalemia
29	Urinary volume is increased by all the following except :	diabetes insipidus	diabetes mellitus	sympathetic stimulation	increased renal arterial pressure	sympathetic stimulation
30	Significant buffers for hydrogen ions generated in the body from anaerobic metabolism include all the following except :	extracellular bicarbonate	plasma proteins	plasma lactate	inorganic phosphate	plasma lactate
31	Extracellular bicarbonate ions serve as effective buffer for all the following except :	phosphate acid	lactic acid	carbonic acid	ß- hydroxybutyric acid	carbonic acid
32	All the following statements are true of the H+ secreted into the lumen of the distal nephron except :	can combine with NH4+	can combine with HCO3	can combine with HPO	can remains as free H	can combine with NH4+
33	The glomerular filtration barrier is composed of all the following except :	fenestrated capillary endothelium .	macula densa .	basement membrane .	podocytes .	macula densa .

34	The amount of H+ excreted as titratable acid bound to phosphate would be increased by all the following except :	an increase in the amount of phosphate filtered at the glomerulus .	an increase in the pH of the urine .	an increase in the dietary intake of phosphate	an increase in the level of plasma parathyroid hormone (PTH	an increase in the pH of the urine .
35	Carbonic anhydrase plays an important role in all the following except :	the renal handing of HCO3- within the cells of the proximal tubule .	the renal handling of HCO3- within the lumen of proximal tubule .	the renal handling of HCO3- within the cells of the tubules of the distal nephron	the renal handling of HCO3 – within the lumen of the tubules of the distal nephron	the renal handling of HCO3 – within the lumen of the tubules of the distal nephron
36	About the proximal convoluted tubules , all are true except :	reabsorb most of Na+ ions in glomerular filtrate	reabsorb most of Cl- ions in glomerular filtrate	reabsorb most of K+ ions in glomerular filtrate	contains JGCs which secrete renin	contains JGCs which secrete renin
37	About urea , all are true except :	concentration rises in tubular fluid as the glomerular filtrate passes down the	nephron	is actively secreted by the renal tubular cells	concentration in the blood rises slightly after a high protein diet	nephron
38	Which of the following would cause an increase in both glomerular filtration rate (GFR) and renal plasma flow (RPF)?	Hyperproteinemia	A ureteral stone	Dilation of the afferent arteriole	Dilation of the efferent arteriole	Dilation of the afferent arteriole
39	Subjects A and B are 70 kg men. Subject A drinks 2 L of distilled water, and subject B drinks 2 L of isotonic NaCl. As result of these ingestions, subject B will have a	greater change in intracellular fluid (ICF) volume	higher positive free-water clearance (CH2O)	greater change in plasma osmolarity	higher urine osmolarity	higher urine osmolarity

40	Use the values below to answer the following question. Glomerular capillary hydrostatic pressure=47 mmHg; Bowman’s space hydrostatic pressure=10 mmHg. At what value of glomerular capillary oncotic pressure would glomerular filtration stop	57 mmHg	47 mmHg	37 mmHg	10 mmHg	10 mmHg
41	Glucose reabsorption occurs in the	proximal tubule	loop of Henle	distal tubule	cortical collecting duct	proximal tubule
42	Which agent is released or secreted after a hemorrhage and causes an increase in renal Na+ reabsorption?	Aldosterone	Angiotensin Ⅰ	Angiotensin Ⅱ	Antidiureis hormone（ADH）	Aldosterone
43	Which of the following causes hyperkalemia?	Exercise	Alkalosis	Insulin injection	Decreased serum osmolarity	Exercise
44	In the presence of vasopressin， the greatest fraction of filtered water is absorbed in the	proximal tubule	loop of Henle	distal tubule	cortical collecting duct	proximal tubule
45	On which of the following does aldosterone exert its greatest effect?	Proximal tubule	Thin portion of the loop of Henle	Thick portion of the loop of Henle	Cortical collecting duct	Cortical collecting duct
46	What is the clearance of a substance when is concentration in the plasma is 10 mg/dl， its concentration in the urine is 100 mg/dl， and urine flow is 2 ml/min？	2 ml/min	10 ml/min	20 ml/min	200 ml/min	20 ml/min

47	As urine flow increases during osmotic diuresis	the osmolality of urine falls below that of plasma	the osmolality of urine increases because of the increased amounts of nonreabsorbable solute in the urine	the osmolality of urine approaches that of plasma because plasma leaks into the tubules	the osmolality of urine approaches that of plasma because an increasingly large fraction of the excreted urine is isotonic proximal tubular fluid	the osmolality of urine approaches that of plasma because an increasingly large fraction of the excreted urine is isotonic proximal tubular fluid
48	If the clearance of a substance which is freely filtered is less than that of insulin	there is net reabsorption of the substance in the tubules	there is net secretion of the substance in the tubules	the substance is neither secreted nor reabsorbed in the tubules	the substance becomes bound to protein in the tubules	there is net reabsorption of the substance in the tubules
49	A negative free-water clearance (-CH2O) will occur in a person who	drinks 2 L of distilled water in 30 minutes	begins excreting large volumes of urine with an osmolarity of 100 mOsm/L after a severe head injury	is receiving lithium treatment for depression， and has polyuria that is unresponsive to the administration of antidiuretic hormone（ADH）	has an oat cell carcinoma of the lung， and excretes urine with an osmolarity of 1000 mOsm/L	has an oat cell carcinoma of the lung， and excretes urine with an osmolarity of 1000 mOsm/L
50	At plasma concentrations of glucose higher than occur at transport maximum（Tm）， the	clearance of glucose is zero	excretion rate of glucose equals the filtration rate of glucose	reabsorption rate of glucose equals the filtration rate of glucose	excretion rate of glucose increases with increasing plasma glucose concentrations	excretion rate of glucose increases with increasing plasma glucose concentrations

51	One gram of mannitol was injected into a woman. After equilibration, a plasma sample had a mannitol concentration of 0.8 g/L. During the equilibration period, 20% of the injected mannitol was excreted in the urine. The subject's	extracellular fluid（ECF）volume is 1 L	intracellular fluid (ICF) volume is 1 L	ECF volume is 10 L	ICF volume is 10 L	ECF volume is 10 L
52	Which of the following would produce an increase in the reabsorption of isosmotic fluid in the proximal tubule?	Increased filtration fraction	Extracellular fluid (ECF) volume expansion	Decreased peritubular capillary protein concentration	Increased peritubular capillary hydrostatic pressure	Increased filtration fraction
53	Which of the following is an action of parathyroid hormone（PTH）on the renal tubule?	Stimulation of adenlate cyclase	Inhibition of distal tuble K+ secretion	Ingibition of distal tuble Ca2+ reabsorption	Stimulation of proximal tubular phosphate reabsorption	Stimulation of adenlate cyclase
54	At plasma para-aminohippuric acid（PAH）concentrations below the transport maximum（Tm）, PAH	reabsorption is not saturated	clearance equals inulin clearance	secretion rate equals PAH excretion rate	concentration in the renal vein is close to zero	concentration in the renal vein is close to zero
55	Compared with a person who ingests 2 L of distilled water, a person with water deprivation will have a	lower plasma osmolarity	lower circulating level of antidiuretic hormone（ADH）	higher tubular fluid/plasma（TF/P）osmolarity in the proximal tubule	higher rate of H2O reabsorption in the collecting ducts	higher rate of H2O reabsorption in the collecting ducts

56	Which of the following would best distinguish an otherwise healthy person with severe water deprivation from a person with the syndrome of inappropriate antidiuretic hormone（SIADH）	Free-water clearance（CH2O）	Urine osmolarity	Plasma osmolarity	Circulating levels of antidiuretic hormone（ADH）	Plasma osmolarity
57	Which of the following causes a decrease in renal Ca2+ clearance?	Hypoparathyroidism	Treatment with chlorothiazide	Treatment with furosemide	Extracellular fluid（ECF）volume expansion	Treatment with chlorothiazide
58	Which of the following substances has the highest renal clearance?	Para-aminohippuric acid（PAH）	Inulin	Glucose	Na+	Para-aminohippuric acid（PAH）
59	A woman runs a marathon in 90 °F weather and replaces all volume lost in sweat by drinking distilled water. After the marathon, she will have	decreased total body water（TBW）	decreased hematocrit	decreased intracellular fluid（ICF）volume	decreased plasma osmolarity	decreased plasma osmolarity
60	The glomerular filtration rate in ml/min is:	120	180	240	400	120

KARPAGAM ACADEMY OF HIGHER EDUCATION

(Deemed University Established Under Section 3 of UGC Act 1956)
Coimbatore - 641021.
(For the candidates admitted from 2018 onwards)

DEPARTMENT OF BIOCHEMISTRY

SUBJECT : ENDOCRINOLOGY
SEMESTER : III
SUBJECT CODE : 18BCP303 CLASS : M.Sc., Biochemistry

UNIT IV

Unit IV: Hormone action

Protein and steroid hormone receptors and their signaling cascades; non-genomic actions; Ras-Raf-MAPK signaling - PI3K signaling. Genomic actions of hormones - thyroid hormone nuclear receptor superfamily. Renin-angiotensin system, atrial natriuretic hormones. Vasopressin and water retention.

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

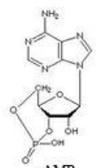
Second messengers are intracellular signaling molecules released by the cell to trigger physiological changes such as proliferation, differentiation, migration, survival, and apoptosis. Secondary messengers are therefore one of the initiating components of intracellular signal transduction cascades. 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

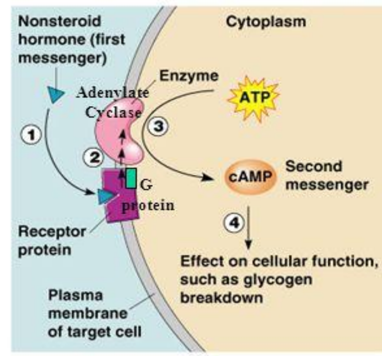
Two Mechanisms of Hormone Action

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).

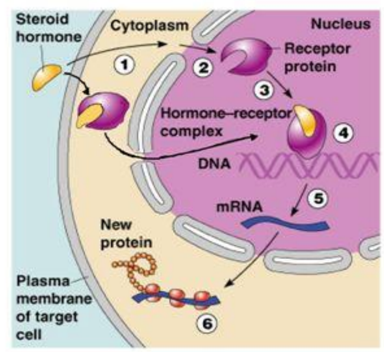




(b) Nonsteroid hormone action

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



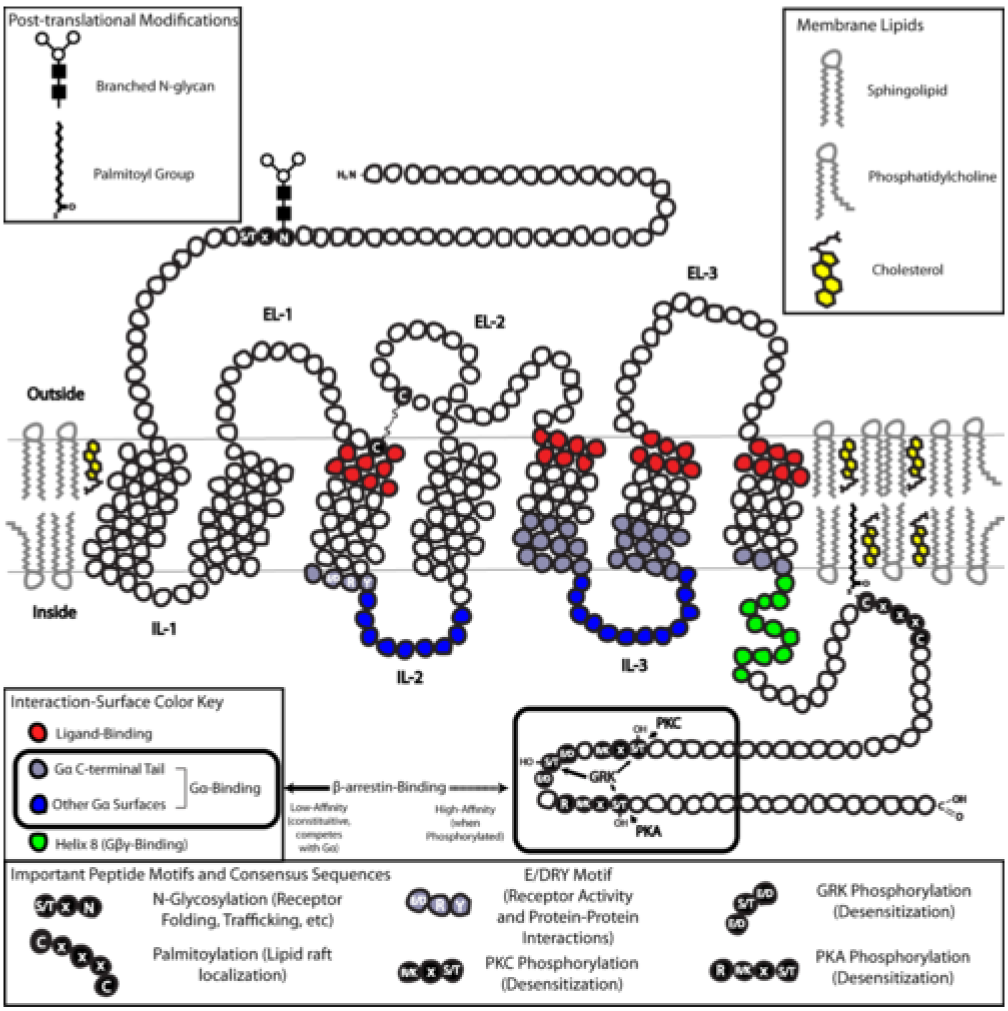
(a) Steroid hormone action

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)

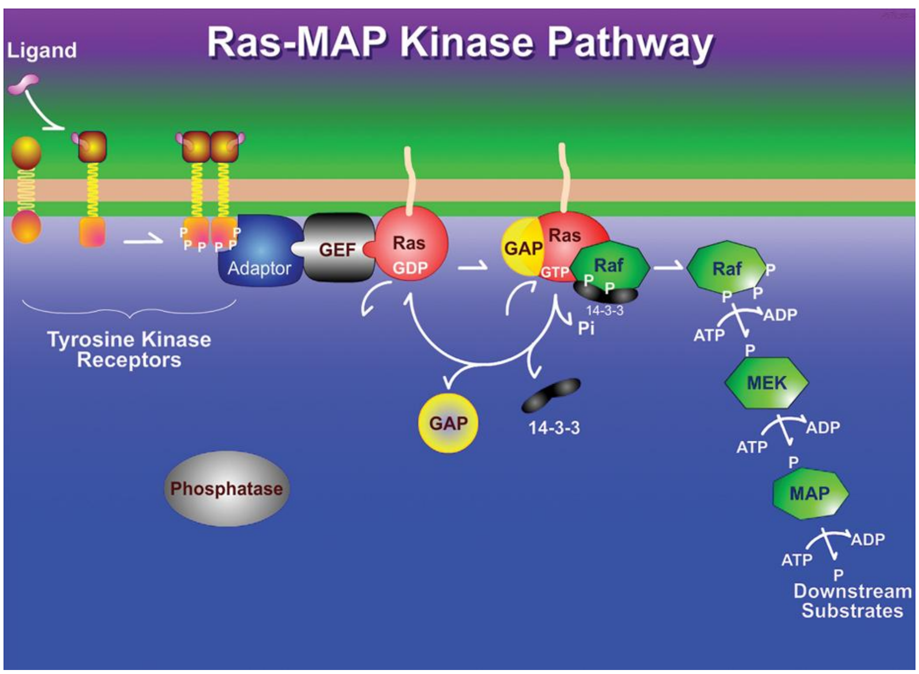
Glucagon – Stimulates glycogen breakdown in the liver

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.

Ras-Raf-MAPK signaling:

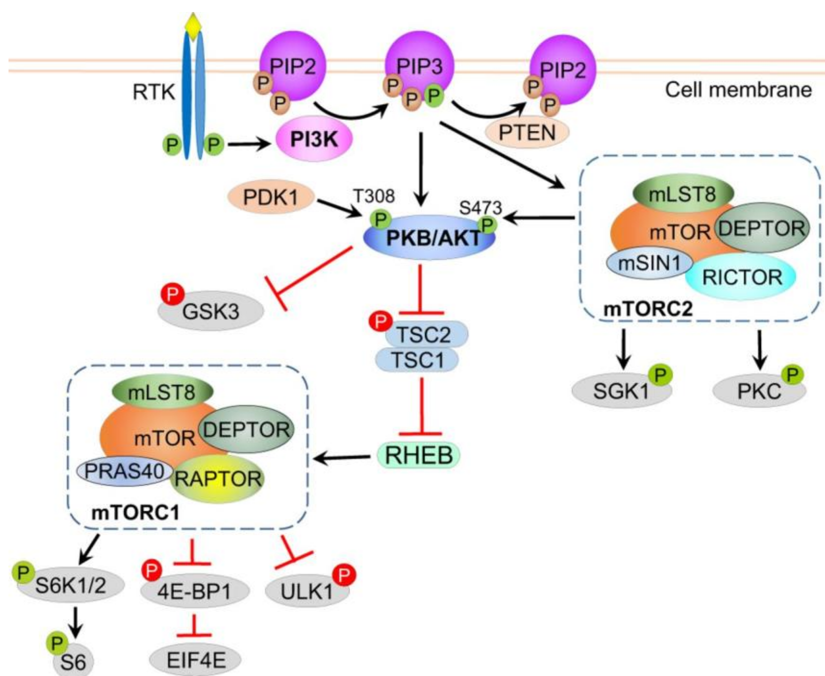
- The **MAPK/ERK pathway** (also known as the **Ras-Raf-MEK-ERK pathway**) is a chain of proteins in the cell that communicates a signal from a receptor on the surface of the cell to the DNA in the nucleus of the cell.
- The signal starts when a signaling molecule binds to the receptor on the cell surface and ends when the DNA in the nucleus expresses a protein and produces some change in the cell, such as cell division.
- The pathway includes many proteins, including MAPK (mitogen-activated protein kinases, originally called ERK, extracellular signal-regulated kinases) which communicate by adding phosphate groups to a neighboring protein (phosphorylating it), which acts as an "on" or "off" switch.
- When one of the proteins in the pathway is mutated, it can become stuck in the "on" or "off" position, which is a necessary step in the development of many cancers. Components of the MAPK/ERK pathway were discovered when they were found in cancer cells.



PI3K signaling:

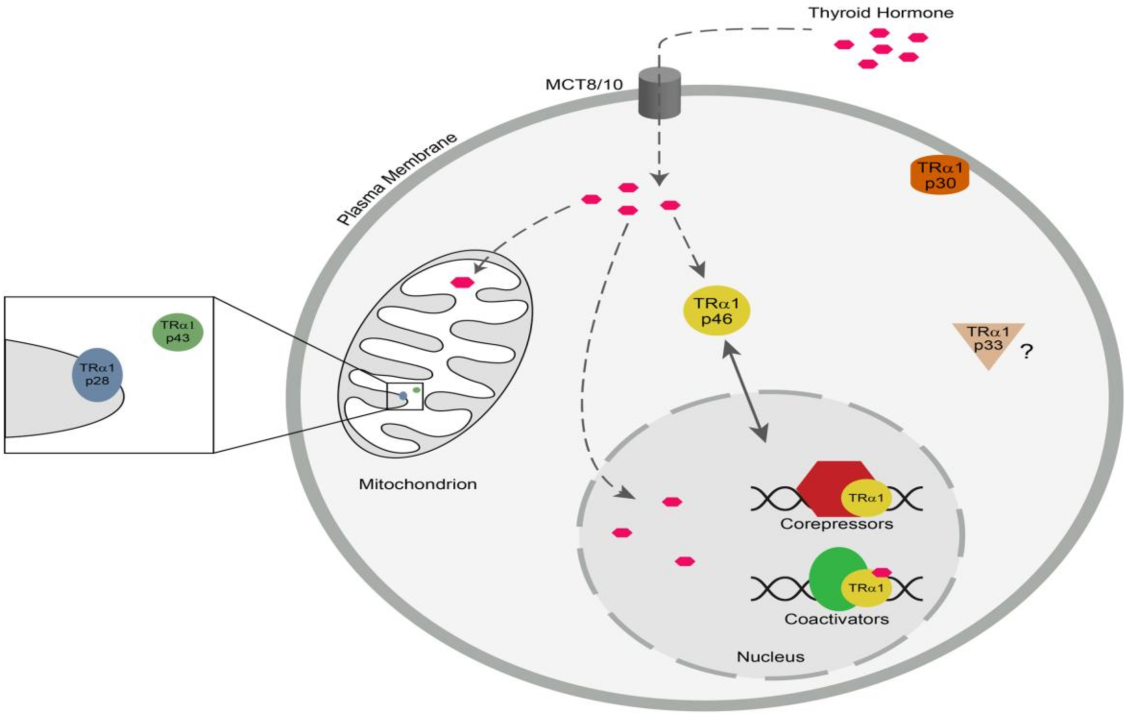
- The **PI3K/AKT/mTOR pathway** is an intracellular signaling pathway important in regulating the cell cycle. PI3K activation phosphorylates and activates AKT, localizing it in the plasma membrane.

- This pathway is necessary, however, to promote growth and proliferation over differentiation of adult stem cells, neural stem cells specifically.
- It is the difficulty in finding an appropriate amount of proliferation versus differentiation that researchers are trying to determine in order to utilize this balance in the development of various therapies. Additionally, this pathway has been found to be a necessary component in neural long term potentiation.



Thyroid hormone nuclear receptor superfamily:

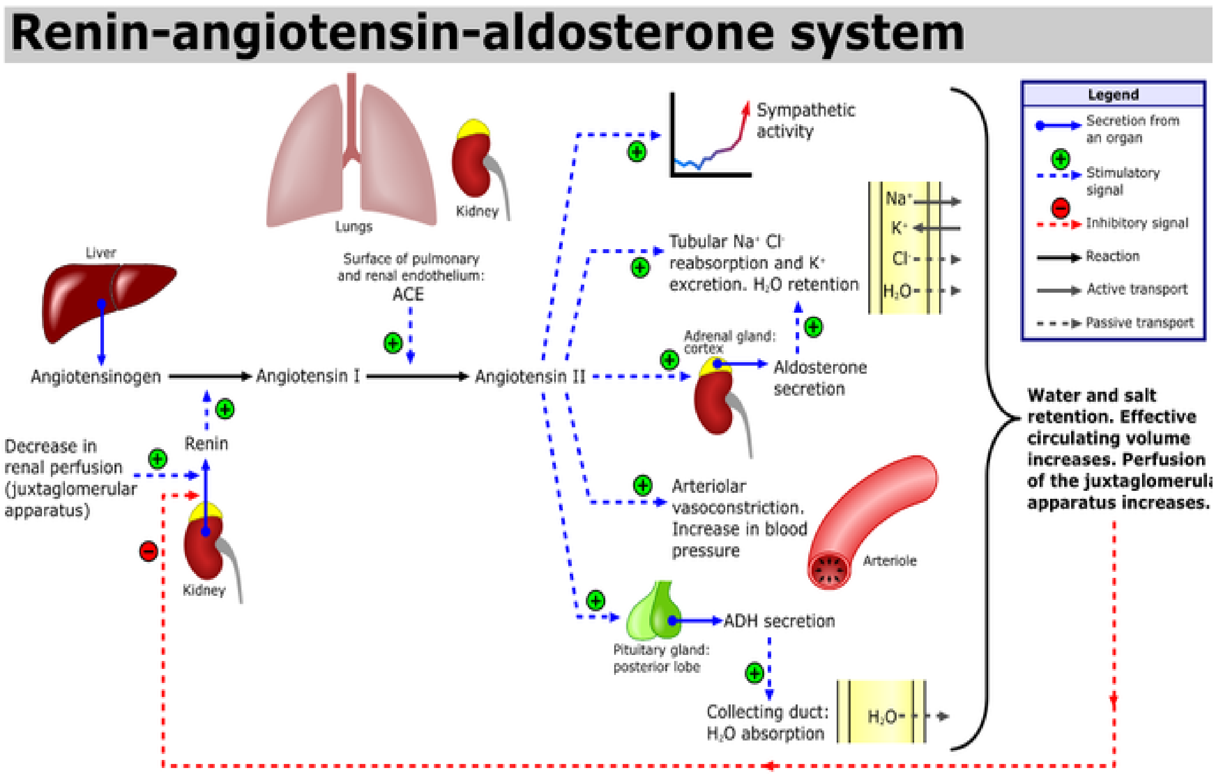
- The thyroid hormone receptors (TRs) are members of the nuclear receptor superfamily that exhibit a dual role as activators or repressors of gene transcription in response to thyroid hormone (T3) and provide a model system for investigating complex networks of cellular trafficking and gene expression.
- TRs act as transcription factors, ultimately affecting the regulation of gene transcriptionand translation. These receptors also have non-genomic effects that lead to second messenger activation, and corresponding cellular response



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.

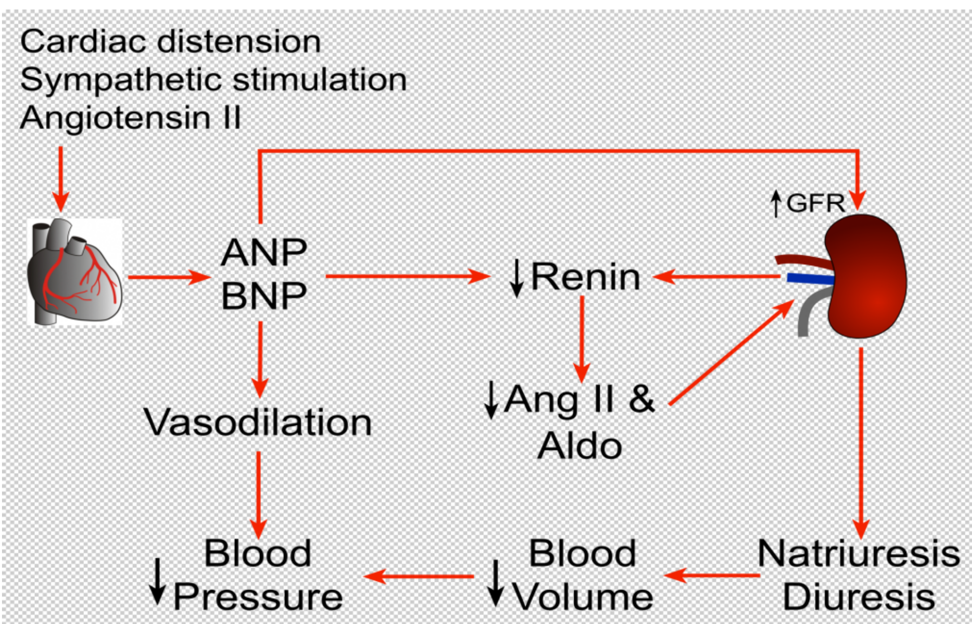
Direct renin inhibitors can also be used for hypertension. The drugs that inhibit renin are aliskiren and the investigational remikiren.

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

Atrial natriuretic hormones:

- The atrial natriuretic hormone (ANP) is a cardiac hormone which gene and receptors are widely present in the body. Its main function is to lower blood pressure and to control electrolyte homeostasis.
- Its main targets are the kidney and the cardiovascular system but ANP interacts with many other hormones in order to regulate their secretion. The adrenal glands are the first endocrine target.

- Steroidogenesis, especially mineralocorticoid synthesis, is inhibited by ANP, but glucocorticoid production seems to be depressed too.
- As ANP synthesis is enhanced by the latter, it suggests a regulatory loop. Moreover ANP inhibits the thyroid synthesis whereas its production is enhanced by thyroid hormone. The hypothalamo-hypophyseal axis is another important target.
- ANP inhibits ACTH release and arginine vasopressin secretion. Vasopressin enhances ANP synthesis while GH decreases it.
- Finally the endocrine effects of ANP strengthen the cardiovascular and renal effects of the hormone, antagonizing the salt and water retention due to aldosterone and AVP. Because of a local production, ANP may also act as a paracrine hormone that influences the function of many endocrine systems (ovarian function for instance).
- In the central nervous system, ANP acts as a neurotransmitter in order to regulate pituitary and vegetative functions. Plasma ANP levels are impaired in several endocrine diseases : the plasma hormone levels increase in hypercortisolism, hyperaldosteronism, thyrotoxicosis and inappropriate antidiuretic hormone secretion; it decreases in hypothyroidism.
- In case of Addison's disease, ANP may be used to assess the quality of mineralocorticoid treatment, in association with the other biological criteria.



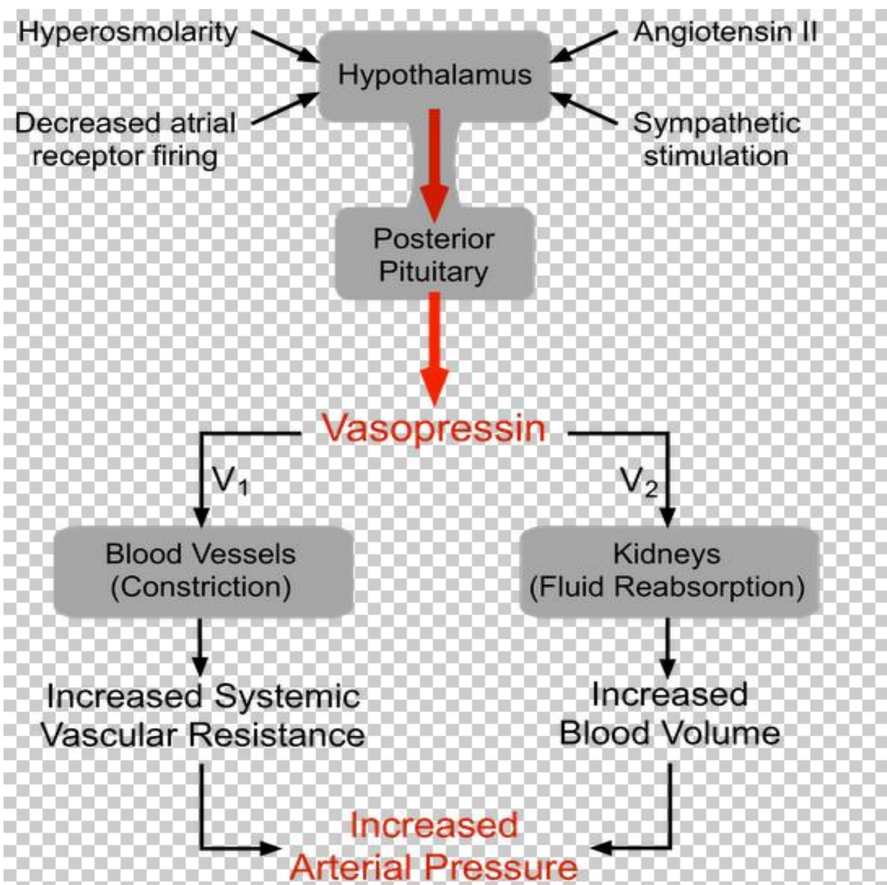
Vasopressin and water retention:

- ADH is also called arginine vasopressin. It's a hormone made by the hypothalamus in the brain and stored in the posterior pituitary gland. It tells your kidneys how much water to conserve.

- ADH constantly regulates and balances the amount of water in your blood. Higher water concentration increases the volume and pressure of your blood. Osmotic sensors and baroreceptors work with ADH to maintain water metabolism.

- Osmotic sensors in the hypothalamus react to the concentration of particles in your blood. These particles include molecules of sodium, potassium, chloride, and carbon dioxide.

- When particle concentration isn't balanced, or blood pressure is too low, these sensors and baroreceptors tell your kidneys to store or release water to maintain a healthy range of these substances. They also regulate your body's sense of thirst.



S. No.	Question	Opt A	Opt B	Opt C	Opt D	Answer
1	Slow waves in small intestinal smooth muscle cells are	action potentials	phasic contractions	tonic contractions	oscillating resting membrane potentials	oscillating resting membrane potentials
2	Which of the following substances is released from neurons in the GI tract and produces smooth muscle relaxation?	Secretin	Gastrin	Cholecystokinin (CCK)	Vasoactive intestinal peptide (VIP)	Vasoactive intestinal peptide（VIP）
3	Which of the following is characteristic of saliva?	Hypotonicity relative to plasma	A lower HCO3- concentration than plasma	The presence of proteases	Secretion rate that is increased by vagotomy	Hypotonicity relative to plasma
4	Which of the following is the site of secretion of gastrin?	Gastric antrum	Gastric fundus	Duodenum	Ileum	Gastric antrum
5	Secretion of which of the following substances is inhibited by low pH?	Secretin	Gastrin	Cholecystokinin（CCK）	Vasoactive intestinal peptide（VIP）	Gastrin
6	When parietal cells are stimulated, they secrete	HCl and intrinsic factor	HCl and pepsinogen	HCl and HCO3-	HCO3- and intrinsic factor	HCl and intrinsic factor
7	Which of the following abolishes “receptive relaxation”of the stomach?	Parasympathetic stimulation	Sympathetic stimulation	Vaotomy	Administration of gastrin	Vaotomy
8	Which of the following is the site of secretion of intrinsic factor?	Gastric antrum	Gastric fundus	Duodenum	Ileum	Gastric fundus

9	Which of the following is true about the secretion from the exocrine pancreas?	It has a higher Cl- concentration than does plasm	It is stimulated by the presence of HCO3- in the duodenum.	Pancreatic HCO3- secretion is increased by gastrin.	Pancreatic enzyme secretion is increased by cholecystokinin（CCK）.	Pancreatic enzyme secretion is increased by cholecystokinin（CCK）.
10	Which of the following are incorrectly paired?	Pancreatic amylase：starch	Elastase：tissues rich in elastin	Enteropeptidase：polypeptides	Rennin：coagulated milk	Enteropeptidase：polypeptides
11	Which of the following has the highest pH?	Gastric juice	Bile in the gallbladder	Pancreatic juice	Saliva	Pancreatic juice
12	Cholecystokinin (CCK) has some gastrin like properties because both CCK and gastrin	are released from G cells in the stomach	are released from I cells in the duodenum	are members of the secretin-homologous family	have five identical C-terminal amino acids	have five identical C-terminal amino acids
13	Which of the following is the site of Na+-bile acid cotransport?	Gastric antrum	Gastric fundus	Duodenum	Ileum	Ileum
14	Peristalsis of the small intestine	mines the food bolus	is coordinated by the central nervous system（CNS）	involves contraction of smooth muscle behind and in front of the food bolus	involves contraction of smooth muscle behind the food bolus and relaxation of smooth muscle in front of the bolus	involves contraction of smooth muscle behind the food bolus and relaxation of smooth muscle in front of the bolus
15	Which of the following changes occurs during defecation?	Internal anal sphincter is relaxed	External anal sphincter is contracted	Rectal smooth muscle is relaxed	Intra-abdominal pressure is lower than when at rest	Internal anal sphincter is relaxed
16	In infants, defecation of ten follows a meal. The cause of colonic contractions in this situation is	the gastroileal reflex	increased circulating levels of CCK	the gastrocolic reflex	increased circulating levels of somatostatin	the gastrocolic reflex

17	Water is absorbed in the jejunum, ileum, and colon and excreted in the feces. Arrange these in order of the amount of water absorbed or excreted from greatest to smallest（　）	colon，jejunum，ileum，feces	feces，colon，ileum，jejunum	jejunum，ileum，colon，feces	colon，ileum，jejunum，feces		jejunum，ileum，colon，feces
18	Which of the following substances must be further digested before it can be absorbed by specific carriers in intestinal cells?	Fructose	Sucrose	Alanine	Dipeptides		Sucrose
19	The pathway from the intestinal lumen to the circulating blood for a short-chain fatty acid (<10 carbon atoms) is	intestinal mucosal cell→chylomicrons→lymphatic duct→systemic venous blood	intestinal mucosal cell→hepatic portal vein blood→systemic venous blood	space between mucosal cells→lymphatic duct→systemic venous blood	space between mucosal cells→chylomicrons→lymphatic duct→systemic venous blood		intestinal mucosal cell→hepatic portal vein blood→systemic venous blood
20	Which type of hepatitis can be transmitted through feco-oral?	hepatitis A	hepatitis B	hepatitis G	hepatitis D		hepatitis A
21	What is type III primary biliary cirrhosis?	Positive LKM	No auto antibodies detected	All antibodies negative, positive antibodies against soluble liver antigen (SLA)	Positive ANA and ASMA, raised IgG		All antibodies negative, positive antibodies against soluble liver antigen (SLA)
22	________ measurement is sensitive in detecting mild cirrhosis.	AST	GGT	ALP	ALT		GGT
23	The best liver function test is:	AST/ALT	Alkaline phosphatase	Bilirubin	INR		INR

24	Feaces gets	Hard and wet in constipation	Soft and dry in constipation	Hard and dry in constipation	Soft and wet in constipation	Hard and dry in constipation
25	Main cause of indigestion of food is due to	Lack of chewing	Lack of water in the body	Lack of Saliva	Infection	Lack of chewing
26	Diarrhea takes out too much water and minerals which causes	Dehydration	Hunger	Dryness	Lack of energy	Dehydration
27	Diarrhea takes place due to	Mosquitoes	Infected Food	Infected Syringes	Cold	Infected Food
28	Liver synthesizes all, except	C3 complement component	Haptoglobin	Fibrinogen	Immunoglobulin	Immunoglobulin
29	The hepatocyte	is usually diploid and uninucleate	closest to the portal tract is said to be centrilobular	has great variation in size, depending on the level of cellular activity	is supplied principally by hepatic arterial blood	is usually diploid and uninucleate
30	The primary diseases of the liver include all of the following except	hepatitis C	alcoholic liver disease	ascending cholangitis	hepatocellular carcinoma	ascending cholangitis
31	The most common cause for chronic liver disease in the West is	Hepatitis C	alcoholic liver disease	non-alcoholic fatty liver disease	drug induced hepatitis	hepatitis C
32	Concerning patterns of hepatic injury	centrilobular necrosis is rare	alcoholic fatty liver affects virtually every hepatocyte	fibrotic change is generally considered reversible in the liver	necrosis is usually liquefactive, and hence causes cystic change	alcoholic fatty liver affects virtually every hepatocyte
33	Regarding hepatic failure	60-70% of hepatic capacity must be eroded before hepatic failure ensues	Mortality of hepatic failure without transplantation is 60%	Paracetamol overdose is the most common cause of massive hepatic necrosis	Hepatitis C is a cause of massive hepatic necrosis	Paracetamol overdose is the most common cause of massive hepatic necrosis

34	Regarding the clinical findings in hepatic failure	patients suffering from hepatic encephalopathy are flaccid and hyporeflexic	patients are often prothrombotic	asterixis is the non rhythmic movement of the extremities	jaundice occurs in 60% of patients	asterixis is the non rhythmic movement of the extremities
35	Regarding hepatic failure (old paper)	60% of hepatic capacity must be eroded before hepatic failure ensues	Encephalopathy is the result of increased ammonia formation	The liver is the predominant site of albumin synthesis	Encephalopathy is universally irreversible	The liver is the predominant site of albumin synthesis
36	Regarding hepatorenal syndrome (old paper)	it is irreversible	the ability to concentrate urine is lost	the urine is high is sodium	the urine is hyperosmolar devoid of proteins and sediment and low in sodium	the urine is hyperosmolar devoid of proteins and sediment and low in sodium
37	Cirrhosis of the liver (old paper)	results in changes to the vascular channels	shows a basically normal liver architecture with chronic hepatocyte necrosis	rapid development of fibrosis allows for the development of large nodules	can usually be reversed if the causative agent is treated or removed	results in changes to the vascular channels
38	Clinical features of cirrhosis include all except	osteoporosis	atrophy of the spleen	anorexia	development of hepatocellular carcinoma	atrophy of the spleen
39	In cirrhosis (old paper)	fibrosis is confined to delicate bands around the central veins	nodularity is uncommon	vascular architecture is preserved	The Ito cell is a major source of excess collagen	The Ito cell is a major source of excess collagen
40	Which of the following is most correct regarding portal hypertension (old paper)	prehepatic + splenic vein thrombosis	intrahepatic + Budd Chiari syndrome	post hepatic + cirrhosis	schistosomiasis + prehepatic	intrahepatic + Budd Chiari syndrome

41	Oesophageal varices (old paper)	occur in one third of all cirrhosis patients	account for more than 50% of haematemesis episodes	are most often as a result of hepatitis C induced cirrhosis	have a 40% mortality during the first episode of rupture	have a 40% mortality during the first episode of rupture
42	Ascites	is clinically detectable when 200mL has accumulated	caused by cirrhosis results in a decrease in hepatic lymphatic flow	can cause a hydrothorax, usually on the left	with the presence of red cells points to possible disseminated intra-abdominal cancer	with the presence of red cells points to possible disseminated intra-abdominal cancer
43	Bilirubin	is formed exclusively from the breakdown of senescent erythrocytes	is produced in quantities of 0.2-0.3g per day	is formed in the liver	is soluble in aqueous solution at physiological pH	is produced in quantities of 0.2-0.3g per day
44	Conjugated hyperbilirubinaemia results from (old paper)	Gilbert's syndrome	Physiologic jaundice	Excess production of bilirubin	Cholestasis	Cholestasis
45	Regarding jaundice (old paper)	Unconjugated bilirubin is excreted in the urine	Excess conjugated bilirubin causes kernicterus in adults	Unconjugated bilirubin does not colour the sclera	Unconjugated bilirubin is tightly bound to albumin	Unconjugated bilirubin is tightly bound to albumin
46	Which of the following conditions is associated with an unconjugated hyperbilirubinaemia	Haemolysis	Rotor syndrome	Dubin Johnson syndrome	Pancreatic cancer	Haemolysis
47	Hepatitis A	has a chronic carrier state	has an associated mortality of up to 10%	infection is not affected by alcohol consumption	has an incubation period of 2-6 weeks	has an incubation period of 2-6 weeks
48	Regarding hepatitis B	HBe antigen amounts to active replication by the virus	IgG anti Hepatitis A virus amounts to recent infection	Anti He antibody amounts to increased infectivity	it has an incubation period of 2 weeks	HBe antigen amounts to active replication by the virus

49	In hepatitis B	anti-HBs appears soon after HBsAg	infection is not associated with hepatocellular carcinoma	HBsAg appears soon after overt disease	acute infection causes sub-clinical disease in 65% of cases	acute infection causes sub-clinical disease in 65% of cases
50	Hepatitis C	has a high association with sexual transmission	transmission increases in pregnancy	causing fulminant hepatitis is a common presentation	infections become chronic in greater than 50% of infected patients	infections become chronic in greater than 50% of infected patients
51	Hepatitis D	is a double stranded DNA virus	induces anti-HD surface immunoglobulin	is unable to replicate independently	does not cause fulminant hepatitis	is unable to replicate independently
52	Hepatitis E infection (old question)	is transmitted primarily parentally	accounts for a greater than 20% mortality in pregnant mothers	is common in Russia	is associated with chronic disease and cirrhosis	accounts for a greater than 20% mortality in pregnant mothers
53	Regarding acute viral hepatitis infection	Acute viral hepatitis is common with Hepatitis C infection	Chronic disease results in chronic icterus	Icterus is common in adults with hepatitis A infection, but is rare in children	Most patients with acute disease have a serum sickness-like syndrome	Icterus is common in adults with hepatitis A infection, but is rare in children
54	Concerning biliary lithiasis p928	stones are produced exclusively in the gallbladder	50% of stones are symptomatic	50% are cholesterol stones	Caucasian women are twice as likely to be affected than men	Caucasian women are twice as likely to be affected than men
55	Concerning the pathogenesis of cholesterol stones, all the following defects are required except	Infection of the biliary tract by E coli	Bile must be supersaturated with cholesterol	Gallbladder hypomotility which promotes nucleation	Cholesterol nucleation acceleration	Infection of the biliary tract by E coli

S. No.	Question	Opt A	Opt B	Opt C	Opt D	Answer
1	_______ Hormone stimulates leydig cells to secrete testosterone	Scrotum	Epididymis	prostrate gland	cowpers gland	scrotum
2	Acetylcholinesterase is	nodes of Ranvier	dendrites	synapses	Schwann cells	Schwann cells
3	Action potentials	serotonin	dopamine	neuropeptides	norepinephrine	neuropeptides
4	After passing stimulus from receptors to sensory neurons , it passes then to	urea	concentrated urine	uric acid	ammonia	concentrated urine
5	All of the following neurotransmitters are biogenic amines except	axons	dendrites	neuron cell bodies	myelin sheaths	dendrites
6	Autonomic nervous system controls	motor neurons	sensory neurons	associative neurons	relay neurons	motor neurons
7	Autonomic nervous system is further divided into	voluntary movements	reflex actions	semi-voluntary movem	involuntary movements	involuntary movements
8	Between two neurons a microscopic gap exists which is the contact point of neurons called	sleep membrane potent	resting membrane poter	passive membrane pot	dormant membrane potential	resting membrane potential
9	Corpus luteum secretes	Placenta	Pregnancy	Fertilization	Ejaculation	Pregnancy
10	During saltatory conduction, a nerve impulse jumps from one _______________ to another.	neuromuscular junction:	nodes of Ranvier	inhibitory synapses	excitatory synapses	inhibitory synapses
11	Each testis is encased by a white fibrous membrane known as	Spermatogenesis	spermatic cord	spermiation	spermetazoa	spermiation
12	Fertilisation of human ovum is due to	Aldosterone	Testosterone	Coticosterone	Vasopressin	Testosterone
13	For each impulse autonomic nervous system utilizes only	axons	dendrites	cell body	myelin	myelin
14	GABA (gamma aminobutyric acid) is normally found at	dendrites	axon	myelin sheaths	hormones	dendrites
15	Graded potentials may become action potential by	are summable	are amplifiable	result from facilitated (	are all-or-nothing events	are all-or-nothing events
16	Human spermatozoa	Penetration of the ovum	Only one sperm is allow	May occur one week a	Usually occurs at the ampullary –Isthu	Penetration of the ovum by the sperm brought about by a lysosomal enzyme present

17	In hydra nervous system is a network of neurons present between the	effectors	motor neurons	associative neurons	Back to receptors	associative neurons
18	In myelinated neurons the impulse jumps from node to node. This is called	node of ranvier	neuron bridges	synapse	gaps	synapse
19	In normal menstrual cycle	Require temperature lov	They are motile even wl	In the absence of fertil	Take about 45 min to pass from the o	Require temperature lower than that of the interior of body for their genesis
20	In sensory neurons, stimuli are received by the	summation	multiplication	hypopolarization	decreasing frequency	summation
21	Interstial cells of Leydig secrete	Prostrate gland	Epidymis	Seminiferous tubules	Ampulla	Seminiferous tubules
22	Leutinizing hormone releasing hormone is secreted in	Thyroxin	Calcitonin	Estrogen	Progesterone	Progesterone
23	Most of the sperms are stored in	Castration	Enuuchism	Frohlich's syndrome	Fibro adenoma	Castration
24	Name the hormone that regulates the water reabsorption in the distal tubule	Spermatogenesis	Cytogenesis	Oogenesis	Embryogenesis	Spermatogenesis
25	Nephrons have extensive blood supply by	cortical nephrons	medullar nephrons	juxtamedullary nephro	cortical and medullar nephrons	juxtamedullary nephrons
26	Nerve impulses are normally carried toward a neuron cell body by the neuron's	neurotransmitter	synapse	node of Ranvier	threshold	synapse
27	Neurons at rest (non-conducting neuron) has electric potential called	ectoderm and mesoderr	ectoderm and endodern	endoderm and mesode	mesoderm and pericarp	ectoderm and endoderm
28	Neurotransmitters are released from vesicles at the	a neurotransmitter	an enzyme that breaks c	a stimulant that trigge	a hormone	an enzyme that breaks down a neurotransmitter
29	Oxytocin is secreted in	LH	Growth hormone	ACTH	PRL	LH
30	Postsynaptic membranes are most likely to be found on	myelin sheath	synapse	node of Ranvier	dendrite	node of Ranvier
31	Prolactin is secreted by	Vasderferens	Spermatids	Spermatogonia	Sertoli cells	Vasderferens
32	Semen also contains a hormone like substance known as	graffian follicle	zona pellucida	ovulation	ophorous	zona pellucida
33	Somatic nervous system is made up of	four neurons and two ga	two neurons and one ga	one neuron and one ga	one neuron and two ganglions	two neurons and one ganglion
34	Spermatogenesis occurs in	Pituitary gland	Ovaries	Hypothalamus	Adrenal gland	Hypothalamus
35	Sympathetic nervous system is associated with	three parts	two parts	four parts	five parts	two parts
36	The cell membrane of the oocyte is called as	Ovulation	cumulus oophorous	corpus leuteum	theca interna	Ovulation
37	The development of the young within the female reproductive system from the time of conception to childbirth is called	4 phases	3 phases	5 phases	6 phases	4 phases

38	The formation of sperm is known as	Sperm	Ovum	Both	None	Ovum
39	The hormone which is responsible for ovulation,formation of the corpus luteum and the secretion of the luteal hormone progesterone is	Diuretic hormone	Antidiuretic hormone	Lutenizing hormone	Follicle stimulating hormone	Antidiuretic hormone
40	The hormone which stimulus secretion of "Uterine milk" is	Adrenal gland	Posterior pituitary	Anterior pituitary	Parathyroid gland	Posterior pituitary
41	The inner end of nephrons is a cup shaped swelling structure known as	hormonal secretions	fear and rage	skeletal muscles	fight and flight	fight and flight
42	The junction between a neuron and its target cell is called a	cell body	dendrite	cell nucleus	presynaptic membrane	presynaptic membrane
43	The juxtamedullary nephrons are specialized for the production of	renal veins	renal arteries	hepatic arteries	peritoneal veins	renal arteries
44	The male organ for copulation is	Testosterone	Androgens	cumulus oophorus	antaglutins	Androgens
45	The menstrual fluid is normally non clotting because of the presence of	Proliferation	Ovulation	Secretory phase	Menstrual phase	Ovulation
46	The meta estrone phase is otherwise termed as	LH	Aldosterone	Vasopressin	FSH	FSH
47	The midbrain of vertebrates is also called the	cerebrum	forebrain	midbrain	hindbrain	hindbrain
48	The myelin sheath is formed by _______________, which wrap around the axons of some neurons.	maintain proper ionic co	generate the nerve impu	transmit the nerve imp	provide a source of Na+ and K+ by spl	maintain proper ionic concentration gradients across the neuron membrane
49	The nephrons which are arranged along the border of medulla looping deep in inner medulla are called	glomerulus	Bowman's capsule	medulla	cortex	Bowman's capsule
50	The neurotransmitter at neuromuscular junctions is	an unmyelinated, small (	an unmyelinated, large (	a myelinated, small dia	a myelinated, large diameter nerve	an unmyelinated, small diameter nerve
51	The outer surface of the ovary is covered by	Thrombolysin	Proteolysin	Anticoagulin	Fibrinolysin	Fibrinolysin
52	The phenomenon of the release of ovum from the graffian follicle is described as	LH	FSH	Relaxin	Progesterone	Progesterone
53	The primary function of the Graffian follicle is to form	Hypothalamus	Posterior pituitary	Anterior pituitary	Adrenal cortex	Anterior pituitary
54	The progestational phase of the endometrial cycle occur after	Pre-ovulatory phase	Ovulatory phase	Post ovulatory phase	None of the above	Ovulatory phase
55	The release of sperms from the sertoli cells is known as	Penis	Spermetagenisis	Spermetocytes	Spermetazoa	Penis

56	The role of the Na+/K+ pump in the nervous system is to	GABA	serotonin	acetylcholinesterase	acetylcholine	acetylcholine
57	The testes are small ovoid organs lodged in a pouch like structure called as	Tunica albicans	tunica albuginea	tunica degeneratum	septum	tunica albuginea
58	The testicular hormones are known as	Primordial follicles	Ligaments	Mesovaria	prostaglandins	prostagladins
59	When a boy loses his testes prior to puberty it leads to a condition called	Primodial follicle	Hilar connective tissue	Germinal epithelium	Fallopian tubes	Germinal epithelium
60	Which of the following should have the slowest conduction velocity?	medulla	mesencephalon	diencephalon	hypothalamus	mesencephalon