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.P.Anusooriya
SUBJECT NAME: Endocrinology

SUB.CODE:17BCP303
SEMESTER: III CLASS: II M.Sc (BC)

Sl. No	LECTURE DURATION	TOPICS	BOOK REFERENCE	PAGE NO	WEB REFERENCE
Unit-1					
1	1	**General Introduction**, Hypothalamo-hypophyseal axis	T1:481-485		
2	1	Chemical signaling – endocrine, paracrine, autocrine, intracrine and neuroendocrine mechanisms	R1:29-32		
3	1	Chemical classification of hormones.	R1:22-28		
4	1	transport of hormones in the circulation and their half-lives.	R1:32-33		
5	1	Hormone receptors – extracellular, transmembrane and intracellular. Receptor – hormone binding, Scatchard analysis,	R1:39-45		
6	1	recycling and degradation of receptors. Releasing/release-inhibiting hormones	R1:46-51		
7	1	TRH, GnRH, CRH	R2: 599-604		
8	1	GHRH, somatostatin, dopamine, their structure, secretion and regulation.	R2: 605-607		
9	1	Revision and Possible QP discussion			
Total: 9 hours					
Unit-2					
1	1	GH, prolactin, ACTH	T1: 554-556		
2	1	insulin, glucagon, PTH and calcitonin	T1:497-504		
3	1	TSH, FSH, LH	T1:486-496		
4	1	Steroid Hormones and their transport	R2: 601-603		
5	1	Structure, synthesis, secretion of T3 & T4	R2: 601-603		
6	1	Transport of T3 &T4	T1: 492-496		

7	1	Metabolism & regulation of T3 &T4	T1: 492-496		
8	1	Revision and Possible QP discussion			
Total: 8 hours					
Unit-3					
1	1	Physiological action of hormones in the regulation of spermatogenesis	T1: 572-574		
2	1	sperm maturation, oogenesis and menstrual/estrus cycles.	T1: 575-577		
3	1	Gonadal and adrenal steroidogenesis.,	R1: 370-375		
4	1	Cell-cell communication – Two cell concept.	R2: 584-592		
5	1	Hormonal control of implantation	R1: 436-438		
6	1	Gestation and lactation.	R1: 444-447		
7	1	Hormonal contraception.	R1: 447-449		
8	1	Revision and Possible QP discussion			
Total: 8 hours					
Unit-4					
1	1	Protein and steroid hormone receptors and their signaling cascades.	R2: 601-603		
2	1	non-genomic actions	R2: 617-627		
3	1	Ras-Raf-MAPK signaling	R2: 617-627		
4	1	PI3K signaling. Genomic actions of hormones	R2: 617-627		
5	1	thyroid hormone nuclear receptor superfamily	R2:612-616		
6	1	Renin-angiotensin system, atrial natriuretic hormones.	R1:344-346		
7	1	Vasopressin and water retention.	T1:535-537		
8	1	Revision and Possible QP discussion			
Total: 8 hours					
Unit-5					
1	1	Hormone assays, RIA, IRMA, ELISA, Radio receptor assay.	R1:74-76		
2	1	Extraction, purification	R1: 69-71		
3	1	quantification of hormone receptors	R1: 69-71		
4	1	cell surface, cytosolic and nuclear receptors.	T1: 574-576		
5	1	Radiolabeling techniques – Radioiodination	R1: 75-78		

		of peptides			
6	1	autoradiography	R1: 75-78		
7	1	Properties of different types of radioisotopes commonly used in biology, radioactivity	R1: 76-87		
8	1	detection and measurement of radioactivity, safely guidelines and disposal procedures.	R1: 76-87		
9	1	Revision and Possible QP discussion			
Total: 9 hours					
PREVIOUS YEAR END SEMESTER EXAMINATION QUESTION PAPER DISCUSSION					
1	1	Previous year ESE question paper discussion			
2	1	Previous year ESE question paper discussion			
Total: 2 hours					
Grand Total: 48 hours					

REFERENCE

T1: Sarada Subrammaniyamm & mmadhanakutty.k Text book of Physiology (2006), 6th Edition

R1: Hadley, M.C., and Levine, J.E., (2007) Endocrinology 6th ed.,. Pearson Education (New Delhi), Inc. ISBN: 978-81-317-2610-5.

R2 : 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.

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Coimbatore – 641 021.

SYLLABUS

STAFF NAME: Dr.P.Anusooriya
SUBJECT NAME: Endocrinology

SUB.CODE:17BCP303
SEMESTER: III CLASS: II M.Sc (BC)

Course objectives

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

Course outcome

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

Unit I: 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, 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.

REFERENCES

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.

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

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

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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.

KARPAGAM ACADEMY OF HIGHER EDUCATION
DEPARTMENT OF BIOCHEMISTRY
II-M.Sc., BIOCHEMISTRY
ENDOCRINOLOGY (17BCP303)
MULTIPLE CHOICE QUESTIONS

S. N	Question	Opt A	Opt B	Opt C	Opt D	Answer
1	“Adam’s apple” is used to refer to	the trachea	the epiglottis	the thyroid cartilage	the larynx	the thyroid cartilage
2	A rapid and shallow ventillation is called	Apnea	Hyperpnea	Hyperventillation	Tachypnea	Tachypnea
3	Amount of air in the lungs that remains afte	Dead space	Residual volume	Vital capacity	Ventilation rate	Residual volume
4	As you breathe, this contracts and flattens t	Larnynx	Lung balloon	Diaphragm	Bronchiole	Diaphragm
5	At high altitude, RBCs of human blood will	Increase in number	Decrease in number	Decrease in size	Increase in size	Increase in number
6	At rest, the average breathing rate of an ad	60 to 65 breaths per m	100 + breaths per min	3 to 5 breaths per min	12 to 15 breaths per m	12 to 15 breaths per minute
7	Bronchi branch into the tubes of smaller dia	Microtrachea	Bronchioles	Alveoli	Eustachian tubes	Bronchioles
8	Coagulation factor IX is:	Stuart-Prower factor	Hageman factor	Anti-hemophilic acid	Christmas factor	Christmas factor
9	Coagulation factor VIII is:	Stuart-Prower factor	Hageman factor	Anti-hemophilic acid	Christmas factor	Anti-hemophilic acid
10	Coagulation factor X is:	Stuart-Prower factor	Hageman factor	Anti-hemophilic acid	Christmas factor	Stuart-Prower factor
11	Coagulation factor XII is:	fibrinogen	Stuart-Prower factor	FSF	Hageman factor	Hageman factor
12	Complete the following statement using the	less than the pressure	greater than the press	equal to the pressure i	greater than the intra-	greater than the pressure in the atmosphere.
13	Complete the following statement using the	less than the pressure	greater than the press	equal to the pressure i	greater than the intra-	greater than the pressure in the atmosphere
14	During inspiration, how does alveolar press	Alveolar pressure is gr	Alveolar pressure is les	Alveolar pressure is th	Alveolar pressure is on	Alveolar pressure is less than atmospheric.
15	During swallowing of food, _____ is the op	Glottis	Trachea	Epiglottis	Larynx	Trachea
16	Human lungs are situated in	Abdominal cavity	Thoracic cavity	Inside diaphragm	Without any cavity	Thoracic cavity
17	In a hot summer after noon, if your body's h	Positive feedback	Negative feedback	Osmoregulation	Feed back	Negative feedback
18	In case of low blood glucose concentration,	To avoid sweets	to workout	to rest	convert glycogen to gl	convert glycogen to glucose
19	In expiration, diaphragm becomes	Flattened	Relaxed	Straightened	Arched	Relaxed
20	In which disease lung tissue degenerate?	Bronchitis	Pneumonia	Emphysema	Asthma	Emphysema
21	In which of these compartments is Na+ con	interstitial fluid	plasma	intracellular fluid	extracellular fluid	intracellular fluid
22	Intrapulmonary pressure is the _____.	pressure within the pl	pressure within the alv	negative pressure in th	difference between at	pressure within the alveoli of the lungs
23	Lack of pulmonary surfactant produces	Asthma	Respiratory distress sy	Cystic fibrosis	Emphysema	Emphysema
24	Opening to the trachea is covered by a sma	Glottis	Trachea	Epiglottis	Larynx	Epiglottis
25	Patients with which of the following disease	von Willebrand’s disea	Hemophilia A	Hemophilia B	Factor V Leiden	von Willebrand’s disease
26	Protection of internal environment from ha	Thermoregulation	Homeostasis	Osomoregulation	nerve impulse	Homeostasis
27	Proteins C and S are dependent on which vi	Vitamin A	Vitamin B	Vitamin E	Vitamin K	Vitamin K

28	Respiration rate is the lowest during	Running	Playing	Eating	Sleeping	Sleeping
29	The _____ produces red blood cells, whic	Liver; oxygen; mineral	Liver; oxygen; carbon (	Bone marrow; oxygen;	Bone marrow; oxygen;	Bone marrow; oxygen; carbon dioxide
30	The amount of air a person takes in during r	Deadspace	Tidal volume	Vital capacity	Ventilation rate	Tidal volume
31	The average percentage of oxygen in inhale	0%	21%	16%	25%	16%
32	The life span of RBC is	100 days	110 days	120 days	130 days	120 days
33	The lowermost portion of the pharynx is the	oropharynx	nasopharynx	laryngopharynx	pharyngeal tonsils	laryngopharynx
34	The major sign of hypoventilation is	Cyanosis	Dyspnea	Hypercapnia	Hypoxia	Hypercapnia
35	The metal ion present in haemoglobin is	Iron	Magnesium	Copper	Zinc	Iron
36	The most powerful respiratory stimulus for	loss of oxygen in tissue	increase of carbon dio	pH (acidosis)	pH (alkalosis)	increase of carbon dioxide
37	The nose, pharynx, and associated structure	respiratory division	upper respiratory syste	lower respiratory syste	bronchial tree	upper respiratory system
38	The relationship between the pressure and	Boyle's law	Henry's law	Charles' law	Dalton's law	Boyle's law
39	The term “Red Puffers” describes a person v	Emphysema	Bronchitis	Tuberculosis	ARDS	Emphysema
40	The type of hypoxia present in high altitute	Anemic hypoxia	Hypoxic hypoxia	Stagnant hypoxia	Histotoxic hypoxia	Hypoxic hypoxia
41	The volume of air that can be exhaled durin	residual volume	expiratory reserve volu	vital capacity	total lung capacity	expiratory reserve volume
42	The walls of the alveoli are composed of tw	secrete surfactant	trap dust and other de	replace mucus in the a	protect the lungs from	secrete surfactant
43	The walls of the alveoli are composed of tw	secrete surfactant	trap dust and other de	replace mucus in the a	protect the lungs from	secrete surfactant
44	This disease is due to allergens	Bronchitis	Pneumonia	Emphysema	Asthma	Asthma
45	Tidal volume in adult is	125 ml	500 ml	1500 ml	2200 ml	500 ml
46	What is another name for the windpipe?	Lungs	Larynx	Trachea	Oesophagus	Trachea
47	What is pulmonary edema?	Excessive leakage of fl	Excessive leakage of fl	Excessive leakage of fl	Edema of the larynx	Excessive leakage of fluid into the interstitial compartm
48	What is pulmonary embolism?	A blood clot obstructir	A blood clot obstructir	A blood clot in the dee	Right sided heart failur	A blood clot obstructing a pulmonary artery
49	What is the instrument that measures the a	Sphygmomanometer	Hygrometer	Stethoscope	Spirometer	Spirometer
50	When a person takes a very deep breath of	tidal volume	vital capacity	residual volume	inspiratory reserve vol	inspiratory reserve volume
51	When the “wind” is knocked out of a footba	tidal volume	vital capacity	residual volume	inspiratory reserve vol	residual volume
52	Which lung disorder is related to profession	Silicosis	Emphysema	Pneumonia	Asthma	Silicosis
53	Which of the following cations is required fo	Ca2+	Fe2+	Mg2+	Mn2+	Ca2+
54	Which of the following initiates the coagula	Factor XII	Thrombin	Tissue factor	Factor X	Tissue factor
55	Which of the following is known as Royal di	Sickle cell anaemia	Haemophilia	Alzheimer’s disease	Color blindness	Haemophilia
56	Which of the following is not a form of lung	adenocarcinoma	Kaposi's sarcoma	small cell carcinoma	squamous cell carcinor	Kaposi's sarcoma
57	Which of the following is not an event nece	pulmonary ventilation	blood pH adjustment	internal respiration	external respiration	blood pH adjustment
58	Which of the following is the correct order f	trachea, bronchus, bro	bronchus, alveoli, tracl	bronchus, trachea, bro	trachea, alveoli, broncl	trachea, bronchus, bronchiole, alveoli
59	Which statement concerning body fluid con	Intracellular fluid cont	Interstitial fluid contai	Extracellular fluid cont	Extracellular fluid cont	Extracellular fluid contains a higher concentration of so
60	Why can't Heparin be administered orally?	It is large	It is negatively chargec	It contains too much n	It is large and negative	It is large and negatively charged

ıent in the lungs

ıdium than intracellular fluid.

CLASS: II MSC BC
COURSE CODE: 17BCP303

COURSE NAME: ENDOCRINOLOGY
UNIT: I - **General Introduction**
BATCH- 2017-2019

UNIT I

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."

Classification of hormones

Chemical structure and synthesis of hormones

FUNCTIONS OF HORMONES

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

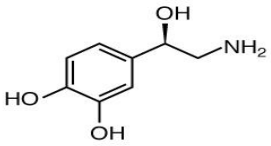
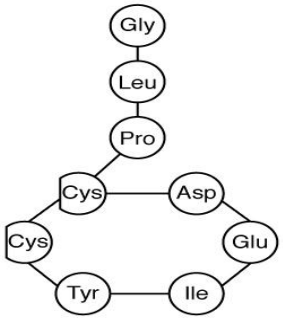
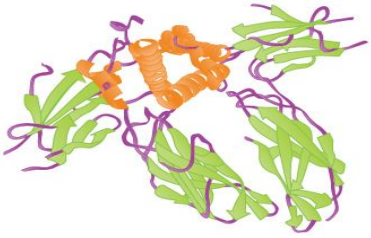
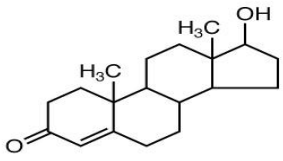
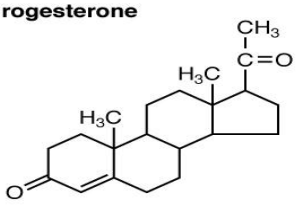
	Tri-iodothyronine (T3)	Most tissues	Acts to regulate the body's metabolic rate
Parathyroid glands	**Parathyroid hormone (PTH)**	Kidney, Bone cells	Increases blood calcium levels in the blood when they are low
	Calcitonin	Kidney, Bone cells	Decreases blood calcium levels when they are high
Adrenal cortex	**Cortisol**	Most tissues	Involved in a huge array of physiological functions including blood pressure regulation, immune system functioning and blood glucose regulation
	Aldosterone	Kidney	Acts to maintain blood pressure by causing salt and water retention
	Androgens	Most tissues	Steroid hormones that promote development of male characteristics. Physiological function unclear
Adrenal medulla	**Adrenaline and noradrenaline (the catecholamines)**	Most tissues	Involved in many physiological systems including blood pressure regulation, gastrointestinal movement and patency of the airways
Pancreas	**Insulin**	Muscle, fat tissue	Acts to lower blood glucose levels
	Glucagon	Liver	Acts to raise blood glucose levels
	Somatostatin	Pancreas	Acts to inhibit glucagon and insulin release
Ovary	**Oestrogens**	Breast, Uterus, Internal and external genitalia	Acts to promote development of female primary and secondary sexual characteristics. Important role in preparing the uterus for implantation of embryo
	Progesterone	BreastUterus	Affects female sexual characteristics and important in the maintenance of pregnancy
Testis	**Testosterone**	Sexual organs	Promotes the development of male sexual characteristics including sperm development
Stomach	**Gastrin**	Stomach	Promotes acid secretion in the stomach
	Serotonin (5-HT)	Stomach	Causes constriction of the stomach muscles
Duodenum and jejunum	**Secretin**	Stomach, Liver	Inhibits secretions from the stomach and increases bile production
	Cholecystokinin (CCK)	Liver, Pancreas	Stimulates release of bile from the gall bladder and causes the pancreas to release digestive enzymes
Kidney	**Erythropoietin**	Bone marrow	Stimulates red blood cell development in the bone marrow
Heart	**Atrial natiuretic factor (ANF)**	Kidney	Lowers blood pressure by promoting salt and water loss
Skin	**Vitamin D**	Small intestine, Kidney, Bone cells	Stimulates the uptake of calcium in the small intestine, retention of calcium and release of calcium from bone stores

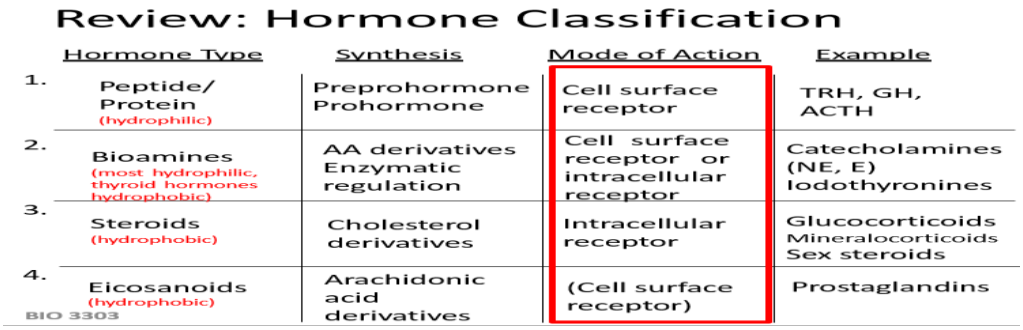
Intracrine refers to a hormone that acts inside a cell, regulating intracellular events. Steroid hormones act through intracellular (mostly nuclear) receptors and, thus, may be considered to be intracrines. In contrast, peptide or protein hormones, in general, act as endocrines, **autocrines**, or **paracrines**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

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

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

Chemical Classification of Hormones

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



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

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

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

Hormones and homeostasis

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

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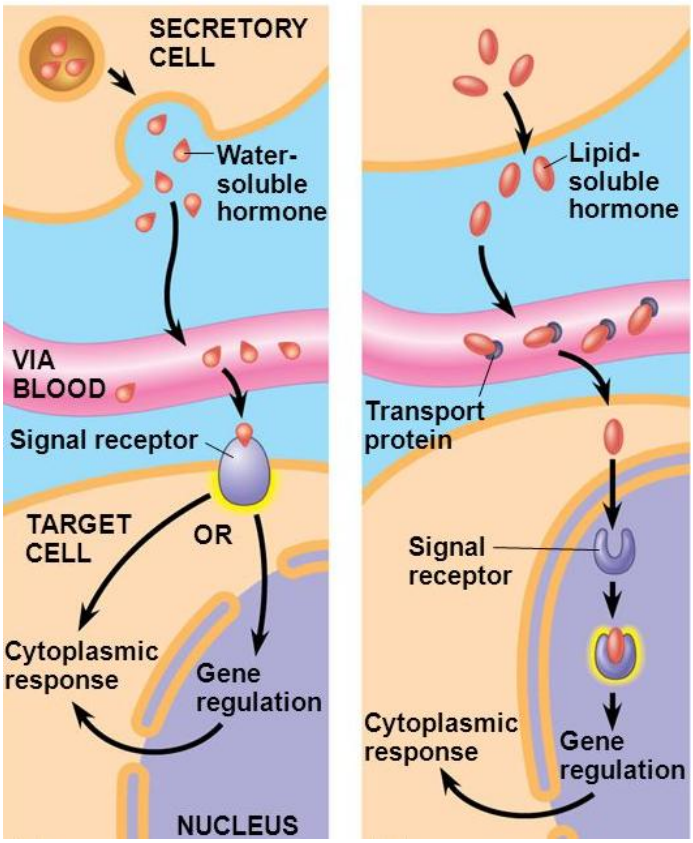


Hormonal secretion and transport

HORMONAL CLEARANCE

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

CONTROL OF HORMONAL SECRETION

Up and Down Regulation

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

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

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

MECHANISM OF HORMONE ACTION

RECEPTORS

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

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

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

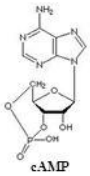
SECOND MESSENGERS

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

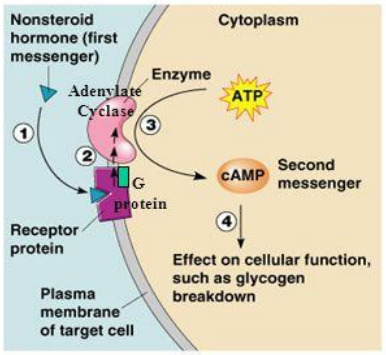
Two Mechanisms of Hormone Action

Non-steroid hormone action

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



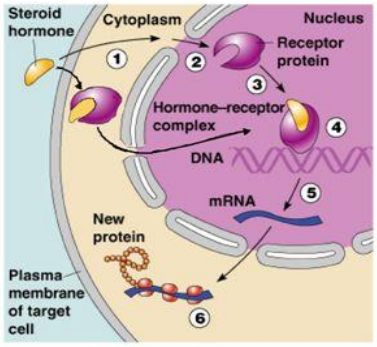
(A few peptide hormones activate Ca^{+2} release via second messengers in the PIP_2 calcium signaling system).



(b) Nonsteroid hormone action

Steroid hormone action

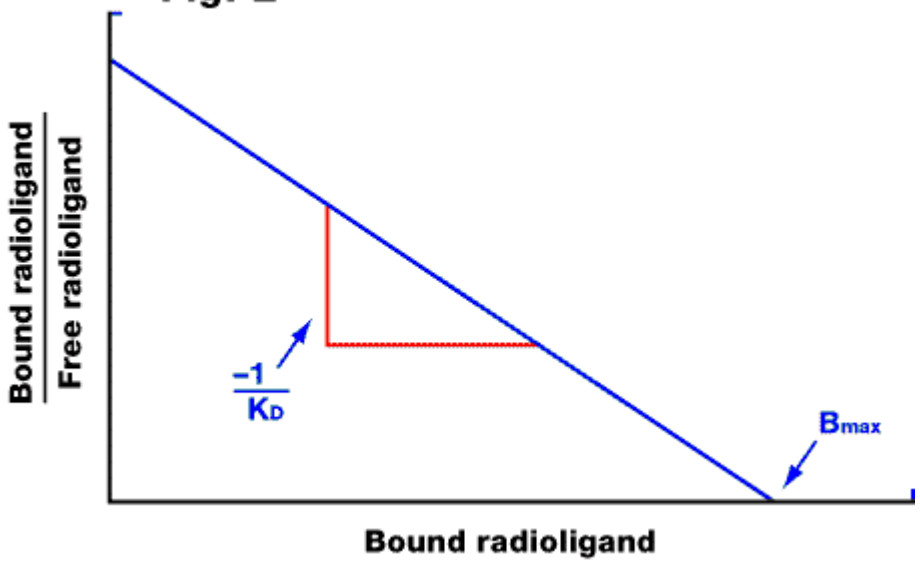
1. Diffuses through the plasma membrane of target cells
2. Enters the nucleus or binds to cytoplasmic receptor
3. Binds to a specific protein within the nucleus if not already bound
4. Binds to specific sites on the cell's DNA
5. Activates genes that result in synthesis of new proteins



(a) Steroid hormone action

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

Fig: E



Application of Scatchard Plot

To assess the number of ligand binding sites in the receptor

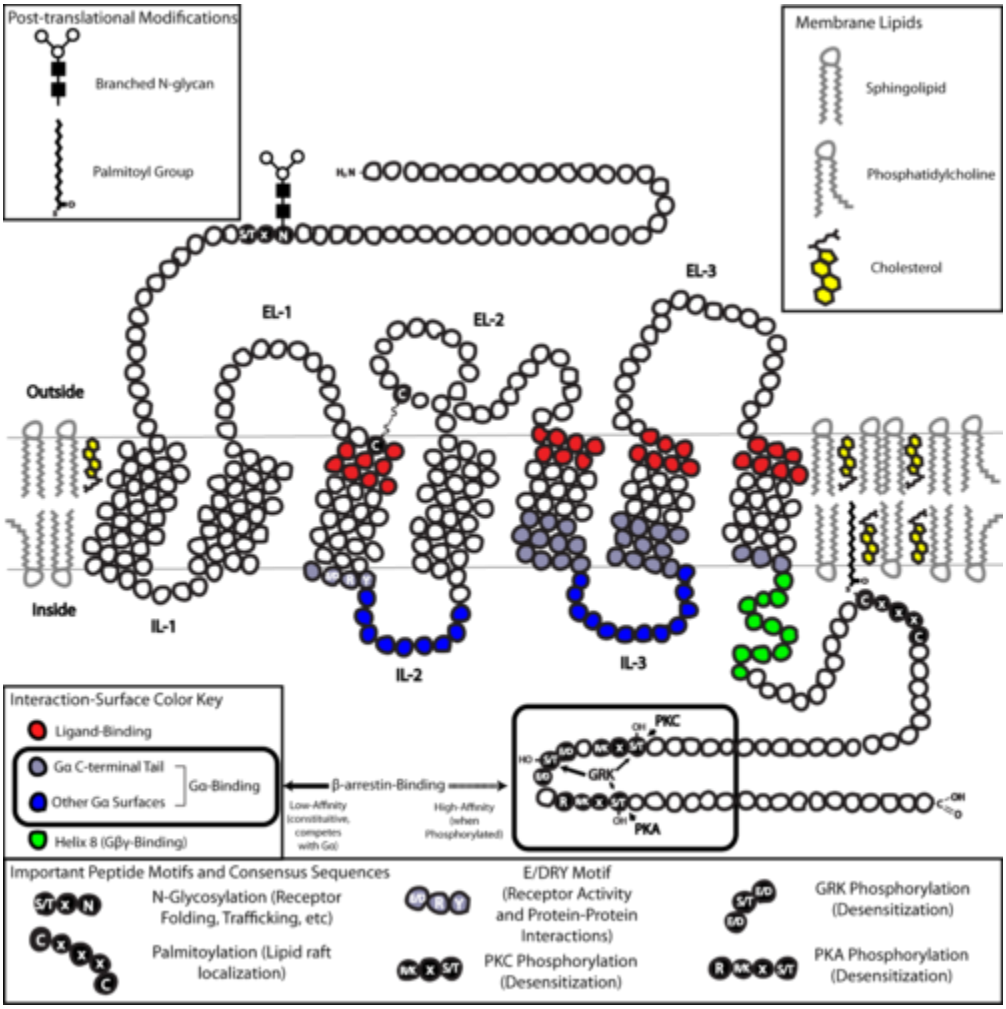
To determine the IC50, ED50 of the drugs

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

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

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

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



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

* cAMP signal pathway
* phosphatidylinositol signal pathway

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

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

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

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

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

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

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

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

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

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

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

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

Glucagon – Stimulates glycogen breakdown in the liver

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

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

Unit II

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.

Hypothalamic - pituitary axis.

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

The anterior pituitary

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

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

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

These hormones are released in response to stimulation by the appropriate releasing hormones. These are peptide hormones secreted by nerve cells in the hypothalamus. They travel through the portal system of vessels in the pituitary stalk to the secretory cells of the anterior pituitary. There, they cause the production and release of pituitary hormones into the bloodstream. For Growth Hormone and Prolactin there are also hypothalamic inhibitory hormones which stop their release, providing a control mechanism.

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

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

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

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

Some of the diseases involving the pituitary gland are:

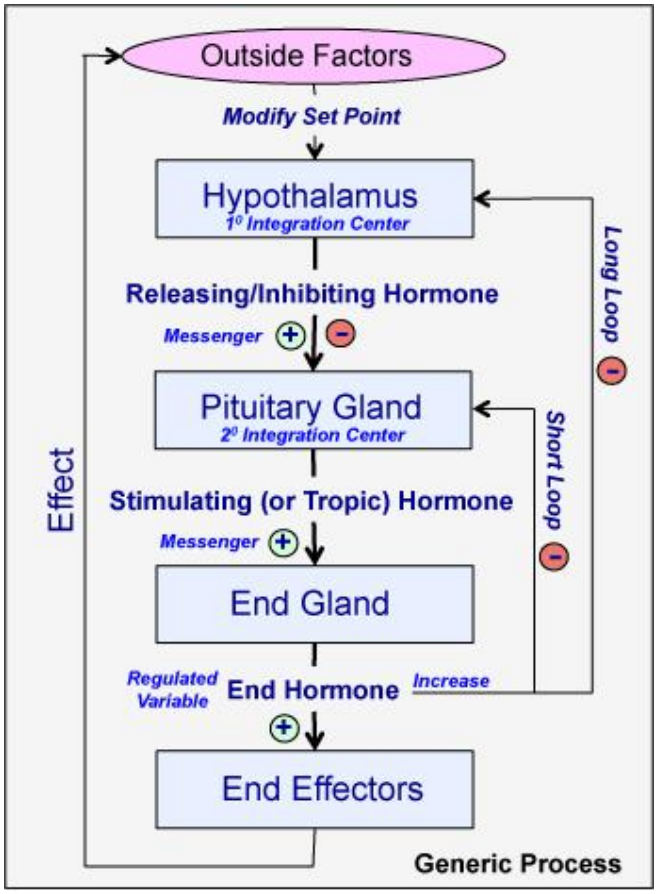
* Central diabetes insipidus caused by a deficiency of vasopressin.
* Gigantism and acromegaly caused by an excess of growth hormone in childhood and adult respectively.

- Hypothyroidism caused by a deficiency of thyroid-stimulating hormone.
- Hyperpituitarism, the increased (hyper) secretion of one or more of the hormones normally produced by the pituitary gland.
- Hypopituitarism, the decreased (hypo) secretion of one or more of the hormones normally produced by the pituitary gland.
- Panhypopituitarism a decreased secretion of most of the pituitary hormones.
- Pituitary tumours.
- Pituitary adenomas, noncancerous tumors that occur in the pituitary gland.

Feedback Regulation

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

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



PTH

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

hyperparathyroidism, or paraneoplastic syndromes) can wreak havoc in the form of bone disease, hypocalcaemia, and hypercalcaemia.

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

Biosynthesis

The formation of parathyroid hormone (PTH) in the parathyroid gland occurs via two successive proteolytic cleavages from larger biosynthetic precursors. The initial product coded for by PTH mRNA is pre-proparathyroid hormone (PreProPTH), a polypeptide of 115 amino acids. Within 1 min of synthesis, the polypeptide, proparathyroid hormone (ProPTH), is formed as a result of the proteolytic removal of the NH_2-terminal 25 amino acids from Pre-ProPTH. After a delay of 15-20 min, the NH_2-terminal six-amino acid sequence of ProPTH is removed to give PTH of 84 amino acids. To investigate the subcellular sites in the parathyroid cell where the biosynthetic precursors undergo specific proteolytic cleavages, from 15 to 30 min they migrated within secretory vesicles still in the Golgi region and then migrated to mature secretory granules outside the Golgi area. Electrophoretic analyses showed that Pre-ProPTH disappeared rapidly (by 5 min) and that conversion of ProPTH to PTH was first detectable at 15 min and was completed by 30 min. At later times of incubation (30-90 min), autoradiographic grains within the secretion glanules migrated to the periphery of the cell and to the plasma membrane, in correlation with the release of PTH first detected by 30 min. Proteolytic conversion of Pre-ProPTH to ProPTH takes place in the RER and that subsequent conversion of ProPTH to PTH occurs in the Golgi complex.

Vitamin D

Vitamin D refers to a group of fat-soluble secosteroids responsible for increasing intestinal absorption of calcium, magnesium, and phosphate, and multiple other biological effects. In humans, the most important compounds in this group are vitamin D3 (also known as

cholecalciferol) and vitamin D2 (ergocalciferol).[1] Cholecalciferol and ergocalciferol can be ingested from the diet and from supplements.[1][2][3] Only a few foods contain vitamin D. The major natural source of the vitamin is synthesis of cholecalciferol in the skin from cholesterol through a chemical reaction that is dependent on sun exposure (specifically UVB radiation). Dietary recommendations typically assume that all of a person's vitamin D is from taken by mouth, as sun exposure in the population is variable and recommendations about the amount of sun exposure that is safe are uncertain in view of the skin cancer risk.

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

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

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

Rickets

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

majority of cases occur in children suffering from severe malnutrition, usually resulting from famine or starvation during the early stages of childhood.

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

Osteoporosis

Osteoporosis is a disease where increased bone weakness increases the risk of a broken bone. It is the most common reason for a broken bone among the elderly.Bones that commonly break include the vertebrae in the spine, the bones of the forearm, and the hip. Until a broken bone occurs there are typically no symptoms. Bones may weaken to such a degree that a break may occur with minor stress or spontaneously. Chronic pain and a decreased ability to carry out normal activities may occur following a broken bone. Osteoporosis may be due to lower than normal bone mass and greater than normal bone loss. Bone loss increases after menopause due to lower estrogen levels.

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

Gastrointestinal Hormones

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

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

Hormone or	**Molecular weight**	**Number of amino**	**Main gut**	**Principal physiologic actions**

peptide	(Da)	acids	localization	
Gastrin family				
Cholecystokinin	3918	33 (also 385, 59)	Duodenum and jejunum, Enteric nerves	Stimulates gallbladder contraction and intestinal motility; stimulates secretion of pancreatic enzymes, insulin, glucagon, and pancreatic polypeptides; has a role in indicating satiety; the C-terminal 8 amino acid peptide cholecystokinin (CCK)-8 retains full activity
Little gastrin	2098	17	Both forms of gastrin are found in the gastric antrum and duodenum	Gastrins stimulate the secretion of gastric acid, pepsinogen, intrinsic factor, and secretin; stimulate intestinal mucosal growth; increase gastric and intestinal motility
Big gastrin	3839	34		
Secretin-glucagon family				
Secretin	3056	27	Duodenum and jejunum	Stimulates pancreatic secretion of HCO_3, enzymes and insulin; reduces gastric and duodenal motility, inhibits gastrin release and gastric acid secretion
Vasoactive intestinal polypeptide (VIP)	3326	28	Enteric nerves	Relaxes smooth muscle of gut, blood vessels, and genitourinary system; increases water and electrolyte secretion from pancreas and gut; releases hormones from

				pancreas, gut, and hypothalamus
Glucose-dependent insulinotropic	4976	42	Duodenum and jejunum	Stimulates insulin release; reduces gastric and intestinal motility; increases fluid and electrolyte secretion from small intestine

Insulin

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

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

If beta cells are destroyed by an autoimmune reaction, insulin can no longer be synthesized or be secreted into the blood. This results in type 1 diabetes mellitus, which is characterized by abnormally high blood glucose concentrations, and generalized body wasting. In type 2 diabetes mellitus the destruction of beta cells is less pronounced than in type 1 diabetes, and is not due to an autoimmune process. Instead there is an accumulation of amyloid in the pancreatic islets, which likely disrupts their anatomy and physiology. The pathogenesis of type 2 diabetes is not

well understood but patients exhibit a reduced population of islet beta-cells, reduced secretory function of islet beta-cells that survive and peripheral tissue insulin resistance Type 2 diabetes is characterized by high rates of glucagon secretion into the blood which are unaffected by, and unresponsive to the concentration of glucose in the blood glucose. Insulin is still secreted into the blood in response to the blood glucose. As a result, the insulin levels, even when the blood sugar level is normal, are much higher than they are in healthy persons. There are a variety of treatment regimens, none of which is entirely satisfactory. When the pancreas's capacity to secrete insulin can no longer keep the blood sugar level within normal bounds, insulin injections are given.

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

Functions of Insulin

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

- Increase of cellular intake of certain substances, most prominently glucose in muscle and adipose tissue (about two-thirds of body cells)
- Increase of DNA replication and protein synthesis via control of amino acid uptake
- Modification of the activity of numerous enzymes.
- The actions of insulin (indirect and direct) on cells include:
- Stimulates the uptake of glucose – Insulin decreases blood glucose concentration by inducing intake of glucose by the cell. This is possible because Insulin causes the insertion of the GLUT4 transporter in the cell membranes of muscle and fat tissues which allows glucose to enter the cell.

* Induce glycogen synthesis – When glucose levels are high, insulin induces the formation of glycogen by the activation of the hexokinase enzyme, which adds a phosphate group in glucose, thus resulting in a molecule that cannot exit the cell. At the same time, insulin inhibits the enzyme glucose-6-phosphatase, which removes the phosphate group. These two enzymes are key for the formation of glycogen. Also, insulin activates the enzymes phosphofructokinase and glycogen synthase which are responsible for glycogen synthesis.

* Increased potassium uptake – forces cells synthesizing glycogen (a very spongy, "wet" substance, that increases the content of intracellular water, and its accompanying K+ ions) to absorb potassium from the extracellular fluids; lack of insulin inhibits absorption. Insulin's increase in cellular potassium uptake lowers potassium levels in blood plasma. This possibly occurs via insulin-induced translocation of the Na+/K+-ATPase to the surface of skeletal muscle cells.

* Decreased gluconeogenesis and glycogenolysis – decreases production of glucose from noncarbohydrate substrates, primarily in the liver (the vast majority of endogenous insulin arriving at the liver never leaves the liver); increase of insulin causes glucose production by the liver from assorted substrates.

* Increased lipid synthesis – insulin forces fat cells to take in blood glucose, which is converted into triglycerides; decrease of insulin causes the reverse.

* Increased esterification of fatty acids – forces adipose tissue to make neutral fats (i.e., triglycerides) from fatty acids; decrease of insulin causes the reverse.

* Decreased lipolysis – forces reduction in conversion of fat cell lipid stores into blood fatty acids and glycerol; decrease of insulin causes the reverse.

* Decreased proteolysis – decreasing the breakdown of protein

* Decreased autophagy – decreased level of degradation of damaged organelles. Postprandial levels inhibit autophagy completely.

* Increased amino acid uptake – forces cells to absorb circulating amino acids; decrease of insulin inhibits absorption.

* Decreased renal sodium excretion.

Diabetes Mellitus

There are several conditions in which insulin disturbance is pathologic:

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

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

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

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

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

There is correlation with diet, with sedentary lifestyle, with obesity, with age and with metabolic syndrome. Causality has been demonstrated in multiple model organisms including mice and monkeys; Importantly, non-obese people do get Type 2 diabetes due to diet, sedentary

lifestyle and unknown risk factors. It is likely that there is genetic susceptibility to develop Type 2 diabetes under certain environmental conditions

Treatment:

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

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

Adiponectin

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

Adiponectin effects:

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

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

Endocrine Disorders

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

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

Signs and symptoms

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

* Soft tissue swelling visibly resulting in enlargement of the hands, feet, nose, lips and ears, and a general thickening of the skin
* Soft tissue swelling of internal organs, notably the heart with attendant weakening of its muscularity, and the kidneys, also the vocal cords resulting in a characteristic thick, deep voice and slowing of speech
* Generalized expansion of the skull at the fontanelle
* Pronounced brow protrusion, often with ocular distension (frontal bossing)

- Pronounced lower jaw protrusion (prognathism) with attendant macroglossia (enlargement of the tongue) and teeth spacing
- Hypertrichosis, hyperpigmentation and hyperhidrosis may occur in these patients.[9]:499
- Acrochordon (skin tags)
- Carpal tunnel syndrome

Complications

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

Treatment

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

Pygmies and Dwarfs

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

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

Causes:

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

Diabetes Insipidus

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

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

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

Thyroid Gland

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

Biosynthesis of thyroid hormone

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

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

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

Regulation

The production of thyroxine and triiodothyronine is primarily regulated by thyroid-stimulating hormone (TSH), released by the anterior pituitary gland. TSH release in turn is stimulated by

thyrotropin releasing hormone (TRH), released in a pulsatile manner from the hypothalamus. The thyroid hormones provide negative feedback to the thyrotropes TSH and TRH: when the thyroid hormones are high, TSH production is suppressed. This negative feedback also occurs when levels of TSH are high, causing TRH production to be suppressed

Functions of thyroid hormone

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

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

These include:

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

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

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

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

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

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

Disorders of thyroid gland

Cretinism and Myxodema

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

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

Treatment

Sporadic and genetic cretinism results from abnormal development or growth of the foetal thyroid gland. This type of cretinism has been almost completely eliminated in developed

countries by early diagnosis by newborn screening schemes followed by lifelong treatment with thyroxine (T4).

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

Comparison between Cretinism and Myxedema:

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

Hashimoto Thyroiditis

Hashimoto's thyroiditis, also known as chronic lymphocytic thyroiditis and Hashimoto's disease, is an autoimmune disease in which the thyroid gland is gradually destroyed. Early on there may be no symptoms. Over time the thyroid may enlarge forming a painless goiter. Some people eventually develop hypothyroidism with its accompanying weight gain, feeling tired, constipation, depression, and general pains. Hashimoto's thyroiditis is thought to be due to a combination of genetic and environmental factors. Risk factors include a family history of the condition and having another autoimmune disease. Diagnosis is confirmed with blood tests for TSH, T4, and antithyroid antibodies.

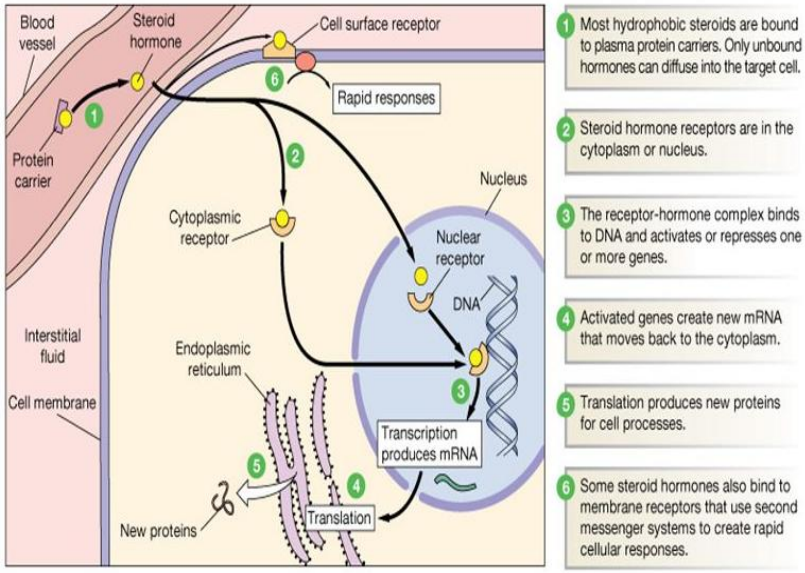
Steroid Hormones

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

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

Mechanism of Action

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



The first identified mechanisms of steroid hormone action were the genomic effects. In this pathway, the free hormones first pass through the cell membrane because they are fat soluble. In the cytoplasm, the steroid may or may not undergo an enzyme-mediated alteration such as reduction, hydroxylation, or aromatization. Then the steroid binds to a specific steroid hormone receptor, also known as a nuclear receptor, which is a large metalloprotein. Upon steroid binding, many kinds of steroid receptors dimerize: two receptor subunits join together to form one functional DNA-binding unit that can enter the cell nucleus. Once in the nucleus, the steroid-receptor ligand complex binds to specific DNA sequences and induces transcription of its target genes.

KARPAGAM ACADEMY OF HIGHER EDUCATION
DEPARTMENT OF BIOCHEMISTRY
II-M.Sc., BIOCHEMISTRY
ENDOCRINOLOGY (17BCP303)
MULTIPLE CHOICE QUESTIONS

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

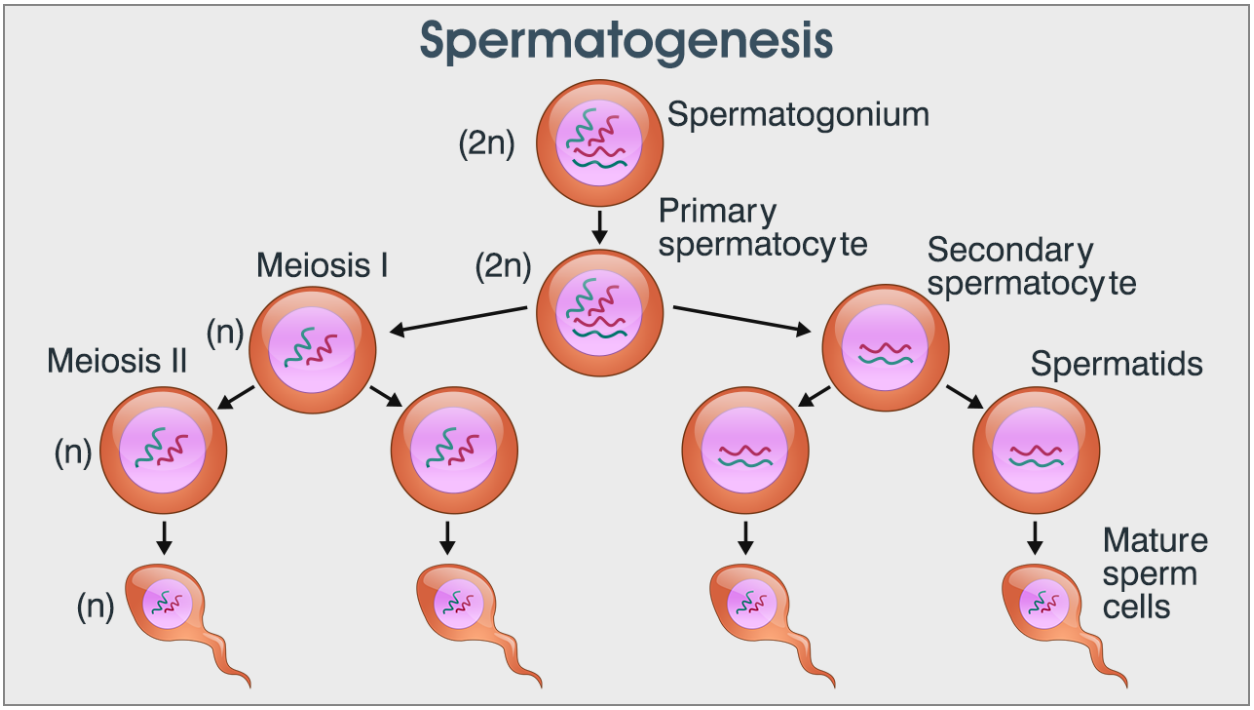
41	The pericardium is the double sac membrane that:	encloses the heart	line the aorta	makes up the heart valves	is found only in the capillaries	encloses the heart
42	The PR interval of ECG corresponds to	ventricular repolarization	ventricular repolarization	atrial repolarization and conduction through 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

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.

Spermatogenesis, the origin and development of the sperm cells within the male reproductive organs, the testes. The testes are composed of numerous thin, tightly coiled tubules known as the seminiferous tubules; the sperm cells are produced within the walls of the tubules. Within the walls of the tubules, also, are many randomly scattered cells, called Sertoli cells that function to support and nourish the immature sperm cells by giving them nutrients and blood products. As the young germ cells grow, the Sertoli cells help to transport them from the outer surface of the seminiferous tubule to the central channel of the tubule.



Sperm cells are continually being produced by the testes, but not all areas of the seminiferous tubules produce sperm cells at the same time. One immature germ cell takes as long as 74 days to reach final maturation, and during this growth process there are intermittent resting phases.

The immature cells (called spermatogonia) are all derived from cells called stem cells in the outer wall of the seminiferous tubules. The stem cells are composed almost entirely of nuclear material. (The nucleus of the cell is the portion containing the chromosomes.) The stem cells begin their process by multiplying in the process of cell duplication known as mitosis. Half of the new cells from this initial crop go on to become the future sperm cells, and the other half remain as stem cells so that there is a constant source of additional germ cells. Spermatogonia destined to develop into mature sperm cells are known as primary sperm cells. These move from the outer portion of the seminiferous tubule to a more central location and attach themselves around the Sertoli cells. The primary sperm cells then develop somewhat by increasing the amount of cytoplasm (substances outside of the nucleus) and structures called organelles within the cytoplasm. After a resting phase the primary cells divide into a form called a secondary sperm cell. During this cell division there is a splitting of the nuclear material. In the nucleus of the primary sperm cells there are 46 chromosomes; in each of the secondary sperm cells there are only 23 chromosomes, as there are in the egg. When the egg and sperm combine and their chromosomes unite, the characteristics of both individuals blend and the new organism starts to grow.

The secondary sperm cell still must mature before it can fertilize an egg; maturation entails certain changes in the shape and form of the sperm cell. The nuclear material becomes more condensed and oval in shape; this area develops as the head of the sperm. The head is covered partially by a cap, called the acrosome, which is important in helping the sperm to gain entry into the egg. Attached to the opposite end of the head is the tailpiece. The tail is derived from the secondary sperm cell's cytoplasm. In the mature sperm, it consists of a long, slender bundle of filaments that propel the sperm by their undulating movement. Once the sperm has matured, it is transported through the long seminiferous tubules and stored in the epididymis of the testes until it is ready to leave the male body.

Spermatozoa maturation steps

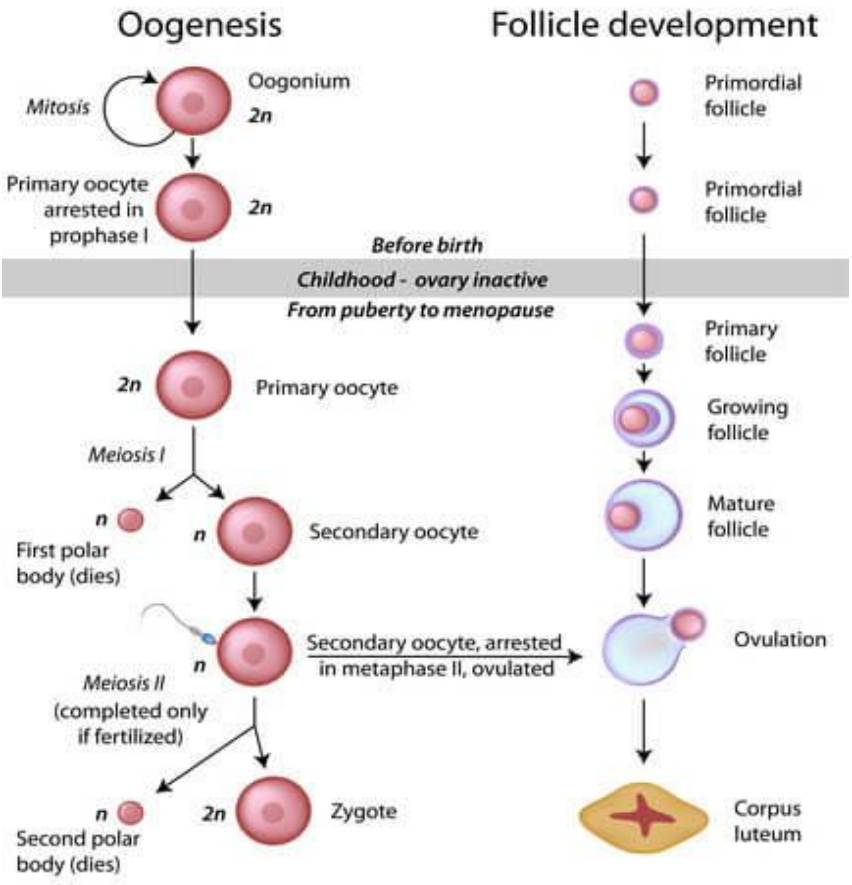
There are parallels between getting the spermatozoa ready and the maturation of an oocyte but there are also clear differences. The spermatozoa have to go through several **temporal maturation steps in a series of different locations** in order to be capable of penetrating into the oocyte. While the oocyte's maturation steps involve the storing of yolk and the process of meiosis, functional maturation steps are required with the spermatozoa, which mainly involve their **motile abilities** along with their **ability to penetrate** through the egg covering.

The spermatozoa experience an initial maturation step during the time they are "stored" in the **epididymis**. When the **ejaculation** occurs, a second step follows that leads to a **sudden activation of their motility**. The third step takes place during their **stay** in the female genital tract, especially during the **ascension** towards the ovary through the uterus and fallopian tube.

The spermatozoa experience thereby the so-called **capacitation**. Finally, the last activation step follows: the **acrosome reaction** in the immediate **vicinity of the oocyte**.

Oogenesis

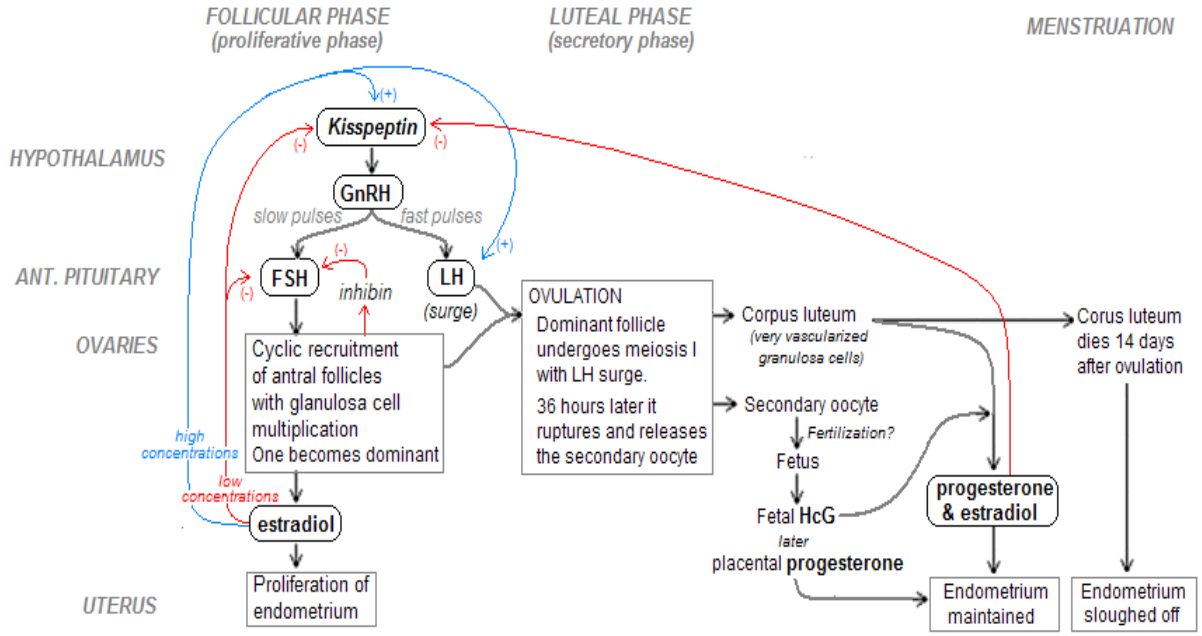
Oogenesis is the process of development of female gametes or ova or egg that takes place in ovaries. The process of oogenesis begins before birth with the formation of diploid germ cells, called oogonia that have the ability to develop into mature ova. These oogonia are formed during fetal life when the female child isn't born yet. However, the majority of these oogonia degenerate prior to birth and the remaining enter first meiotic division as primary oocytes. After duplicating their genetic material post-birth, primary oocytes are arrested in prophase I and remain arrested at this stage of development for years until they are prepared to shed the first egg (i.e. until the first ovulation period). The immature ova then resume the cell division where they left off until they finish the meiosis I.



This yields two daughter cells, each receiving an equal number of chromosomes. Nonetheless, this is not the case with the cytoplasm of the primary oocytes, as the entire cytoplasm remains with one of the daughter cells, which is then designated as the secondary oocyte. The other daughter cell that lacks cytoplasm develops into a first polar body. The polar body is nonfunctional, and therefore, degenerates or gives rise to 2 more polar bodies. The secondary oocyte is released from the ovary during ovulation. It is destined to become a mature ovum but still contains two copies of each chromosome. A mature ovum should have a single set of chromosomes and not two. So, the oocyte has to undergo a second meiotic division. The secondary oocyte is arrested in metaphase II until fertilization. The penetration the sperm into the secondary oocyte induces the second meiotic division. The second meiotic division finally yields a mature ovum and since this division is also unequal, half of the chromosomes are transferred to the second polar body and the other half is conserved by the ovum along with all of the cytoplasm. Hence, while the mature ovum acquires its single set of chromosomes, it retains the cytoplasm. If the secondary oocyte is not fertilized by a sperm within a day, it degenerates.

Reproductive Cycle

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



Disorders

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

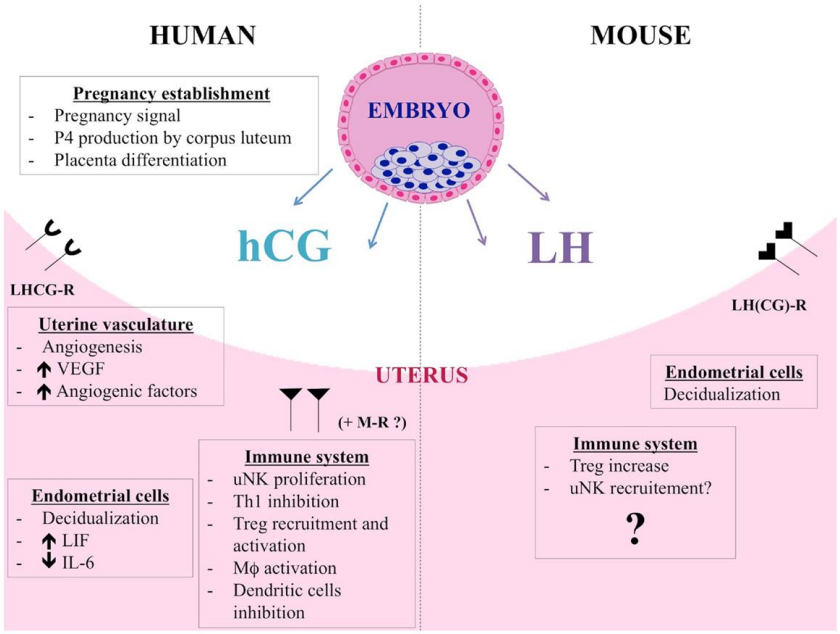
Very little flow (less than 10 ml) is called hypomenorrhea. Regular cycles with intervals of 21 days or fewer are polymenorrhea; frequent but irregular menstruation is known as metrorrhagia. Sudden heavy flows or amounts greater than 80 ml are termed menorrhagia.

Endocrinology of Pregnancy

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

Some of the most significant hormones in pregnancy are:

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



Aldosterone

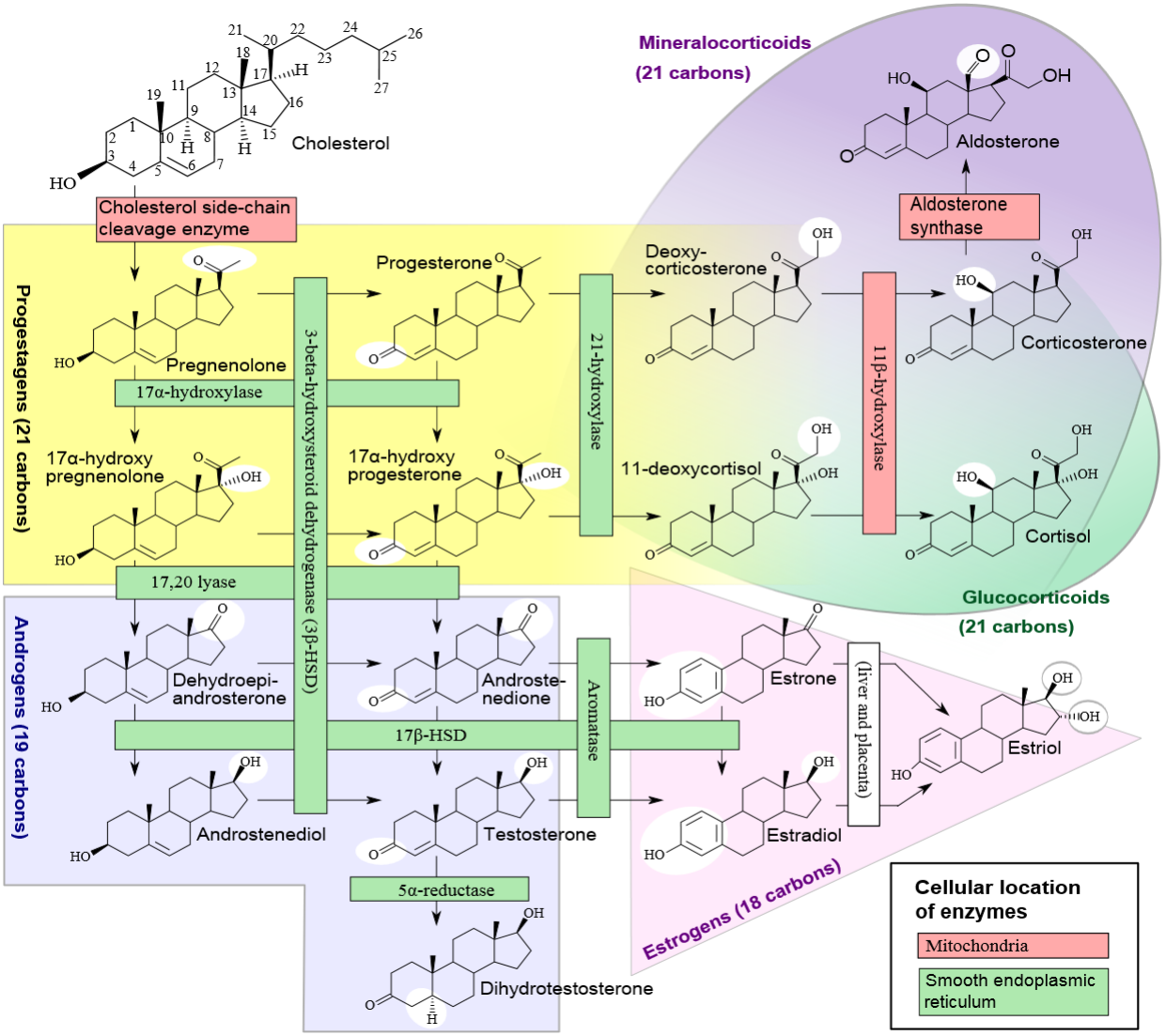
Aldosterone, the main mineralocorticoid hormone, is a steroid hormone produced by the zona glomerulosa of the adrenal cortex in the adrenal gland. It is essential for sodium conservation in the kidney, salivary glands, sweat glands and colon. It plays a central role in the homeostatic regulation of blood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

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

drugs stimulate the excretion of sodium and water in urine, while they block the excretion of potassium.

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

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



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

Aldosterone and corticosterone share the first part of their biosynthetic pathways. The last parts are mediated either by the aldosterone synthase (for aldosterone) or by the 11β-hydroxylase (for corticosterone). These enzymes are nearly identical (they share 11β-hydroxylation and 18-hydroxylation functions), but aldosterone synthase is also able to perform an 18-oxidation. Moreover, aldosterone synthase is found within the zona glomerulosa at the outer edge of the adrenal cortex; 11β-hydroxylase is found in the zona glomerulosa and zona fasciculata.

Functions

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

* Acting on the nuclear mineralocorticoid receptors (MR) within the principal cells of the distal tubule and the collecting duct of the kidney nephron, it upregulates and activates the basolateral Na+/K+ pumps, which pumps three sodium ions out of the cell, into the interstitial fluid and two potassium ions into the cell from the interstitial fluid. This creates a concentration gradient which results in reabsorption of sodium (Na+) ions and water (which follows sodium) into the blood, and secreting potassium (K+) ions into the urine (lumen of collecting duct).

* Aldosterone upregulates epithelial sodium channels (ENaCs) in the collecting duct and the colon, increasing apical membrane permeability for Na+ and thus absorption.

* Cl^- is reabsorbed in conjunction with sodium cations to maintain the system's electrochemical balance.

* Aldosterone stimulates the secretion of K+ into the tubular lumen.

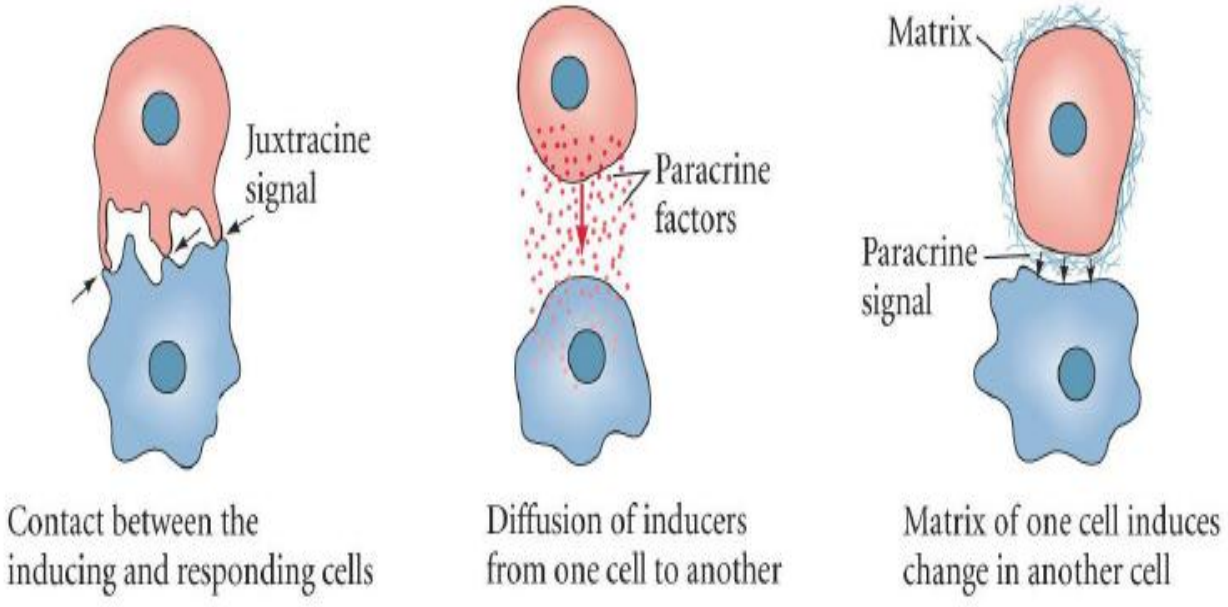
* Aldosterone stimulates Na+ and water reabsorption from the gut, salivary and sweat glands in exchange for K+.

* Aldosterone stimulates secretion of H+ via the H+/ATPase in the intercalated cells of the cortical collecting tubules

* Aldosterone upregulates expression of NCC in the distal convoluted tubule chronically and its activity acutely.

Cell –Cell Commuication

Cell– cell interaction refers to the direct interactions between cell surfaces that play a crucial role in the development and function of multicellular organisms. These interactions allow cells to communicate with each other in response to changes in their microenvironment. This ability to send and receive signals is essential for the survival of the cell. Interactions between cells can be stable such as those made through cell junctions. These junctions are involved in the communication and organization of cells within a particular tissue. Others are transient or temporary such as those between cells of the immune system or the interactions involved in tissue inflammation. These types of intercellular interactions are distinguished from other types such as those between cells and the extracellular matrix. The loss of communication between cells can result in uncontrollable cell growth and cancer.



Cells develop in the context of their environment, including:

-their immediate cellular neighborhood

-their tissue identity-their position in the body.

Developing cells receive signals from each of these locations, and they, in turn, signal the cells around them.

1) A signal

2) A receptor for that signal

3) A mechanism to translate and/or transport the signal

4) A mechanism to translate the signal to a stimulation (or repression) of gene expression.

Endocrinology of pregnancy

- Make no mistake, the placenta is a temporary endocrine organ; **the placenta produces several important hormones for the maintenance of pregnancy**.
- The placenta produces progesterone, estrogen:
    - Recall that estrogen and progesterone from the follicle and corpus luteum (follicular and luteal phases of the ovarian cycle) conditioned the female genital tract (uterus, cervix, vagina) for fertilization and implantation (the proliferative and secretory stages of the uterine cycle).
    - So, it makes sense that the placenta would make progesterone and estrogen in order to maintain the microenvironment of the genital tract.

The placenta produced human chorionic gonadotropin:

- hCG is produced by trophoblast cells of the placenta.
- hCG is an alpha-beta protein (alpha constant, beta unique) just like LH and FSH.
- hCG binds the LH receptors.
- Recall that the corpus luteum has granulosa cells and theca cells; recall, too, that theca cells have LH receptor throughout development of the follicle

and **granulosa cells begin to express LH receptor** as the follicle matures to ovulation.

- Therefore, it makes sense that **hCG is called a gonadotropin** because **hCG extends the life of the corpus luteum** and elevates production of progesterone (by the reciprocal action of granulosa and theca cells).
- **hCG peaks at 10-15 weeks.**
- We suspect that hCG has a critical role throughout pregnancy.

The **placenta produces placental lactogen**:

- hPL is produced by syncitiotrophoblasts of the placenta.
- hPL promotes milk-production (**lactogenic**) and somatic growth (**growth-hormone-like**).
- hPL ensures adequate fuel supplies for the parasite fetus by reducing mother's glucose use and mobilizing mother's adipose reserves.

Steroid hormones of pregnancy

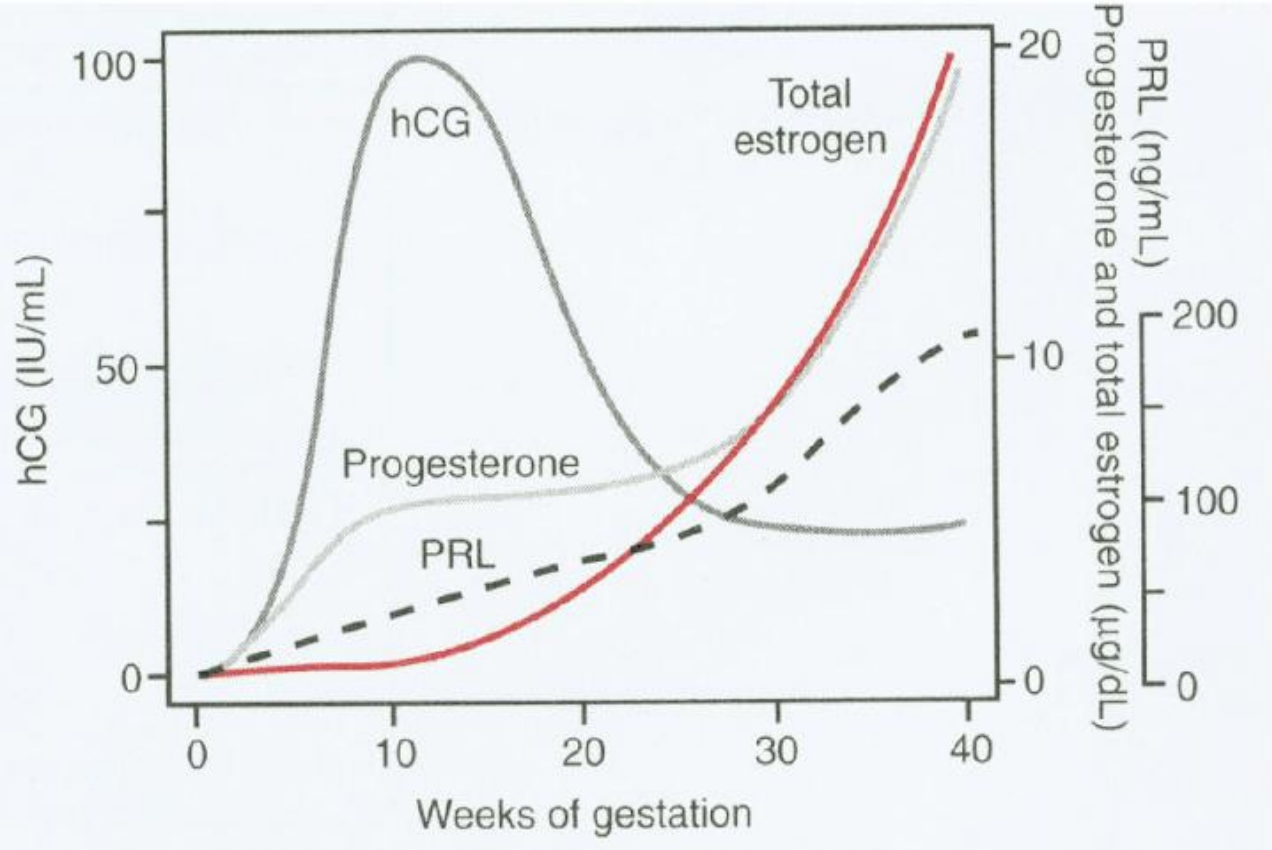
- The two major steroid hormones of pregnancy are progesterone and estrogen.
  - Recall that progesterone and estrogen serve to condition the genital tract microenvironment for pregnancy.
  - **Progesterone:**
    - Produced for the first 8 weeks primarily by the corpus luteum.
    - Recall that the trophoblasts of the placenta produce hCG which is a gonadotropin that maintains the life of the corpus luteum beyond the 2 weeks it would normally produce progesterone / estrogen while degrading during the luteal phase of the ovarian cycle.
    - After 8 weeks, the trophoblasts of the placenta are the primary producers of progesterone.

- **Trophoblasts have LDL receptors** that collect LDL cholesterol from the mother's blood supply and convert it into progesterone.
- **Progesterone levels rise throughout pregnancy**.
- Progesterone conditions the genital tract in three ways: **inhibits utrine contraction**, **inhibits prostaglanding formation**, and **inhibits immune response at the uterus**.
- Specifically, progesterone **binds to uterine smooth muscle cells to inhibit contraction**.
- Specifically, progesterone **inhibits T cell response** at the uterus to provide **temporary immune privilege** to the uterus.

Estrogen / estradiol:

- Recall that estrogen is produced by the granulosa cells of the corpus luteum throughout the luteal phase (~2 weeks w/o pregnancy, extended to 8 weeks with hCG from placenta).
- Production of estrogens require a functional **fetoplacental unit** (that is, a functional connection between the fetus and the mother).
- **Estrogen levels rise throughout pregnancy just like progesterone**.
- Estrogen serves to condition the mother's genital tract: **increases uterine size** and **increases uterine blood flow**.
- **Estrogen also affects fetal development**; estrogen augments organ development and affects breast and adipose development.
- Lastly, **estrogen is involved in implantation**.

Hormone production during pregnancy



Maternal changes of pregnancy

- The physical presence of the growing fetus, along with estrogen, progesterone, and human placental lactogen cause changes to the mother's physiology.
- Recall that progesterone inhibits contractions, inhibits prostaglandins, and inhibits immune response at the uterus.
- Progesterone's inhibition of uterine contractions affects other smooth muscle, too, causing **gastroesophageal reflux** and **constipation**.

- Recall that the lower esophageal sphincter is smooth muslce (lower 1/3 is all smooth muscle) and the colon requires periodic smooth muscle peristalsis to move feces along so they do not dry out.
- Progesterone also causes **increased minute ventilation**.
- Recall that estrogen causes uterine growth and increased uterine blood flow.
- Estrogens cause increased blood flow systemically which can lead to **sinus congestion**, **bleeding gums**, and **sensations of warmth**.
- Estrogens cause **increased perfomance of the cardiovascular system** in general: increased blood volume, increased cardiac output, and increased heart rate.
- Recall that hPL (human placental lactogen from the **synciotrophoblasts**) causes milk production, reduced glucose use and increased adipose energy store mobilization in the mother.
- The mother will **gain weight to ensure enough energy** for fetal peak growth and in the case of starvation.

Endometriosis

- Recall that endometrial cells line the inside of the uterus and respond to estrogen and progesterone by proliferation.
- When endometrial cells exist outside of the uterus (like on the ovaries), they can proliferate and cause pathology.
- S&S include **pelvic pain that worsens with the menstruation cycle**.
- It makes sense that pain would increase during during the follicular uterine cycle and the luteal phase of the ovarian cycle because estrogen levels will be high.
- Endometriosis is in 5-10% of women--usually during the reproductive years.
- Endometriosis is **a common cause of infertility.**

Parturition

- Parturition is a poorly understood concept in general.
- We do know that there are both fetal and maternal factors that play a role.
- We know that there are both hormonal and mechanical factors.
- We suspect that **paracrine factors may be the most important** kind of hormone signaling involved in parturition.
- There are 5 major hormones that affect parturition: estrogen, progesterone, oxytocin, relaxin, placental-corticotropin releasing hormone (pCRH).
- We know that **estrogen is generally pro-parturition and progesterone is generally anti-parturition**.
  - **Estrogen's role in parturition:**
    - Recall estrogen is generally pro-parturition.
  - **Oxytocin's role in parturition:**
  - Oxytocin augments labor but doesn't increase uterine responsiveness or density (that is, it doesn't cause uterine contractions to be more forceful or more common).
  - Recall that **myometrial cells (uterine smooth muscle cells) can coordinate via gap junctions**.
  - **Cervical and vaginal dilation causes explosive, pulsatile release of oxytocin** during parturition.
  - We believe that this release of oxytocin developed to help mother's deliver the subsequent litter-mates (and in humans the placenta).
  - Note that **women with a posterior pituitary defect proceed through parturition normally**.
  - Recall that the posterior pituitary releases oxytocin generated by the neurons of the nuerohyophysis.

- The role of relaxin is in parturition is unclear.
- pCRH's (placental corticotropin releasing hormone) role in parturition:
- pCRH (placental corticotropin releasing homrone) seems to affect the estrogen-progesterone ratio in sheep and humans.
- In general, **pCRH increases exponentially near parturition**.
- **pCRH shifts production from progesterone to estrogen**.
- This makes sense; recall that estrogen is pro-parturition and progesterone is anti-parturition.
- Recall that progesterone inhibits prostaglandins; so it makes sense that **elevated pCRH is associated with elevated prostaglandins** because pCRH causes a relative decrease in progesterone to estrogen.
- Additional evidence of the importance of pCRH:
- Sheep without anterior pituitary function or adrenal function (that is, lacking ACTH and cortisol) have longer gestation periods (that is, delayed parturition).
- Women who deliver early show elevated levels of pCRH within 24-48 before parturition.

Lactation

- Lactation is the production of milk by a woman.
- Lactation is primary controlled by the maternal pituitary gland.
- Recall that lactotropes (mammotropes) of the anterior pituitary produce prolactin.
- Recall that neurons of the neurohypophysis (posterior pituitary) produce and release oxytocin.
- Lactation **requires suckling upon the nipple** to be maintained; that is, neural sensation at the nipple is required for milk production by the mammary glands.
- Maternal milk is the "perfect nutrition source" for newborns because it is **easy to digest**, **sterile**, and **the perfect temperature**.

- Breast-milk infers several health advantages on the child: decreased risk of obesity, decreased ear infections, decreased food allergies, decreased GI illnesses.

Development of the mammary glands

- Mammary gland precursor cells develop along the **bilateral mammary ridges** in both boys and girls.
- **Accessory nipples** can result from poor degenerative signaling that usually limits nipple development to just two, symmetrical nipples.
- There is an initial development and maturation of the mammary glands throughout fetal and post-natal development.
- This initial development is **identical in boys and girls** and allows the glands to be responsive to hormonal signals.
- Note that this development stage sets the mammary glands up to either be **signaled to develop further by the relatively high estrogen levels pregnancy** or to remain under-developed in boys.
- Secondary development is characterized by the change of **connective tissue to milk ducts** and occurs in response to hormone elevation during pregnancy.

Anatomy of the breast

- Breast tissue contains epithelial milk producing cells arranged in alveola, myoepithelial cells surrounding the alveoli, and epithelial lined tracts.
- Cuboidal epithelial cells that make up the alveoli are signaled by **prolactin** to produce milk and secrete it into the epithelial **secretory alveoli** (the beginning of the ductule system).
- Myoepithelial cells around the alveoli are signaled by oxytocin to contract, thus squeezing milk along the tracts.
- The epithelial ductule system of mammary glands begins as the tract within alveoli called **secretory alveoli**, progresses to **intralobular ducts**, and then to **collecting ducts** that converge on the nipple.

Characteristics of human milk

- The characterisitics of human milk change over a short time frame post-parturition.
- The **initial milk produced is called colostrum** and is **high in lymphocytes and antibodies** which is good for helping the baby deal with its new, infectious environment.
- The milk matures from colostrum into **hindmilk** within three days.
- Hindmilk contains higher fat content which promotes satiety in the newborn.
- Note that pregnancy and lactogenesis are well coordinated because **lactogenesis occurring with pre-term delivery generates milk with a higher protein and fat concentration** which makes sense because the newborn has some extra growing to do.

Lactogenesis

- Milk production begins in the 5th (~20 weeks) month of gestation.
- Note that **only colostrum is produced before and immediately following parturition**.
- **Production of hindmilk is inhibited by high progesterone and estrogen levels of pregnancy**.
- Recall that estrogen and progesterone are produced by the placenta so it is not until the placental source is arrested (via parturition) that hindmilk can be produced.
- **Progesterone and estrogen are prolactin antagonists**.

Role of prolactin

- Recall that prolactin is produced by lactotrophs of the anterior pituitary.
- Estrogen increases prolactin production during pregnancy. (Recall that estrogen levels rise throughout pregnancy and that estrogen is a prolactin antagonist).
- Note that **estrogen increases prolactin levels but decreases prolactin's ability to have an effect at the mammary gland tissue**.
- Recall that **dopamine is constantly expressed in non-pregnant females to inhibit prolactin production at the anterior pituitary.**

- Prolactin has several effects at the mammary tissue: **increases milk production, stimulates lactose production, and stimulates expression of milk-protein genes**.
- Prolactin production increases at each nursing (that is, it is produced as a result of suckling stimulation).

Role of suckling

- An infant suckles on the nipple in a back-to-front action.
- Stimulation at the nipple by an infant has a short term and a long term effect via neuronal-hormonal reflex arcs: milk secretion and milk production.

  {The infant does not suckle "on the nipple". To stimulate Prolactin the infant must be deeply attached to the breast with breast tissue filling the cheeks.}
- The afferent (at the CNS) signal for these reflex arcs is physical stimulation of the neurons that innervate the nipple.
- The short term, milk-secretion arc occurs through neuronal secretion of oxytocin (the hormonal efferent--exit the CNS signal) from the neurohypophysis (posterior pituitary) which stimulates the myoepithelial cells surrounding the mammary gland alveoli to contract, secreting milk for the infant.
- The long term, milk-production arc occurs through increased prolactin production (the hormonal efferent--exit the CNS signal) which causes increased milk production by signalling the epithelial cells of the mammary gland alveoli.
- Milk-let down is the release of milk from the lactiferous ducts to the lactiferous sinus.

  {Lactiferous sinuses have been disproven. You are using outdated information}
- The **let down effect may be secondary to CNS effects** (meaning stimulation at the nipple gets to the posterior pituitary via the CNS and causes oxytocin release).

Role of oxytocin

- Oxytocin has social-behavioral effects in addition to the direct physical effects previously described (think myoepithelial signaling, milk-secretion, dilation of cervix and vagina).
- Indeed, oxytocin has been considered a *love potion*.

- Oxytocin acts as a nuerotransmitter in the brain and is associated with maternal nurturing behavior, trust, decreased fear, increased empathy.
- Oxytocin is also associated with female orgasm and a habit of long-term mating.

Sustaining lactation

- Lactation can be maintained for years after parturition given regular stimulation of the nipple.
- The supply of milk produced by the mother is determined by the need of the baby.
- Maximum volume production falls within 800-1200 ml / day.
- High levels of prolactin (which can be maintained through regular breast-feeding) can suppress pulsatile release of GnRH and therefore prevent ovulation and pregnancy.
- GnRH from the hypothalamus stimulates LH / FSH release and that LH / FSH serve to mature the follicle and thus regulate ovulation.
- **Semen analysis**

  Semen analysis, also known as a sperm count test, analyzes the health and viability of a man's sperm. Semen is the fluid containing sperm (plus other sugar and protein substances) that's released during ejaculation. A semen analysis measures three major factors of sperm health:

  - the number of sperm
  - the shape of the sperm
  - the movement of the sperm, also known as "sperm motility"

  Sperm counts can vary on a daily basis. Taking an average of the sperm samples can give the most conclusive result.

KARPAGAM ACADEMY OF HIGHER EDUCATION
DEPARTMENT OF BIOCHEMISTRY
II-M.Sc., BIOCHEMISTRY
ENDOCRINOLOGY (17BCP303)
MULTIPLE CHOICE QUESTIONS

S. No.	Question	Opt A	Opt B	Opt C	Opt D	Answer
1	An increase in the concentration of plasma potassium causes	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	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	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	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	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	water	ammonia	urea	sodium	urea
11	substances will be more concentrated at the end of the proximal tubule than at the	glucose	creatinine	sodium	bicarbonate	creatinine

12	When a person is dehydrated, hypotonic fluid will be found in	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 .	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	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	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	sodium	hemoglobin	chloride	albumin	hemoglobin
27	The hypothalamus will effect the release of ADH in response to all	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	extracellular bicarbonate	plasma proteins	plasma lactate	inorganic phosphate	plasma lactate
31	Extracellular bicarbonate ions serve as effective buffer for all	phosphate acid	lactic acid	carbonic acid	ß- hydroxybutyric acid	carbonic acid
32	All the following statements are true of the H+ secreted into the	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	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	Hyperproteinemia	A ureteral stone	Dilation of the afferent arteriole	Dilation of the efferent arteriole	Dilation of the afferent arteriole
39	Subject A drinks 2 L of distilled water， and subject B drinks 2 L of isotonic NaCl. As result of the following question.	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	Glomerular capillary hydrostatic pressure=47 mmHg; Bowman’s space hydrostatic pressure=10	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	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	proximal tubule	loop of Henle	distal tubule	cortical collecting duct	proximal tubule

45	On which of the following does aldosterone exert its greatest	Proximal tubule	Thin portion of the loop of Henle	Thick portion of the loop of Henle	Cortical collecting duct	Cortical collecting duct
46	substance when is concentration in the plasma is 10 mg/dl, its concentration in the urine is 100	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	injected into a woman. After equilibration， a plasma sample had a mannitol concentration of 0.8 g/L. During the equilibration	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 tuble?	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	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	best distinguish an otherwise healthy person with severe water deprivation from a person	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	Para-aminohippuric acid（PAH）	Inulin	Glucose	Na+	Para-aminohippuric acid（PAH）
59	90 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	120	180	240	400	120

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.

Steroid hormone receptors (SRs) are transcription factors regulating the expression of target genes . Binding of steroid hormones to the specific SR ligand-binding domain (LBD) induces a conformational modification of the receptor, followed by the separation of the receptor from cytoplasmic chaperone proteins such as heat shock protein 90 (Hsp90) and by the exposure of nuclear localization sequences. This allows nuclear translocation and homo/heterodimerization of the ligand-bound receptors, and their binding to steroid response elements (i.e. nucleotide sequences specifically recognized by SRs) on the promoter regions of the target genes, thus regulating gene expression by interacting with the transcription machinery.

However, the observation of effects elicited by steroid hormones which are too rapid to be mediated by activation of RNA and protein synthesis has prompted the search for alternative signaling mechanisms. Additional indications for new ways of steroid signaling have been provided by the discovery of receptor sub fractions localized at the cell membrane level, that have been indicated as potentially responsible for the non-nuclear effects of steroid hormones. Different terms have been used to distinguish these non-conventional signaling mechanisms, the more popular being ‘non-genomic’ or ‘non-nuclear’. However, these mechanisms may be more properly indicated as ‘non-transcriptional’, so as to underline that DNA binding of the receptors and RNA synthesis are not required.

The classification of these effects is still poor, due to the incomplete knowledge of the molecular basis, which explains the different phenomena that have been described as ‘non-genomic’ actions of SRs. The definition itself of these mechanisms is a ‘negative’ one, defining what these phenomena are not, instead of one describing their specific characteristics. As practical rules, non-transcriptional effects can be indicated as:

(i) actions that are too rapid to be compatible with RNA and protein synthesis (i.e. that ensue within seconds to minutes from the challenge with the hormone)

(ii) actions that can be reproduced in the presence of inhibitors of RNA or protein synthesis;

(iii) actions that can be reproduced by using steroid hormones coupled.

Signal Transduction

Extracellular signals are received at the membrane and then *transduced* to the cytoplasm at the cell membrane

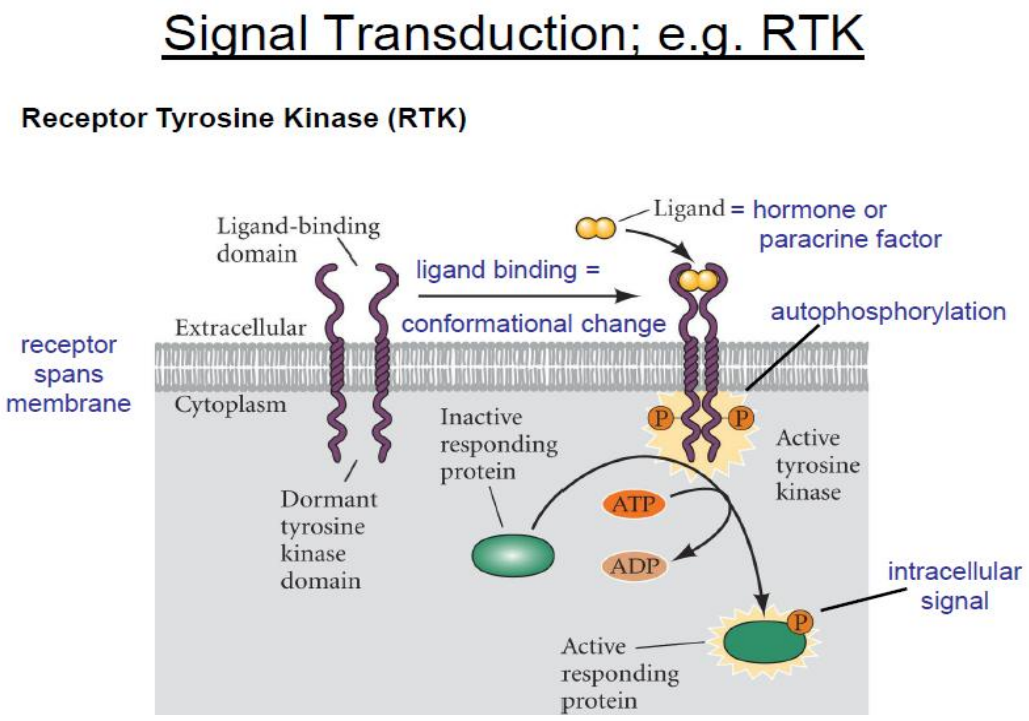
- external signal is transmitted into the interior of the cell

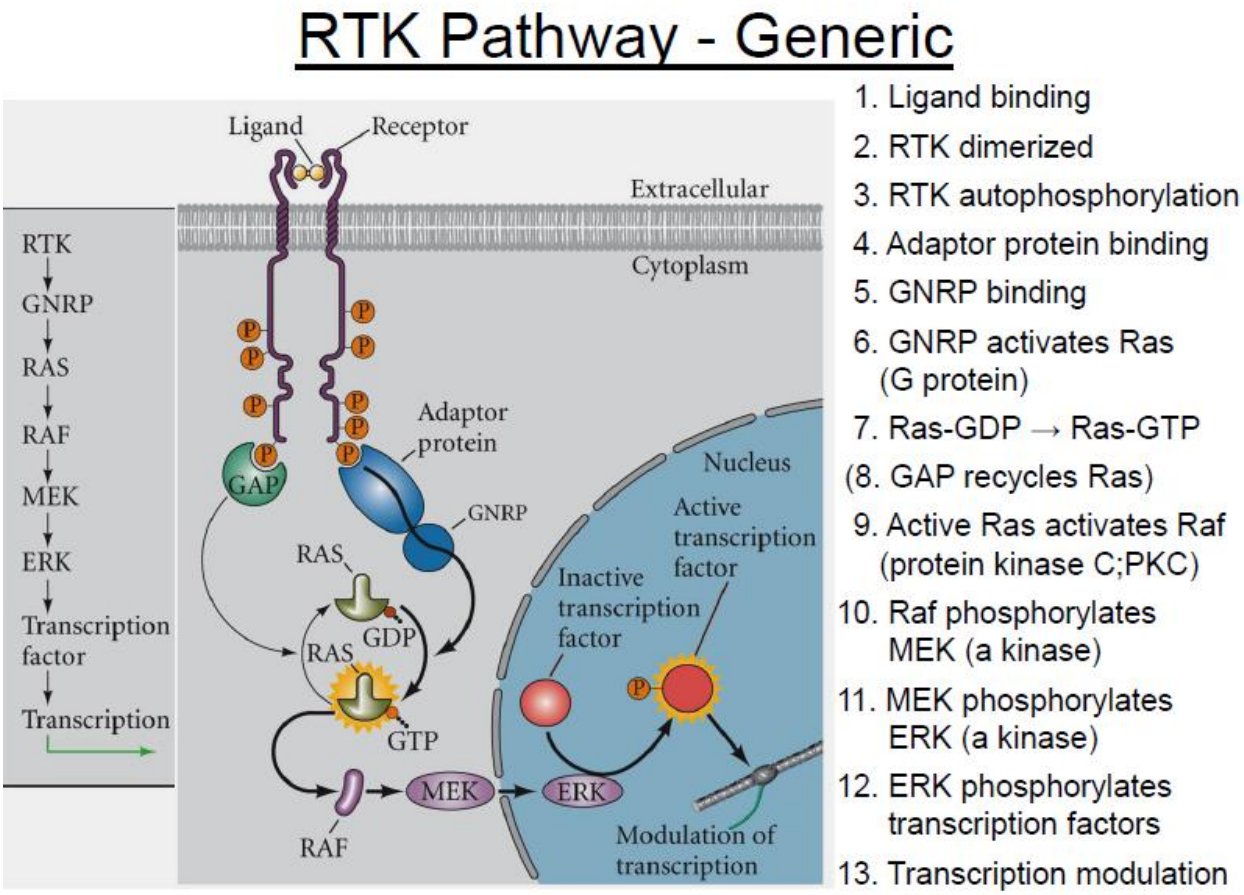
e.g. receptor tyrosine kinase (RTK)

(kinase = enzyme that phosphorylates a protein)

- most intercellular and intracellular signals are part of larger sets of pathways signal transduction cascades

- activated products or intermediates trigger other pathways



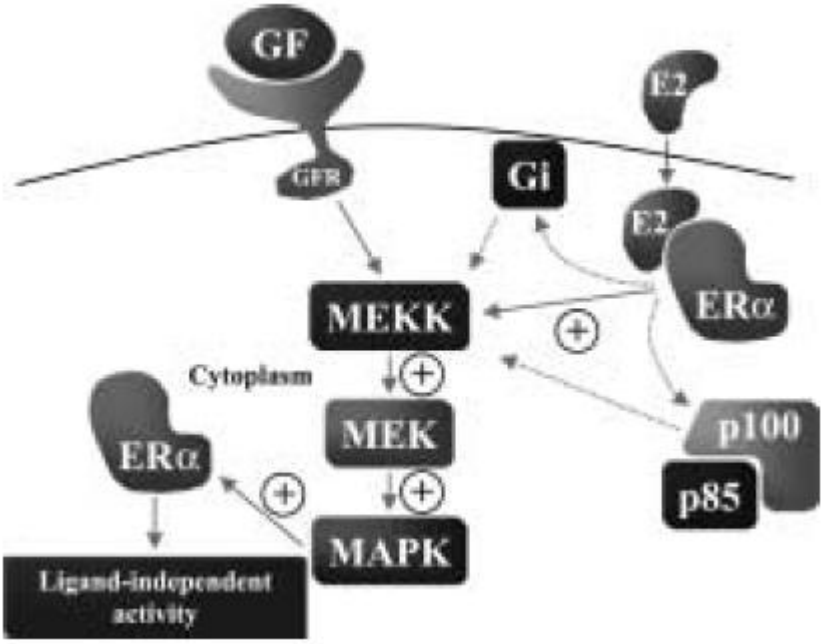


Protein kinase signaling pathways

Between the signaling machineries that are regulated by sex steroids are the MAPK cascades, several tyrosine kinases and lipid kinases. These pathways are ubiquitous transducers of the signals coming from different growth factors, and their activation is linked to a variety of important cellular events including gene expression, cell proliferation and survival.

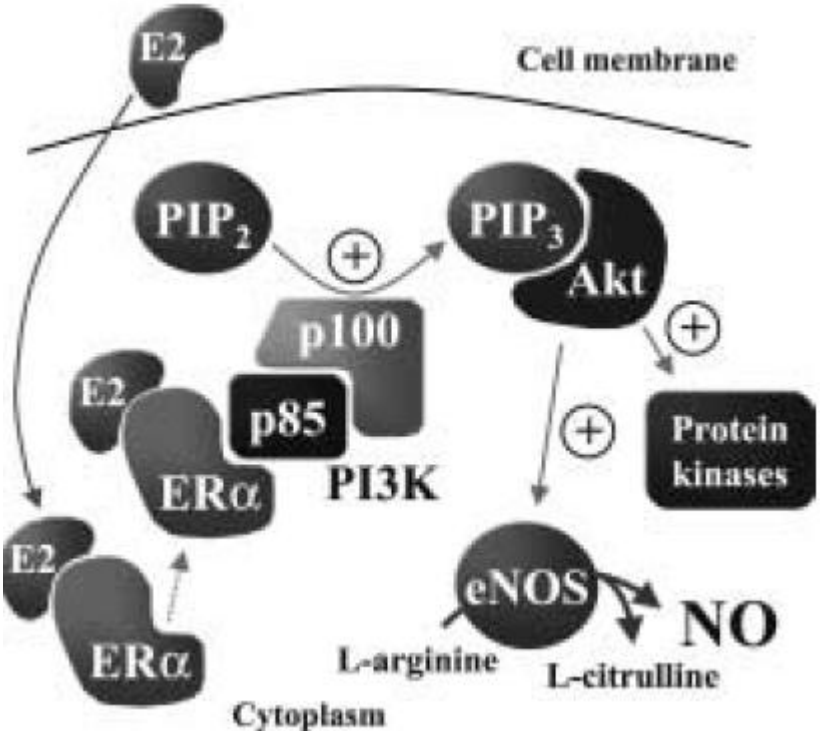
MAPKs and tyrosine kinases

The activation of the MAPK pathways by sex steroids has been characterized in several tissues. Although large overlaps exist, MAPKs are organized in three step-modules, where an upstream kinase phosphorylates and activates the downstream MAPK. Three main cascades are described, the extracellular signal-regulated kinase (ERK) 1/2, the p38 and the stress-activated protein kinase (SAPK) or c-Jun NH2-terminal kinase (JNK) cascades.



PI3K

In addition to protein kinase signaling pathways, non-transcriptional actions of sex steroid hormones can be mediated by the recruitment of lipid kinases. Indeed, upon binding with E2, ERa physically and functionally couples with the regulatory subunit of the lipid kinase PI3K, thus triggering an activation of the catalytic subunit and increasing intracellular production of phosphoinositides. PI3K phosphorylates the D-3 position of the phosphatidylinositol ring, catalyzing the synthesis of lipid mediators that act as second messengers transferring the signaling cascade to intracellular protein kinases. One of the principal targets of this cascade is the serine-threonine protein kinase Akt/protein kinase B. Activation of Akt mediates many of the downstream cellular effects of PI3K triggered by E2, including rapid activation of the endothelial isoform of the nitric oxide (NO) synthase (eNOS).



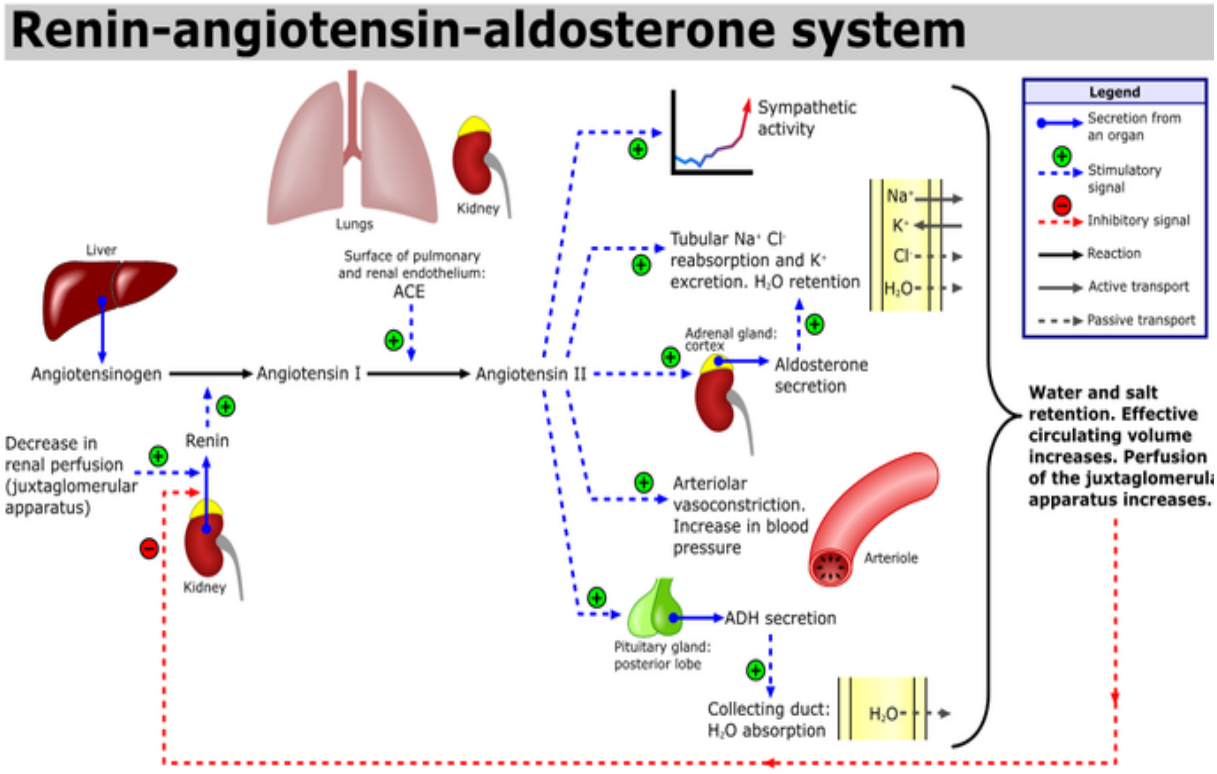
The relevance of this interaction has been confirmed in vivo, where estrogen induces a dramatic reduction in leukocyte adhesion to endothelium in vessels after ischemia/ reperfusion, which is completely reversed by treatment with PI3K as well as eNOS inhibitors. Activation of PI3K by estrogens is important also in breast cancer cells, where E2 rapidly triggers association of ERa with Src and p85. This ternary complex probably favors hormone activation of Src- and PI3Kdependent pathways, which converge on cell cycle progression.

Renin-Angiotensin System

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

When renal blood flow is reduced, juxtaglomerular cells in the kidneys convert the precursor – prorenin, already present in the blood into renin and secrete it directly into the circulation. Plasma renin then carries out the conversion of angiotensinogen, released by the liver, to angiotensin I. Angiotensin I is subsequently converted to angiotensin II by the enzyme

angiotensin-converting enzyme (ACE) found in the lungs. Angiotensin II is a potent vasoconstrictive peptide that causes blood vessels to narrow, resulting in increased blood pressure. Angiotensin II also stimulates the secretion of the hormone aldosterone from the adrenal cortex. Aldosterone causes the renal tubules to increase the reabsorption of sodium and water into the blood, while at the same time causing the excretion of potassium (to maintain electrolyte balance). This increases the volume of extracellular fluid in the body, which also increases blood pressure.



Clinical Significance

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

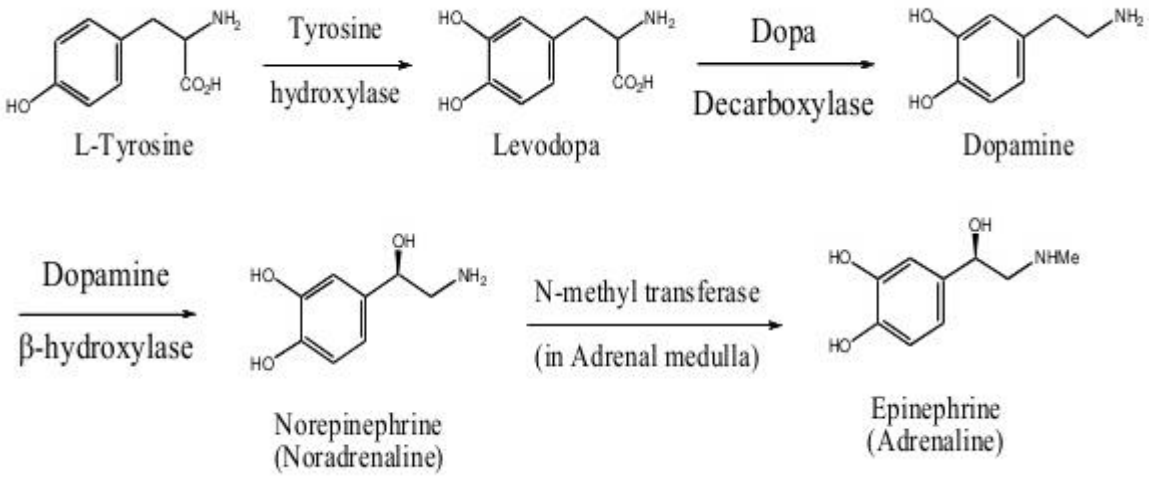
Angiotensin II receptor antagonists, also known as angiotensin receptor blockers, can be used to prevent angiotensin II from acting on its receptors.

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

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

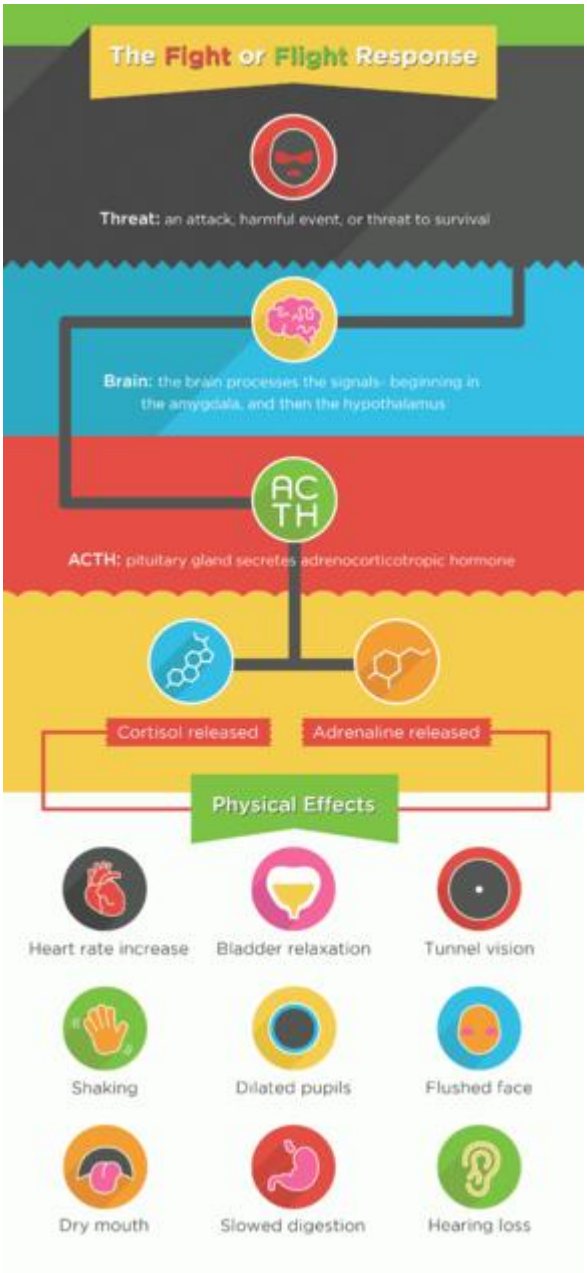
Epinephrine:

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



Fight-or-flight response

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



Addison Disease

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

Characteristic symptoms are:

- Sudden penetrating pain in the legs, lower back, or abdomen
- Severe vomiting and diarrhea, resulting in dehydration
- Low blood pressure
- Syncope (loss of consciousness and ability to stand)
- Hypoglycemia (reduced level of blood glucose)
- Confusion, psychosis, slurred speech
- Severe lethargy
- Hyponatremia (low sodium level in the blood)
- Hyperkalemia (elevated potassium level in the blood)
- Hypercalcemia (elevated calcium level in the blood)
- Convulsions
- Fever

Causes:

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

Treatment

Treatment for Addison's disease involves replacing the missing cortisol, sometimes in the form of hydrocortisone tablets, or prednisone tablets in a dosing regimen that mimics the physiological concentrations of cortisol. Alternatively, one-quarter as much prednisolone may be used for

equal glucocorticoid effect as hydrocortisone. Treatment is usually lifelong. In addition, many patients require fludrocortisone as replacement for the missing aldosterone.

Cushing Syndrome

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

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

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

Signs and symptoms

* Rapid weight gain
* Moodiness, irritability, or depression
* Muscle and bone weakness
* Memory and attention dysfunction
* Osteoporosis

* Diabetes mellitus
* Hypertension
* Immune suppression
* Sleep disturbances
* Menstrual disorders such as amenorrhea in women
* Decreased fertility in men
* Hirsutism
* Baldness

Treatment:

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

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

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

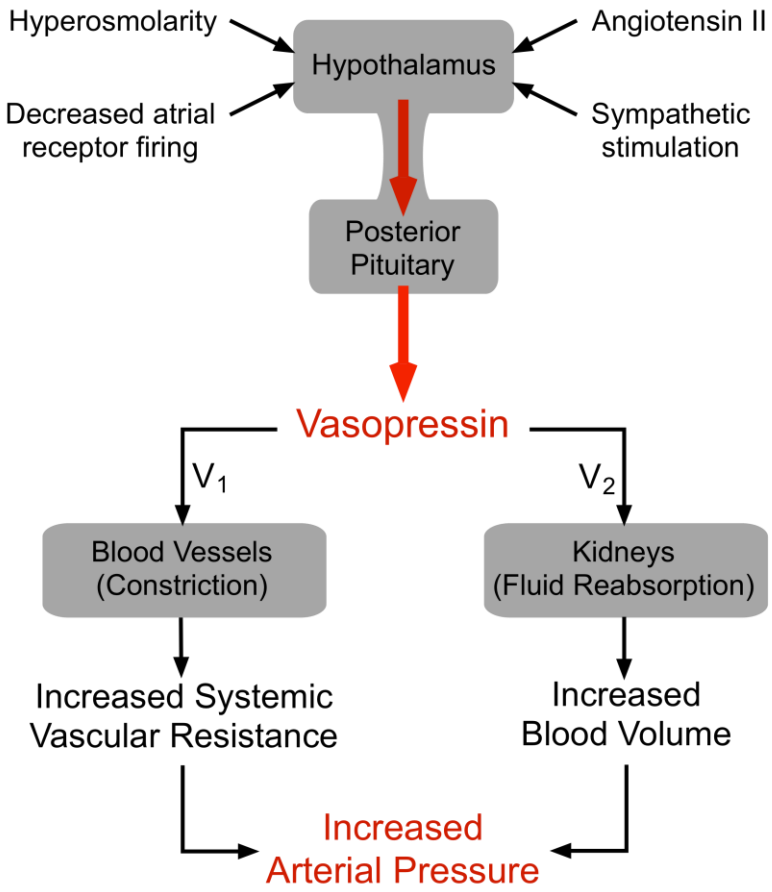
Vasopressin, also named antidiuretic hormone (ADH), arginine vasopressin (AVP) or argipressin, is a hormone synthesized as a peptide prohormone in neurons in the hypothalamus, and is converted to AVP. It then travels down the axon of that cell, which terminates in the posterior pituitary, and is released from vesicles into the circulation in response to extracellular fluid hypertonicity (hyperosmolality). AVP has two primary functions. First, it increases the amount of solute-free water reabsorbed back into the circulation from the filtrate in the kidney tubules of the nephrons. Second, AVP constricts arterioles, which increases peripheral vascular resistance and raises arterial blood pressure. A third function is possible. Some AVP may be released directly into the brain from the hypothalamus, and may play an important role in social behavior, sexual motivation and pair bonding, and maternal responses to stress.

Function

Vasopressin regulates the tonicity of body fluids. It is released from the posterior pituitary in response to hypertonicity and causes the kidneys to reabsorb solute-free water and return it to the circulation from the tubules of the nephron, thus returning the tonicity of the body fluids toward normal. An incidental consequence of this renal reabsorption of water is concentrated urine and reduced urine volume. AVP released in high concentrations may also raise blood pressure by inducing moderate vasoconstriction. AVP also may have a variety of neurological effects on the brain. It may influence pair-bonding in voles. The high-density distributions of vasopressin

receptor AVPr1a in prairie vole ventral forebrain regions have been shown to facilitate and coordinate reward circuits during partner preference formation, critical for pair bond formation.

A very similar substance, lysine vasopressin (LVP) or lypressin, has the same function in pigs and is used in human AVP deficiency.



Kidney

Vasopressin has three main effects:

Increasing the water permeability of initial and cortical collecting tubules (ICT & CCT), as well as outer and inner medullary collecting duct (OMCD & IMCD) in the kidney, thus allowing water reabsorption and excretion of more concentrated urine, i.e., antidiuresis. This occurs through increased transcription and insertion of water channels (Aquaporin-2) into the apical

membrane of collecting tubule and collecting duct epithelial cells. Aquaporins allow water to move down their osmotic gradient and out of the nephron, increasing the amount of water re-absorbed from the filtrate (forming urine) back into the bloodstream. This effect is mediated by V2 receptors. Vasopressin also increases the concentration of calcium in the collecting duct cells, by episodic release from intracellular stores. Vasopressin, acting through cAMP, also increases transcription of the aquaporin-2 gene, thus increasing the total number of aquaporin-2 molecules in collecting duct cells.

Increasing permeability of the inner medullary portion of the collecting duct to urea by regulating the cell surface expression of urea transporters, which facilitates its reabsorption into the medullary interstitium as it travels down the concentration gradient created by removing water from the connecting tubule, cortical collecting duct, and outer medullary collecting duct. Acute increase of sodium absorption across the ascending loop of henle. This adds to the countercurrent multiplication which aids in proper water reabsorption later in the distal tubule and collecting duct.

Central nervous system

Vasopressin released within the brain may have several actions:

Vasopressin is released into the brain in a circadian rhythm by neurons of the suprachiasmatic nucleus. Vasopressin released from centrally projecting hypothalamic neurons is involved in aggression, blood pressure regulation, and temperature regulation. Recent evidence suggests that vasopressin may have analgesic effects. The analgesia effects of vasopressin were found to be dependent on both stress and sex.

Regulation

Many factors influence the secretion of vasopressin:

Ethanol (alcohol) reduces the calcium-dependent secretion of AVP by blocking voltage-gated calcium channels in neurohypophyseal nerve terminals in rats. Angiotensin II stimulates AVP secretion, in keeping with its general pressor and pro-volumic effects on the body. Atrial natriuretic peptide inhibits AVP secretion, in part by inhibiting Angiotensin II-induced stimulation of AVP secretion. Cortisol inhibits secretion of antidiuretic hormone.

Production and secretion

The physiologic stimulus for secretion of vasopressin is increased osmolality of the plasma, monitored by the hypothalamus. A decreased arterial blood volume, (such as can occur in cirrhosis, nephrosis and heart failure), stimulates secretion, even in the face of decreased osmolality of the plasma: it supersedes osmolality, but with a milder effect. In other words, vasopressin is secreted in spite of the presence of hypoosmolality (hyponatremia) when the arterial blood volume is low.

The AVP that is measured in peripheral blood is almost all derived from secretion from the posterior pituitary gland (except in cases of AVP-secreting tumours). Vasopressin is produced by magnocellular neurosecretory neurons in the Paraventricular nucleus of hypothalamus (PVN) and Supraoptic nucleus (SON). It then travels down the axon through the infundibulum within neurosecretory granules that are found within Herring bodies, localized swellings of the axons and nerve terminals. These carry the peptide directly to the posterior pituitary gland, where it is stored until released into the blood.

KARPAGAM ACADEMY OF HIGHER EDUCATION
DEPARTMENT OF BIOCHEMISTRY
II-M.Sc., BIOCHEMISTRY
ENDOCRINOLOGY (17BCP303)
MULTIPLE CHOICE QUESTIONS

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	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	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	Parasympathetic stimulation	Sympathetic stimulation	Vaotomy	Administration of gastrin	Vaotomy
8	Which of the following is the site of secretion of intrinsic	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	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	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	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	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	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	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	hepatitis C	alcoholic liver disease	ascending cholangitis	hepatocellular carcinoma	ascending cholangitis
31	The most common cause for chronic liver disease in the West	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	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

KARPAGAM ACADEMY OF HIGHER EDUCATION
DEPARTMENT OF BIOCHEMISTRY
II-M.Sc., BIOCHEMISTRY
ENDOCRINOLOGY (17BCP303)
MULTIPLE CHOICE QUESTIONS

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 moven	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 pote	passive membrane pot	dormant membrane potenti	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 ampull	Penetration of the ovum by the sperm brough
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 lo	They are motile even wl	In the absence of fertil	Take about 45 min to pass fr	Require temperature lower than that of the in
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 nephr	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 endoderr	endoderm and mesod	mesoderm and pericarp	ectoderm and endoderm
28	Neurotransmitters are released from vesicles at the	a neurotransmitter	an enzyme that breaks d	a stimulant that trigge	a hormone	an enzyme that breaks down a neurotransmit
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 ganglio	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	maintain proper ionic concentration gradients
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 d	an unmyelinated, large d	a myelinated, small dia	a myelinated, large diamete	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

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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.

Hormonal analyses

Most hormone assays performed today are of the competitive-binding variety. For a competitive-binding assay to be of value it must be practical and reliable.

RIA

The RIA is the conventional prototype of a competitive-binding assay. There are three fundamental components to the RIA - radioactive ("hot") hormone, unlabeled ("cold") hormone (standard or sample), and antibody. Radioisotopes of tritium (b emitter) and iodine (high specific activity g emitter) are incorporated into steroid and protein (Tyr or His residues) hormones, respectively; this must be done without significant damage to the immunoreactivity of the hormone. Tracer and standard or unknown sample compete for a limited number of binding sites on the antibody. Amounts of (excess) tracer and antibody for each reaction are held constant, while quantities of standard hormone are increased step-wise. Reactions are allowed to proceed to equilibrium, and free (unbound) hormone is segregated from antibody-hormone complexes. Emission of energy from the bound complex is monitored by radiation detection equipment. As content of standard is increased from 0 (ie., 100% of antibody is bound by tracer), the amount of antibody-bound tracer declines reciprocally - a standard curve is constructed from these data. Reaction tubes containing sample in place of standard are assayed simultaneously. Estimates of mass of hormone within a sample are interpolated from the standard curve.

Antibodies belong mainly to the gamma globulin (IgG) class of immunoglobulins. Each Fab arm of the (bivalent) antibody can bind a molecule of ligand. Binding is mediated by weak noncovalent forces (ionic interactions, hydrogen bonding, hydrophobic attractions, van der Waals attraction); therefore, like that of enzyme-substrate binding, the reaction is reversible.

Antisera can be generated by injecting purified hormone into a species of animal that is capable of mounting an immunological reaction to that hormone (ie., do not produce the hormone in a chemical form that is exactly similar). Some small molecules (haptens) are not antigenic on their own (eg., steroid and peptide hormones, prostaglandins) and must first be coupled (at a nonactive site) to an immunogenic carrier (eg., albumin, keyhole limpet hemocyanin) before injection.

Even under the best of conditions of immunization, antisera can contain antibodies (polyclonal) that cross-react with related substances - the development of technology using monoclonal (homogenous) antibodies has helped in this respect. To obtain monoclonal antibodies an animal (eg., mouse) is injected with purified antigen, spleen cells capable of secreting a single type of antibody (clones) are screened and isolated, and selected cells are fused with myeloma (immortal) cells to produce a hybridoma. Cells maintained in culture provide a continuous source of antibody. A single hybridoma can yield approximately 1000 specific molecules of antibody per second.

A convenient method to separate antibody-hormone complexes from free hormone is to adhere the antibody to a solid phase, such as to the walls of a test tube. The free hormone can then be decanted (a centrifugation step is not required). Because proteins attach nonspecifically to plastic (eg., polyvinyl chloride or polystyrene), tubes can be coated by simply incubating with a solution containing antibody. Remaining unoccupied sites are then filled with an irrelevant protein, such as serum albumin or gelatin. One criticism of antibody-coated tubes is adsorption can mask immunoreactive (Fab) sites: to overcome this problem, protein A, a molecule derived from staphylococcus aureus that binds the Fc tail of IgG, can be coated to the solid phase (this permits extraction of IgG from the fluid-phase reaction mixture). Alternatively, precipitation of hormone-antibody complexes can be achieved using ammonium sulfate, magnetically-activated antibody, or with a second antibody generated against the first antibody (ie., anti-IgG). Adsorption of free (low molecular weight ligand) can be achieved with dextran-coated charcoal.

Other analytical systems that exploit the same basic principle as the RIA include the protein-binding assay, radioreceptor assay (RRA), scintillation proximity assay (SPA), enzyme immunoassay (EIA), fluoroimmunoassay (FIA), and chemiluminescent assay (CIA). Protein-binding and radioreceptor assays are radioligand assays that utilize an endogenous plasma protein (eg., for steroid hormones) or cellular receptor, respectively - instead of an antibody. Protein-binding assays lack the specificity of an immunoassay. The radioreceptor assay has an advantage over the RIA in that it only detects bioactive hormone (ie., antibodies can interact with sites on the hormone molecule not involved in receptor binding). Notwithstanding, it is difficult

to isolate abundant quantities of stable receptor for routine analyses. Fortunately, data obtained from RIAs and RRAs are usually comparable.

A newly-developed methodology, SPA, does not require separation of bound from free ligand. Competitive binding of labeled ligand in proximity to antibody- or receptor-coated fluoromicrospheres allows the energy emitted to excite the fluor and produce detectable light that can be measured in a scintillation counter without liquid cocktail. Unbound tracer is too far from the microsphere to enable energy transfer before it is absorbed by the aqueous solution.

In the EIA, FIA ,and CIA, radioactive hormone is replaced by an enzyme-, fluorescein- or luminol-tagged ligand, respectively. Quantification is accomplished with a fluorometer in FIA and a luminometer in CIA. In EIA an extra step is required first - addition of substrate. An example of an enzyme commonly used in enzyme immunoassays is horseradish peroxidase: hydrogen peroxide (substrate) is reduced by this enzyme, and in the process an appropriate hydrogen donor (eg., o-phenylenediamine) is oxidized, causing a change in color of solution - appearance of product is measured by spectrophometric analysis of color reactions (ie., absorbance) to graded concentrations of hormone.

Antibody-excess immunoassays include the immunoradiometric assay (IRMA) and enzyme-linked immunosorbent assay (ELISA). In the IRMA cold ligand is "sandwiched" between an antibody coated to a solid phase and a second radiolabeled antibody raised against a different hormonal epitope (this works best with macromolecular hormones); sensitivity is not mandated by competition, and therefore, reactions can be carried out expeditiously over a wide range of detection. In a sandwich ELISA, hormone is bound to an antibody attached to a solid phase, and then an antibody-enzyme conjugate and substrate are added (Figure 2-39). These methods engender a direct relationship between radioactivity measured in the final complex and concentration of standard or analyte (in contrast to the inverse correlation between bound radioactivity and standard or sample concentrations in an RIA).

Non radio isotopic procedures, such as ELISAs, are becoming popular because of lowered equipment costs, reduced hazard to users and the environment (ie., associated with handling and disposal of radionuclides), and can be adapted (subjective appraisal of color-change) for in-the-home or on-the-farm/ranch diagnostics. However, ELISAs tend to be less sensitive than the RIA.

A reverse hemolytic plaque assay is used to detect secretion of hormone from individual cells (eg., gonadotropes) contained within a heterogeneous population. The concept is that a secretory product of a cell can be measured by specific antibodies in the presence of erythrocytes coated with protein A and added complement. Interaction of hormone with binding sites on the antibody causes stearic alterations in the antibody allowing for fixation of complement by juxtaposed Fc. Complement-induced hemolysis leads to the formation of a clear zone of erythrocyte membrane "ghosts" (ie., a plaque) surrounding the secretory cell. The plaque technique is sensitive and areas of lysis can be quantitated.

Receptor analyses

It is technically more difficult to monitor changes in populations of hormonal receptors than to evaluate alterations in patterns of secretion of hormones; yet, knowledge of dynamics of cellular receptors is no less important (eg., in diseases of endocrine resistance). The task of receptor measurement can be accomplished by exposing a constant amount of receptor (eg., tissue homogenate) to increasing concentrations of radioactive hormone. Receptor bound with hormone is separated from free radiolabel and each fraction is counted - the Scatchard plot is a common method of data assessment. Receptors not occupied by hormones are generally characterized unless special methods are first used to elute endogenous ligand from its binding site. hormone receptors bind ligands with great specificity and high affinity. Binding of a hormone to a receptor involves the same types of weak interactions — ionic and van der Waals bonds and hydrophobic interactions — that characterize the specific binding of a substrate to an enzyme. The *specificity* of a receptor refers to its ability to distinguish closely related substances; the insulin receptor, for example, binds insulin and a related hormone called insulin-like growth factor 1, but not other peptide hormones.

Hormone binding usually can be viewed as a simple reversible reaction,

$$R + H \longrightarrow RH$$

which can be described by the equation

$$K_D = \frac{[R][H]}{[RH]} \qquad (20\text{-}1)$$

where [R] and [H] are the concentrations of free receptor and hormone (ligand), respectively, and [RH] is the concentration of the receptor-hormone complex. K_D, the dissociation constant of the receptor-ligand complex, measures the *affinity* of the receptor for the ligand. This binding equation can be rewritten as

$$\frac{[RH]}{R_T} = \frac{1}{1 + K_D/[H]} \qquad (20\text{-}2)$$

where R_T is the sum of free and bound receptors: [R] + [RH]. Equation 20-2 is similar in form to the Michaelis-Menten equation used to analyze enzymatic reactions (Section 3.3).

The lower the K_D value, the higher the affinity of a receptor for its ligand. The K_D value is equivalent to the concentration of ligand at which one-half of the receptors contain bound ligand. If [H] = K_D, then from Equation 20-2 we can see that [RH] = 0.5 *R*

Hormone Receptors are detected by binding assays

Hormone receptors are difficult to identify and purify, mainly because they are present in such minute amounts. The surface of a typical cell bears 10,000 – 20,000 receptors for a particular hormone, but this quantity is only ≈10−6 of the total protein in the cell, or ≈10−4 of the plasmamembrane protein. Purification is also difficult because these integral membrane proteins first must be solubilized with a nonionic detergent (see Figure 3-38).

Usually, receptors are detected and measured by their ability to bind radioactive hormones to a cell or to cell fragments. When increasing amounts of a radiolabeled hormone (e.g., insulin) are added to a cell suspension, the amount that binds to the cells increases at first and then tapers off at higher concentrations (Figure 20-7, curve A). Much of the radiolabeled hormone is bound specifically to its receptor, but some is bound nonspecifically to the multitude of other proteins and phospholipids on the cell surface. Nonspecific binding of a labeled hormone can be measured by conducting the binding assay in the presence of a large excess of unlabeled hormone. Because the specific (high-affinity) binding sites are saturable, they all are filled by unlabeled hormone under these conditions and bind no labeled hormone. Nonspecific sites, however, do not saturate, so that binding of labeled hormone in the presence of excess unlabeled hormone represents nonspecific binding (Figure 20-7, curve C). Specific binding is calculated as the difference between total binding and nonspecific binding.

Autoradiography

Autoradiography is employed for the detection of materials that possess radioactive properties. By using X-ray films, autoradiography determine the relative positions and intensities of radiolabeled bands in a gel or blot. In 1867 the first autoradiography was observed accidently when an emulsion of silver chloride and iodide turns black by uranium salts. With the advent of photographic emulsions and photographic films after World War II, autoradiography was used as a biological technique for the detection of radioactive substances or materials labelled with radioactive isotopes.

Mechanism

Penetration of negatively charged beta particles emitted by radioactive salts through silver halide film emulsion causes activation of silver present in the emulsion. Activated silver crystals are very unstable therefore quickly reduced to black silver particles which is easily detectable. Autoradiography sensitivity is improved by carrying the detection process at 70°C and preflashing the film before use. Preflashing needs only one hit per crystal deposited to increases sensitivity.

Sequential steps of autoradiography

• Brief exposure of living cells to a pulse of specific radioactive material for a variable time.

• Preparation of samples are for microscopy either light or electron.

• Dissection of samples into sections for coverage with thin film of photographic emulsion which are then incubated in the dark for few days for radioactive decay. The exposure time depends on isotope activity, temperature and the background radiation.

Development of photographic emulsion.

• Toluidine blue is used for counter staining to reveal tissue histology. Instead Osmium or dipping emulsion can be used for pre-staining of the entire tissue before exposure to the photographic emulsion to avoid for individual post- staining each slide.

• Microscopy either light or electron is used to determine the relative position of the silver particles.

• Generation of records in the form of autoradiographs.

Fluorography

Autoradiography sensitivity is greatly enhanced through fluorography which transforms radioactive emissions into light which efficiently penetrates the film to be readily detected. A number of phosphor compounds absorb energy from beta particles and re-emit it as light e.g. Autofluor.

Advantages

• Technically easy not much expertise required,

• Highly specific detection tool,

• Unlike tissue bath preparations, pharmacologically characterize and localize receptors in tissues,

• Enables characterization of receptors in different tissues in different animals or brain regions.

Disadvantages

• Lack of assessment criteria to determine whether the binding site really corresponds to an actual receptor,

• Non-physiological significance of high affinity radiolabelled receptor

• Non-specificity of ligands can easily cause misinterpretation of results.

Autoradiography practical applications

Autoradiography provides qualitative as well as quantitative information regarding a specimen. Some of the following applications of this technique are given below:

• Autoradiography is used to determine receptor distribution and localization while studying neurodegenerative disorders.

• Application of autoradiography in electrophoretic transfer of proteins from polyacrylamide gels to nitrocellulose sheets during blotting.

• To study cytogenesis of the forebrain.

• Applications in radiopharmaceutical research.

• Applications in radioimmunoelectroosmophoresis to study viruses.

• In imaging and analyzing rock porosity.

• In matrix-assisted laser desorption/ionization mass spectrometric imaging (MALDI-MSI), and secondary ion mass spectrometric imaging (SIMS-MSI) for pharmaceutical discovery and development.

• In whole body imaging.

• Tool for genetic studies.

• For comparison of complex mixtures of proteins.

• Applications in microbial ecology.

• Determining gross absorption and utilization of foliar applied nutrients etc