Department of Zoology
Model Answer
M.Sc. Zoology (First Semester) Examination-2015
Paper – LZT 103 (Endocrinology) (AV-8182)

Q 1.

Answer

(i) c	(ii) b	(iii) b	(iv) b	(v) d
(vi) b	(vii) d	(viii) b	(ix) c	(x) b

Q 2.
Answer

Pituitary gland secretes tropic hormones that regulate the functions of other endocrine glands such as thyroid, adrenal, testis and ovary. In other words pituitary gland was considered to exert control over other endocrine glands. So, it was considered as master gland. Later attention was shifted to hypothalamus through which pituitary gland is regulated by means of releasing and inhibiting hormones. The adenohypophysial hormones are classified into three distinct categories. The hormones within each category exhibit considerable overlap in chemical structure and in some cases overlapping biological actions.

Glycoprotein hormones

This category includes thyroid stimulating hormone (TSH), Luteinizing hormone (LH) and Follicle stimulating hormone (FSH). These hormones affect diverse biological processes and yet have remarkable structural similarity. Each hormone consists of two subunits, α and β joined by non-covalent bonding. The α subunits are identical for all these hormones within a species. The specific biological activity is determined by β subunit. In each glycoprotein hormone the α subunit contains two complex asparagine linked oligosaccharides and β subunit has either one or two. The α subunit has five disulfide bonds while β subunit has six.

1. **Gonadotropins**

   These hormones are responsible for Gametogenesis and steroidogenesis in gonads. Each is a glycoprotein with a molecular weight of about 25000.

a. Follicle stimulating hormone

Biological actions

- In females, it promotes follicular growth, prepares the follicle for action of LH and enhances the release of estrogen induced by LH.
- In males, it stimulates seminal tubules and testicular growth and plays an important role in early stages of spermatogenesis.

Plasma FSH concentration increases through puberty from low level, with peaks of the order of 10 fold or more over basal level being reached at or slightly before the time of ovulation.

b. Luteinizing hormone

Biological actions

- In the female, LH stimulates final maturation of Graafian follicle, ovulation and development of corpora lutea. Both estrogen and progesterone secretion are stimulated.
- In ovary LH can stimulate the interstial cells to produce male hormone.
- In males, LH stimulates testosterone production by testis which in turn maintains spermatogenesis and provides for a development of accessory sex organs such as the vas deferens, prostate and seminal vesicles.

The plasma concentration of pituitary content of LH increases through puberty. In human there is cycle of plasma LH level with mid cycle (ovulatory) peaks many times the basal level.

c. TSH

Chemistry

The α subunit of TSH has 89 amino acid residues and β subunit consists of 112 amino acid residues. It has a molecular weight of about 30,000.

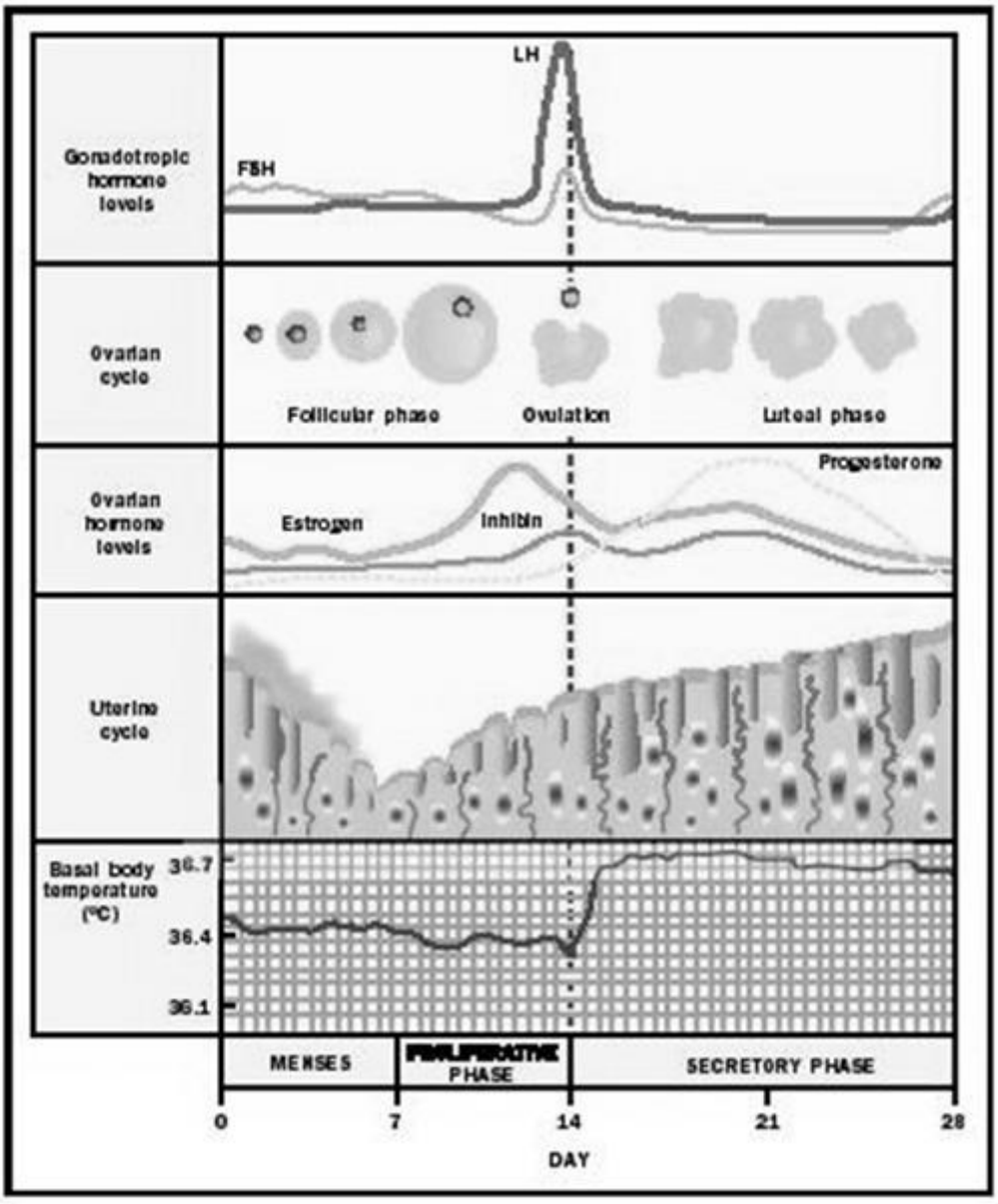
Biological Actions

TSH increases the synthesis of thyroid hormones by thyroid gland. It causes release of stored thyroid hormones and increased iodide uptake by thyroid cells.

Q 3.

Answer

The menstrual cycle is the physiological change that occurs under the control of the endocrine system in fertile women for the purposes of sexual reproduction and fertilization. It is divided into three stages: follicular phase, ovulation, and the luteal phase.



The follicular phase (or proliferative phase) is the phase of the menstrual cycle during which follicles in the ovary mature. It is under control of estradiol.

Follicle-stimulating hormone (FSH) is secreted by the anterior pituitary gland. It begins to rise in the last few days of the previous menstrual cycle. It is highest and most important during the first week of the follicular phase. The rise in FSH levels recruitstertiary-stage ovarian follicles (aka antral follicles) for entry into the menstrual cycle.

Follicle-stimulating hormone induces the proliferation of granulosa cells in the developing follicles and the expression of luteinizing hormone (LH) receptors on these cells. Under the influence of FSH, granulosa cells begin estrogensecretion. This increased level of estrogen stimulates production of gonadotropin-releasing hormone (GnRH), which increases production of LH. LH induces androgen synthesis by thecal cells, stimulates proliferation, differentiation, and secretion of follicular thecal cells, and increases LH receptor expression on granulosa cells.

Throughout the entire follicular phase, rising estrogen levels in the blood stimulates growth of the endometrium and myometrium of the uterus. It also causes endometrial cells to produce receptors for progesterone, which helps prime the endometrium to the late proliferative phase and the luteal phase.

Two or three days before LH levels begin to increase, one (or occasionally two) of the recruited follicles has emerged as dominant. Many endocrinologists believe that the estrogen secretion of the dominant follicle lowers the levels of LH and FSH, leading to the atresia (death) of most of the other recruited follicles. Estrogen levels will continue to increase for several days.

High estrogen levels initiate the formation of a new layer of endometrium in the uterus, the proliferative endometrium. Crypts in the cervix are also stimulated to produce fertile cervical mucus. This mucus reduces the acidity of the vagina, creating a more hospitable environment for sperm. In addition, basal body temperature may lower slightly under the influence of high estrogen levels.

Estrogen levels are highest right before the luteinizing hormone surge begins. The short-term drop in steroid hormones between the beginning of the LH surge and the event of ovulation may cause mid-cycle spotting or bleeding. Under the influence of the preovulatory LH surge, the first meiotic division of the oocytes is completed. The surge also initiates luteinization of thecal and granulosa cells. Ovulation normally occurs 30 (± 2) hours after the beginning of the LH surge.

Ovulation is the process in a female's menstrual cycle by which a mature ovarian follicle ruptures and discharges an ovum (aka oocyte). The time immediately surrounding ovulation is referred to as the ovulatory phase.

In the pre-ovulatory phase of the menstrual cycle, the ovarian follicle will undergo cumulus expansion, which is stimulated by FSH. Then, ovum will leave the follicle through the formed stigma. Ovulation is triggered by a spike in the amount of FSH and LH released from the pituitary gland.

The luteal phase begins with the formation of the corpus luteum stimulated by FSH and LH and ends in either pregnancy or luteolysis. The main hormone associated with this stage is progesterone, which is produced by growing corpus luteum and is significantly higher during the luteal phase than other phases of the cycle. Progesterone plays a vital role in making the endometrium receptive to implantation of the blastocyst and supportive of the early pregnancy; it also raises the woman's basal body temperature.

Several days after ovulation, the increasing amount of estrogen produced by the corpus luteum may cause one or two days of fertile cervical mucus, lower basal body temperatures, or both. This is known as a "secondary estrogen surge".

The hormones produced by the corpus luteum also suppress production of the FSH and LH, which leads to its atrophy. The death of the corpus luteum results in falling levels of progesterone and estrogen, which triggers the end of the luteal phase. Increased levels of FSH start recruiting follicles for the next cycle.

Alternatively, the loss of the corpus luteum can be prevented by implantation of an embryo: after implantation, human embryos produce human chorionic gonadotropin (hCG). Human chorionic gonadotropin is structurally similar to LH and can preserve the corpus luteum. Because the hormone is unique to the embryo, most pregnancy tests look for the presence of hCG. If implantation occurs, the corpus luteum will continue to produce progesterone (and maintain high basal body temperatures) for eight to 12 weeks, after which the placenta takes over this function.

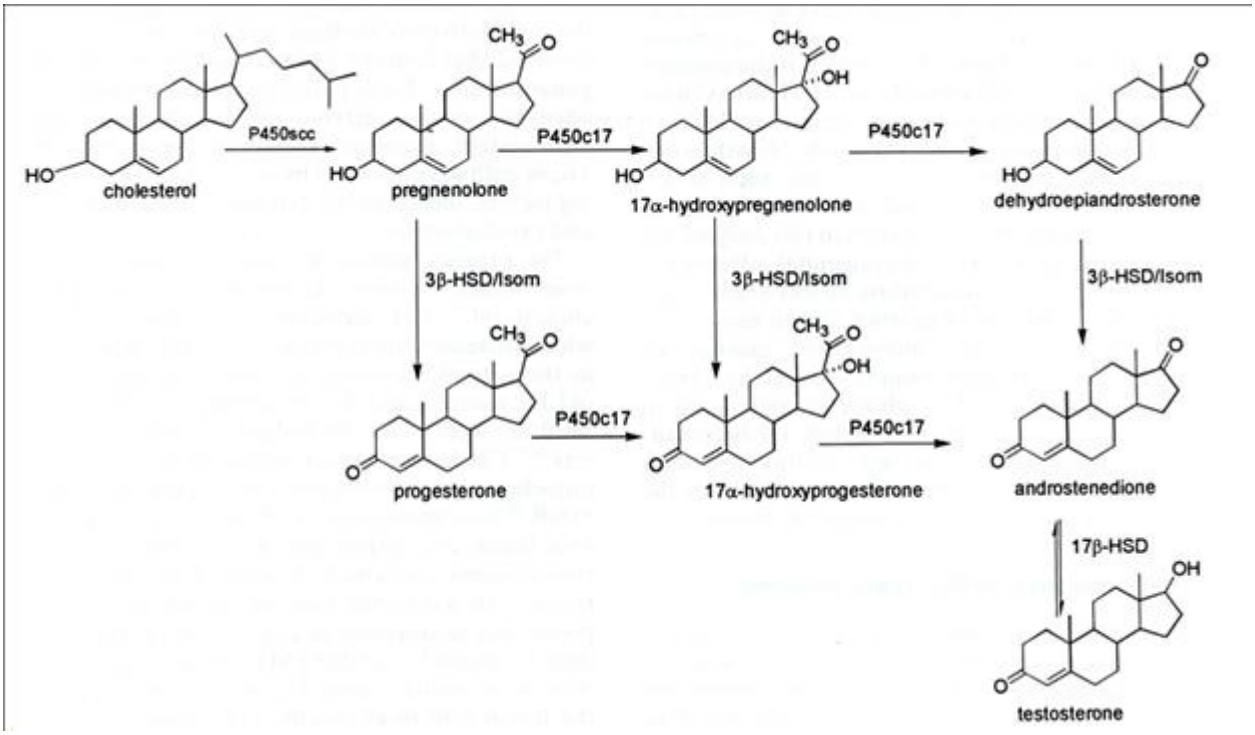
Q 4.

Answer

Steroidogenesis

Testosterone (Te) is the most important local and systemic androgen produced by the testes. Androgens are crucial for male reproduction and general health. Testosterone triggers the

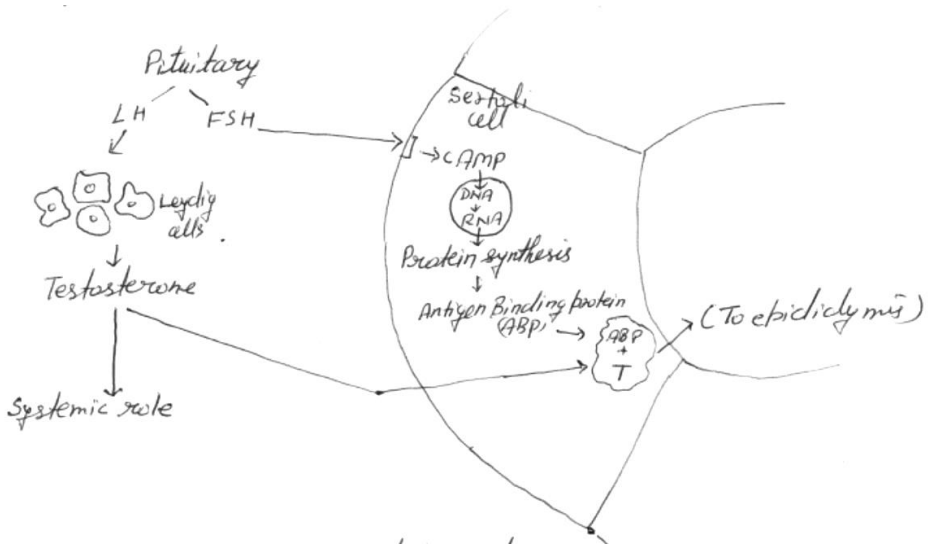
development of male secondary sexual characteristics at puberty, maintains adult sexual behavior and function, and drives late stages of spermatogenesis independently of its metabolite 5α-dihydrotestosterone (DHT). During fetal development Te is essential for differentiation of the internal and DHT the external male urogenital system. Testosterone is synthesized from cholesterol through sequential reactions that are catalyzed by cytochrome P450-containing complexes. Five major steps are involved, namely, (1) cholesterol C20,22- desmolase (CYP11A cholesterol side-chain cleavage), (2) 3β-hydroxysteroid dehydrogenase/Δ4,5-isomerase (3β-OHSDH), (3 and 4) C17,20-desmolase/17α-hydroxylase (CYP17A), and (5) 17β-hydroxysteroid dehydrogenase type III. Cytochrome P450 refers to a 450-nm light-absorbing heme-binding peptide sequence that is critical for stoichiometry. The enzymatically rate-limiting step in steroidogenesis is encoded by CYP11A, which converts cholesterol to pregnenolone in the inner mitochondrial membrane. However, the kinetically rate-limiting step is delivery of LDL-, membrane-, and cholesteryl ester-derived free cholesterol to the inner mitochondrial leaflet by steroidogenic acute regulatory (StAR) protein. LH activates StAR rapidly via posttranslational modification and slowly via increased gene transcription. Combined responses ensure both immediate and sustained access of cholesterol to mitochondrial side-chain cleavage system. Pregnenolone leaves mitochondria and enters endoplasmic reticulum, where subsequent enzymatic modifications occur. Pregnenolone (or its 3β-reduced metabolite, progesterone) undergoes sequential cleavage and hydroxylation via CYP17A-encoded C17,20 lyase/17α-hydroxylase (a single enzyme with dual functions), which constitutes the androgen-committing step. The product is a weak ketosteroid, androstenedione, which must be converted to the potent hydroxysteroid, Te, via 17β-hydroxysteroid dehydrogenase type 3.



Physiological Roles of Androgens

- FSH and testosterone are required for the initiation of spermatogenesis during sexual maturation.
- FSH interacts, with Sertoli cell plasmalemma receptors, results in cAMP production and synthesis of an Androgen Binding Protein (ABP).
- Presumably cAMP activates a protein kinase that leads to genomic production of a mRNA coding for ABP.
- Testicular receptors for LH are specifically localized to Leydig cells.
- In response to LH, cAMP is produced which then causes Leydig cell testosterone production.
- The dramatic development and behavioural changes in male at puberty result from enhanced testosterone secretion by testis.
- The accessory reproductive glands are dependent on testosterone to enable them to contribute secretory products to the semen.
- Sebaceous gland activity is stimulated by androgens most likely derived from testosterone.
- Acne often present in male is due to increased activity of these glands.
- In most vertebrates, skin, hair and feather coluration differ between the sexes. These pigmentary changes are usually androgen dependent.
- Growth and shedding of antlers is under the control of androgens.
- Androgens exert anabolic actions in muscle, cartilage, and other tissues.

- There is an age-associated decrease in serum testosterone level.
- Testosterone is clearly necessary to maintain libido.



Model of FSH and LH actions on Sertoli and Leydig cells

Q 5.
Answer

Several hormones participate in the regulation of carbohydrate metabolism. Four of them are secreted by the cells of the islets of Langerhans in the pancreas: two, insulin and glucagon, with major actions on glucose metabolism and two, somatostatin and pancreatic polypeptide, with modulating actions on insulin and glucagon secretion. Other hormones affecting carbohydrate metabolism include: epinephrine, thyroid hormones, glucocorticoids, and growth hormone.

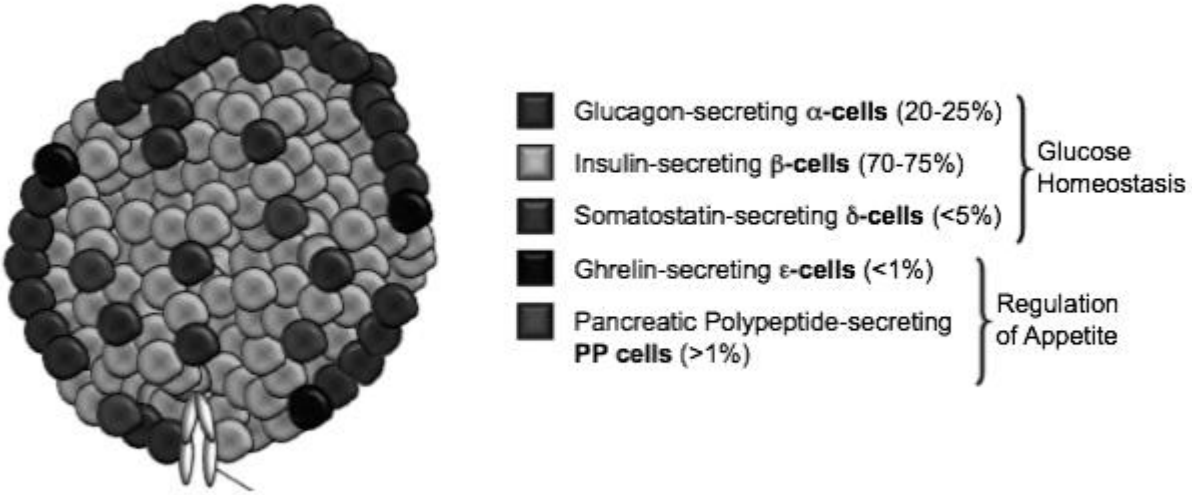
Structure and Function of the Pancreas

The pancreas lies inferior to the stomach, in a bend of the duodenum. It is both an endocrine and an exocrine gland. The exocrine functions are concerned with digestion. The endocrine function consists primarily of the secretion of the two major hormones, insulin and glucagon. Four cell types have been identified in the islets, each producing a different hormone with specific actions:

* A cells produce glucagon;
* B cells produce insulin;

* D cells produce somatostatin; and
* F or D1 cells produce pancreatic polypeptide.

These hormones are all polypeptides. Insulin is secreted only by the B cells whereas the other hormones are also secreted by the gastrointestinal mucosa and somatostatin is also found in the brain.



Both insulin and glucagon are important in the regulation of carbohydrate, protein and lipid metabolism:

Insulin is an anabolic hormone, that is, it increases the storage of glucose, fatty acids and amino acids in cells and tissues.

Glucagon is a catabolic hormone, that is, it mobilizes glucose, fatty acids and amino acids from stores into the blood.

Somatostatin may regulate, locally, the secretion of the other pancreatic hormones; in brain (hypothalamus) and spinal cord it may act as a neurohormone and neurotransmitter. The function

and origin of pancreatic polypeptide are still uncertain although the hormone may influence gastrointestinal function and promote intra-islet homeostasis.

Secretion and Actions of Insulin

Insulin is synthesized in B cells as part of a larger preprohormone - preproinsulin - which includes a 23 amino acid leader sequence attached to proinsulin; this leader sequence is lost upon entrance of the molecule into the endoplasmic reticulum leaving the pro-insulin molecule. Kallikrein, an enzyme present in the islets, aids in the conversion of proinsulin to insulin. In this conversion, a C peptide chain is removed from the proinsulin molecule producing the disulfide-connected A and B chains that are insulin.

Insulin secretion is pulsatile (i.e. increases as needed by bursts) and is regulated by a variety of stimulatory and inhibitory factors, most of them related to glucose metabolism and the effects of cAMP. Insulin secretion is stimulated by high blood glucose levels and reduced when blood glucose is low. Other stimulatory factors include several amino acids, intestinal hormones, acetylcholine (parasympathetic stimulation) and others. Inhibitory factors include somatostatin, norepinephrine (sympathetic stimulation) and others.

Once in the circulation, insulin is degraded within minutes in the liver and kidneys. C-peptide and Kallikrein are also present in the circulation, having been secreted with the insulin. Antibodies to components of islet cells have been detected in a high proportion of patients with insulin-dependent diabetes, that is, diabetes due to insulin deficiency. Antibody attack on B cells leads to extensive loss of these cells, characteristic of insulin-dependent diabetes and initiated by genetic mechanisms.

Insulin binds with specific membrane receptors forming an insulin-receptor complex which is taken into the cell by endocytosis. Insulin receptors are found in almost all cells of the body. The insulin-receptor, a tetramer, is made up of two alpha and two beta glycoprotein subunits. The

beta subunit is a protein kinase that catalyzes the phosphorylation of proteins, an activity resulting in a change in the number of "transporters", i.e. protein carriers of glucose. Intracellular free glucose concentration is low (due to rapid, efficient phosphorylation of glucose); therefore, a certain amount of glucose moves into the cell even in the absence of insulin. With insulin, however, the rate of glucose entry is much increased due facilitated diffusion as mediated by transporters.

The insulin-receptor complex enters the lysosomes where it is cleaved, the hormone internalized and the receptor recycled. Increased circulating levels of insulin reduce the number of receptors--down-regulation of receptors--and decreased insulin levels increase -- up-regulation--the number of receptors. The number of receptors per cell is increased in starvation and decreased in obesity and acromegaly; receptor affinity is decreased by excess glucocorticoids.

The major actions of insulin are:

* 1. facilitation of glucose transport through certain membranes (e.g. adipose and muscle cells)
* 2. stimulation of the enzyme system for conversion of glucose to glycogen (liver and muscle cells);
* 3. slow-down of gluconeogenesis (liver and muscle cells);
* 4. regulation of lipogenesis (liver and adipose cells); and
* 5. promotion of protein synthesis and growth (general effect).

These actions of insulin are mediated by the binding of the hormone to membrane receptors to trigger several simultaneous actions. A major effect of insulin is to promote the entrance of glucose and amino acids in cells of muscle, adipose tissue and connective tissue. Glucose enters the cell by facilitated diffusion along an inward gradient created by low intracellular free glucose and by the availability of a specific carrier called transporter. In the presence of insulin, the rate of movement of glucose into the cell is greatly stimulated in a selective fashion.

In the liver, insulin does not affect the movement of glucose across membranes directly but facilitates glycogen deposition and decreases glucose output. Consequently, there is a net increase in glucose uptake. Insulin induces or represses the activity of many enzymes; however if these actions are direct or indirect is not known. For example, insulin suppresses the synthesis of

key gluconeogenic enzymes and induces the synthesis of key glycolytic enzymes such as glucokinase. Glycogen synthetase activity is also increased. Insulin likewise increases the activity of enzymes involved in lipogenesis.

Glucagon

Glucagon is a peptide hormone, produced by alpha cells of the pancreas that raises the concentration of glucose in the bloodstream. Its effect is opposite that of insulin, which lowers the glucose concentration. The pancreas releases glucagon when the concentration of glucose in the bloodstream falls too low. Glucagon causes the liver to convert stored glycogen into glucose, which is released into the bloodstream. High blood-glucose levels stimulate the release of insulin. Insulin allows glucose to be taken up and used by insulin-dependent tissues. Thus, glucagon and insulin are part of a feedback system that keeps blood glucose levels at a stable level.

Glucagon generally elevates the concentration of glucose in the blood by promoting gluconeogenesis and glycogenolysis. Glucose is stored in the liver in the form of the polysaccharide glycogen, which is a glucan (a polymer made up of glucose molecules). Liver cells (hepatocytes) have glucagon receptors. When glucagon binds to the glucagon receptors, the liver cells convert the glycogen into individual glucose molecules and release them into the bloodstream, in a process known as glycogenolysis. As these stores become depleted, glucagon then encourages the liver and kidney to synthesize additional glucose by gluconeogenesis. Glucagon turns off glycolysis in the liver, causing glycolytic intermediates to be shuttled to gluconeogenesis. Glucagon also regulates the rate of glucose production through lipolysis. Glucagon induces lipolysis in humans under conditions of insulin suppression

Q 6.
Answer

Signal transduction is the process whereby information from outside the cell is conveyed into the cell. This often involves messenger systems. One such system involves a first messenger, such as a hormone, which binds to a cell surface receptor. The binding stimulates production of a second messenger inside the cell. Several molecules have been implicated as second messengers. A

widely use one is cyclic AMP (cAMP). cAMP-dependent signal transduction mechanisms involve three separate proteins:

1. A hormone receptor;
2. Adenylate cyclase; and
3. A G protein

G proteins, also known as guanosine nucleotide-binding proteins, are a family of proteins involved in transmitting signals from a variety of different stimuli outside a cell into the inside of the cell. G proteins function as molecular switches. Their activity is regulated by factors that control their ability to bind to and hydrolyze guanosine triphosphate (GTP) to guanosine diphosphate (GDP). When they bind GTP, they are 'on', and, when they bind GDP, they are 'off'.

G protein is made up of alpha (α), beta (β) and gamma (γ) subunits. Beta and gamma subunits (regulatory subunit) can form a stable dimeric complex referred to as the beta-gamma complex. Alpha subunit is catalytic subunit.

G proteins located within the cell are activated by G protein-coupled receptors (GPCRs) that span the cell membrane. Signaling molecules bind to a domain of the GPCR located outside the cell. An intracellular GPCR domain in turn activates a G protein. The G protein activates a cascade of further signaling events that finally results in a change in cell function. G protein-coupled receptor and G proteins working together transmit signals from many hormones, neurotransmitters, and other signaling factors. G proteins regulate metabolic enzymes, ion channels, transporter, and other parts of the cell machinery, controlling transcription, motility, contractility, and secretion, which in turn regulate diverse systemic functions such as embryonic development, learning and memory, and homeostasis.

In summary, the signal transduction pathway involves the following steps:

1. Binding of extracellular hormone or agonist to a receptor causes a conformational change in the receptor that stimulates it to interact with a nearby molecule of Gs.
2. This in turn stimulates an exchange of bound GDP for GTP--that is, the dissociation of GDP from Gs, to be replaced by GTP. A class of protein factors called guanine nucleotide exchange factors (GEF) assists in the exchange of GDP and GTP.
3. Gs is thereby converted to a protein that activates adenylate cyclase, producing cyclic AMP from ATP.

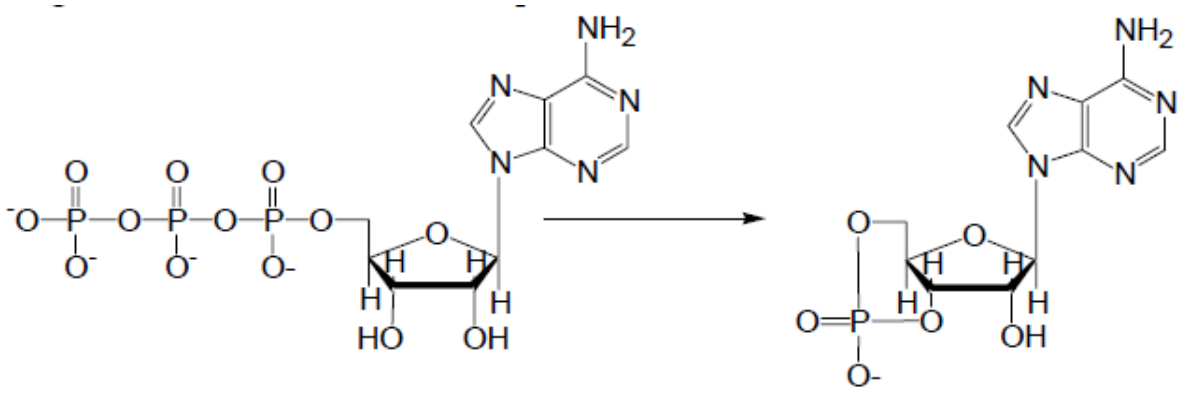
4. This results in activation of cAMP-dependent protein kinase (protein kinase A), with consequent phosphorylation of target proteins, such as phosphorylase b kinase in cells that activate glycogen phosphorolysis.

5. Phosphorylation of target enzymes results in stimulation or inhibition of metabolic reactions.

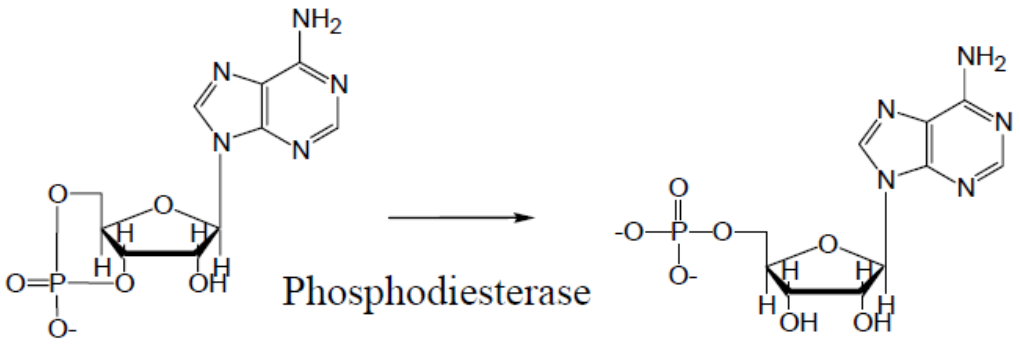
Continued activation of Gs depends on the presence of bound GTP.

The Gi protein functions similarly, but it responds to extracellular signals whose response is the inhibition of adenylate cyclase. Here the binding of GTP provokes an inhibitory interaction of Gi with adenylate cyclase, which decreases the synthesis of cAMP.

Second messengers need to have short half lives so that the response can be rapidly terminated. Phosphodiesterase hydrolyzes the phosphodiester bond to convert cAMP to AMP. The G proteins ultimately need to reset themselves. The Gα subunit has an intrinsic GTPase activity. The bound GTP will slowly be hydrolyzed into GDP and Pi. This GTPase activity is like a built in clock that spontaneously resets the Gα subunit after a short period of time. After the Gα subunit has hydrolyzed GTP it tightly binds the GDP. When the Gα subunit had GDP bound it dissociates from adenylate cyclase turning this enzyme off and reassociates with the Gβγ dimer to reform the heterotrimer. This requires the hormone to be bound to the receptor to keep adenylate cyclase active.



ATP **cAMP**



cAMP **AMP**

Q 7.
Answer

The adrenal glands are two glands that sit on top of kidneys that are made up of two distinct parts.

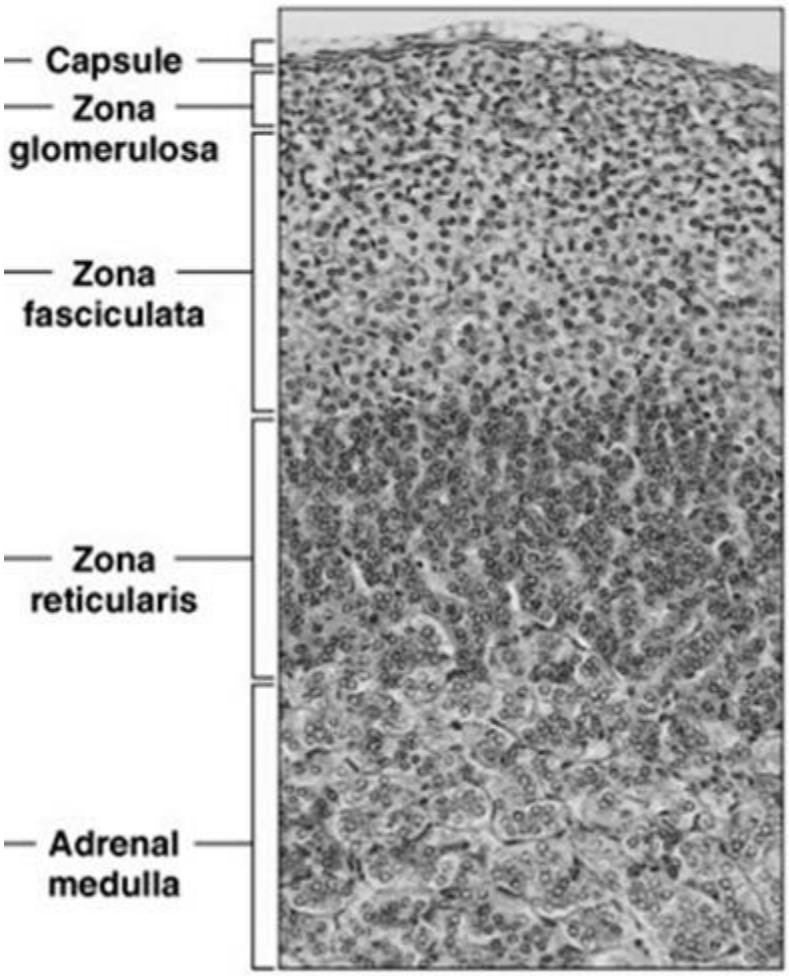
- The adrenal cortex—the outer part of the gland—produces hormones that are vital to life, such as cortisol (which helps regulate metabolism and helps body respond to stress) and aldosterone (which helps control blood pressure).
- The adrenal medulla—the inner part of the gland—produces hormones, such as adrenaline (which helps body react to stress).

Adrenal Cortex

The adrenal cortex consists of three concentric zones of steroid-synthesizing cells called the:

- glomerulosa
- fasiculata, and
- reticularis.

Although the boundaries between these zones are indistinct, each of these zones has a characteristic arrangement of cells.



Cortex

The adrenal cortex is the outermost layer of the adrenal gland. Within the cortex are three layers, called "zones". When viewed under a microscope each layer has a distinct appearance, and each has a different function. The adrenal cortex is devoted to production of hormones, namely aldosterone, cortisol, and androgens.

Zona glomerulosa

The outermost layer of the adrenal cortex is the zona glomerulosa. It lies immediately under the fibrous capsule of the gland. Cells in this layer form oval groups, separated by thin strands of connective tissue from the fibrous capsule of the gland and carry wide capillaries.

This layer is the main site for production of aldosterone, a mineralocorticoid, by the action of the enzyme aldosterone synthase. Aldosterone plays an important role in the long-term regulation of blood pressure.

Zona fasciculata

The zona fasciculata is situated between the zona glomerulosa and zona reticularis. Cells in this layer are responsible for producing glucocorticoids such as cortisol. It is the largest of the three layers, accounting for nearly 80% of the volume of the cortex. In the zona fasciculata, cells are arranged in columns radially oriented towards the medulla. Cells contain numerous lipid droplets, abundant mitochondria and a complex smooth endoplasmic reticulum.

Zona reticularis

The innermost cortical layer, the zona reticularis, lies directly adjacent to the medulla. It produces androgens, mainly dehydroepiandrosterone (DHEA), DHEA sulfate (DHEA-S), and androstenedione (the precursor to testosterone) in humans. Its small cells form irregular cords and clusters, separated by capillaries and connective tissue. The cells contain relatively small quantities of cytoplasm and lipid droplets, and sometimes display brown lipofuscin pigment

Adrenal Cortex	• **Corticosteroids**	**Glucocorticoids** (e.g. cortisol, cortisone, corticosterone) • Utilization of carbohydrate, fat and protein by the body. • Normal response to stress. • Anti-inflammatory effects. • **Hypersecretion of cortisol results in Cushings Syndrome.**
		Mineralocorticoids (e.g. aldosterone) • Regulation of salt and water balance. • **Hypersecretion of Alderosterone decreases the potassium in the body (affecting nerve impulse transmission and leading to muscular paralysis).**

The adrenal gland secretes a number of different hormones which are metabolised by enzymes either within the gland or in other parts of the body. These hormones are involved in a number of essential biological functions.

Corticosteroids

Corticosteroids are a group of steroid hormones produced from the cortex of the adrenal gland, from which they are named. Corticosteroids are named according to their actions:

- Mineralocorticoids such as aldosterone regulate salt ("mineral") balance and blood volume.
- Glucocorticoids such as cortisol influence metabolism rates of proteins, fats and sugars ("glucose").

Mineralocorticoids

The adrenal gland produces aldosterone, a mineralocorticoid, which is important in the regulation of salt ("mineral") balance and blood volume. In the kidneys, aldosterone acts on the distal convoluted tubules and the collecting ducts by increasing the reabsorption of sodium and the excretion of both potassium and hydrogen ions. Aldosterone is responsible for the reabsorption of about 2% of filtered sodium in the kidneys, which is nearly equal to the entire sodium content in human blood under normal glomerular filtration rates. Sodium retention is also a response of the distal colon and sweat glands to aldosterone receptor stimulation. Angiotensin II and extracellular potassium are the two main regulators of aldosterone production.The amount of sodium present in the body affects the extracellular volume, which in turn influences blood pressure. Therefore, the effects of aldosterone in sodium retention are important for the regulation of blood pressure.

Glucocorticoids

Cortisol is the main glucocorticoid in humans. In species that do not create cortisol, this role is played by corticosterone instead. Glucocorticoids have many effects on metabolism. As their name suggests, they increase the circulating level of glucose. This is the result of an increase in the mobilization of amino acids from protein and the stimulation of synthesis of glucose from these amino acids in the liver. In addition, they increase the levels of free fatty acids, which cells can use as an alternative to glucose to obtain energy. Glucocorticoids also have effects not related to the regulation of blood sugar levels, including the suppression of the immune system and a potent anti-inflammatory effect. Cortisol reduces the capacity of osteoblasts to produce new bone tissue and decreases the absorption of calcium in the gastrointestinal tract.

The adrenal gland secretes a basal level of cortisol but can also produce bursts of the hormone in response to adrenocorticotropic hormone (ACTH) from the anterior pituitary. Cortisol is not evenly released during the day – its concentrations in the blood are highest in the early morning and lowest in the evening as a result of the circadian rhythm of ACTH secretion. Cortisone is an

inactive product of the action of the enzyme 11β-HSD on cortisol. The reaction catalyzed by 11β-HSD is reversible, which means that it can turn administered cortisone into cortisol, the biologically active hormone.

Q 8.

Answer

Stress and Adrenal Gland

Stress is the sum total of all mental and physical input over a given period of time. The marker used to measure stress is the adrenal steroid hormone, cortisol. Stress, whether physical or emotional in origin, provokes a response by the adrenal glands. Many hormonal imbalances are the direct result of adrenal insufficiency. The adrenal glands produce two primary hormones, DHEA and cortisol. Both are considered the major shock absorber hormones in the body. They buffer stress and the negative impact it can have on both mental and physical function. Long-term stress can have a serious impact on the adrenal glands and cause them to shrink and reduce production. This causes cellular damage, which sets off a chain reaction affecting all parts of the body, as well as accelerating the aging process. The symptoms associated with adrenal dysfunction are diverse and can involve the digestive, circulatory, respiratory, as well as the brain and nervous systems. In addition, the adrenals can impact the growth and repair of bones, muscles, hair and nails. Cortisol is a steroid hormone made in the adrenal glands. Cortisol's important function in the body includes roles in the regulation of blood pressure and cardiovascular function as well as regulation of the body's use of proteins, carbohydrates, and fats.

Cortisol secretion increases in response to any stress in the body, whether physical (such as illness, trauma, surgery or temperature extremes) or psychological pressures. When cortisol is secreted, it causes a breakdown of muscle protein, leading to release of amino acids into the bloodstream. These amino acids are then used by the liver to synthesize glucose for energy, in a process called gluconeogenesis. Cortisol also leads to the release of energy source from fat cells, for use by the muscles. Taken together, these energy directing processes prepare the individual to deal with stressors and insure that the brain receives adequate energy sources. The body possesses an elaborate feedback system for controlling cortisol secretion and regulating the amount of cortisol in the bloodstream. The pituitary gland, a small gland at the base of the brain, makes and secretes a hormone known as adrenocorticotropic hormone, or ACTH. Secretion of ACTH signals the adrenal glands to increase cortisol production and secretion. The pituitary, in turn, receives signals from the hypothalamus of the brain in the form of the hormone CRH, or corticotrophin-releasing hormone, which signals the pituitary to release ACTH. Almost immediately after a stressful event, the levels of the regulatory hormones ACTH and CRH increase, causing an immediate rise in cortisol levels. When cortisol is present in adequate, or excess amounts, a negative feedback system operates on the pituitary gland and hypothalamus, which alerts these areas to reduce the output of ACTH and CRH, respectively, in order to reduce cortisol secretion when adequate levels are present.

Adrenaline, commonly known as the fight or flight hormone, it is produced by the adrenal glands after receiving a message from the brain that a stressful situation has presented itself. Adrenaline, along with norepinephrine, is largely responsible for the *immediate* reactions we feel when stressed. Along with the increase in heart rate, adrenaline also gives a surge of energy -- which one might need to run away from a dangerous situation -- and also focuses attention.