Lecture No.5

Pituatary Gland:

- It is divisible into two distinct portions,
- the anterior pituitary or adenohypophysis and posterior pituitary or neurohypophysis or pars nervosa.
- The adenohypophysis consists of three portions, viz., the pars distalis, pars tuberalis and the pars intermedia.
- The pars distalis is the largest of the three parts and secrets the tropic hormones.
- The pars tuberalis does not have any endocrine function.
- The pars intermedia produce melanocyte-stimulating hormone (MSH) and regulate the pigmentation in the body.

ADENOHYPOPHYSIS (Anterior Pituitary)

- Adenohypophysis contains two types of cells - **chromophobes and chromophils**
- **The chromophobes are the inactive precursor or a resting type of cells from** which the active (hormone producing) **cells known as chromophils arise**.
- Chromophils are further divided into acidophils and basophils.
- The acidophils and basophils include five types that produce six hormones

	Cells	**Hormone**	**Target organ**	**Biological effect**
I	Chromophobes	Inactive cells	-	-
II	Chromophils	Active cells	-	-

	A) Acidophils			
	a) Somatotrophs	GH	All body cells	Growth, Somatomedin synthesis
	b) Lactotrophs/ mammotrophs	Prolactin	Mammary gland	Milk biosynthesis, luteotropic
	B) Basophils			
	a) Thyrotrophs	TSH	Thyroid gland	Thyroxine synthesis and release
	b) Corticotrophs	ACTH & β-LPH	Adrenal cortex	Glucocorticoid synthesis and release
	c) Gonadotrophs	FSH	Testis, ovary	Spermatogenesis, folliculogenesis, estradiol synthesis
		LH (ICSH)	Leydig cells of testis	Androgen production, spermiogenesis
			Graafian follicle of ovary	Ovulation, CL development, progesterone synthesis

SOMATOTROPIN (STH) or growth hormone (GH)

- Complex protein having **191 amino acids and S-S bridges.**
- The **STH is species specific** and it is structurally related to prolactin of the same species.

Control of STH secretion

- by a balance between the growth hormone releasing hormone (GHRH) and somatostatin.
- A sharp drop in blood glucose and fatty acids levels is the primary cause of GHRH release from the hypothalamus and it results in two to ten fold increases in STH secretion.

Stimuli that increases the GH secretion

- Deficiency of energy - hypoglycaemia, exercise, fasting, insulin
- Stress (trauma, surgery) pyrogen
- Sleep
- **Ghrelin, a 28 amino acid polypeptide hormone secreted from hypothalamus (also from stomach) stimulates GH release**

Stimuli that decreases the GH secretion

  - Increase in glucose, cortisol, free fatty acids, GH
  - Obesity results in reduced GH release and GIH
- STH has a biological role throughout life as an anabolic agent as well as synergistic role by enhancing the actions of ACTH, TSH, LH, and FSH on their target organs.
- Females are more responsive to GH stimuli than males.

PHYSIOLOGICAL EFFECTS OF STH

- Growth hormone has two distinct types of effects
  - Direct effects are the result of **growth hormone binding its receptor on target cells**.

    Fat cells (adipocytes) have growth hormone receptors, and growth hormone stimulates them to lipolysis and reduce uptake of **circulating lipids**.
  - Indirect effects are mediated primarily by an **insulin-like growth factor-I (IGF-I),**

    IGF-I a hormone that is secreted from the liver and other tissues in response to growth hormone.

Normal Effects in the Body

1. The STH does **not have a specific target organ** its effect on **almost all tissues of the body.**

2. STH causes **both increase in size (hypertrophy) and number of cells (hyperplasia),** and promotes growth of all tissues of the body which are capable of growing.
3. GH enhances the **activities of the visceral organs like liver, kidney, intestine, endocrine glands parathyroid, and pancreas.**
4. It stimulates **cardiac output, glomerular filtration and the metabolic activities in liver, skeletal muscle and heart.**
5. Increases **both the soft and osseous tissues of the body and** has a profound effect on **lactation**.

Effects on Growth

1. Growth is a very complex process, and requires the coordinated action of several hormones.
2. GH does not act directly on bone and cartilage, but indirectly by causing the liver to produce **smaller proteins** called **somatomedins** that act on cartilages and bone to promote their growth.
3. Two somatomedins, C and A which structurally similar to insulin and hence they are also known as insulin like growth factors I and II (IGF I & II) respectively.
4. **IGF I is transported in blood bound with specific binding proteins called IGF-binding proteins (IGFBP); this binding of IGF prolongs the half-life of IGF I.**
5. The receptor for IGF is similar to insulin receptors.
6. **IGF I promotes skeletal and cartilage growth and IGF II is functional during foetal period.**
7. The metabolic effects of GH on most of the cells are promoted by stimulating the liver and other tissues to secrete *IGF-I* or somatomedin C.

8. **IGF-I stimulates proliferation of chondrocytes (cartilage cells) resulting in bone growth**. GH also seems to have a **direct effect on bone growth in stimulating differentiation of chondrocytes**. Somatomedin production is inhibited by estrogen and cortisol.
9. *IGF*-I also increase muscle growth. It stimulates both the differentiation and proliferation of myoblasts. It also stimulates amino acid uptake and protein synthesis in muscle and other tissues.

METABOLIC EFFECTS OF GROWTH HORMONE

Protein

1. As a **protein anabolic hormone**
2. GH enhances amino acid metabolism including uptake of Amino acid,
3. Reducing the break down of proteins.
4. Decreased catabolism of protein and amino acids for energy.
5. Protein content of the body is increased by GH.
6. Increased protein synthesis in all cells of the body more specifically the muscle cells.
7. Stimulates the formation of RNA by increasing the transcription process in the nucleus.
8. By enhancing the ribosomal machinery, produces greater number of protein molecules.

Lipid

1. It **stimulates lipolysis** and mobilizes large quantities of free fatty acids from the adipose tissue.
2. It enhances the **conversion of fatty acids to acetyl Co- A**, which is used for energy.
3. Excessive amount of STH at times causes greater amounts of fat mobilization resulting in excess acetyl Co-A which is converted to

acetoacetate, b -OH butyric acid and acetone leading to ketonemia which is called as **ketogenic effect of GH**.

4. It reduces lipid synthesis and leads to leaner animal.
5. GH decreases body fat content and promotes lean body mass.

Carbohydrate

1. GH causes **decreased utilization of glucose for energy** (possibly due to utilization of fat for energy) and **enhanced glycogen deposition**. It diminishes **uptake of glucose by the cells for energy by the muscle and adipose cells, thus increases blood glucose concentration which is known as diabetogenic effect of GH.**
2. GH shows **positive nitrogen balance and phosphorus balance**.
3. In the cow lactation can be induced with STH more easily and with greater regularity than with lactogenic hormone (prolactin). This is due to **galactopoietic effect of STH**
4. In summery, **STH favours economical use of proteins and carbohydrates, encouraging the body to retain these building blocks for tissue growth and development**.
5. Injection of growth hormone increases milk yield by 10-25%, lactose, protein and fat contents of milk.
6. Endogenous plasma concentrations of GH are high in high yielding than low yielding animals.
7. GH partitions nutrients for milk yield and increases fatty acid mobilisation.
8. Exogenous GH increases nitrogen retention and improves carcass quality with improved muscle growth; helps in lean meat production with less adipose tissue in cattle, pigs, sheep.

EFFECTS OF ABNORMAL PRODUCTION

- If the overproduction occurs before the closure of epiphyseal lines in the long bones, it results in lengthening of the long bones and increased deposition of soft tissue, resulting **in gigantism**. This condition occasionally occurs in domestic animals.
- If excess production of STH occurs after the closure of epiphyseal lines, the long bones of the body are thickened and there is excessive soft tissue and this condition is termed as **acromegaly**. This is produced in acidophilic tumours.

THYROTROPIC HORMONE (TSH)

1. The thyrotropic hormone or thyroid-stimulating hormone (TSH) is a **glycoprotein** with two peptide sub units, the α and β. The a sub unit(92) is non-specific, whereas b -sub unit(112) shows some species specificity.
2. TSH has morphological and functional effects on the thyroid.
3. Functionally, the effect of TSH is to increase cell size, number of thyroid follicles and also the activity of thyroid gland which includes

   Uptake of iodide (iodine trapping),

   Production and release of thyroxine by increasing iodination and coupling reactions and Proteolysis of thyroglobulin releasing the thyroid hormones.
4. **TSH enhances DNA, RNA and ribosome activities**, thus **favours synthesis of proteins and phospholipids in thyroid follicle cells**.

5. Exposure to lower environmental temperature or chilling of the animal causes the release of TRH and TSH, thus the thyroxine formation to elevate basal metabolic rate and heat production by non-shivering thermogenesis.

ADRENOCORTICOTROPIC HORMONE (ACTH)

1. **It is a polypeptide containing 39 amino acids in a straight chain in sheep**, pig, cow and man.
2. It stimulates synthesis and immediate release of corticosteriods.
3. The primary physiological function of ACTH is to stimulate the secretion of the adrenal cortex, especially of cortisol and corticosterone.
4. However the mineralocorticoids show lesser effects to ACTH.
5. During haemorrhage it causes aldosterone release.
6. **Stressful stimuli such as haemorrhage, temperature, pain, toxin and emotional states, influence the release of ACTH by stimulating the hypothalamus to release CRH.**
7. **ACTH secretion is influenced by circadian light/darkness cycle**.
8. In human and horses ACTH secretion is high during morning hours (6.00 to 8.00 A.M.), in pigs two peaks occur, one in morning and one in late afternoon.
9. In dogs, there is no peak level.
10. **By long loop servomechanism, the glucocorticoid cortisol regulates CRH release from the hypothalamus, thus decreases ACTH formation in the adenohypophysis.**
11. By short-loop negative feed back action ACTH inhibits CRH release.

PROLACTIN (LACTOGENIC HORMONE)

1. PRL a lactogenic hormone, is a single-chain peptide consisting of 199 amino acids and three disulfide bridges.
2. PRL is structurally similar to GH and **has many overlapping biological functions with GH**.
3. The most important influence of PRL secretion is the **combination of pregnancy, estrogen, and nursing of newborn**.
4. PRL secretion increases steadily during pregnancy.
5. **PRL secretion rises at night similar to GH**.
6. Suckling inhibits dopamine (PIF) secretion, thus stimulates PRL release.
7. **Dopamine, catecholamines, LH - RH** inhibits PRL release.
8. PRL is the **principle hormone responsible for lactogenesis** (milk production).
9. **PRL together with estrogen, progestrone, cortisol and GH cause proliferation of duct system of the mammary gland**.
10. **During pregnancy prolactin, estrogen and progesterone cause development of secretory alveoli in the mammary gland thus causes initiation and maintenance of lactation in domestic animals**.
11. **PRL level increases just prior to parturition and after parturition, milk synthesis and secretion require PRL along with cortisol and insulin.**
12. **PRL induces enzymes necessary for lactose synthesis.**
13. **It provokes synthesis of milk constituents including lactalbumin, casein, and lipids. Prolactin increases in the peripheral blood of the cow during milking.**
14. In pigeon it causes the **crop gland to hypertrophy and stimulates the secretion of crop milk** (this is used in **bioassay of prolactin**).
15. In ewes, **prolactin stimulates corpus luteum referred to as the luteotropic effect; hence it is also referred as luteotropin .**

16. It is necessary for maintenance of CL in rat, dog.
17. An excess of PRL blocks the synthesis and release of LH-RH which inhibits gonadotropin (FSH/LH) secretions from the pituitary and prevents ovulation and spermatogenesis.
18. High PRL concentration also inhibits the synthesis of gonadal steroids both in male and female.
19. In animals PRL provides productive maternal behaviour toward the newborn.
20. Broodiness in birds is controlled by PRL. (**Broodiness** is the action or behavioral tendency to sit on a clutch of eggs to incubate them, often requiring the non-expression of many other behaviors including feeding and drinking.)
21. Prolactin may have a growth mediating role similar to GH and reduces lipid synthesis
22. Helps in partitioning of nutrients.

GONADOTROPINS (FSH & LH)

1. Two hormones from the adenohypophysis, the follicle-stimulating hormone (FSH) and luteinizing hormone (LH/ICSH) in females/males affect the gonadal activity.
2. The basal or tonic output of FSH and LH is pulsatile during the reproductive functions in males and females.
3. **Follicle stimulating hormone (FSH) is a glycoprotein made up of α- (92 amino acids) and β- (118 amino acids) subunits with carbohydrate moiety**.
4. **Luteinizing hormone (LH) or Interstitial-cell stimulating hormone (ICSH) - LH in female and ICSH of the male is the same hormone**.

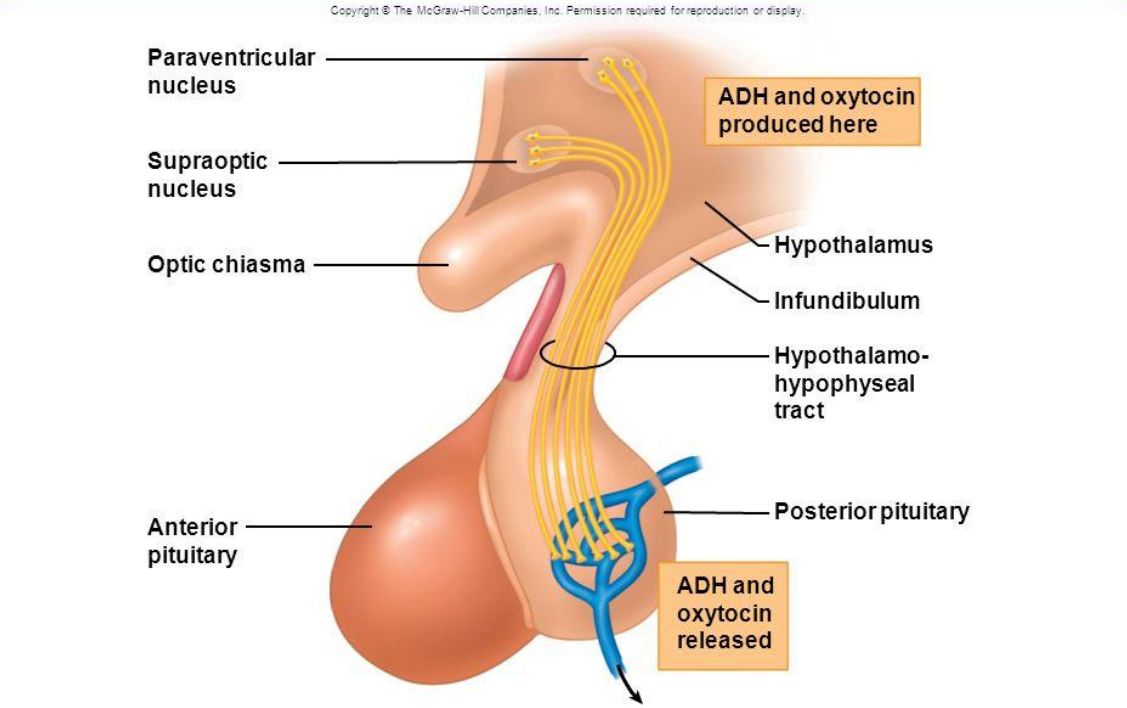
5. **LH is a glycoprotein made up of α- and β- subunits having 92 and 115 amino acids with carbohydrate moiety**.
6. Environmental conditions like changing seasons and day light length is mediated from exteroceptors like eye to the hypothalamus to influence GnRH output.
7. **Basal pulsatile FSH secretion stimulates follicular growth and estrogen secretion in ovaries**.
8. **FSH acts synergistically with LH to effect ovulation**.
9. In the male FSH acts on the seminiferous tubules and stimulates spermatogenesis.
10. The actions of LH and FSH are synergistic.
11. **Increased production of estrogen by the Graafian follicle stimulates LH surge to effect ovulation by positive feedback effect.**
12. LH causes **maturation of ovum, ovulation, and formation of corpus luteum (CL).**
13. The CL produces progesterone which **inhibits LH secretion and prevents further follicular growth and ovulation**, **thus preventing estrus during the period of CL**.
14. In induced ovulators e.g., cat and rabbit, LH secretion is stimulated by neuroendocrine reflex of the hypothalamus. In male **LH stimulates interstitial cells of testis and causes testosterone production**.
15. The **regulation of LH output from the pituitary gland is dependent upon the hypothalamic GnRH by a negative-feedback control mechanism.**
16. During pregnancy, placenta also secretes placental luteotropic hormone.
17. Estrogen and progesterone in large amounts inhibit FSH and LH release from the adenohypophysis and the feedback effect operates through the hypothalamus and anterior pituitary.

18. In addition inhibin secreted from the large graafian follicles in females and Sertoli cells in males inhibits FSH to a major extent and LH to a lesser extent.

OXYTOCIN

1. It is synthesize mainly by paraventricular nucleus of the HPT.
2. It is also synthesize by supraoptic nucleus in small quantity
3. It is transported from HPT to PP(NHP) through the nerve fibre of hypothamo-hypophysial tract and stored in PP where secreted directly in to the blood without partipication of HPPS.(hypophysial portal system)

Hypothalamic Control of the Posterior Pituitary



4. It is a **peptide hormone** containing **8 amino acids**.
5. Cys-Tyr-Ile-glu-asn-cys-pro-leu-gly-NH_2 (CTI- GAC-PLG)
6. Isolleucine at position 3rd is critical for oxytocic effect.
7. **Seven amino acids are common between oxytocin and ADH**.
8. Oxytocin has a half life of 2 min.(1-3minutes)
9. Oxytocin has **specific effects on the smooth muscle of the uterus and the myoepithelial cells of the mammary gland.**
10. It also functions in the **release of prostaglandins from the endometrium**.
11. **Along with estrogen and PGF_2 alpha , it causes powerful contractions in the pregnant uterus and helps in parturition.**
12. It helps **sperm transport in estrogen-primed uterus during follicular phase of estrous cycle**.

13. In male it is released during **mating to cause movement of sperm through the male duct system for ejaculation**.
14. **On the udder it causes contraction of myoepithelial cells which results in milk letdown by a neuroendorcine reflex.**
15. **Suckling stimulates hypothalamus, causes oxytocin release from neurohypophysis**.
16. In birds it has the ability to **lower BP**.
17. **Oxytocin is also secreted by corpus luteum which acts with estrogen and PGF to cause lysis of CL**.
18. CL also produces oxytocin .
19. Gonadotropins, PGF and progesterone stimulate oxytocin from CL. At the end of luteal phase, when progesterone effect on CL is reduced, oxytocin induces luteolysis by initiating release of PGF2 alpha from endometrium.

ANTIDIURETIC HORMONE OR VASOPRESSIN

- It is synthesize mainly by supraoptic nucleus of the HPT.
- It is also synthesize by paraventricular nucleus in small quantity

- It is transported from HPT to PP(NHP) through the nerve fibre of hypothamo-hypophysial tract and stored in PP where secreted directly in to the blood without partipication of HPPS.(hypophysial portal system)
- The vasopressin is a peptide containing 8 amino acids.
- Cys-Tyr-Phe-gln-asn-cys-pro-arg-gly-NH_2 (CTP- GAC-PAG)
- It shows species specificity in its composition.
- In cattle, man and most mammals the main form of vasopressin is arginine-vasopressin (arginine at position 8 is essential for antidiuretic effect).
- In swine it is **lysine-vasopressin**.
- In birds it is **arginine- vasotocin**.
- **ADH has a half-life of 18 minutes**.
- **An increase in osmolality of body fluids due to dehydration of body, hypotension and decreased blood volume, angiotensin II stimulates the osmoreceptrors(anterior HPT) of the hypothalamus and release ADH**.
- ADH acts on the **distal tubule and collecting ducts through cAMP mechanism and causes increased reabsorption of water.**
- Trauma, pain, anxiety and certain drugs also favour the release vasopressin,
- Diluted body fluid and cold environmental temperature inhibit its secretion.
- There is feedback regulation between plasma osmalality and ADH secretion
- A deficiency of this hormone leads to increased urine volume (diuresis) resulting in a condition known as diabetes insipidus in the dog, cat and horse.