

## **MODULE 8 : Endocrine System**

### **Biochemistry – Undergraduate Programme**

**Faculty of Medicine and Allied Sciences**

**Rajarata University of Sri Lanka**

#### ***Broad Objectives***

At the end of this course, the student is expected to know,

1. the hormones and the stimuli for their release from the hypothalamus, pituitary, thyroid, parathyroid, adrenal cortex, adrenal medulla, gonads, pancreas, kidney, the gastrointestinal tract and the vascular endothelium
2. the functions of anterior pituitary and posterior pituitary hormones and their action on metabolism
3. the structure of the thyroid cell and the synthesis, secretion and the biological activity of thyroid hormones and calcitonin
4. the cells that synthesize the parathyroid hormone, its processing, the mode of action in relation to its structure and its function
5. the principle hormones synthesized by the adrenal cortex and the medulla, factors promoting their release and the mode of action
6. the pancreatic cells that produce the four polypeptide hormones, their structure, synthesis, processing, secretion, functions and metabolic derangements associated with abnormal hormone-receptor interaction
7. that the ovaries and testes produce sex hormones and that these affect growth, cell turnover and metabolism
8. the hormones released by the kidney and their mode of action
9. the hormones secreted by the vascular endothelium and platelets, their synthesis, mode of action and functions

#### **Specific Objectives**

##### ***1. Endocrine organs and tissues***

- 1.1. Recall that hypothalamus is the highest centre for co-ordinating the activities of hormones in the body and that release or inhibition of hormone release is initiated through releasing hormones of the hypothalamus.
- 1.2. Recall that the hypothalamus, pituitary and the target endocrine glands form a series of closed loop regulatory systems. (Physiology)
- 1.3. List the important organs and tissues that secrete hormones into the blood.
- 1.4. Name the hormones that are released by those mentioned in 1.3.
- 1.5. State the chemical stimuli for the secretion of the hormones named in 1.4.
- 1.6. Group the hormones mentioned in 1.4 according to the hormone receptor.
- 1.7. Explain the mechanisms of action of hormones at cellular level based on the hormone - receptor involved

##### ***2. Pituitary***

- 2.1. Know the hormones of the pituitary gland and their mode of action and functions

## 2.2. Anterior Pituitary

- 2.2.1. Recall the hormones that are synthesized in the anterior pituitary
- 2.2.2. Explain the importance of TSH in the regulation of plasma T3 and T4 levels
- 2.2.3. Recall that ACTH has a role to play in stress and its direct and indirect action on energy and protein metabolism
- 2.2.4. Recall that growth hormone (GH) is synthesized in somatotropes and that these are the most abundant cells in the gland
- 2.2.5. Recall that growth hormone is a single polypeptide of 70,000 MW that acts on the membrane by phosphorylation of the receptor
- 2.2.6. Recall that growth hormone is essential for post natal growth and for normal carbohydrate, protein, lipid and mineral metabolism
- 2.2.7. Recall that growth related effects are primarily mediated by IGF-I
- 2.2.8. Recall that growth hormone increases the transport of amino acids into myocytes and increases the synthesis of DNA and RNA in some tissues
- 2.2.9. Recall that the growth hormone antagonizes the effects of insulin
- 2.2.10. Recall that the administration of growth hormone is followed by decreased peripheral utilization of glucose and increased hepatic production via gluconeogenesis, resulting in increased liver glycogen
- 2.2.11. Explain the action of growth hormone on adipose tissue
- 2.2.12. Recall that GH promotes positive calcium balance, where it promotes growth of long bones at the epiphyseal plates of growing children and the growth of extremities in adults
- 2.2.13. Recall that GH has a structure similar to prolactin and binds to lactogenic receptors mimicking the effects of prolactin
- 2.2.14. Explain the effect of GH on skeletal muscle, hepatocytes, adipocytes, beta cells of the Islets of Langerhan
- 2.2.15. Recall that GH will not bring about nitrogen retention unless insulin is present. Explain its amino acid sparing action
- 2.2.16. Explain why prolonged elevation of GH may result in diabetes mellitus.
- 2.2.17. Recall that there is a marked surge of GH secretion during sleep
- 2.2.18. Recall that plasma GH is consistently higher in kwashiorkor, but not in marasmus, and that secretion of GH in kwashiorkor is not suppressed by glucose
- 2.2.19. State the immediate and long term effects of thyrotropin on the thyroid gland
- 2.2.20. Explain how the secretion of thyrotropin is controlled
- 2.2.21. Recall that prolactin of 23,000 MW is secreted by lactotropes which increase in number and size during pregnancy
- 2.2.22. Recall that it is involved in initiation and maintenance of lactation
- 2.2.23. Recall that physiological levels act only on breast tissue primed by female sex hormones
- 2.2.24. Recall that high levels of plasma prolactin maybe associated with amenorrhoea and galactorrhoea in women and gynaecomastia and impotence in men

### 2.3. **Posterior Pituitary**

- 2.3.1. Recall that both vasopressin and oxytocin are structurally closely related nanopeptides containing a disulphide linkage between 1 and 6 amino acids
- 2.3.2. State the sites of action of these hormones and the functions they perform
- 2.3.3. Explain why vasopressin is also known as the anti-diuretic hormone
- 2.3.4. Recall that disorders due to vasopressin may arise due to deficiency of the hormone or a receptor defect
- 2.3.5. Explain what is meant by 'diabetes insipidus' and how it may arise

### 3. ***Thyroid***

- 3.1. Recall that thyroid is made up of acini and describe their appearance under the microscope (Histology)
- 3.2. Recall that thyroglobulin is present in a colloidal form within the acini
- 3.3. Explain the mechanism involved in the uptake of iodine into the thyroid cell and its inhibition by molecules of similar size
- 3.4. Describe the synthesis of  $T_4$  highlighting iodine uptake, organification, coupling and the processing involved
- 3.5. Describe the transport of thyroid hormones in the blood and recall that it is the free form that is biologically active
- 3.6. State the immediate and the long term effects of thyrotropin (TSH) on the thyroid gland
- 3.7. Recall that only the L-isomer of  $T_4$  is active and that the D-isomer has a blood cholesterol lowering effect
- 3.8. Recall the signs and symptoms associated with a) hypothyroidism and b) hyperthyroidism (Physiology) and explain the biochemical basis of these wherever possible.
- 3.9. Distinguish between  $T_3$  and  $rT_3$  in structure, synthesis and function.
- 3.10. Recall the two types of de-iodinases present and their structural and functional differences
- 3.11. Recall that very little hormone crosses the placenta from the mother to the foetus
- 3.12. Explain why  $rT_3$  in the amniotic fluid is considered to be indicative of foetal thyroid activity
- 3.13. State the effect of fasting and feasting on the plasma level of  $T_4$ ,  $T_3$  and  $rT_3$
- 3.14. Recall that thyroiditis may be caused by antibodies against TSH receptors. (Physiology)
- 3.15. Recall that parafollicular cells (clear cells, 'C' cells) synthesize and secrete calcitonin
- 3.16. Recall that calcitonin is a polypeptide hormone and that its mode of action is different from that of thyroid hormone
- 3.17. Explain the role of calcitonin in calcium homeostasis

### 4. ***Parathyroid***

- 4.1. Recall the cells that synthesize PTH
- 4.2. Describe the processing of pre-pro PTH and the release of active PTH
- 4.3. Explain the functions of the different segments of the pre-pro PTH

- 4.4 . Explain how PTH regulates calcium and phosphate homeostasis
- 4.5 . Explain how hypo-parathyroidism may result from
  - 4.5.1. accidental removal of the gland during surgery,
  - 4.5.2. autoimmune destruction of the parathyroid gland, and accompanying disorders in calcium metabolism (Physiology).
- 4.6. Explain the biochemical changes seen in the blood, bone and the kidneys in hyperparathyroidism

## 5. *Adrenals*

### 5.1 General

- 5.1.1. Know the classes of the hormones of the adrenals and their mode of action and functions

### 5.2. *Adrenal Cortex*

- 5.2.1. Recall that glucocorticoids, mineralocorticoids and androgens are the three classes of hormones released
- 5.2.2. Recall that cortisol is the major glucocorticoid hormone that affects protein and energy metabolism in the fasting state
- 5.2.3. Recognize the structures of cortisone, corticosterone and cortisol and know their difference in structure from those of sex hormones.
- 5.2.4. List their effects on the metabolism of carbohydrate, protein and lipid & explain how these effects are brought about.
- 5.2.5. Recall that aldosterone is the major mineralocorticoid that affects sodium and potassium concentration of the plasma.
- 5.2.6. Recall that the major androgen precursor produced is dehydroepiandrosterone and that a small amount of it is converted to testosterone and oestrogen.
- 5.2.7. Recall that in post menopausal women, testosterone produced by the adrenal could be converted to oestrogen by peripheral aromatization.
- 5.2.8. Recall that ACTH is a peptide hormone with a  $t_{1/2}$  of 3 minutes.
- 5.2.9. Outline the events in the adrenal cortex following the administration of ACTH that result in the secretion of corticosteroids, and in cellular proliferation.
- 5.2.10. Explain how circulating corticosteroids affect feedback control over secretion of ACTH
- 5.2.11. Describe the biological functions of ACTH and its action on adipocytes

### 5.3. *Adrenal Medulla*

- 5.3.1. Recall that the adrenal medulla is a specialized ganglion without axonal extensions that produce catecholamine hormones
- 5.3.2. Recall that epinephrine, norepinephrine and dopamine are released in response to severe stress and their action is aided by glucocorticoids, growth hormone, glucagon and angiotensin II
- 5.3.3. Recall that epinephrine is synthesized from tyrosine
- 5.3.4. Recall that tyrosine hydroxylase is the rate limiting step in the catecholamine biosynthesis and that it is competitively inhibited by alpha-methyl-tyrosine and is under feedback inhibition by catecholamines which compete with the enzyme for the pteridine co-factor necessary for the reaction.

- 5.3.5. Recall that catecholamines cannot cross the blood-brain barrier, but that L-dopa, the precursor of dopamine does cross this barrier.
- 5.3.6. Recall the use of L-dopa in the treatment of Parkinson's disease.
- 5.3.7. Recall that the neural stimulation of the adrenal medulla leads to the release of norepinephrine and is calcium dependant
- 5.3.8. Recall that neuronal re-uptake of catecholamines is important for conserving these hormones and for quickly terminating neurotransmitter activity.
- 5.3.9. Recall that catecholamines are loosely bound to albumin in plasma and have a very short half life and rapidly metabolized by the liver.
- 5.3.10. Recall that catecholamines are rapidly metabolized by catechol-'O'-methyl transferase (COMT) and mono amine oxidase (MAO) and that MAO inhibitors are used to a limited extent to treat depression and hypertension.
- 5.3.11. Recall that vanilyl mandelic acid (VMA) is a product of epinephrine and norepinephrine that is readily excreted in the urine and is used in clinical diagnosis.
- 5.3.12. Recall that the action of catecholamines may be classified according to the type of receptor they are bound to, namely  $\alpha_1$ ,  $\alpha_2$ ,  $\beta_1$ ,  $\beta_2$
- 5.3.13. Recall that catecholamine receptors are G protein-linked and that catecholamines act by increasing or decreasing the intracellular cAMP level. Explain the molecular mechanisms involved, using a schematic diagram.
- 5.3.14. Recall that a response to an increase in norepinephrine and epinephrine is an increase in the blood glucose resulting from glycogenolysis and gluconeogenesis and that this is primarily due to  $\beta$  adrenergic activity
- 5.3.15. Recognize the formulae of epinephrine and norepinephrine and state their sites of origin
- 5.3.16. List the factors that stimulate their secretion
- 5.3.17. Explain how epinephrine increases blood glucose and decreases blood glucose utilization by the muscle
- 5.3.18. Describe how epinephrine ensures an energy supply to muscle by increased lipolysis and glycogen break down in times of stress

## 6. *Pancreas*

### 6.1 General

- 6.1.1. Describe the islets of Langerhan
- 6.1.2. Enumerate the different types of cells in the islets and indicate their functions
- 6.1.3. Recall that the islets make up 1-2% of the weight of the pancreas and that in humans there are 1-2 million islets

### 6.2. Insulin

- 6.2.1. Describe the synthesis of pre-proinsulin, functions of the different segments in it, processing and secretion of insulin
- 6.2.2. Sketch the structure of insulin
- 6.2.3. Recall that there are minor differences in the amino acid composition of the insulin molecules from species to species

- 6.2.4. Recall that the differences in amino acid composition are generally not sufficient to affect the biological activity of particular insulin in heterologous species but are sufficient to make the insulin antigenic
- 6.2.5. Explain why porcine insulin has low antigenicity compared to bovine insulin
- 6.2.6. Recall that human insulin produced in bacteria by recombinant DNA technology is widely used to avoid antigenic effect of insulin
- 6.2.7. State why C-peptide level provides an index of B cell function in patients receiving exogenous insulin
- 6.2.8. List the compounds that stimulate insulin secretion and explain their mode of action
- 6.2.9. Know the effects of glucagon, ACTH, GH, adrenaline & neural
- 6.2.10. Describe the effect of gastro-intestinal hormones on insulin secretion
- 6.2.11. Explain the fate of insulin in the body.
- 6.2.12. Explain how insulin facilitates glucose entry into muscle and adipose tissue
- 6.2.13. Explain how insulin facilitates glucose entry into liver cells
- 6.2.14. List and explain the effects of insulin on adipose tissue, muscle and liver
- 6.2.15. Describe the effects of insulin on extracellular  $K^+$  concentration
- 6.2.16. Explain why failure to grow is a symptom of diabetes in children.
- 6.2.17. Recall that diabetes is due to relative deficiency of insulin and describe the aetiology and the metabolic dysfunctions resulting from such disorders
- 6.2.18. Explain the biochemical tests used to diagnose diabetes and the rationale for the use of such tests
- 6.2.19. Explain Glucose Tolerance Test (GTT) and its applications
- 6.2.20. Recall the changes in the blood and urine in untreated diabetes
- 6.2.21. State the signs and symptoms associated with diabetes mellitus
- 6.2.22. Relate wherever possible, the signs and symptoms of diabetes mellitus to biochemical alterations
- 6.2.23. Explain syndrome X

### 6.3 Glucagon

- 6.3.1. List the stimuli that provoke the secretion of pancreatic glucagon
- 6.3.2. Explain the effect of glucagon on the  $\beta$ -cells of the Islets of Langerhan
- 6.3.3. State how the effect of glucagon on pancreatic glycogen phosphorylase is brought about
- 6.3.4. Explain the effect of glucagon on liver and adipocyte lipase and on hepatic gluconeogenesis
- 6.3.5. Explain how glucagon brings about ketonaemia
- 6.3.6. State how the actions of glucagon differ from those of adrenaline
- 6.3.7. Describe the effect of starvation on blood glucagon concentration

### 6.4 Somatostatin

- 6.4.1. List the compounds that stimulate somatostatin secretion
- 6.4.2. State the functions of somatostatin

## 7. *Gonads*

See objectives under 'The Reproductive System' (sex hormones)

**8. *Kidney***

- 8.1. State the two polypeptide hormones synthesized in the kidney and their functions
- 8.2. Explain how hypoxia promotes erythropoiesis
- 8.3. Recall that erythropoietin interacts with the red cell progenitor causing it to proliferate and differentiate
- 8.4. Recall that recombinant erythropoietin is available for treatment in renal failure
- 8.5. Describe the importance of hydroxylation of 25- hydroxyl cholecalciferol in plasma calcium homeostasis
- 8.6. Explain the role of renin in the synthesis of angiotensin I
- 8.7. State the factors that stimulate/inhibit the release of renin (Physiology)

**9. *Vascular Endothelium and Platelets***

See objectives under 'The Reproductive System' (Eicosanoids)

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*Saliyapura, 2006-2011*