Chapter-2 | Pharmacotherapeutics | (C) Endocrine System

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- Diabetes
- Thyroid disorders- Hypo and Hyperthyroidism

Endocrine System.

Introduction- Endocrine system is defined as the complex glandular structure (cell modification or aggregation) which secrete the hormones and neurotransmitter in the body and regulate the body physiology and major participate in the defensive mechanism of the body.

Hormones are non-nutrient chemicals which act as intercellular messengers and are produced in trace amounts. Most hormones enter interstitial fluid and then the bloodstream. In endocrine system we have discussed about two types of glands.

1. **Exocrine glands**—Exocrine glands secrete their products (enzymes) into ducts, that carry the secretions into body cavities, into the lumen of an organ, or to the outer surface of the body. Exocrine glands include sudoriferous (sweat), sebaceous (oil), mucous, and digestive glands
2. **Endocrine gland**—Endocrine glands secrete their products (Hormone) into the interstitial fluid surrounding the secretory cells rather than into ducts. From the interstitial fluid, hormones diffuse into blood capillaries and blood carries them to target cells throughout the body. It is depending upon the heart for distribution of products.

Clinical consideration— when the hormonal secretion impaired due to any reason include external as well as internal reason leads to disease like-

- Diabetes mellitus.
- Hashimoto thyroiditis.
- Grave's disease
- Polycystic ovarian.
- Hypothyroidism.
- Hyperthyroidism

Diabetes.

Definition—Diabetes mellitus is the group of metabolic disorders sharing the common feature of hyperglycaemia. Hyperglycaemia in diabetes results from defects in insulin secretion, insulin action or both. The chronic hyperglycaemia and attendant metabolic dysregulation may be associated with secondary damage in multiple organ systems, especially the kidney, eyes, nerves, and blood vessels.

Diabetes is associated with endocrine pancreas.

Pancreas consists of clusters of cells which contains the four major type of cell types

1. **β cell— The β cells** produce insulin, which regulates glucose utilization in tissues and reduces blood glucose levels, as will be detailed in the discussion of diabetes
2. **α cell— α cells** secrete glucagon, which stimulates glycogenolysis in the liver and thus increases blood sugar.
3. **δ cell— δ cells** secrete somatostatin, which suppresses both insulin and glucagon release.
4. **PP (pancreatic polypeptide) cells— PP cells** secrete pancreatic polypeptide, which exerts several gastrointestinal effects, such as stimulation of secretion of gastric and intestinal enzymes and inhibition of intestinal motility.

The World Health Organization estimates that as many as 346 million people suffer from diabetes worldwide, with India and China being the largest contributors to the world's diabetic load.

- Blood glucose is normally maintained in a very narrow range of 70 to 120 mg/dL. According to the ADA and WHO, diagnostic criteria for diabetes include:
    1. **A fasting plasma glucose ≥ 126 mg/dL.**
    2. **A random plasma glucose ≥ 200 mg/dL.**
    3. **2-hour plasma glucose ≥ 200 mg/dL during an oral glucose tolerance test (OGTT) with a loading dose of 75 gm.**
    4. **A glycated haemoglobin (HbA1C) level ≥ 6.5%.**

Classification of diabetes mellitus— Although all forms of diabetes mellitus share hyperglycaemia as a common feature, the underlying abnormalities involved in the development of hyperglycaemia vary widely-

- **Type 1 diabetes** is an autoimmune disease characterized by pancreatic β cell destruction and an absolute deficiency of insulin. It accounts for approximately 5% to 10% of all cases.
- **Type 2 diabetes** is caused by a combination of peripheral resistance to insulin action and an inadequate secretory response by the pancreatic β cells ("relative insulin deficiency"). Approximately 90% to 95% of diabetic patients have type 2 diabetes.

Etiopathogenesis—

Type 1 diabetes mellitus— Also called 'Insulin dependent diabetes mellitus' (IDDM). It is an autoimmune disease in which islet destruction is caused primarily by immune effector cells reacting against endogenous β-cell antigens. type 1 diabetes require insulin for survival; without insulin they develop serious metabolic complications such as ketoacidosis and coma. It usually occurs in children.

Type 2 diabetes mellitus— Also called 'Insulin Independent diabetes mellitus' (IIDDM). Type 2 diabetes is a complex disease that involves an interplay of genetic and environmental factors and a proinflammatory state. Unlike type 1 diabetes, there is no evidence of an autoimmune basis. It usually occurs in middle age.

Clinical manifestations—

- Excessive hunger and thirst.
- Frequent urination.
- Progressively weight loss.
- Sudden vision changes.
- Tingling or numbness in the hands or feet.
- Very dry skin and sometime skin disorder also.
- Obstruction in blood vessel (blood supply hampered).
- Cardiac diseases also induced
- Slow healing wounds.

Pharmacological managements—

1. **Insulin.**
    - Long acting— Ex- Insulin degludec, Insulin glargine.
    - Intermediate acting— Ex- Insulin Zinc suspension.

- Short acting— Ex- Biphasic Insulin.
- Rapid acting— Ex- insulin aspart, Insulin lispro.
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2. Oral drugs.

A. Enhance insulin secretion.

- Dipeptidyl peptidase-4 inhibitors.
  Ex- Alogliptin, Linagliptin, Saxagliptin, Sitagliptin, Teneligliptin, Vidagliptin.
- Glucagon like peptide-1 agonists.
  Ex-Albiglutide, Dulaglitide, Exenatide, Liraglutide, Lixisenatide, Semaglutide.
- K-ATP channel blockers.

B. Overcome Insulin Resistance.

- Biguanides- Ex- Buformin, Metformin, Phenformin.
- Dual peroxisome Proliferator-activator receptor agonists- Ex-

C. Miscellaneous drugs.

- Aldose reductase inhibitors- Ex- Epalrestat.
- Alpha Glucosidase Inhibitors- Ex- Acabose, Miglitol, Voglibose.
- Amylin Analogue- Ex- Pramlintide.
- Dopamine D_2 Agonist- Ex- Bromocriptine.

Non-pharmacological management—

- Increasingly sedentary life styles and poor eating habits have contributed to the simultaneous escalation of diabetes and obesity, which some have called the diabesity epidemic.
- Avoid the any type of injury.
- Make the diet plan because, in diabetes condition sugar level maintenance is the major task.
- More hunger and thrust is the common condition in the diabetes so, availability of things is very important.
- Exercise and yoga are regular require because it help in the metabolism (BMR) process of the body and maintain the glucose level.
- Try to avoid the stress and depression and visit those places where we feel happy and pleasant.
- We also take ayurvedic/natural remedies and avoid the allopathic medications.

Thyroid Disorders.

- The thyroid gland, usually located below and anterior to the larynx, consists of two bulky lateral lobes connected by a relatively thin isthmus.
- The thyroid is divided by thin fibrous septae into lobules composed of about 20 to 40 evenly dispersed follicles, lined by a cuboidal to low columnar epithelium.

A.Hypothyroidism.

Definition— Diseases of the thyroid include conditions associated with thyroid hormone deficiency is considered as hypothyroidism. It is a condition caused by a structural and functional derangement that interferes with the production of thyroid hormone. Hypothyroidism is a fairly common disorder in female than in male. Some times on the factors involving it is divided in two-

1. **Primary hypothyroidism—** it is arising due to intrinsic abnormality in the thyroid itself, or occurs as a result of pituitary and hypothalamic disease.
    - Primary hypothyroidism accounts for the vast majority of cases, and may be accompanied by an enlargement in the size of the thyroid gland (goitre). It can be congenital (due to iodine deficiency in the diet), autoimmune or iatrogenic.
2. **Secondary hypothyroidism—** It is arising from processes outside of the thyroid gland.

Etiopathogenesis—

- **Congenital hypothyroidism—** Congenital hypothyroidism is most often the result of endemic iodine deficiency in the diet. Other rare form of congenital include inborn errors of thyroid metabolism.
  In rare instances there may be complete absence of thyroid parenchyma or gland may be greatly reduced in size due to germline mutations in genes responsible for thyroid development.

- **Autoimmune hypothyroidism—** Autoimmune hypothyroidism is the most common cause of hypothyroidism in iodine-sufficient areas of the world. The vast majority of cases of autoimmune hypothyroidism are due to Hashimoto thyroiditis. Circulating autoantibodies, including anti microsomal, antithyroid peroxidase, and antithyroglobulin antibodies, are found in this disorder, and the thyroid is typically enlarged.
- **Iatrogenic hypothyroidism—** This can be caused by either surgical or radiation-induced abnormality. A large resection of the gland (total thyroidectomy) for the treatment of hyperthyroidism or a primary neoplasm can lead to hypothyroidism. Drug also decreased the thyroid secretion ex- methimazole, propylthiouracil etc.

Clinical manifestations—

Pharmacological managements— 1. Levothyroxine 2. Triiodothyronine.

Non-pharmacological management—

- Make the diet plan according to indication of physician, because iodine level maintenance in the major task during thyroid disorders.
- Avoid consumption of goitrogenic foods such as broccoli and cauliflower.
- Increase intake of yellow vegetables, egg, carrots.
- Coconut water and green tea helps to control the hypothyroidism and aids in weight loss.
- Avoid the allergic causing substances.
- Try to avoid the stress and depression and visit those places where we feel happy and pleasant.
- Follow the exercise and yoga regularly.

B. Hyperthyroidism.

Definition— Diseases of the thyroid include conditions associated with excessive release of thyroid hormones is called as hyperthyroidism. Some times on the factors involving it is divided in two-

1. **Primary hyperthyroidism—** It is arising from an intrinsic thyroid abnormality, such as Grave's disease an autoimmune disease.
2. **Secondary hyperthyroidism—**It is arising from processes outside of the thyroid, such as a TSH-secreting pituitary tumour.

Etiopathogenesis—Thyrotoxicosis is a hypermetabolic state caused by elevated circulating levels of free T3 and T4. Because it is caused most commonly by hyperfunction of the thyroid gland, it is often referred to as hyperthyroidism. Three most common cause for the hyperfunctioning for the gland include as-

- Diffuse hyperplasia of the thyroid associated with Graves' disease (approximately 85% of cases).
- Hyper functional multinodular goitre.
- Hyper functional thyroid adenoma

Hyperthyroidism also cause by the—

- Genetic defects in thyroid development.
- Thyroid hormone resistance syndrome.
- Congenital biosynthetic defect.
- Hashimoto thyroiditis.
- Iodine deficiency.
- Hypothalamic/pituitary failure (Rare).

Clinical manifestations—

- Tachycardia
- Tremors.
- Heat intolerance.
- Infertility.
- Polyphagia
- Palpitations

- Fatigue and muscle pain.
- Hair loss.
- Swelling at base of neck.

Pharmacological managements—

- Thioamides— Methimazole, Propylthiouracil.
- Iodide salts— Lugol's solution.
- Iodinated contrast media— Ipodate.
- Beta blocker— Propranolol, Esmolol.
- Anion inhibitor— Thiocyanate, perchlorate.

Non-pharmacological management—

- Make the diet plan according to indication of physician, because iodine level maintenance (low iodine) in the major task during thyroid disorders.
- Take diet rich in calcium, vitamin D, magnesium, selenium.
- Avoid intake of sugar, caffeine, alcohol etc. products.
- Avoid the allergic causing substances.
- Try to avoid the stress and depression and visit those places where we feel happy and pleasant.
- Follow the exercise and yoga regularly.