

# LECTURE NO-2

## HISTORICAL BACKGROUND OF ENDOCRINOLOGY

- How did scientists first find out what endocrine glands do?
  - Scientists first removed the gland and monitored the organism for changes (like in hormone deficiency).
  - Then scientists replaced the gland or gave an extract of the gland to see if the abnormalities disappeared (like in replacement therapy).
  - Then scientists implanted the gland or gave extract to a normal individual to see the symptoms (like in hormone excess).
  - Once a gland was identified as a source of hormones, extracts from the gland were purified and a test was designed to calibrate the activity of the hormone in another organism (known as a *bioassay*).
- The writings of Hippocrates and Aristotle as early as BC 460 to 322 contain some information that there might be internal control over body functions
- First recorded endocrine experiment was published by Berthold (1849). He discovered castrated cockerels failed to develop their combs and wattles and also failed to exhibit male behaviour. Replacement of one or both testes back into abdominal cavity restored the lost function.
- In 1889, von Mering and Minkowski demonstrated that surgical removal of pancreas from dog produced a disease later to be known as diabetes mellitus. This led to the recognition of insulin in the control of diabetes mellitus in man and dogs.
- **In 1902**, Canadian physiologists *Bayliss and Starling* discovered that a substance liberated by small intestinal mucosa stimulates the pancreatic juice flow. The active substance was named as *secretin*. They coined the word

“hormone” (from the Greek "*I arouse to activity*" or "*I excite*") to this newly discovered substance.

- **Banting and Best** (1921) isolated the potent pancreatic extract containing insulin
- In 1949, Hench and co workers isolated a hormone from adrenal cortex- cortisone or compound E that relieved some of the symptoms of rheumatoid arthritis.
- In 1953, Simpson and Tait found that unidentified steroid present in adrenal gland was aldosterone. In the same year, **Sanger** established the amino acid sequence for insulin for which he bagged the **Nobel Prize**.
- In 1953, Du Vigneaud and his co-workers determined the structure of oxytocin and vasopressin.
- In 1955, Harris provided the data suggesting that the release of pituitary hormones was controlled by humoral factors of hypothalamic origin.
- In 1962, Earl Sutherland described the presence of cyclic AMP in biological materials.
- In 1978, insulin was synthesized by a strain of genetically engineered *E.coli*.
- For the development of RIA for hormone analysis, **Rosalyn Yalow** received the Nobel prize in 1978.

## DEFINITION

- The term hormone means "to excite" or "arouse".
- Hormones are chemicals secreted at variable rates in response to external or internal stimuli by an endocrine gland or a group of cells in very low concentrations (nanomolar to picomolar –  $10^{-9}$  to  $10^{-12}$  M) directly into the blood for transport to some distant target organs/cells where they alter already existing reactions but cannot initiate new reactions.

## CLASSIFICATION BASED ON CHEMICAL NATURE

- Hormones are chemically classified into the following categories
  1. **Amines** - are derivatives of the amino acids **tyrosine and tryptophan (e.g) epinephrine, norepinephrine.**
  2. **Iodinated aminoacids** – (e.g) **Thyroxine**
  3. **Peptides** - consist of **chains of amino acids**. Examples of small peptide hormones are **TRH and vasopressin**
  4. **Proteins:** Peptides composed of numerous amino acids are referred to as proteins. Examples of protein hormones include **insulin and growth hormone.**
  5. **Glycoprotein:** More complex protein hormones bear carbohydrate side chains and are called **glycoprotein hormones(e.g) LH, FSH and TSH.**
  6. **Steroids** - derived from **cholesterol and contains basic cyclopentano perhydro phenanthrene nucleus.** (e.g) **Estrogen, progesterone, cortisol.** Being non-polar, they are able to pass through the phospho-lipid membrane of a cell and enter the cytoplasm .
  7. **Fatty acids derivatives - Eicosanoids** - they are a large group of molecules derived from **Arachadonic acid. The principal groups of hormones of this class are prostaglandins, prostacyclins, leukotrienes and thromboxanes.** These hormones are rapidly inactivated by being metabolized, and are typically active for only a few seconds.

## CHEMICAL CLASSIFICATION OF HORMONES

- Chemical structure determines ,solubility and transport characteristics ,degradation rate (plasma half-life),storage and route of exogenous administration

Sn.		<b>Peptides</b>	<b>Amines</b>	<b>Steroids</b>
-----	--	-----------------	---------------	-----------------

1.	Solubility	<b>hydrophilic</b>	<b>hydrophilic</b>	lipophilic
2.	Synthesis	<b>rough ER, packaged in Golgi complex</b>	cytosol	stepwise modification of cholesterol molecule in various intracellular compartments (in the endocrine gland , blood and target tissues)
3.	Storage	secretory granules	secretory (chromaffin) granules	hormones not stored, only precursor (cholesterol) stored.
4.	Secretion	exocytosis	exocytosis	diffusion
5.	Transport	<b>mostly as a free hormone</b>	as a <b>free hormone and bound to plasma proteins</b>	mostly bound to plasma proteins
6.	Receptor site	<b>surface of target cell</b>	surface of target cell	inside of target cell
7.	Action:	<b>channel changes or sms</b>	second messenger system (sms)	direct effects on genes for production of new proteins

### PHYSIOLOGICAL CLASSIFICATION OF HORMONES

1. Hormones Regulating **Energy Metabolism** :Insulin, Glucagon, Glucocorticoids, Epinephrine, ACTH, Thyroid
2. **Mineral Metabolism**:Aldosterone, Renin-Angiotensin II & Natriuretic hormone, PTH, CT , Vitamin D3
3. **Growth**:GH, Insulin, Estrogen, Androgen, Somatostatin, Thyroxine and Cortisol

4. **Reproduction:** GnRH, FSH, LH /ICSH, Estrogen, Inhibin Progesterone, Testosterone, Oxytocin, Prostaglandins and Relaxin, GnIH, Thyroxin, Cortisol, Prolactin and Gonadocrnin
5. **Milk Secretion:** Prolactin, TSH, ACTH, GH, Glucocorticoid, Placental Lactogen, Thyroxin, Insulin and Oxytocin
6. **Blood Pressure:**Renin-Angiotensin, Epinephrine, Norepinephrine, Vasopressin, ACTH , Vasotocin, ADH and ANP
7. **Water Balance:** Vasopressin (ADH), Renin-Angiotensin, Glucocorticoids & Insulin
8. **Local Hormones:**PGs, Histamine, Serotonin
9. **Gut Hormones:**Gastrin, Secretin, CCK, Gastric inhibitory peptide (GIP), Vasoactive intestinal Polypeptide