

INTRODUCTION TO HORMONES

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What are hormones?

- Cells in multi-cellular organisms communicate with one another to coordinate their growth and metabolism;
- Cell to cell communicate is mainly via Extracellular signaling molecules or Hormones;
- Hormones carry information from **Sensor Cells**, that sense changes in the environment, to **Target Cells** that respond to the changes;
- Hormones tend to coordinate various metabolic processes in the body;

How are hormones classified?

Hormones are classified by various criteria:

- By Proximity of their site of synthesis to their site of action,
- By their chemical structure,
- By their degree of solubility in aqueous medium

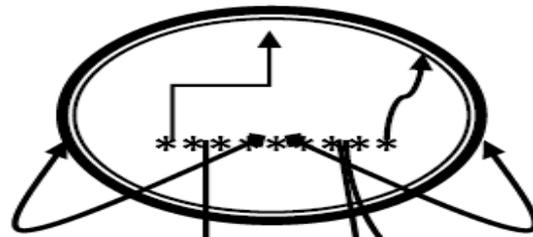
How are hormones classified by proximity of site of synthesis to site of action?

- **3 classes of hormones** based on proximity of site of Synthesis to Site of Action: (**Fig. 1**)
 - **Autocrine Hormones:** those that act on the same cells that synthesize them;
 - **Paracrine Hormones:** those that are synthesized very close to their site of action;
 - **Endocrine Hormones:** those that are synthesized by endocrine glands and transported in the blood to target cells that contain the appropriate receptors;

Fig. 1:

Diagrams for classification of hormones by sites of synthesis to site of action

Autocrine



Target cell

Paracrine



Target cell

Endocrine



Blood vessel

Target cell with receptors

How are hormones classified according to Chemical Structure?

4 classes of hormones based on chemical structure:

- **Peptides or Protein hormones:**

- They are synthesized as peptides or large polypeptides precursors that undergo processing before secretion;

Examples:

- Thyrotropin Releasing Hormone (TRH), made up of three amino acid residues;
- Insulin, made up of 51 amino acid residues;
- Pituitary Gonadotrophins, made up of large Glycoproteins with subunits;

- **Amino acid derivatives:** Examples:
 - Adrenaline, Catecholamines, Thyroid Hormones;
- **Fatty acid derivatives:** Examples:
 - Eicosanoids (Prostaglandins);
- **Steroid hormones:**
 - These are derivatives of Cholesterol; Example:
 - Estradiol, Testosterone, Cortisol, Aldosterone;

How are hormones classified according to solubility in aqueous medium in cells?

- **Two classes** of hormones based on solubility in aqueous medium;
- **Hydrophilic Hormones** (Lipophobic Hormones);
- **Lipophilic Hormones** (Hydrophobic Hormones);
- Location of receptors for each class of hormone is different;

- **Hydrophilic Hormones (Lipophobic Hormones):**
 - Hormones that are soluble in aqueous medium;
 - They cannot cross the cell membrane,
 - Thus, they bind to **receptor molecules on the outer surface** of target cells, initiating reactions within the cell that ultimately modifies the functions of the cells;
 - Examples: Insulin, Glucagon, Epinephrine,

- **Lipophilic Hormones (Hydrophobic Hormones):**
 - Hormones that are not soluble in aqueous medium, but soluble in lipid;
 - They can easily cross the cell membrane,
 - Thus, they can enter target cells and bind to **intracellular receptors** to carry out their action;
 - Examples: Thyroid hormones, Steroid hormones;

Acronyms of some hormones

Hormones	Acronym
AdrenoCorticoTrophic Hormone (Corticotrophin)	ACTH
Arginine Vasopressin (Anti-Diuretic Hormone)	AVP (ADH)
Corticotrophin Releasing Hormone	CRH
Follicular Stimulating Hormone	FSH
Gonadotrophin Releasing Hormone	GnRH
Growth Hormone	GH (HGH)
Growth Hormone Releasing Hormone	GHRH
Luteinizing Hormone	LH
Parathyroid Hormone	PTH
Thyroid Stimulating Hormone	TSH
Thyrotrophin Releasing Hormone	TRH
Tri-iodothyronine	T ₃
Thyroxine	T ₄

How do hormones exit in blood plasma?

- Hormones are normally present in blood plasma at very low concentrations;
- In blood, hormone binds to **Specific Plasma Carrier Protein**, forming a complex, which is then transported in the plasma to distant target cells;
- Plasma carrier proteins exist for all classes of endocrine hormones;

What are the functions of carrier proteins for hormones?

Carrier proteins for:

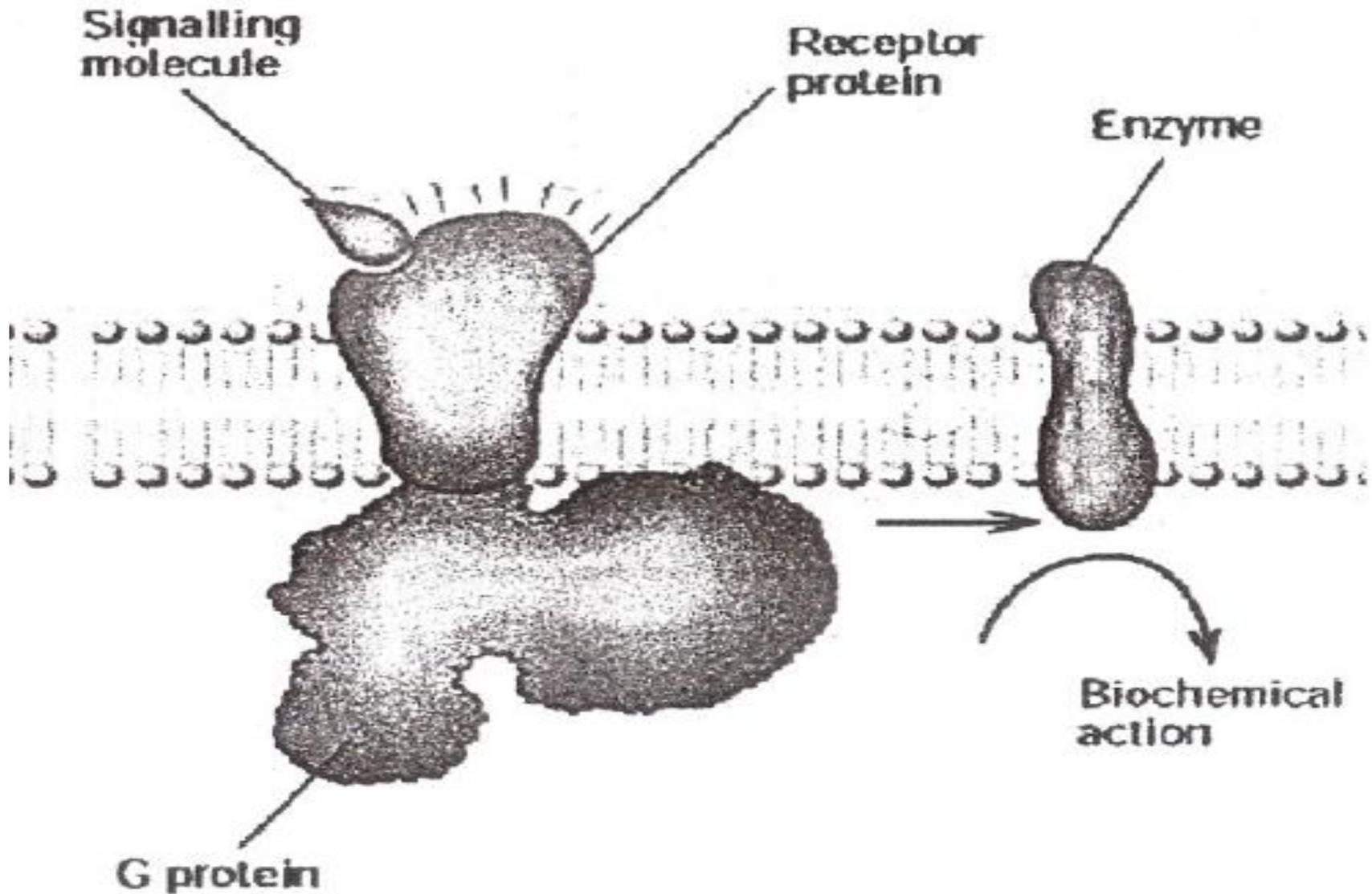
- **Peptide Hormones** prevent destruction of peptide hormones by Protease enzymes in plasma;
- **Steroid Hormones and Thyroid Hormones** significantly increase the solubility of these very hydrophobic compounds in plasma;
- **Small, Hydrophilic Amino Acids – derived hormones** prevent their filtration by the kidneys, thus greatly prolonging their circulating half-life;

Outline the mechanism of action of Hydrophilic hormones with receptors in target cells

- Mechanism of action of Hydrophilic hormones with receptors in target cells is called “Second Messenger”;
- Receptors for Hydrophilic Hormones are located on the Plasma membrane of target cells;
- Hormone (**First messenger**) interacts with the receptor on the cell membrane, forming the **Hormone-Receptor Complex**;

- Hormone-receptor complex causes conformational change in membrane proteins;
- Results in production within the cell of a “**Second Messenger**”, such as, **Cyclic-AMP**, or **Cyclic-GMP**;
- Increase in the cell of the Second Messenger leads to a rapid alteration in cellular function;
 - Example: Action of Glucagon on Glycogen metabolism is via the Second Messenger, which is cyclic-AMP;

Second Messenger System



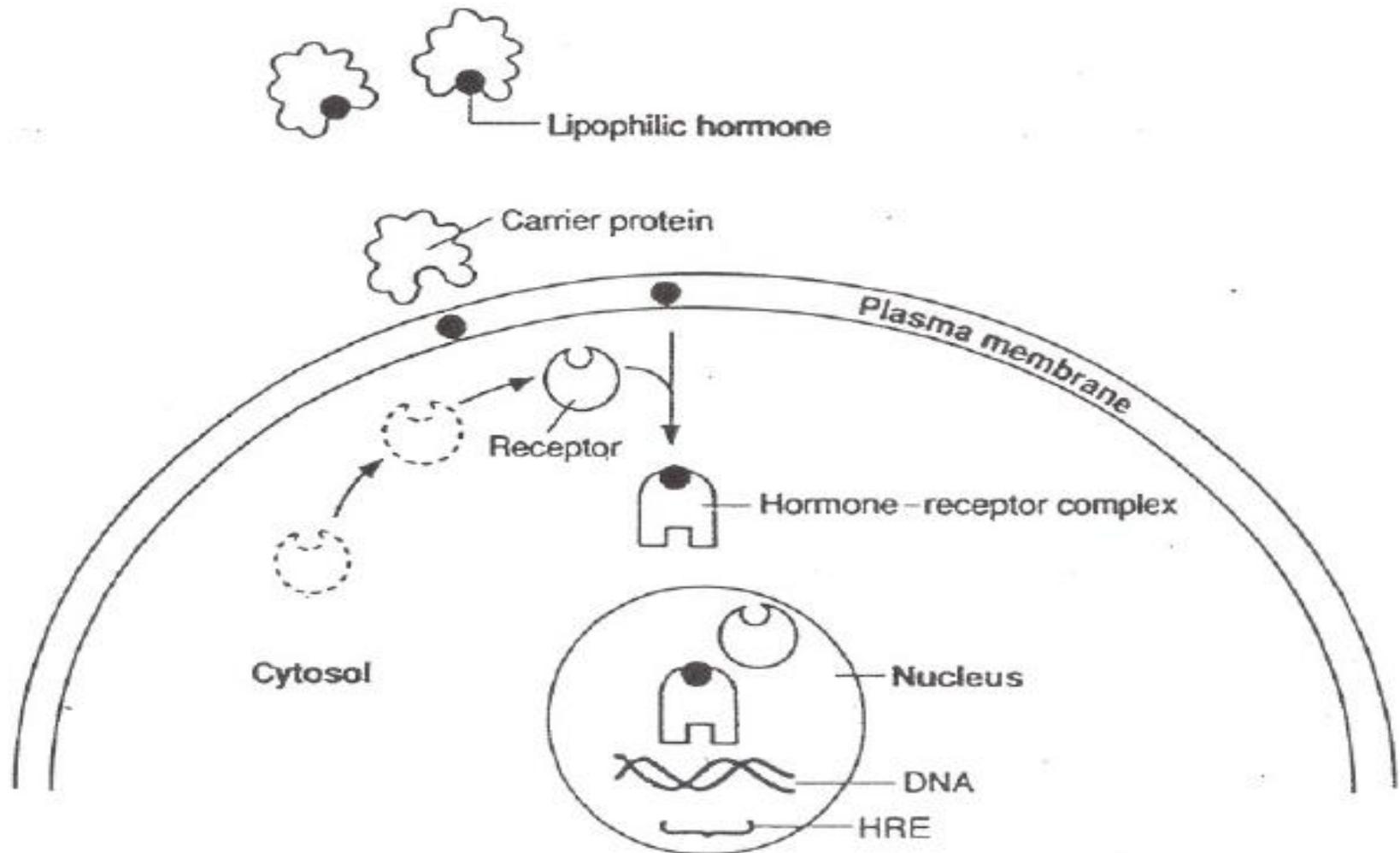
List some properties of Hydrophilic hormones receptors

- They are large, integral or transmembrane proteins with specificity and high affinity for a given hormone;
- Binding between hormone and receptor is reversible;
- Action of hormone depends on plasma level of hormone;
- Hydrophilic hormones initiate a response without entering target cells;
- Hydrophilic hormones causes a more rapid response and have a shorter duration of action than lipophilic hormones;
- Action of hydrophilic hormone can last seconds to hours;
- G – proteins are associated with hormone receptors on the cytosolic side of the cell membrane;
- G – protein is a protein that binds either GTP or GDP;

Outline the mechanism of action of Lipophilic hormones with receptors in target cells

- Lipophilic hormone crosses cell membranes to bind with Intracellular Receptor, forming **Hormone-Receptor Complex**;
- Hormone-Receptor Complex then bind to Specific Sequence of Nucleotide Bases in DNA called **Hormone Response Element (HRE)**;
- Binding of Hormone-Receptor Complex to HRE results in synthesis of **Messenger-RNA** required for biosynthesis of specific protein;
- Lipophilic hormones are slower to act and have longer duration of action than Hydrophilic hormones;
- Duration of action may range from hours to days;

Action of Lipophilic (Hydrophobic) Hormones



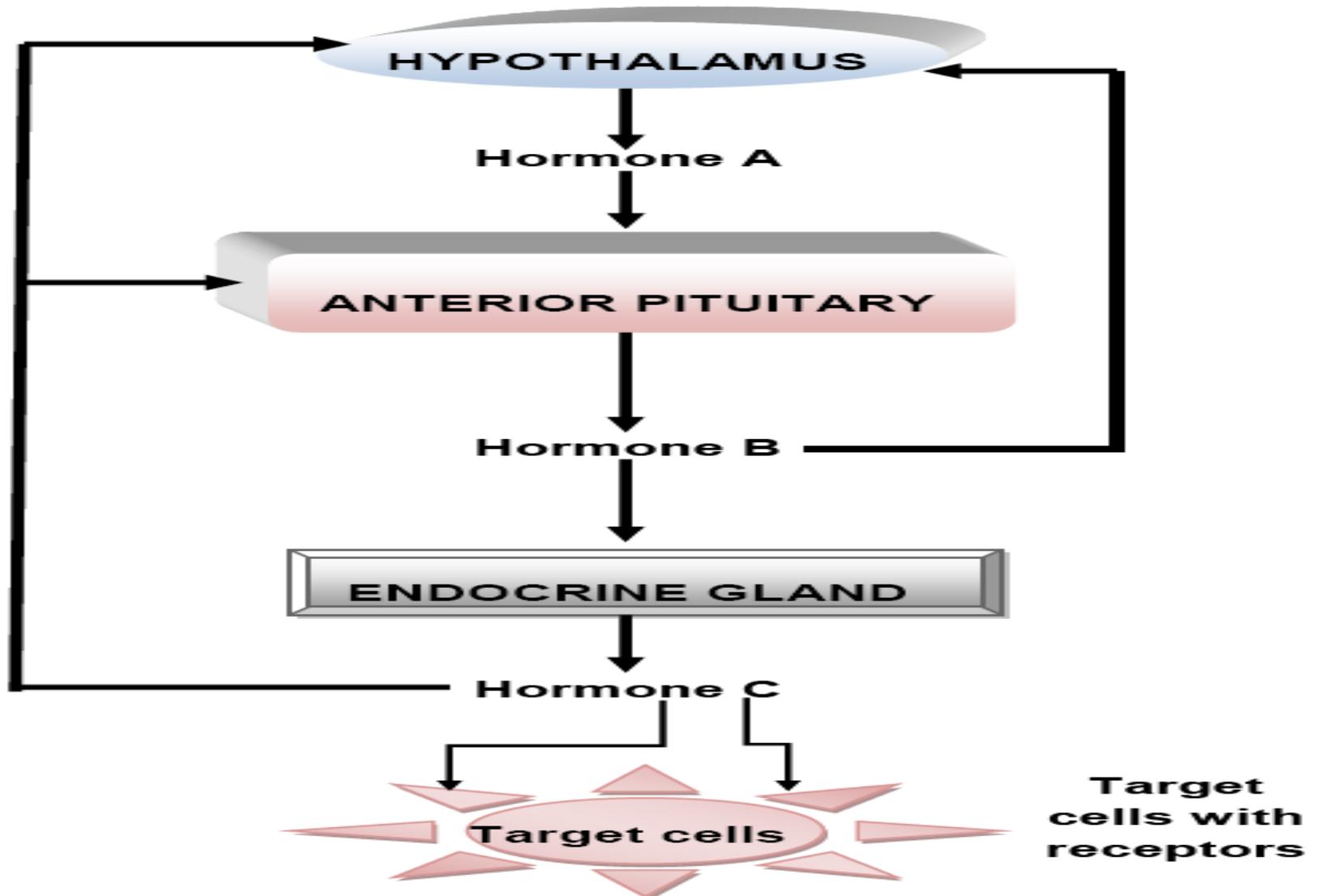
What is Negative-Feedback Mechanism for Regulation of Hormone secretion?

- Regulation of secretion of some hormones from endocrine glands is controlled via “**Negative-Feedback**” Mechanism, (Long-Loop, Short-Loop negative Feedback):
- Hormone released from one gland regulates the release of another hormone from a second gland, which then controls hormone production from the endocrine gland;
- Plasma level of the hormone itself or of a substance produced by the target tissue in response to the hormone may inhibit further release of the hormone;
 - Example: Negative-Feedback control of Thyroid hormones;

**Feedback hormonal control
(Hypothalamic-Pituitary-Endocrine gland)**

**Long Loop
feedback**

**Short loop
feedback**



What are some of the factors controlling hormone secretion?

- Hormone secretion is influenced by variety of factors:
 - Stimulatory and Inhibitory agents, such as: Hypothalamic Peptides or Neurotransmitters;
 - Other hormones: Gonadotrophin Releasing Hormone (GnRH), are released in a pulsatile fashion;
 - Some hormones exhibit Circadian Rhythm:
 - Adreno-Cortico-Trophic Hormone (ACTH),
 - Cortisol;
 - Prolactin, TSH, GH and PTH have peak secretion at different times during the day or night;

- Stress can increase hormone synthesis and release (e.g., ACTH, GH and Prolactin);
- Hormones synthesized by target cells may regulate release by Negative Feed Back control;
- Changes in metabolic products caused by hormone action may exert feedback control;
- Other hormones or drugs may modulate normal endocrine responses;