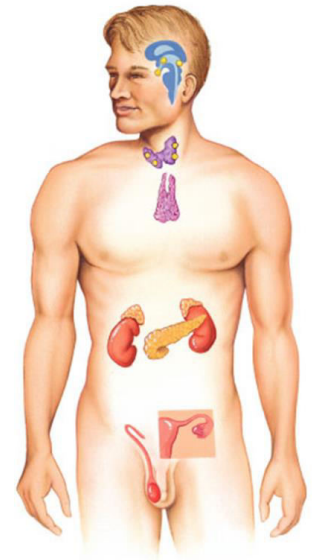


# General Endocrinology

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# Learning outcomes

- Introduction to endocrine system
- Features of hormones
- Organs of the endocrine system
- Types of hormones and their modes of action
- Synthesis and feedback mechanisms of hormone secretion
- Hypo and hypersecretion of hormones

# Introduction

- Homeostasis (constancy) of the internal environment is maintained by two systems.
- They are the **endocrine system** and the **autonomic nervous system**.
- The **autonomic** nervous system brings about very **rapid changes**, while the **endocrine system** brings about **slow and more precise** changes

# Introduction

- The endocrine system influences the metabolic activities of the body by secretions known as **hormones** . (The word 'hormone' is known to have the meaning 'to excite' in Greek).

- Ernest Starling in 1905 first described the term "Hormone".

- Hormones are secreted by several glands of the body.

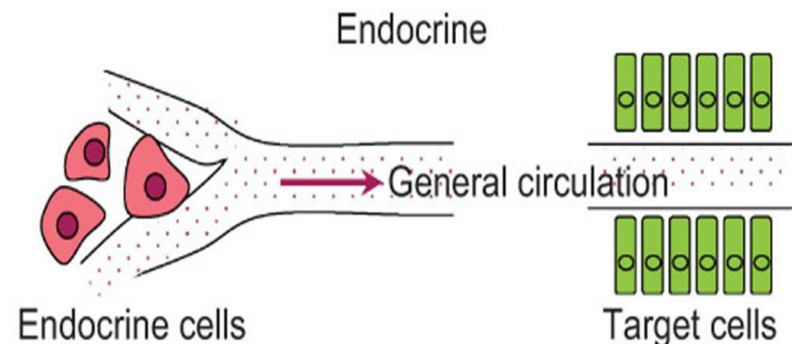


# Introduction

- Compared with other organs of the body, the **endocrine organs are small**.
- Endocrine organs are widely scattered throughout the body.
- Endocrine glands are also called **ductless glands** as they produce hormones and release it to the blood stream without ducts.
- They release their **hormones** into the surrounding tissue fluid or the blood
- The endocrine organ generally has a **rich vascular and lymphatic drainage**.

# Hormones

- Hormones can be defined as **chemical signals** secreted into the blood stream that act on **distinct tissues**, usually in a regulatory fashion.
- Organ influenced by the a particular hormone is called a **target organ**.
- When the **target organ is an endocrine gland** the hormone is called **trophic hormone**. eg anterior pituitary hormones.



# Hormones

- Target cells contain specific hormone binding sites within its cellular organelles.
- When a hormone binds to a hormone binding site in a cell, it stimulates specific responses .
- Initiated responses can go on for a few seconds to even days. Therefore the responses activated by the endocrine system are much **slower** in action.
- The actions of hormones continue to go on for a **prolonged period** than those activated by the nervous system

### Comparison of nervous and hormonal control systems

Feature	Nervous	Hormonal (endocrine)
Made up of	Neurones	Secretory cells
Form of transmission	Electrical impulses	Chemical (hormones)
Transmission pathway	Nerves fibres (axons and dendrons)	Blood plasma
Speed of transmission	Fast	Slow
Duration of effect	Short term	Long term
Response	Localised	Widespread (although there may be a specific target organ)



# Cell to cell communication

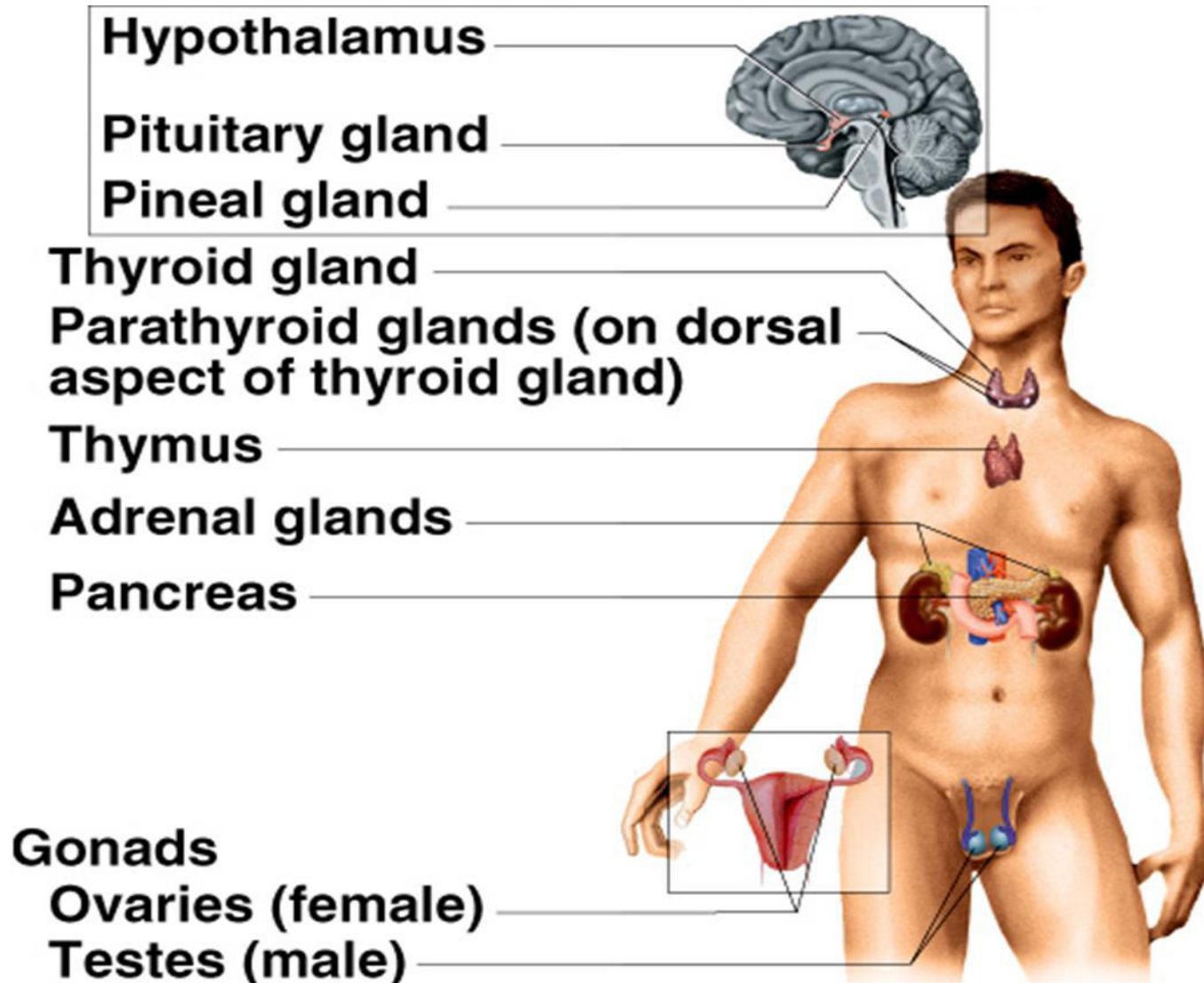
- **Chemical communications**

- Endocrine
- Autocrine
- Paracrine
- Neurocrine

- **Neural communications**

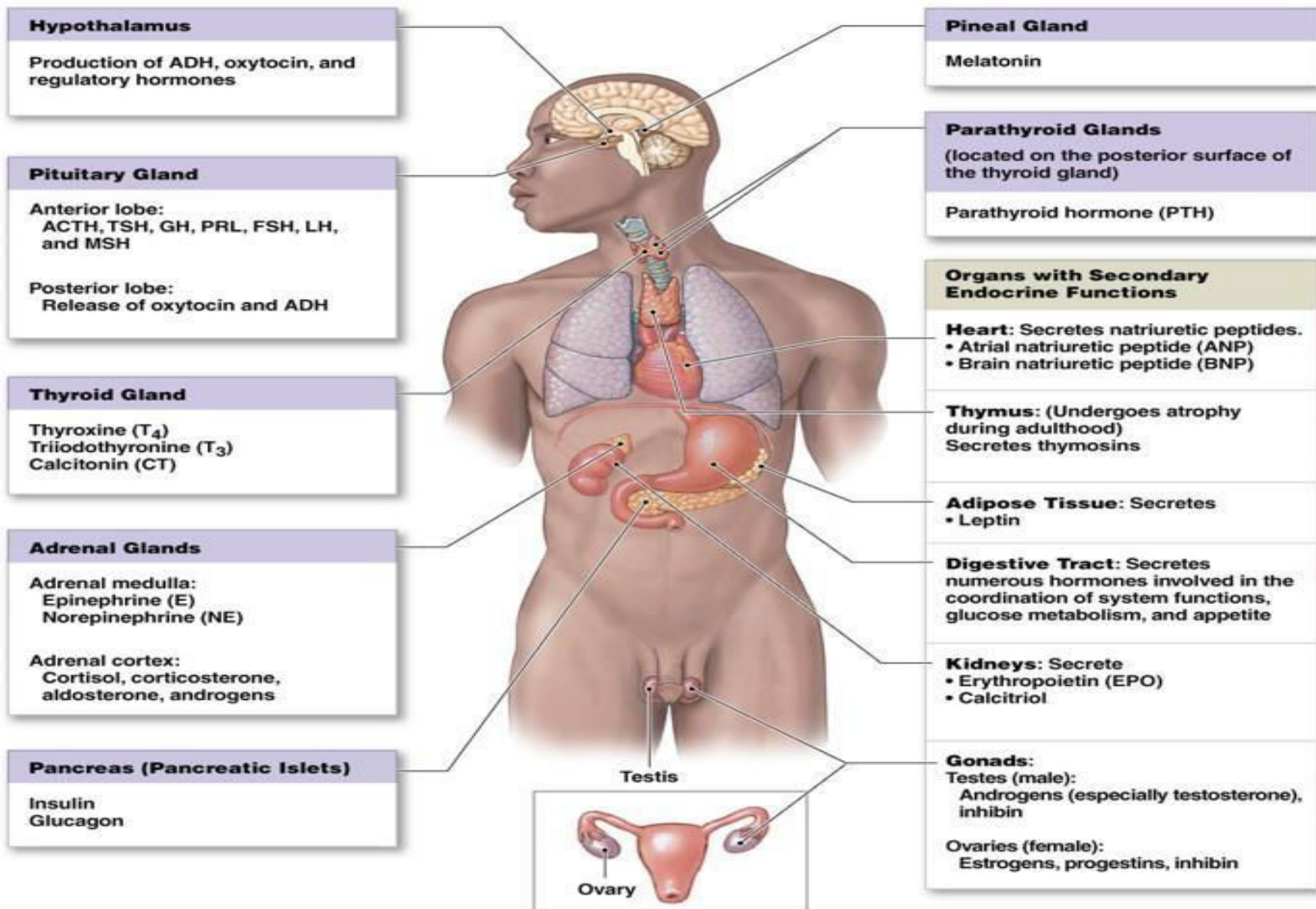
- Transmitted along the nerve fibres
- Electrical signals
- Call as nerve impulses or action potentials

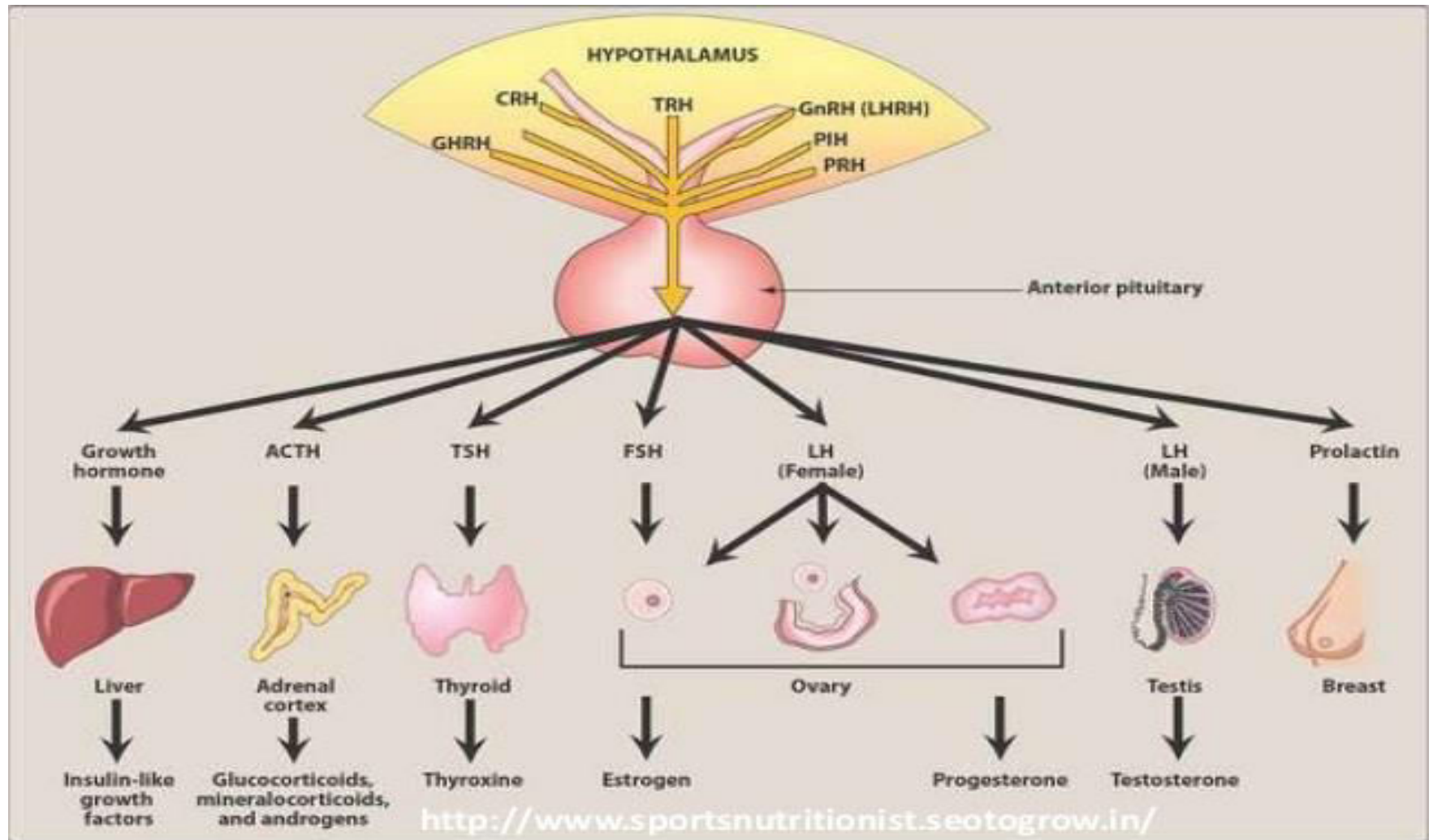
# Organs of the Endocrine system



# Endocrine Glands

- Purely endocrine organs
  - Pituitary gland
  - Pineal gland
  - Thyroid gland
  - Parathyroid glands
  - Adrenal: 2 glands
    - Cortex
    - Medulla
- Endocrine cells in other organs
  - Pancreas
  - Thymus
  - Gonads
  - Hypothalamus





# Self Assessment Questions

- Can you explain the importance of the endocrine system?
- Can you list the organs of the endocrine system?
- Can you list the hormones secreted by each endocrine gland?

# Hormones

- **3 types of hormones**

## **1. Peptides**

Large or small peptides

Secreted by pituitary gland, parathyroid glands, pancreas and placenta ('P' s)

Eg- Growth Hormone, Insulin, TSH, LH, FSH, Prolactin

## **2. Steroids**

Formed from cholesterol or its derivatives

Secreted by adrenal cortex, gonads and placenta.

Eg- Testosterone, Estrogen, Progesterone, Cortisol, Aldosterone

# Hormones ctd..

## 3. Tyrosine Derivatives

Derived from AA called Tyrosine

Thyroid and adrenal medullary hormones

Eg- Catecholamine, Thyroxine, Dopamine



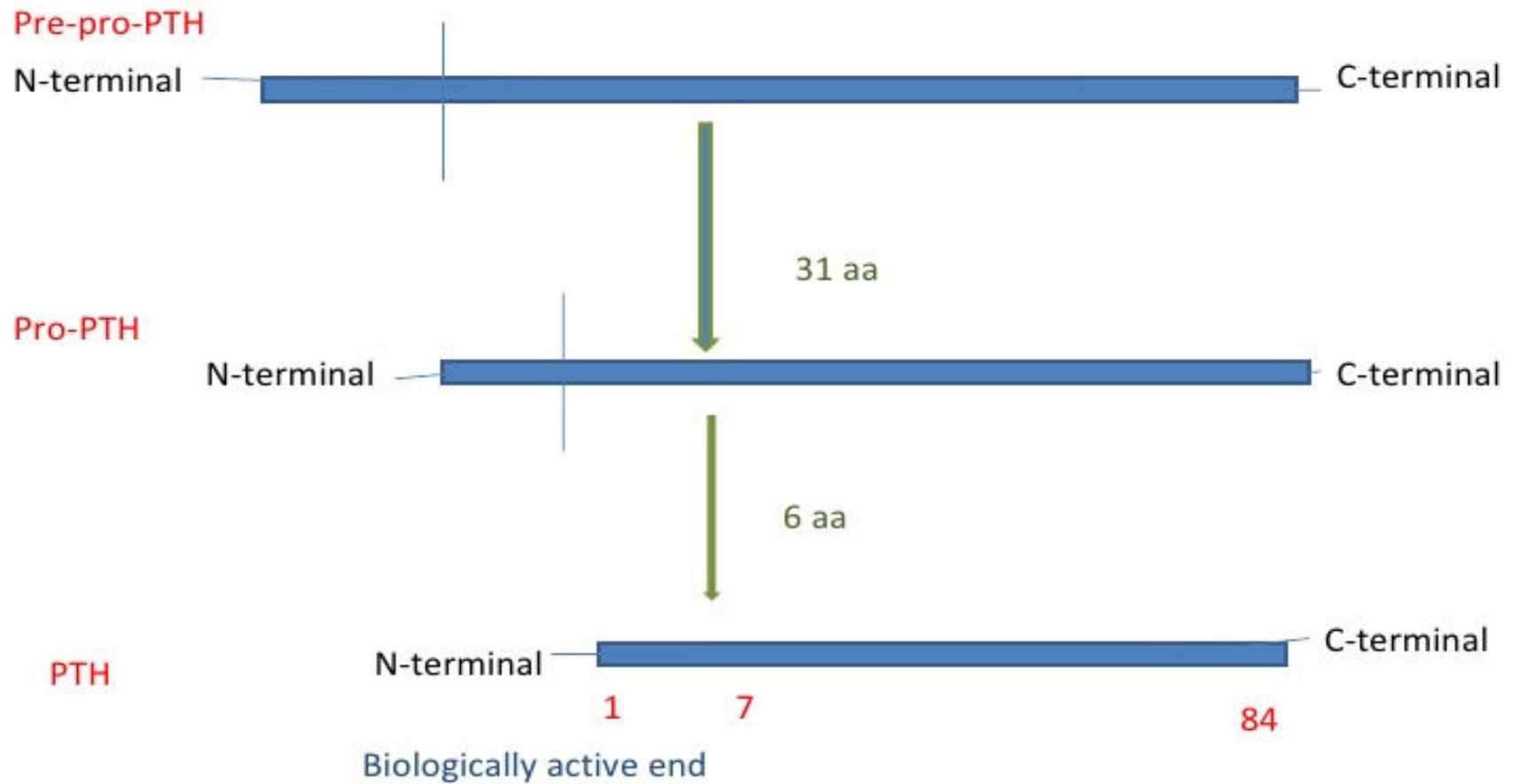
# Hormone synthesis

- Hormones are synthesized in response to biochemical signals generated by various modulating systems.
- Regulation of hormone synthesis will depend on the chemical structure.

# Hormone synthesis

- Peptide hormones –controlled mainly at gene transcription.
- Eg- high glucose load will stimulate the transcription of insulin ,mRNA
- Synthesized initially as larger polypeptide chains, which are cleaved to form the final hormone

# SYNTHESIS OF PTH

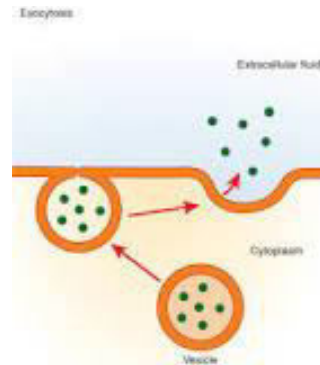


# Hormone synthesis

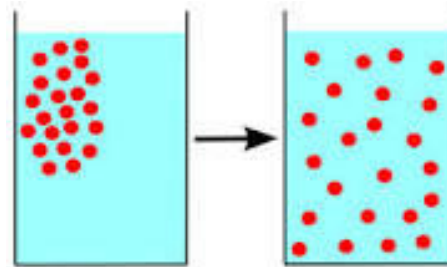
- Steroid Hormone synthesis controlled indirectly by regulating the production of Key synthetic enzymes and substrate availability
- Eg-cAMP dependent Protein Kinase in Cortisol production

# Hormone secretion

- Exocytosis
- Eg-many hormones

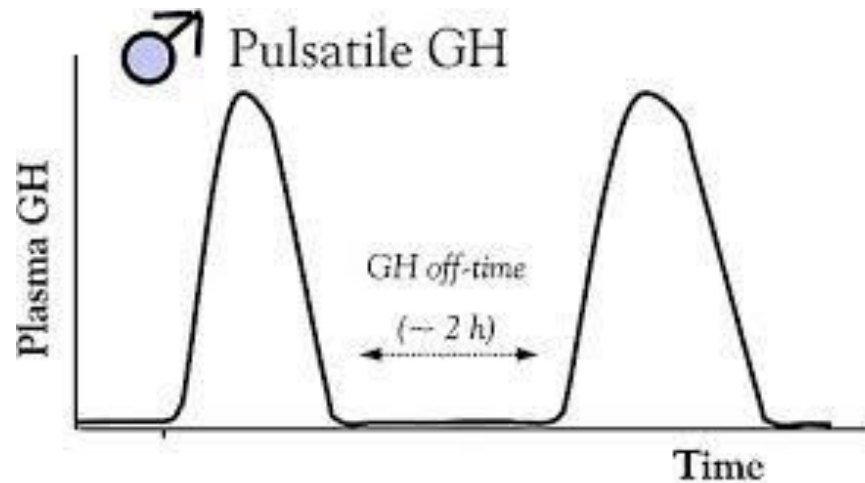


- Diffusion eg-Steroids



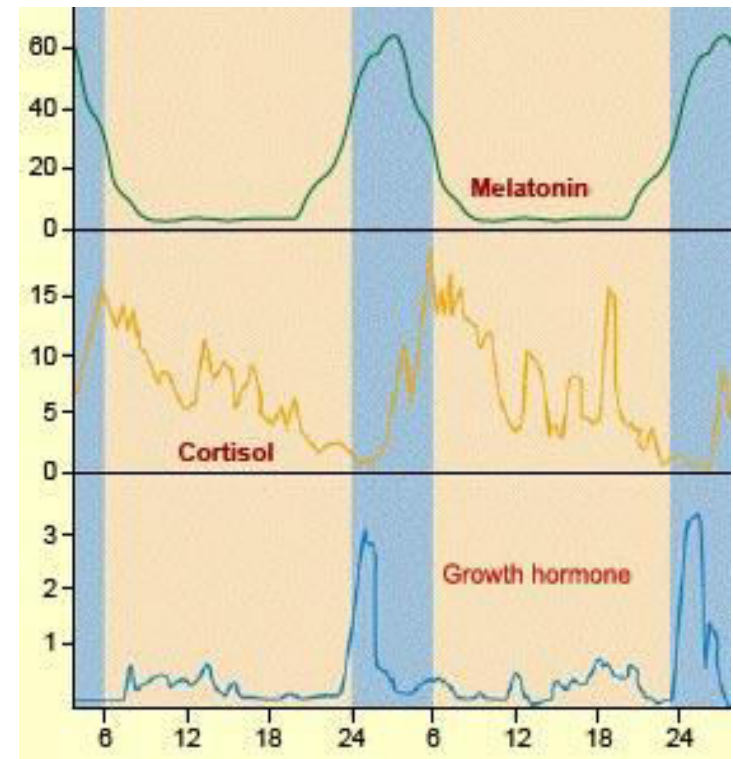
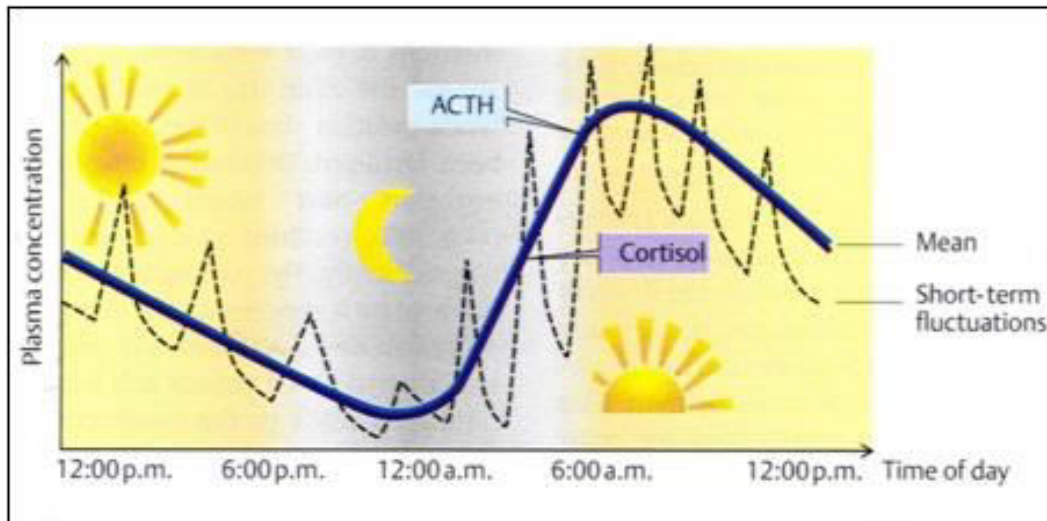
# Hormone secretion

- Pulsatile manner
- Eg-Growth Hormone



# Hormone secretion

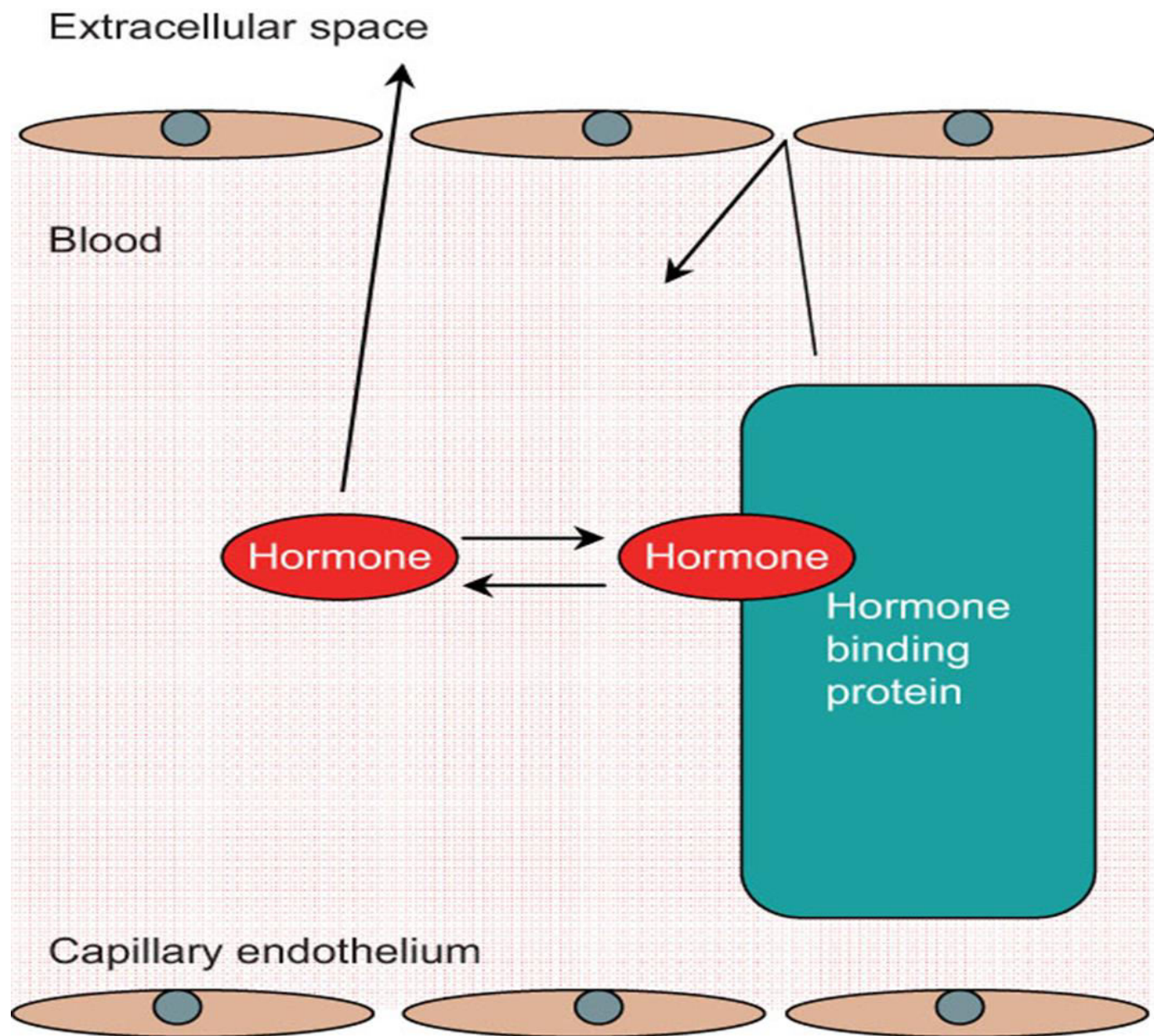
## Diurnal variation



# Hormone transport

- Water soluble hormones
  - Eg-Peptides and catecholamines
- Lipid soluble hormones-bound to large proteins
  - Eg-Steroids and Thyroid hormones





# Binding proteins

- Steroid binding proteins (SBP)
- Eg- Sex hormone-binding globulin(SHBG)  
Binds Testosterone and  $17\beta$  –estrodinol

Transcortin-Progesterone,cortisol

- Functions
  - 1.Increase solubility of lipid based hormones
  - 2.Reduce the rate of loss from urine
  - 3.Source of hormone in the bloodstream

# True or False

1. Endocrine system responses are slower than the nervous system.
2. Oxytocin is a neurohormone
3. Anterior pituitary secretes ADH
4. Thyroxine is a steroid hormone
5. Peptide hormones are produced as prepro hormones
6. Cortisol level is highest in the blood stream at midnight
7. Estradiol is bound to sex hormone binding globulin in the blood stream

# Hormonal Action

- Hormones does not act directly on cellular structures
- First the hormone combines with receptors on the target cells –Hormone –Receptor complex
- This induces various changes or reactions in the target cells

# Hormone receptors

- Large proteins present in target cells
- Each cell has thousands of receptors
- Each receptor is highly specific for one single hormone
- Serve two functions.
  - Firstly, they are required for selectivity.
  - Secondly, they are connected to an effector mechanism in the cell

# Hormone Action

- Water soluble hormones-Bind to cell surface receptors
- Action is fast
- Steroid hormones –Bind mainly to nuclear receptors and some to extranuclear receptors
- Slow action -nuclear receptors
- Fast action - extranuclear receptors

# Location of hormone receptors

## **1.Cell membrane**

- Protein hormones and Catecholamines

## **2.Cytoplasm**

- Sterod hormones

## **3.Nucleus**

- Thyroid hormones

## Activation Of Target Cell

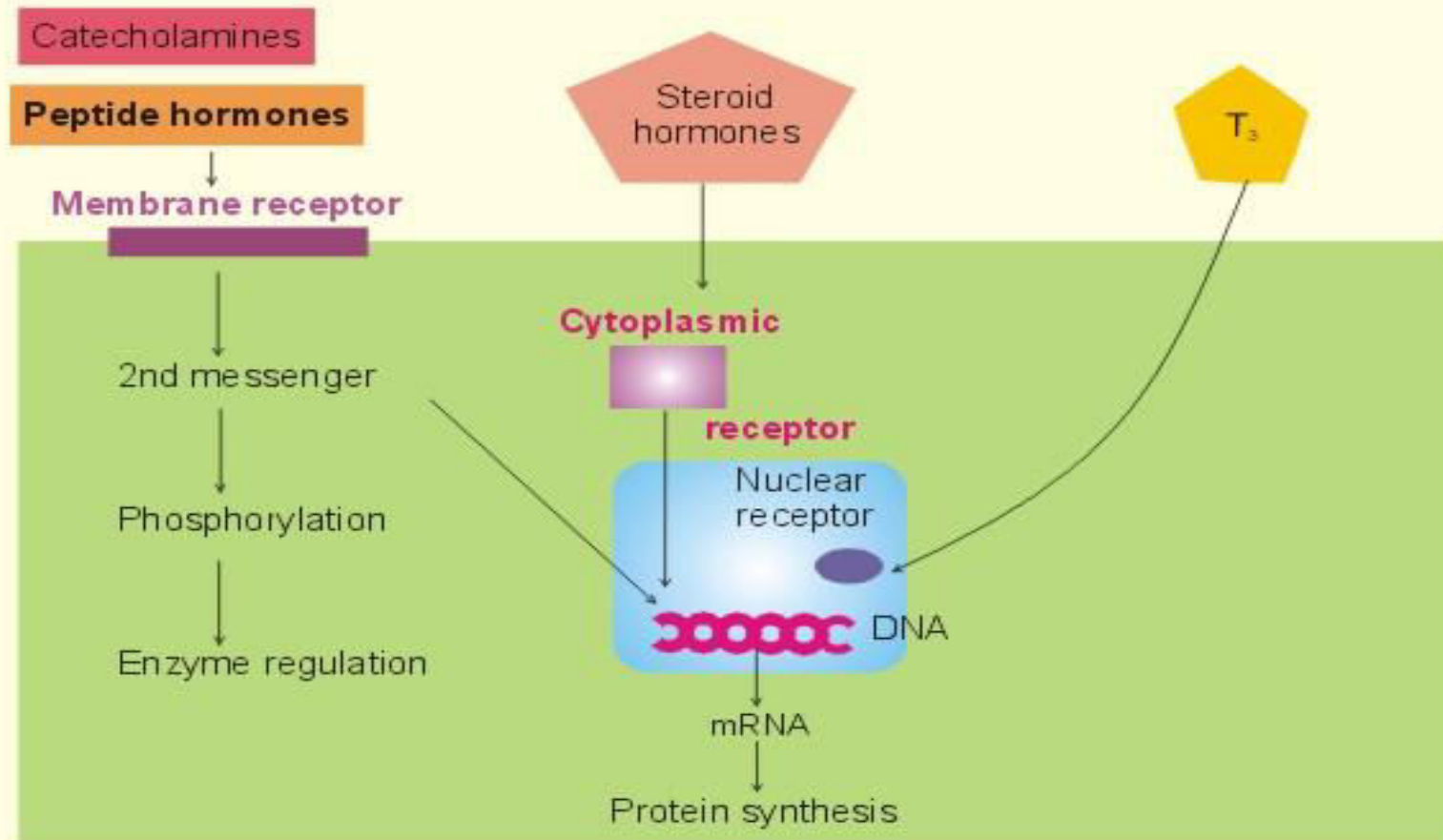
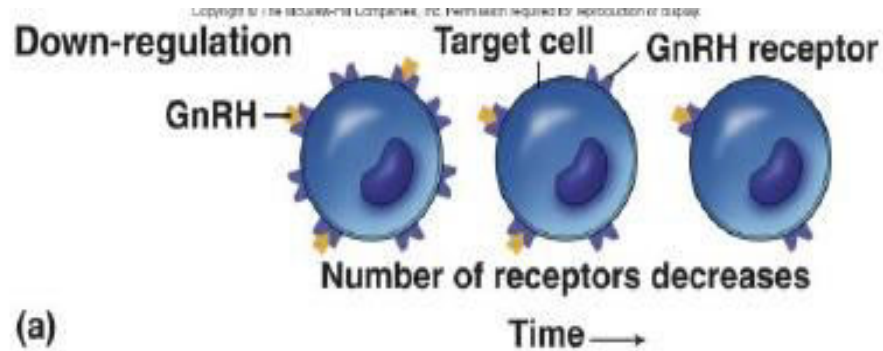


Fig. 26-1

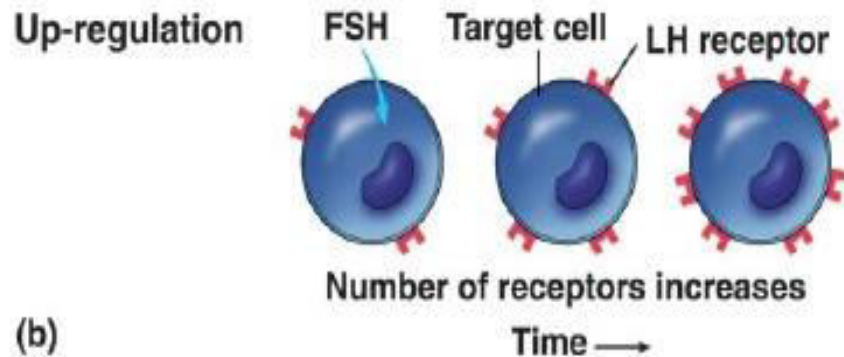


# Regulation of hormone receptors

- Cell membrane and intracellular receptors can change their affinity and number.
- A specific ligand for a receptor is able to modulate the total number of this receptor.
- Increasing the concentration of the ligand (hormone, neurotransmitter, drug) often reduces the number of receptors (down-regulation).
- Hormones recruit their own receptors at low concentrations (up-regulation).
- Maximal effects of hormones are generally observed at receptor occupancy of less than 50%.



(a)



(b)

## ■ Down-regulation

- Number of receptors decreases within target cells

## ■ Up-regulation

- Some stimulus causes number of receptors for a hormone to increase within target cell

# Regulation of hormone receptors

- Hormone -receptor complex enters the target cell by endocytosis -Internalization.
- After internalization some receptors are recycled.
- Many of them are replaced by newly formed receptors in the cell (Takes a long time)

# Mechanisms of hormone action

1.By altering the permeability of the cell membrane.

Eg -Neurotransmitters

2. By activating the intracellular enzymes.

Eg-Protein and catecholamines

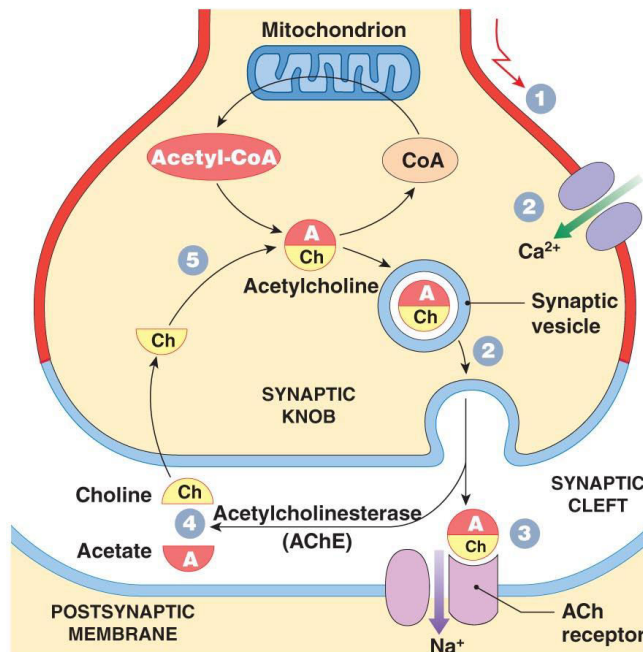
3.By activating the genes.

Eg-Thyroid and steroid hormones

# By altering the permeability of the cell membrane.

- NT in a synapse or a NMJ by changing the permeability of the postsynaptic membrane

The events that occur at a cholinergic synapse



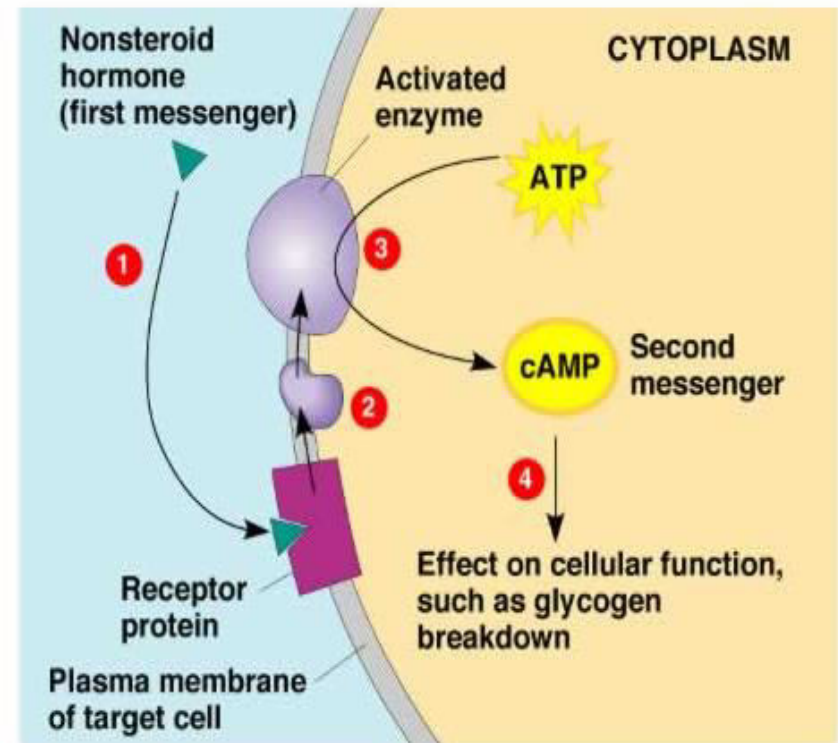
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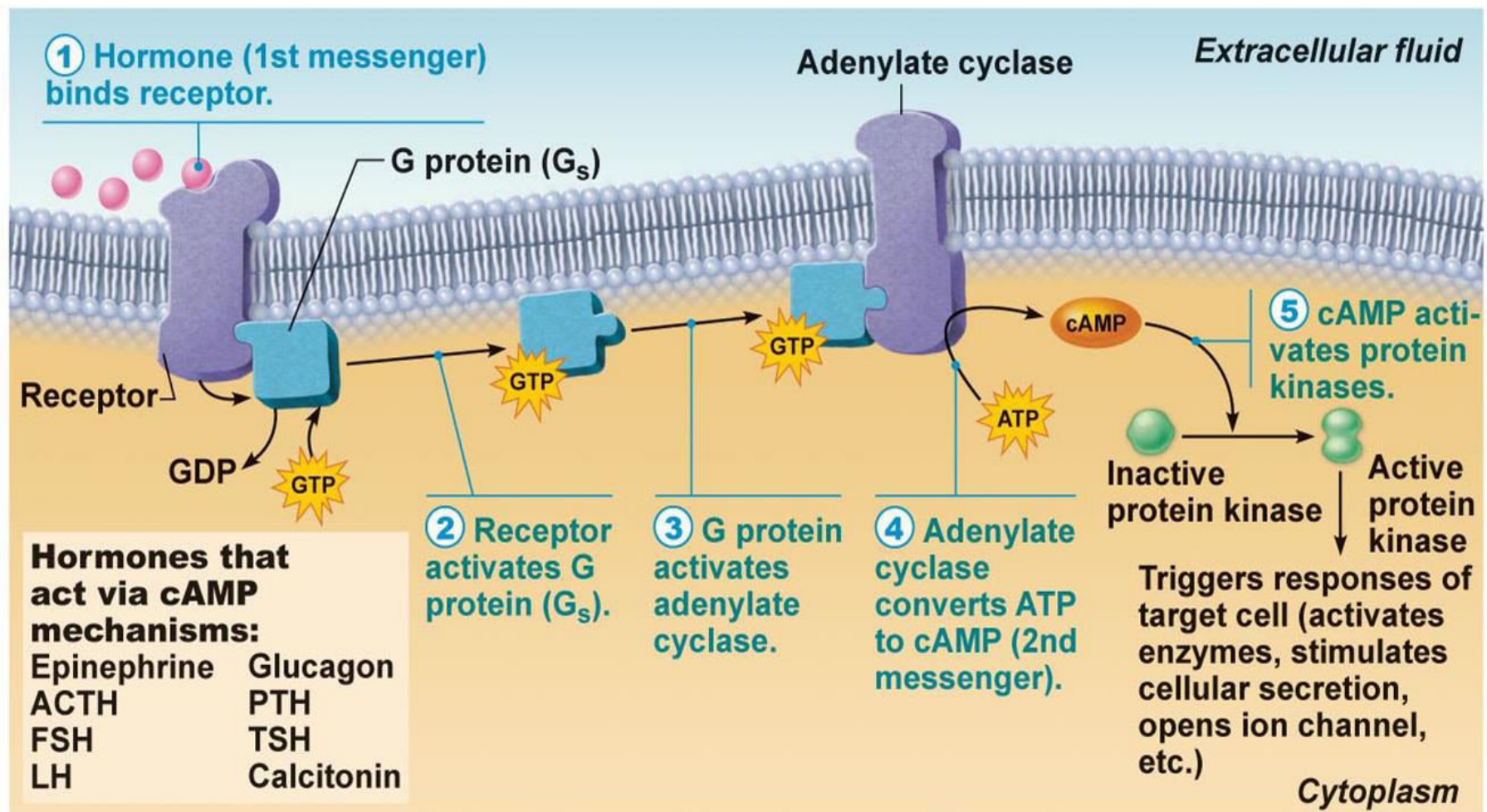
## Events Occurring at Synapse

- 1** An arriving action potential depolarizes the synaptic knob.
- 2** Calcium ions enter the cytoplasm, and after a brief delay, ACh is released through the exocytosis of synaptic vesicles.
- 3** ACh binds to sodium channel receptors on the postsynaptic membrane, producing a graded depolarization.
- 4** Depolarization ends as ACh is broken down into acetate and choline by AChE.
- 5** The synaptic knob reabsorbs choline from the synaptic cleft and uses it to synthesize new molecules of ACh.

# By activating the intracellular enzymes

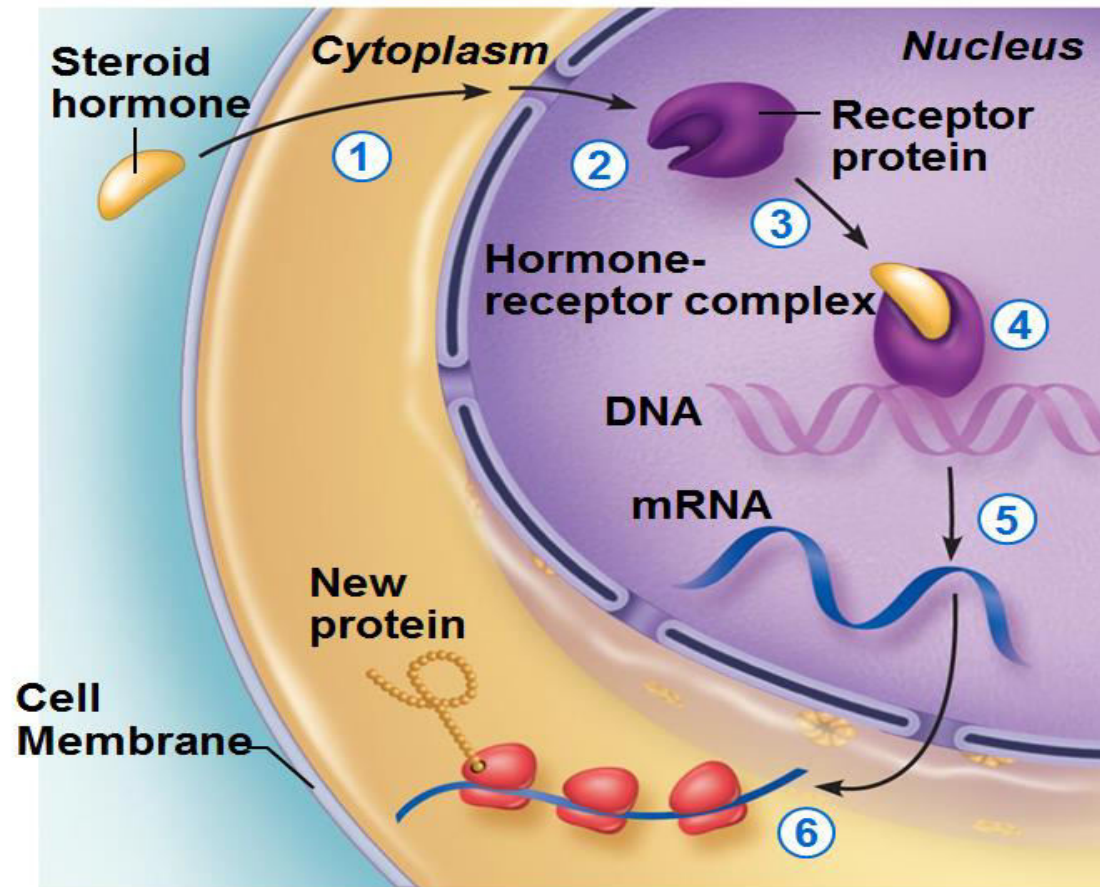
- Hormone receptor complex activates formation of second messengers.
- Commonest Second messenger is cyclic AMP
- Other second messengers are calcium ions and calmodulin, inositol triphosphate







# By acting on genes



(a) Steroid hormone action



# Differences of Peptide and Steroid hormones

	Peptides	Steroids
Structure	hydrophilic, large (polypeptides) or small (amino acid derivatives)	hydrophobic, small
Site of synthesis	rough ER	smooth ER
Regulation of release	stored in vesicles until a signal for secretion is received	synthesized only when needed and then used immediately, not stored
Transport in bloodstream	free	stuck to protein carrier
Specificity	only target cells have appropriate surface receptors (exception: thyroxine = cytoplasmic)	only target cells have appropriate cytoplasmic receptors
Mechanism of effect	bind to receptors that generate second messengers which result in modification of <i>enzyme activity</i>	bind to receptors that alter <i>gene expression</i> by regulating DNA transcription
Timing of effect	rapid, short-lived	slow, long-lasting

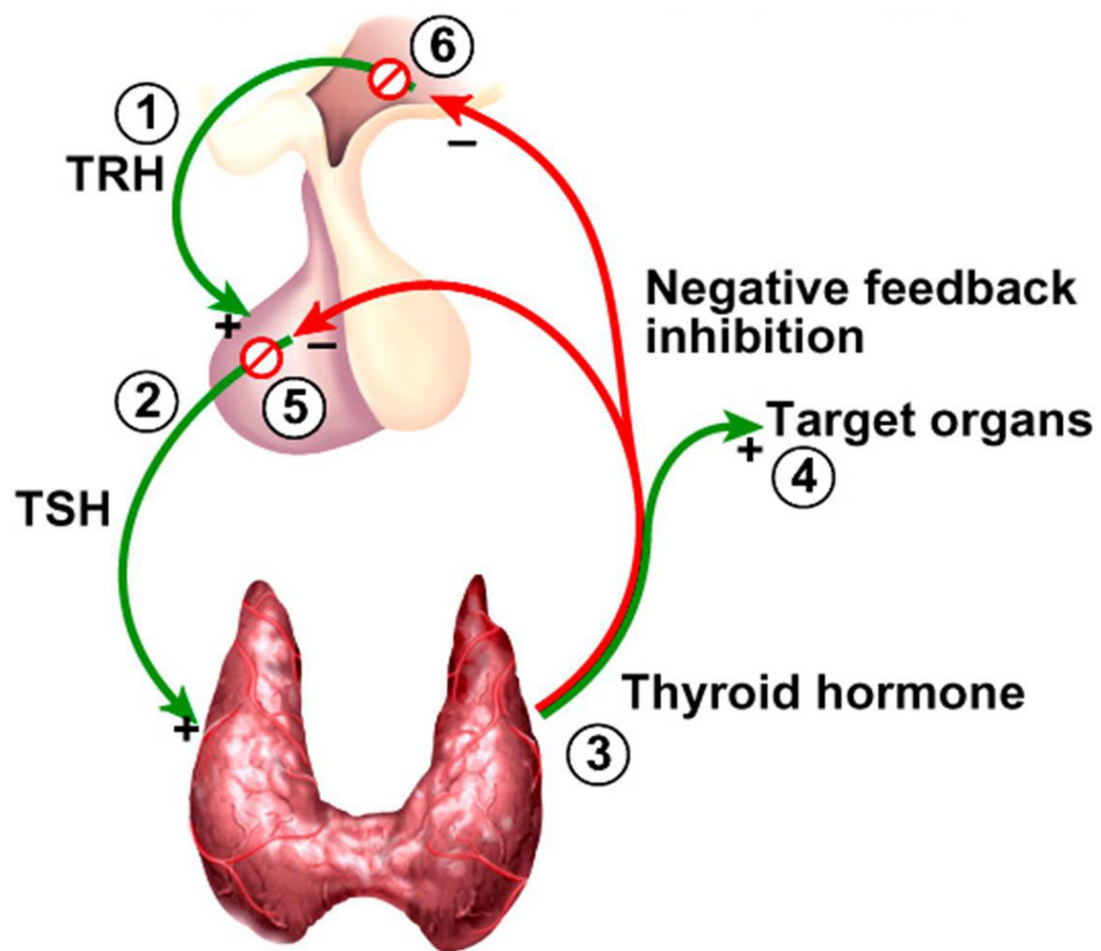
# Regulation of hormone secretion

## Negative feedback

The body senses a change and activates mechanisms that negate (**reverse**) it;

- target organ hormone( pituitary hormones) levels **inhibits** release of tropic hormones

Eg— TRH-TSH-thyroid hormones



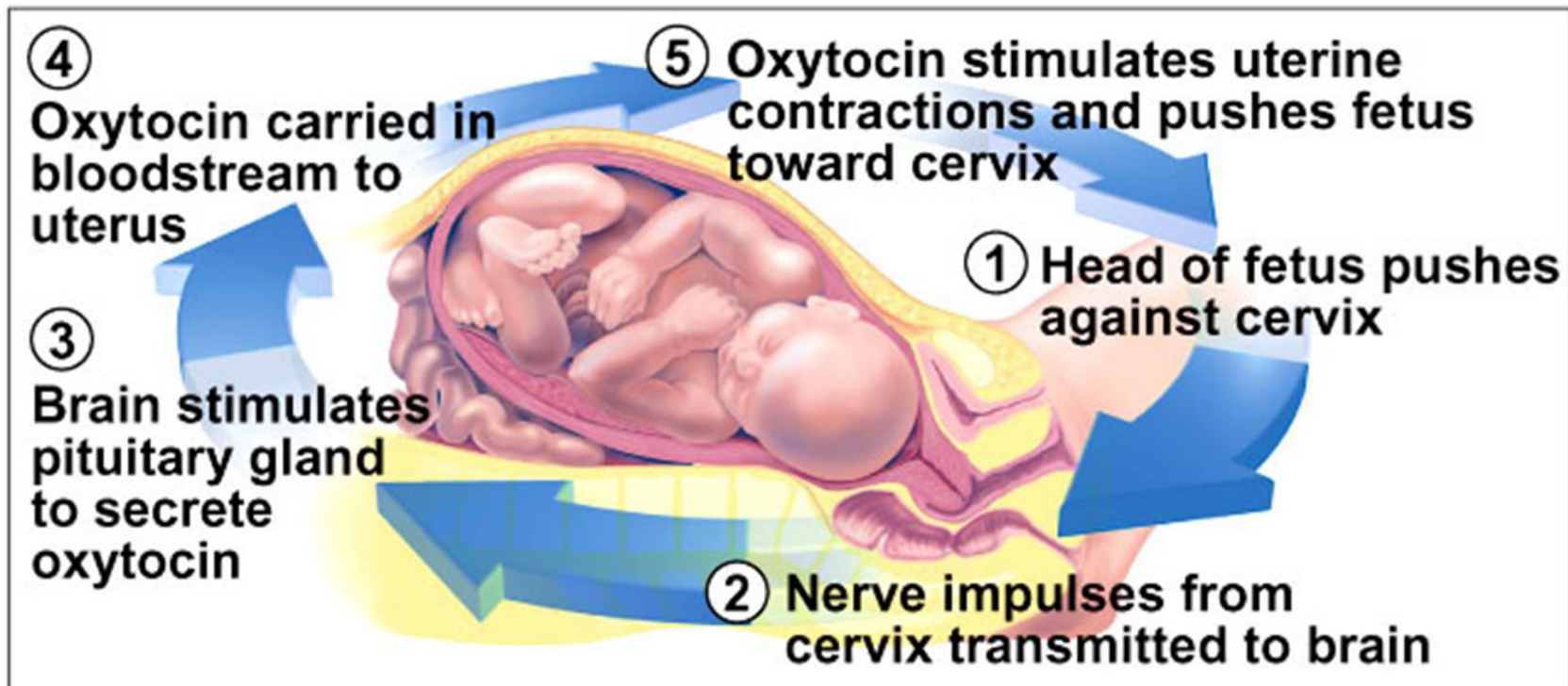
# Regulation of hormone secretion

- Positive feedback

change in a factor triggers a physiological response that AMPLIFIES an initial change

Rarer than negative feedback.

Eg- Parturition



# Types of Endocrine Disorders

- Hormone Deficiency

Due to destruction of the glandular structure which produces hormones

Eg-

Hypothyroidism

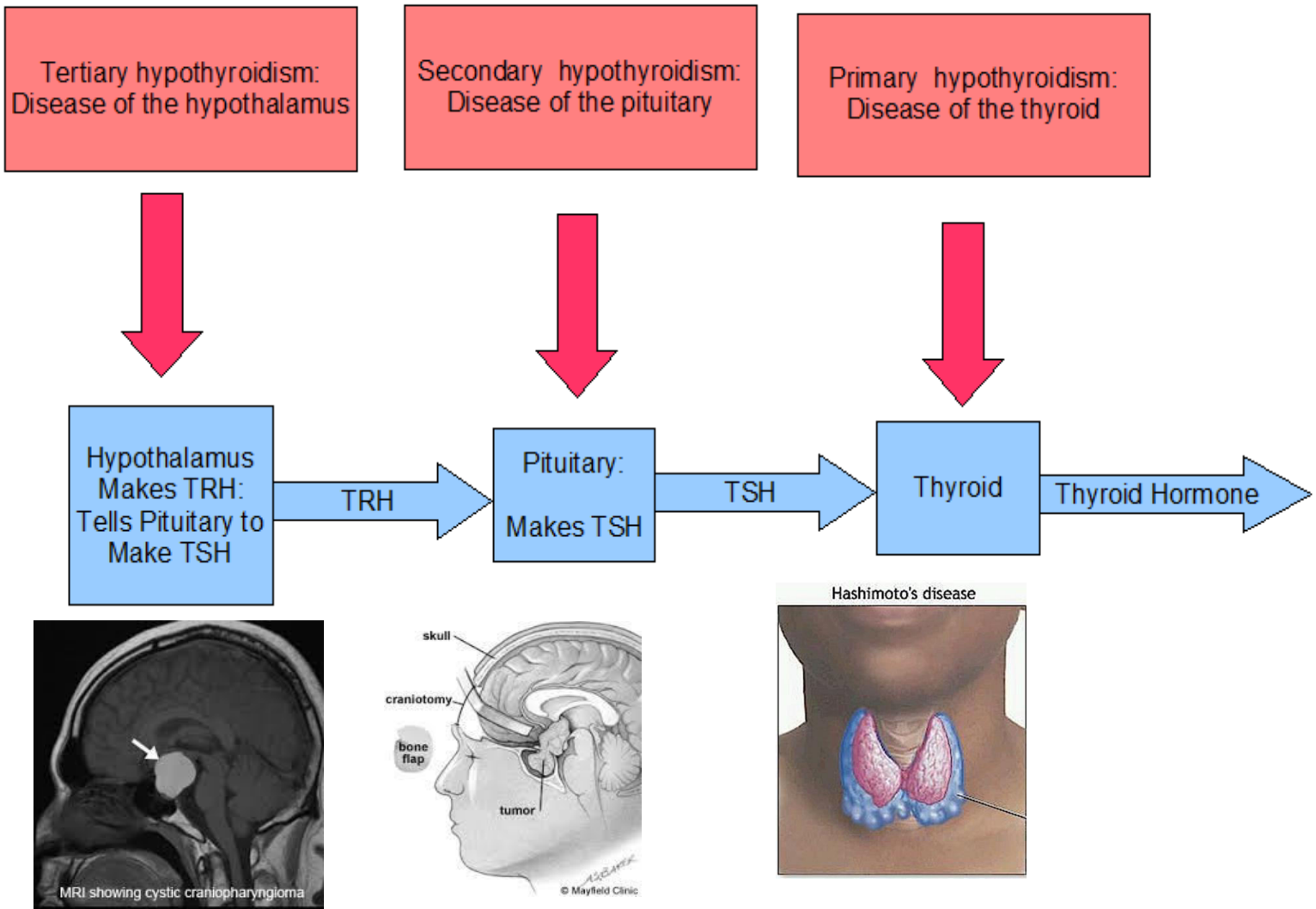
Primary

Secondary

Tertiary



## Primary, Secondary and Tertiary Hypothyroidism



# Types of Endocrine Disorders

- Hormone excess or over stimulation of receptors

Acromegaly due to Growth hormone excess



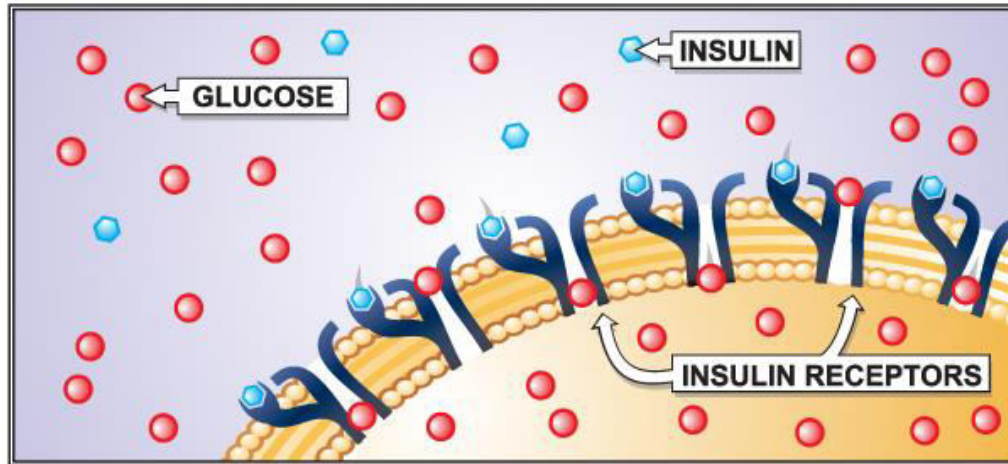
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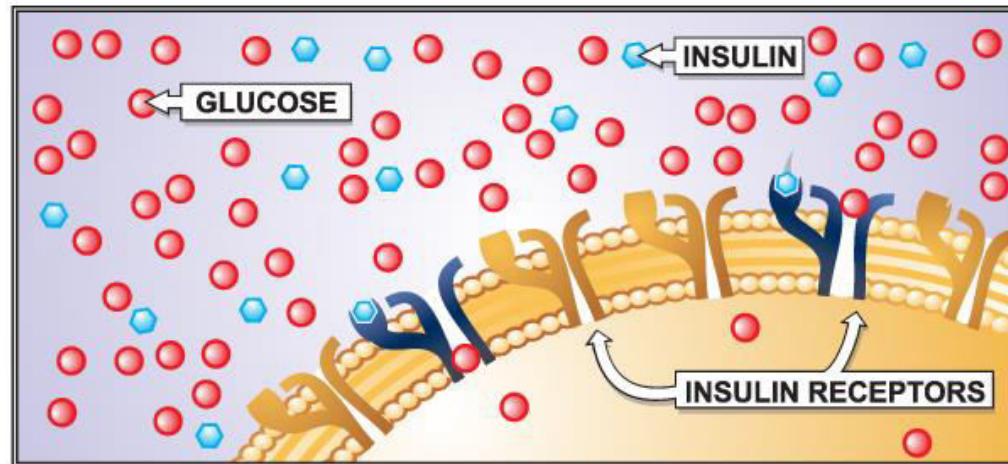
# Types of Endocrine Disorders

- Hormone resistance
- Target tissue becomes resistant to the hormone
- Eg-Insulin receptor resistance causing Diabetes mellitus

## NORMAL CELL



## INSULIN RESISTANT CELL

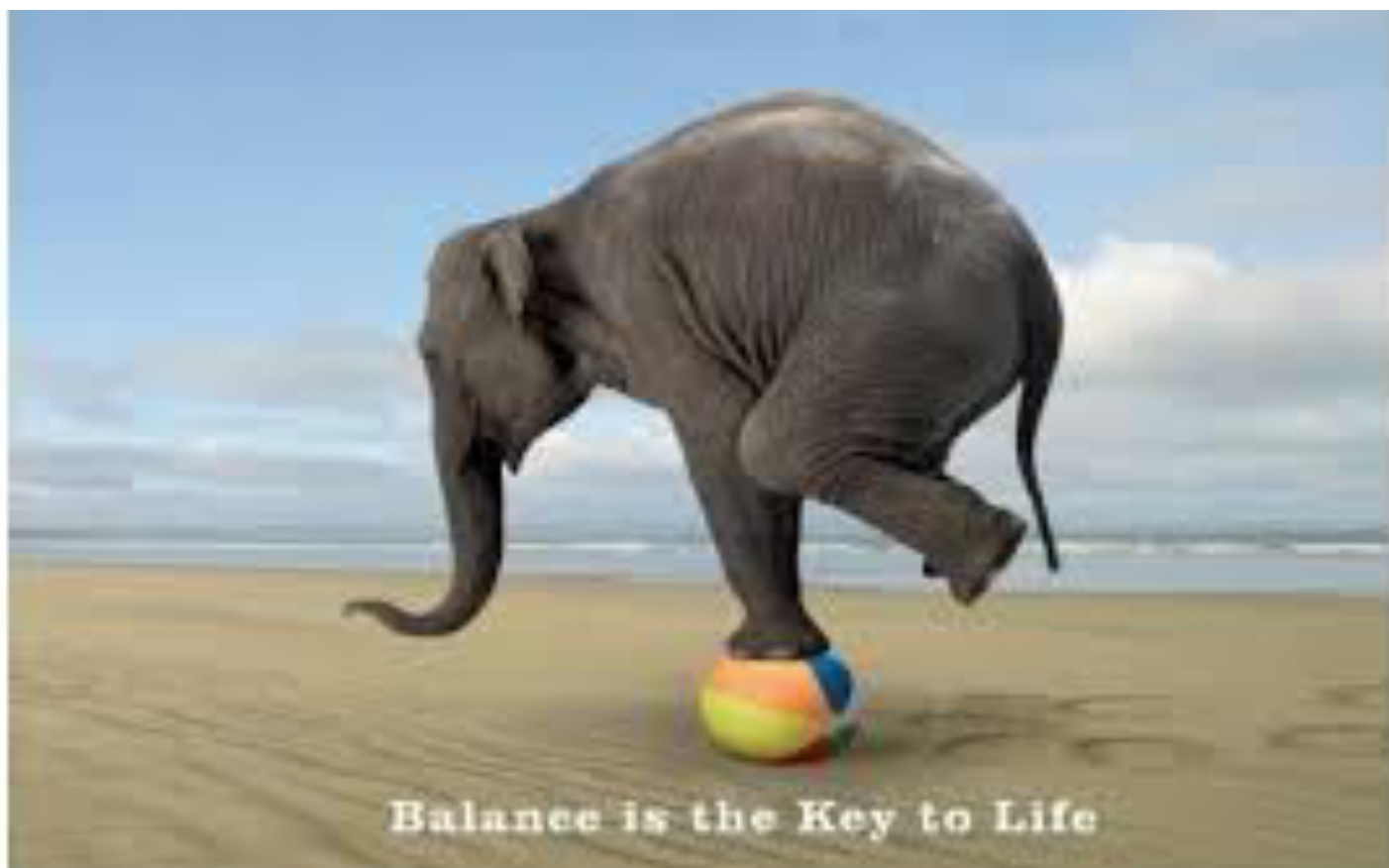


# Summary

- Endocrine system consist of glands and hormones.
- Hormones play a vital role to ensure a relative stability of body systems –homeostasis
- Hormones are divided into peptide, amine (Water soluble) and steroid hormones(Lipid soluble).
- Water soluble hormones bind to cell surface receptors and lipid soluble hormones bind to nuclear receptors.
- Synthesis and release of hormones are regulated by feedback mechanisms

# True or False

1. Hormone deficiencies lead to down regulation of hormones
2. Steroid hormones bind to cytoplasmic receptors
3. Peptide hormones activate intracellular enzymes.
4. c AMP is a second messenger
5. Oxytocin has a negative feedback system
6. Acromegaly is caused by GH excess



Balancee is the Key to Life