

SESSION ONE

ENDOCRINOLOGY INTRODUCTION

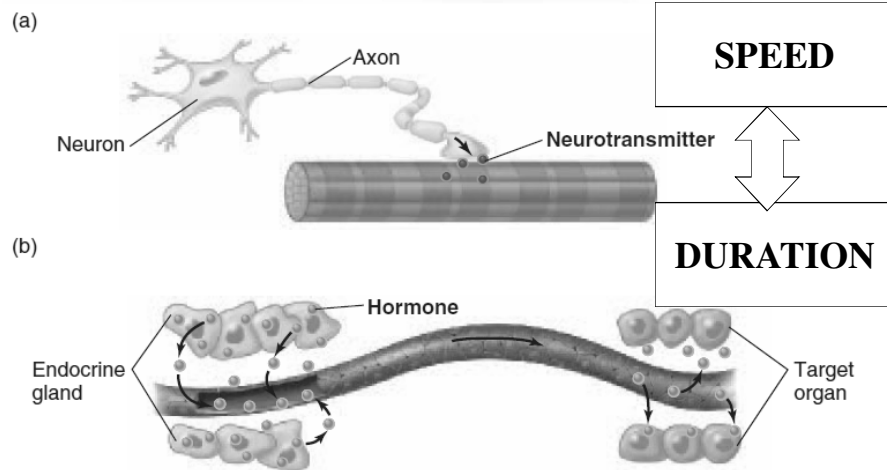
DR SYED SHAHID HABIB
MBBS FCPS DSDM PGDCR
Associate Professor
Dept. of Physiology
College of Medicine & KCUH
King Saud University

OBJECTIVES

At the end of this Session you should be able to:

- **List the general chemical categories of hormones and give examples of hormones within each category.**
- **Explain how different hormones can exert synergistic, permissive, or antagonistic effects.**
- **Explain how hormone concentrations in the blood are regulated**
- **Describe the mechanisms of actions of hormones**

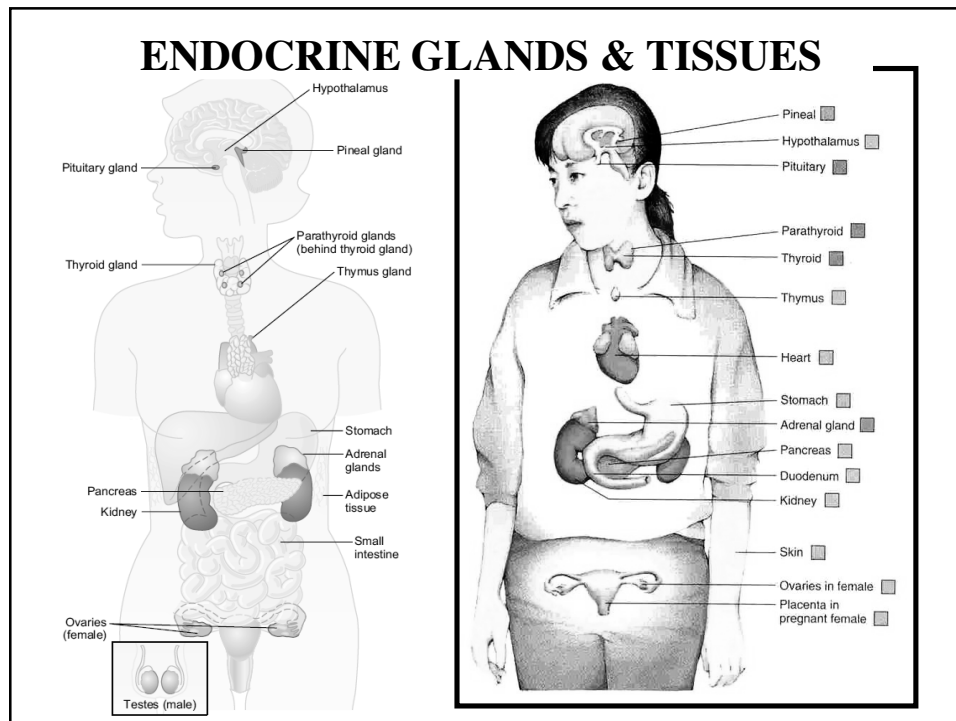
CONTROL SYSTEMS



Two systems control all physiologic processes:

- **THE NERVOUS SYSTEM** exerts point-to-point control through nerves, similar to sending messages by conventional telephone. Nervous control is electrical in nature and fast.
- **THE ENDOCRINE SYSTEM** broadcasts its hormonal messages to essentially all cells by secretion into blood and extracellular fluid. Like a radio broadcast, it requires a receiver to get the message - in the case of endocrine messages, cells must bear a *receptor* for the hormone being broadcast in order to respond.

Endocrinology is the study of hormones, their receptors and the intracellular signalling pathways they invoke



HISTORY

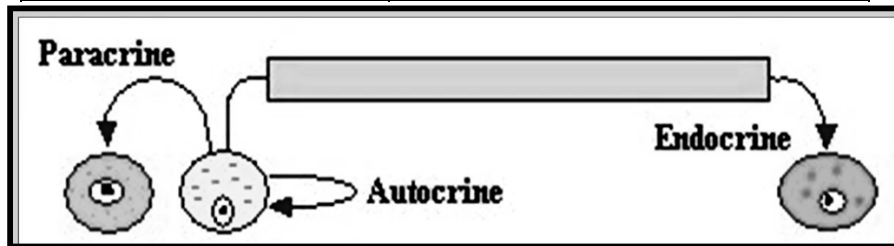
- **The term hormone was used for the first time by E. H Starling in 1905 to describe Secretin**
- **The first hormone to be isolated in pure form was Insulin**

**The term Hormone is derived from Gr.
Word orma`ein to excite**

- A chemical substance formed in one organ and carried in the circulation to another organ on which it exerts a stimulating effect**
- Biologically potent and chemically diverse substances secreted by the ductless glands into the general body circulation and affect the target tissues by activating the second messenger system in target tissues**

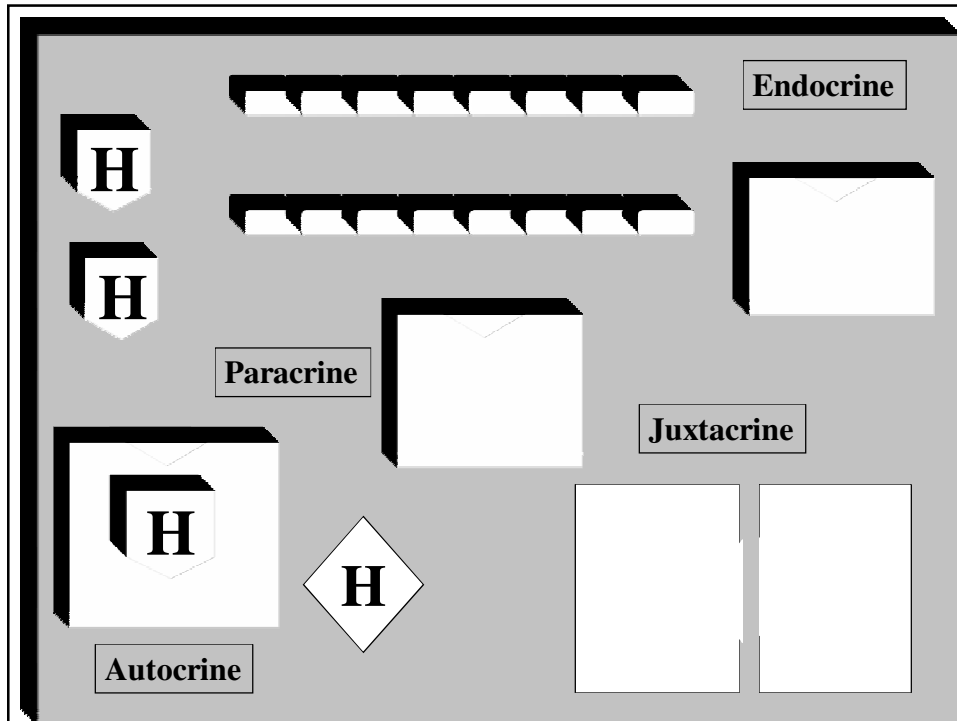
COORDINATION OF BODY FUNCTIONS

Neural	Acetylcholine
Endocrine	Growth Hormone
Neuroendocrin	Glucagon
Paracrine	Gastro Int Hormones
Autocrine	Nor Epinehprine, IGF-1
Juxtacrine	Growth Factors



INTERCELLULAR COMMUNICATIONS

	GAP Junctions	Synaptic	Paracrine & Autocrine	Endocrine
Message transmission	Directly from Cell to Cell	Across synaptic cleft	By diffusion in interstitial fluid	By circulating body Fluids
Local or General	Local	Local	Locally Diffuse	General
Specificity depends on	Anatomic location	Anatomic location & Receptors	Receptors	Receptors



CLASSIFICATION

- **Chemical Structure**
 - Peptides and proteins
 - Steroids
 - Amino acid derivatives
 - Fatty acid derivatives – (Eicosanoids prostaglandins, prostacyclins, leukotrienes and thromboxanes) ??
- **Solubility (Water and Lipid Soluble)**
- **Mechanism Of Action**

Chemical Classification of Hormones

- **1. Amino acid derivatives:**
 - Hormones derived from tyrosine and tryptophan.
 - NE, Epi, T₄.
- **2. Polypeptides and proteins:**
 - Polypeptides:
 - Chains of < 100 amino acids in length.
 - ADH.
 - Protein hormones:
 - Polypeptide chains with > 100 amino acids.
 - Growth hormone.

Glycoproteins

Chemical Classification of Hormones (continued)

- **3. Lipids derived from cholesterol (Steroids).**
 - Are water insoluble hormones.
 - Testosterone.
 - Estradiol.
 - Cortisol.
 - Progesterone.

POINTS TO REMEMBER

- **All hormones secreted by Ovaries, testes and adrenal cortex are steroids**
- **All hormones secreted by adrenal medulla and thyroid are amines except one (Calcitonin, Dopamine [PIH])**
- **All Others are peptides and proteins**

PROPERTIES

- **Half Life**
- **Receptors**
- **Onset of Action**
- **Types of Actions**
- **Storage**
- **Efficient Regulation**

Half Life

Hormone	Half Life
Amines	2-3 min
T3	0.75 days
T4	6.7 days
Polypeptides	4-40 min
Proteins	15-170 min
Steroids	4-120 min

TRANSPORT

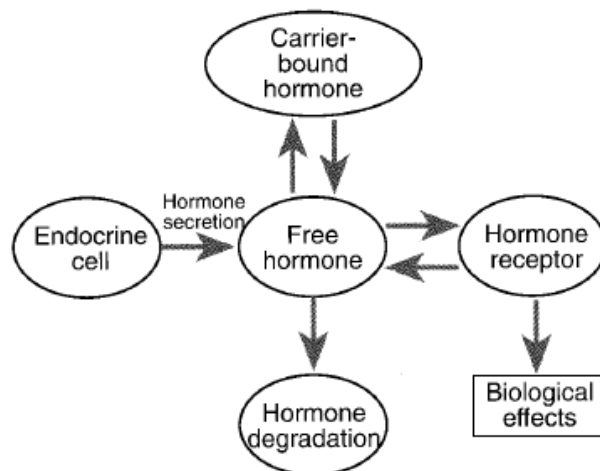
- **Water Soluble Hormones are transported dissolved in Plasma eg: Peptides**
- **Lipid Soluble hormones are reversibly bound to Plasma Proteins (Steroids & Thyroid hormones....thyroid binding globulin, thyroid binding albumin, thyroid binding pre-albumin)**

TABLE 31.2 Circulating Transport Proteins

Transport Protein	Principal Hormone(s) Transported
Specific	
Corticosteroid-binding globulin (CBG, transcortin)	Cortisol, aldosterone
Thyroxine-binding globulin (TBG)	Thyroxine, triiodothyronine
Sex hormone-binding globulin (SHBG)	Testosterone, estrogen
Nonspecific	
Serum albumin	Most steroids, thyroxine, triiodothyronine
Transthyretin (prealbumin)	Thyroxine, some steroids

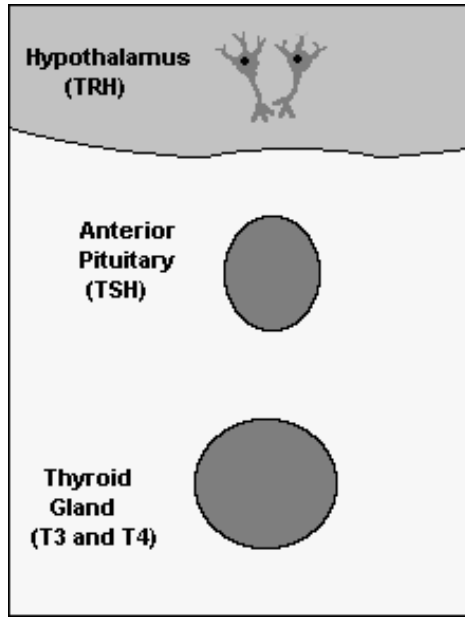
FATE

- **Liver**
- **Kidneys**
- **Other Tissues**



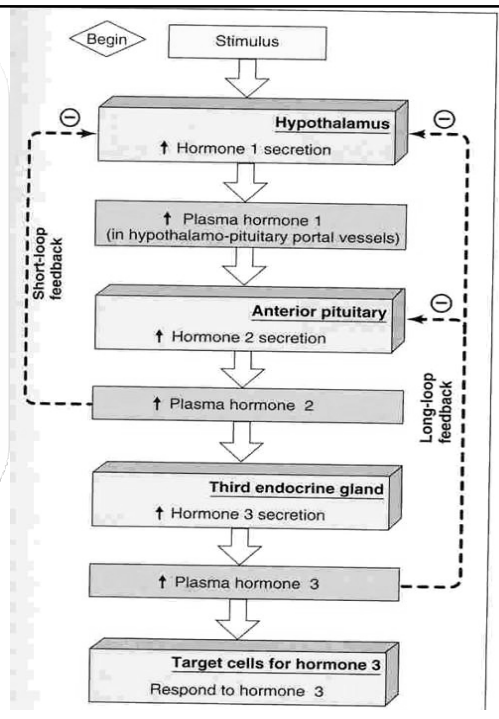
FEEDBACK CONTROLS & RHYTHMS

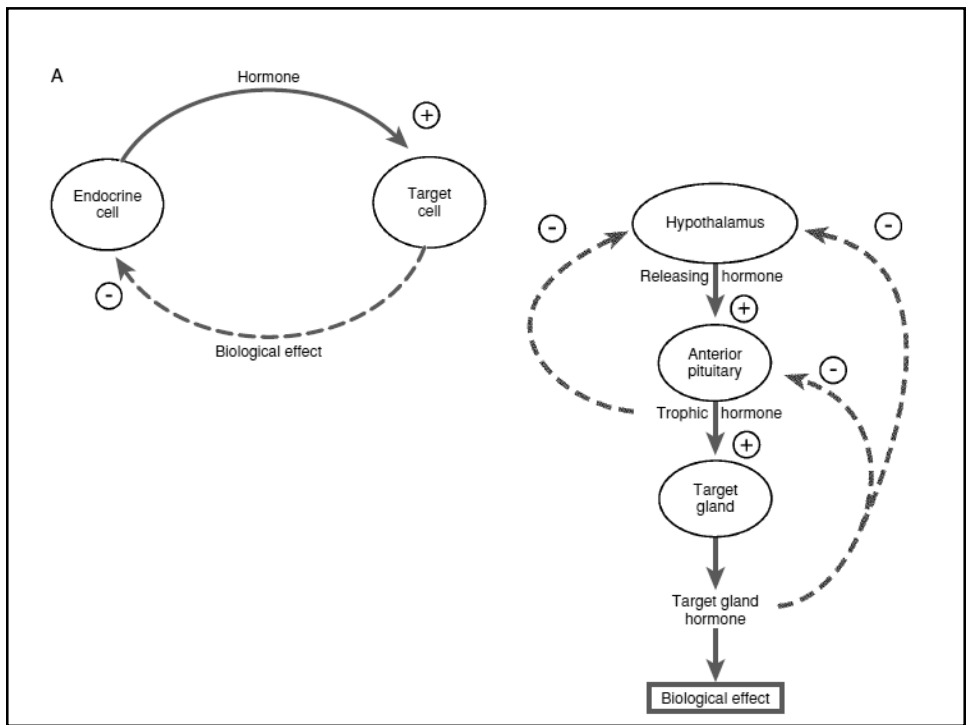
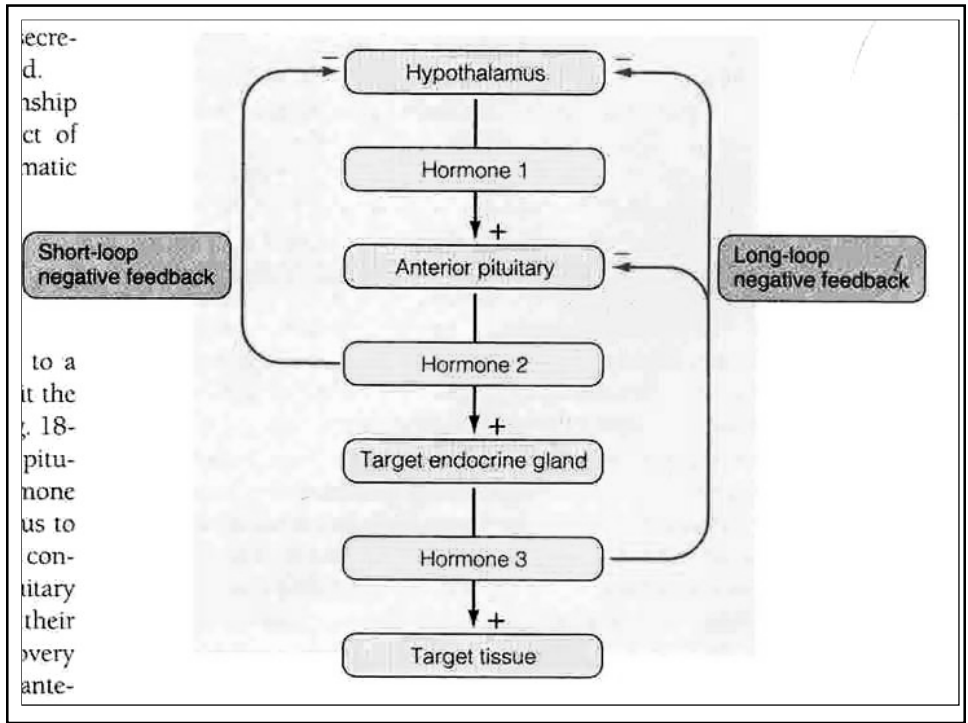
- Positive Feedback Control
- Negative Feedback Control
- Circadian Rhythm
- Circalunar Rhythm
- Cyclic Rhythm



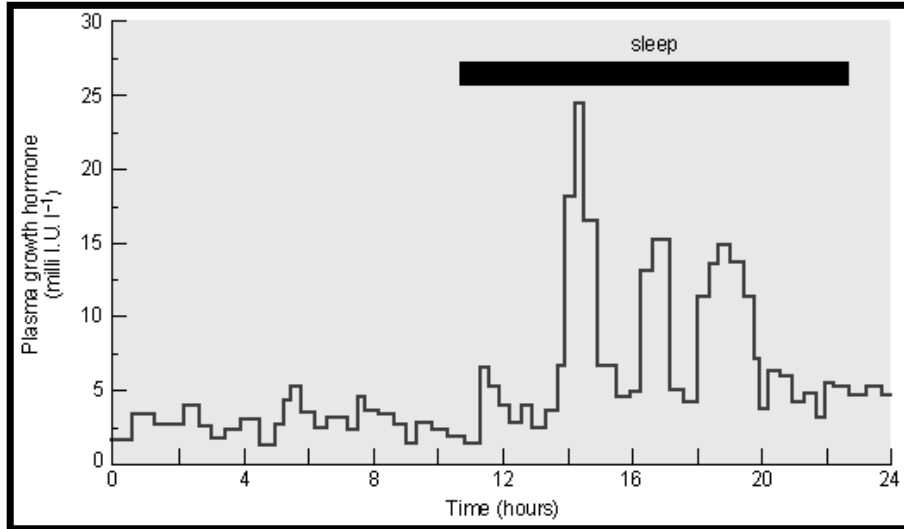
FEEDBACK CONTROL OF HORMONE SECRETION

Short & Long loop Negative & Positive Feedback

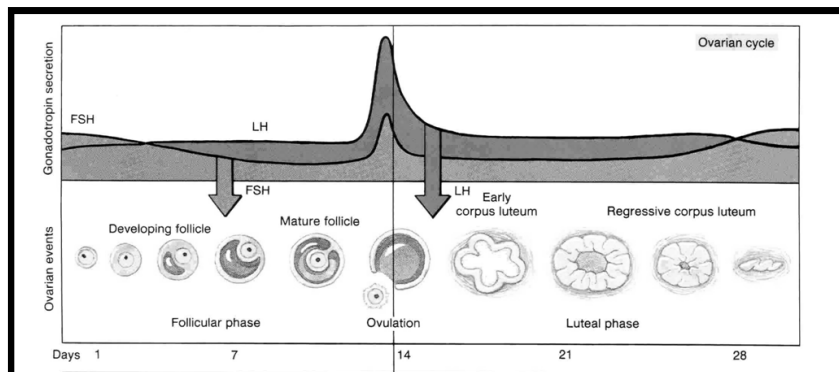




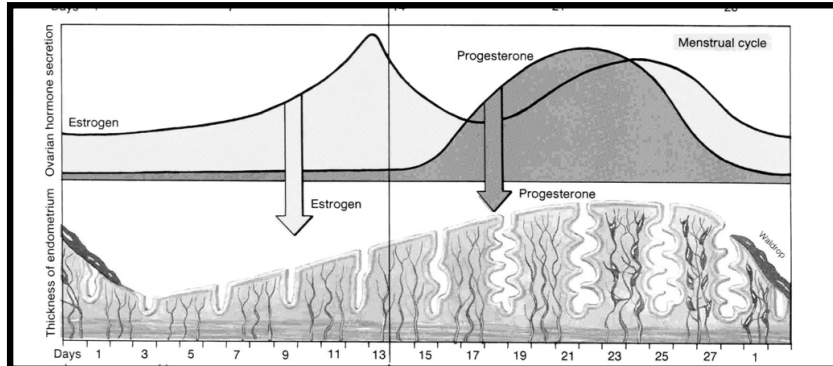
What is this Rhythm?



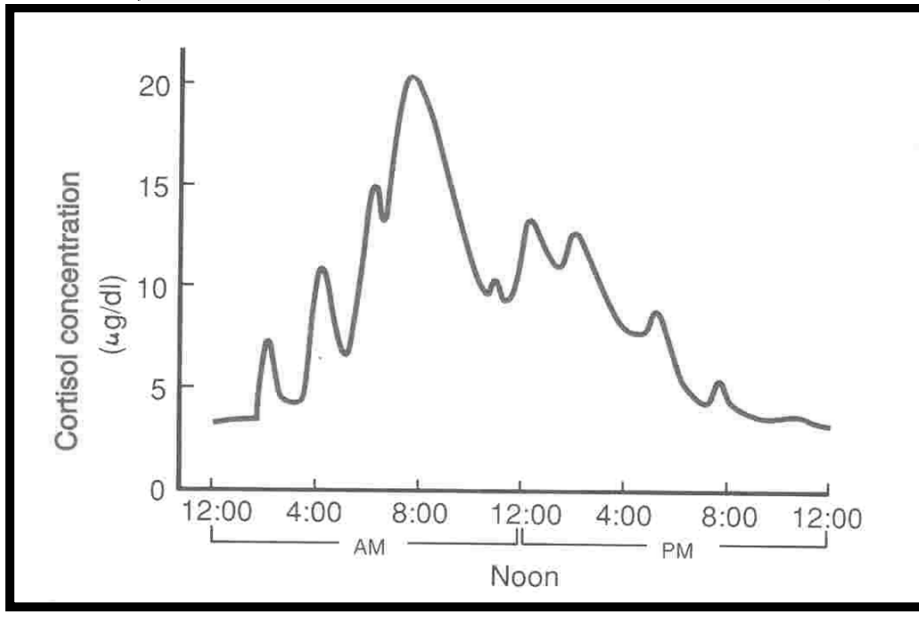
What is this Rhythm ?



What is this Rhythm ?

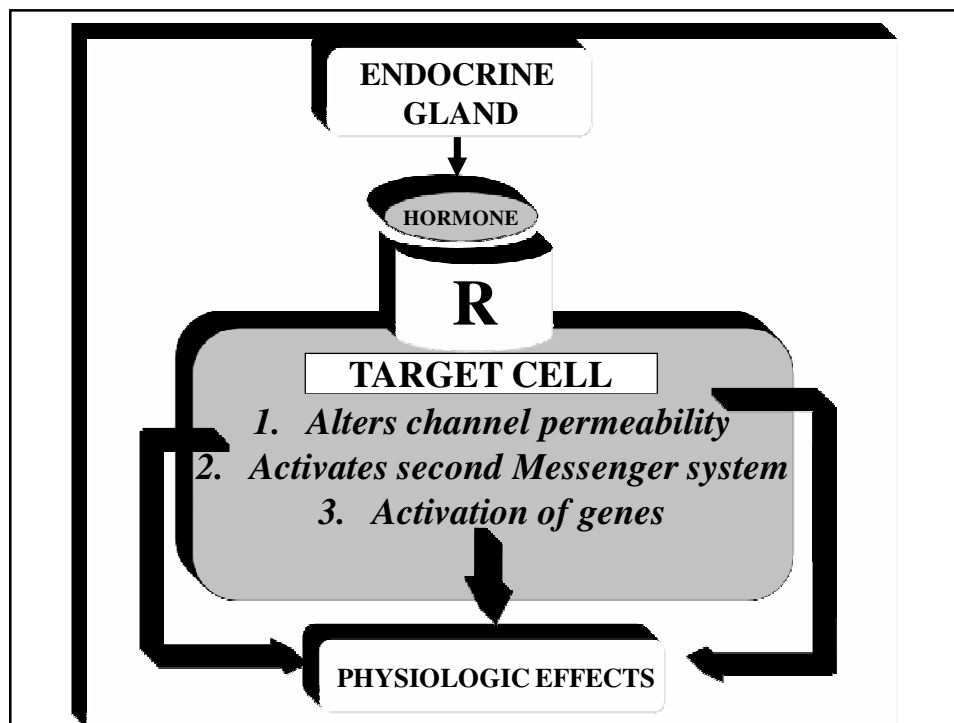


What is this Rhythm ?



MECHANISM OF ACTION

- **RECEPTORS**
 - **CELL MEMBRANE** (Prot, Peptides, Catecholamines)
 - **CYTOPLASM** (Steroids)
 - **NUCLEUS** (Thyroid H)
- **INTRACELLULAR SIGNALLING**
 1. **CHANGE IN MEMBRANE PERMEABILITY**
 2. **ACTIVATION OF INTRACELLULAR ENZYMES**
 3. **ACTIVATION OF GENES TO PRODUCE NEW PROTEINS**

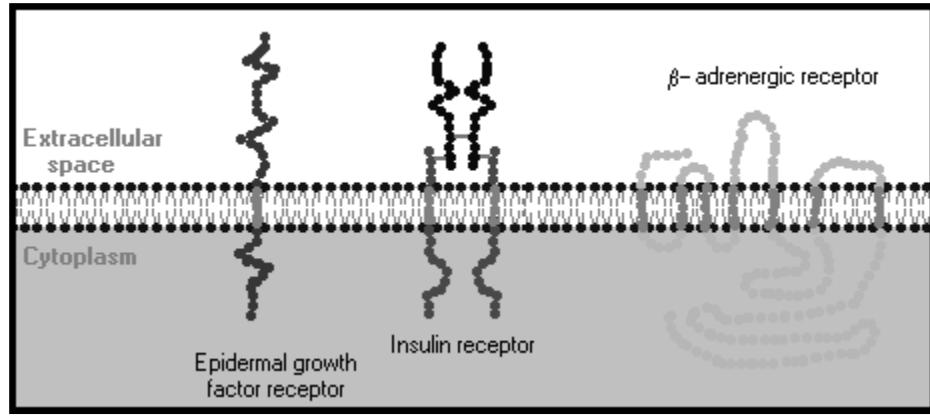


RECEPTORS

Extracellular domains (*ligand-binding domain*)

Transmembrane domains are

Cytoplasmic or intracellular domains (*effector region*)



RECEPTORS

Location of Receptor	Classes of Hormones	Principle Mechanism of Action
Cell surface receptors (plasma membrane)	Proteins and peptides, catecholamines and eicosanoids	Generation of <i>second messengers</i> which alter the activity of other molecules - usually enzymes - within the cell
Intracellular receptors (cytoplasm and/or nucleus)	Steroids and thyroid hormones	Alter transcriptional activity of responsive genes

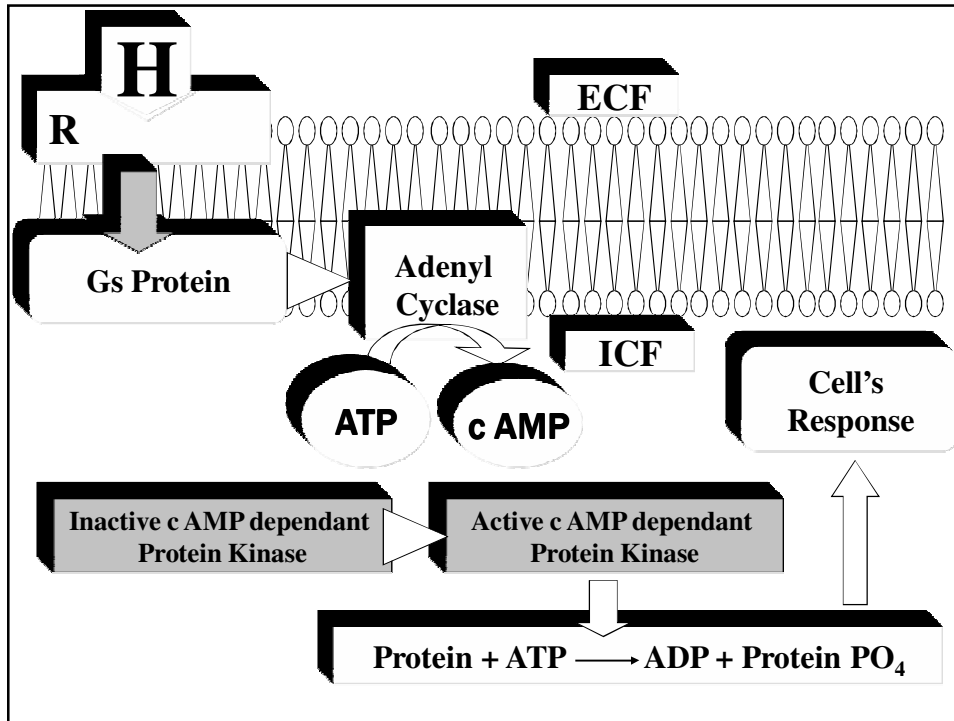


Table 74-2

Some Hormones That Use the Adenylyl Cyclase-cAMP Second Messenger System

- Adrenocorticotrophic hormone (ACTH)
- Angiotensin II (epithelial cells)
- Calcitonin
- Catecholamines (β receptors)
- Corticotropin-releasing hormone (CRH)
- Follicle-stimulating hormone (FSH)
- Glucagon
- Human chorionic gonadotropin (HCG)
- Luteinizing hormone (LH)
- Parathyroid hormone (PTH)
- Secretin
- Somatostatin
- Thyroid-stimulating hormone (TSH)
- Vasopressin (V_2 receptor, epithelial cells)

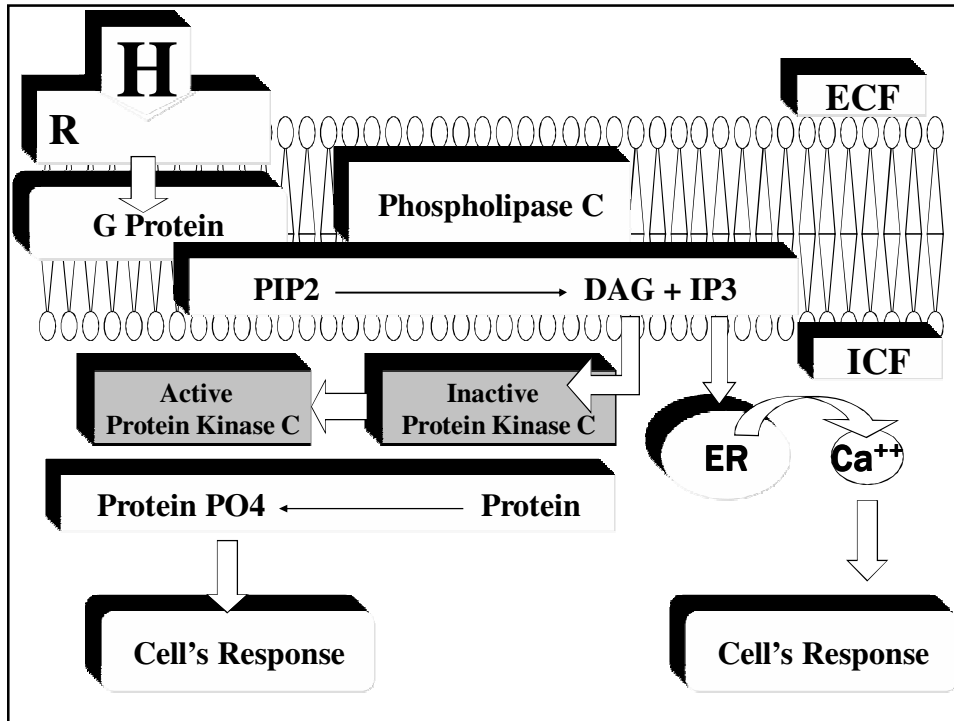
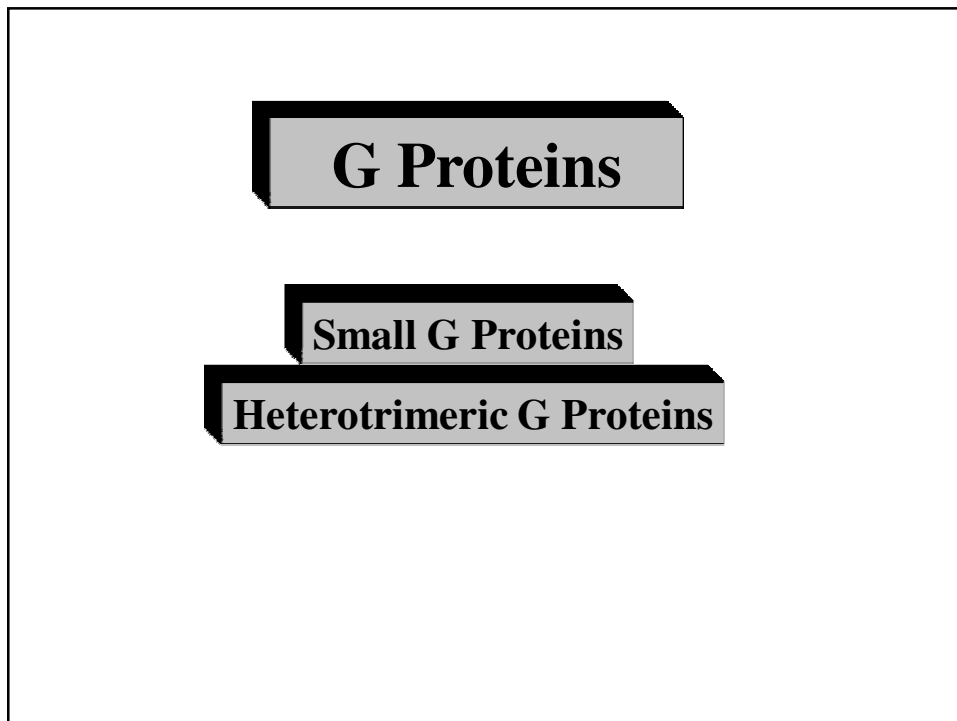
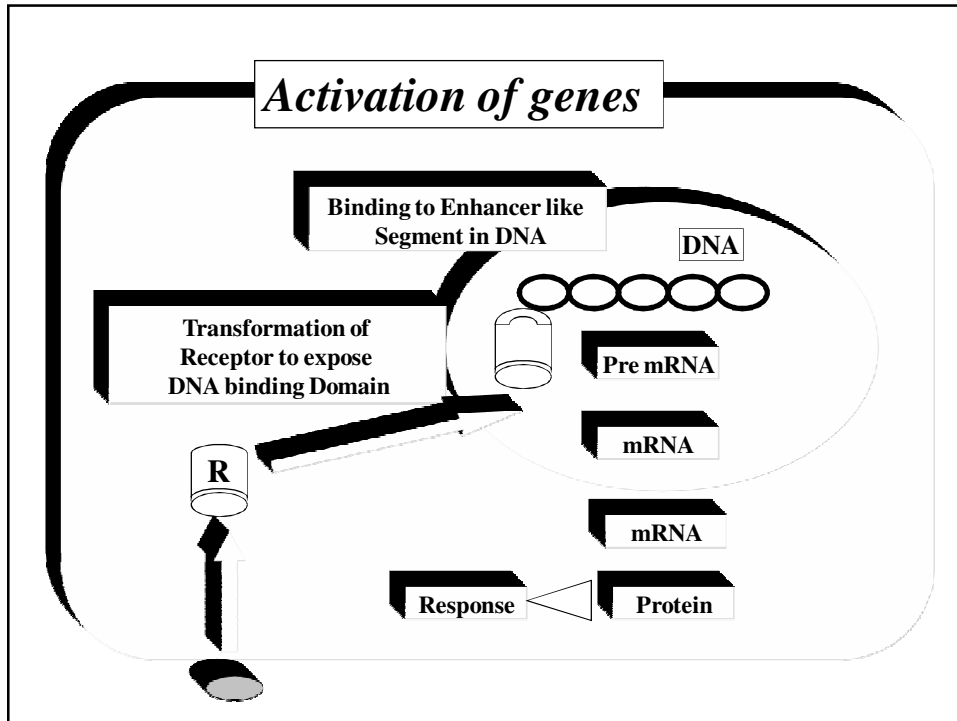
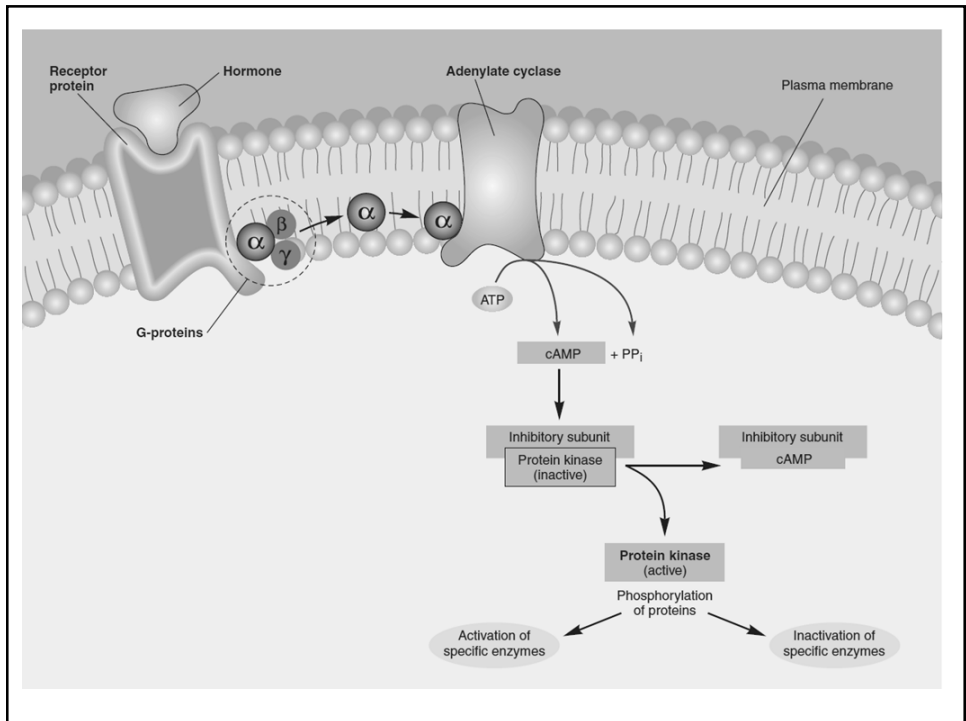
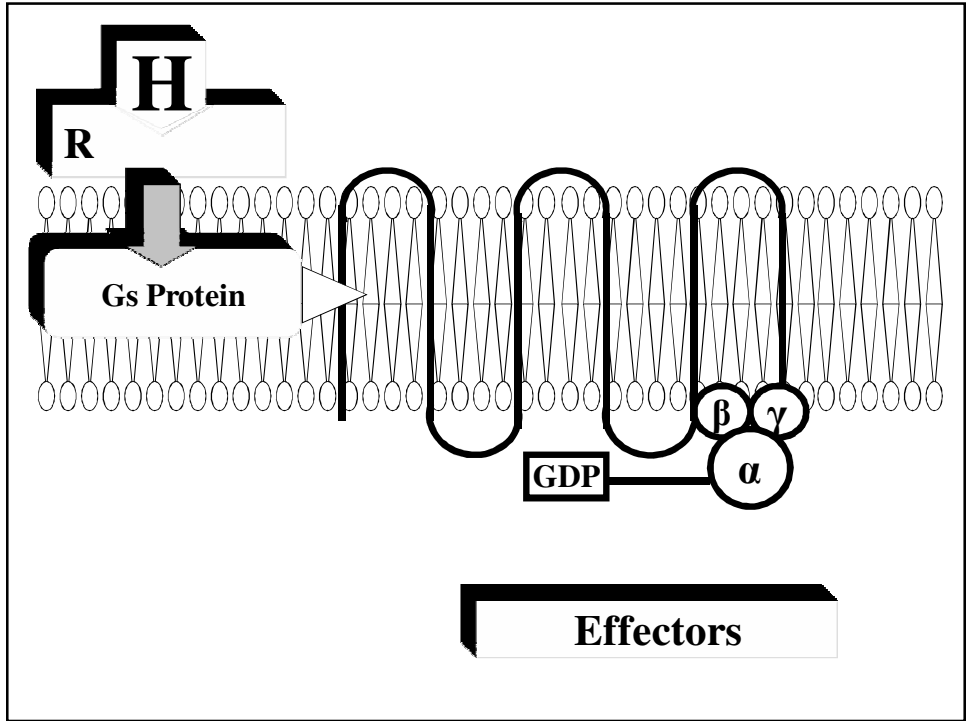


Table 74-3

Some Hormones That Use the Phospholipase C Second Messenger System

- Angiotensin II (vascular smooth muscle)
- Catecholamines (α receptors)
- Gonadotropin-releasing hormone (GnRH)
- Growth hormone-releasing hormone (GHRH)
- Oxytocin
- Thyroid-releasing hormone (TRH)
- Vasopressin (V_1 receptor, vascular smooth muscle)





STORAGE, SYNTHESIS, SECRETION

- **STORAGE**
 - Polypeptide and Proteins are stored in Secretory Vesicles
 - Steroid Hormones are usually not stored
- **SYNTHESIS**
- **SECRETION** Bursts, Volleys, spurts

SYNTHESIS OF PEPTIDES

Ribosomes on Rough ER

Prepro Hormones
Large inactive protein molecules

**Cleaved in
Endoplasmic Reticulum**

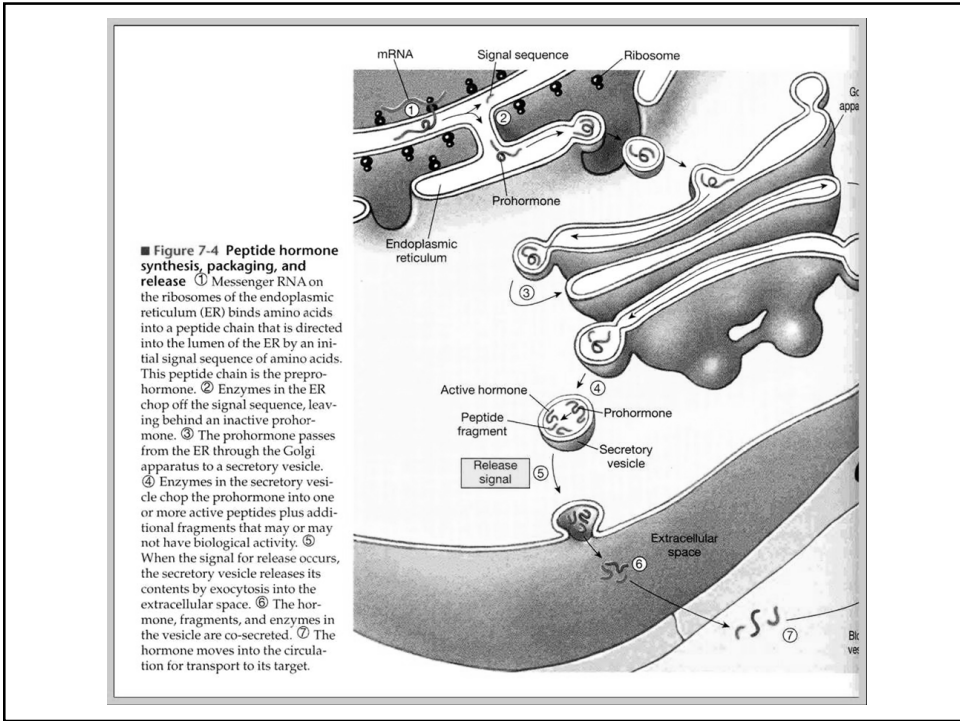
Pro Hormones

**Packed in Golgi App to
Secretory Vesicles**

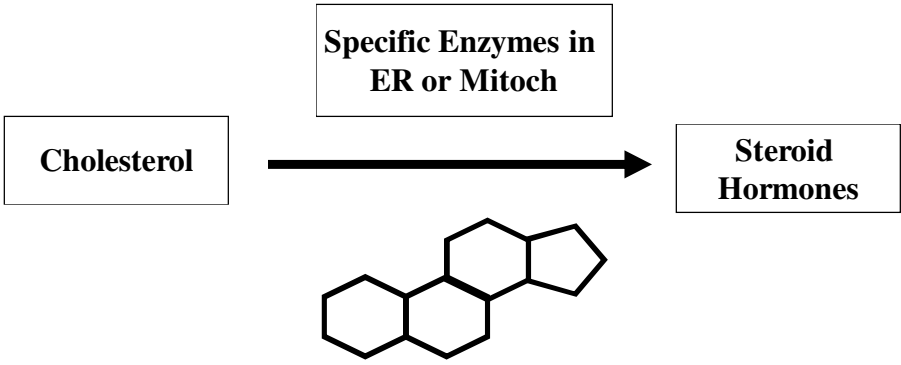
**Active Hormones
Inactive Fragments**

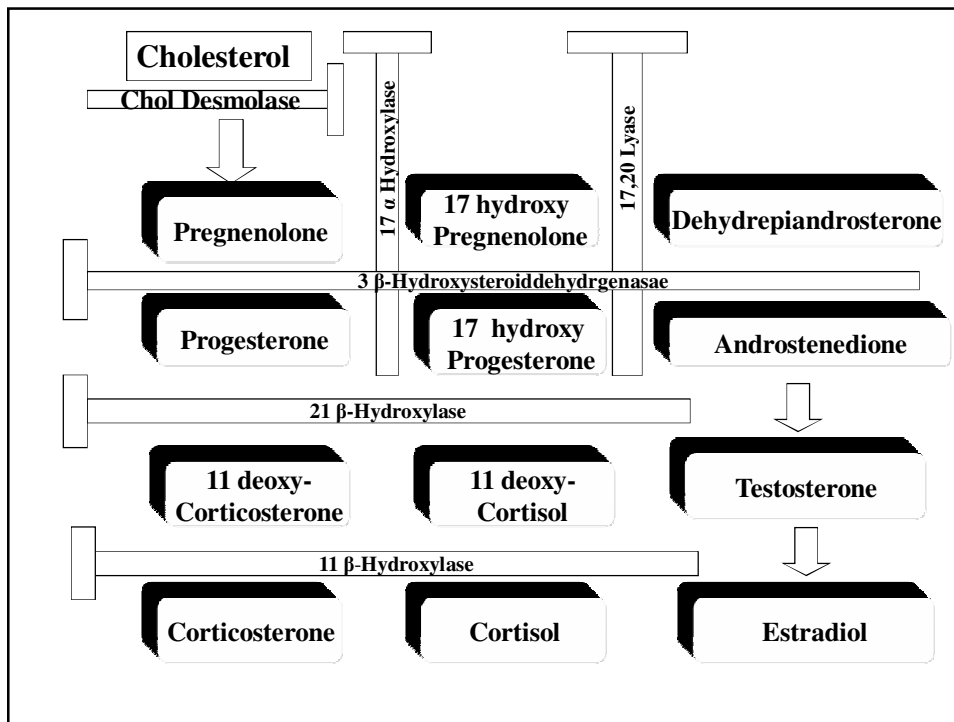
Exocytosis

Active Hormones



SYNTHESIS OF STEROIDS

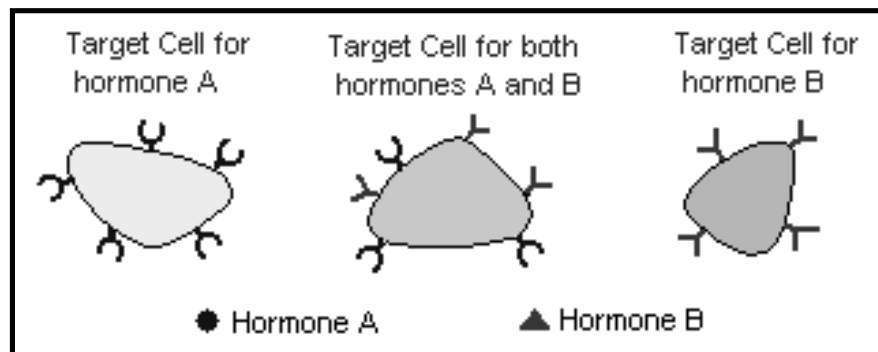




CHARACTERISTICS

- A single endocrine gland may produce multiple hormones (eg: Pituitary)
- A single hormone may be produced by more than one endocrine gland (Somatostatin by hypoth & Pancreas)
- A single hormone can have more than one type of target cells and can induce more than one type of effect (Vasopressin)
- A single target cell may be influenced by more than one hormone (Insulin & Glucagon actions on liver)
- Same chemical substance can be a hormone and neurotransmitter (eg: Norepinephrine)
- Organs can be exclusively endocrine or mixed (Pancreas)
- Some hormones have two names (Somatostatin & GHIH)

HORMONE ACTIONS



HORMONE ACTIONS

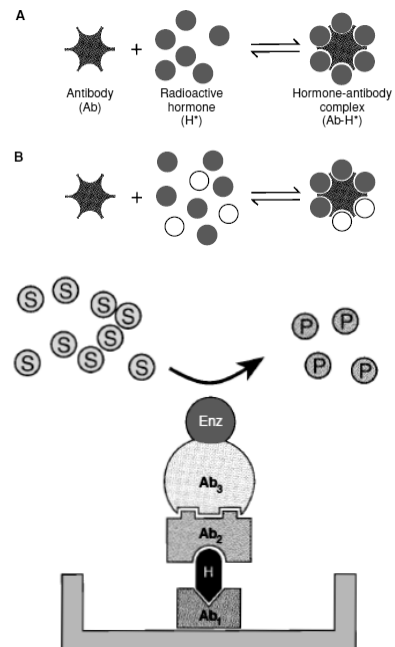
- **Tropic & Non Tropic**
- **Permissive (eg: Thyroid H for GH)**
- **Synergism (Potentiating)**
- **Additive**
- **Agonist and Antagonist**
- **Down Regulation (Desensitization)**
- **Up Regulation (Priming Effect)**

ENDOCRINE DISORDERS

- **HYPOSECRETION**
 - Primary
 - Secondary
- **HYPERSECRETION**
 - Primary
 - Secondary
- **DECREASED TARGET CELL RESPONSIVENESS**

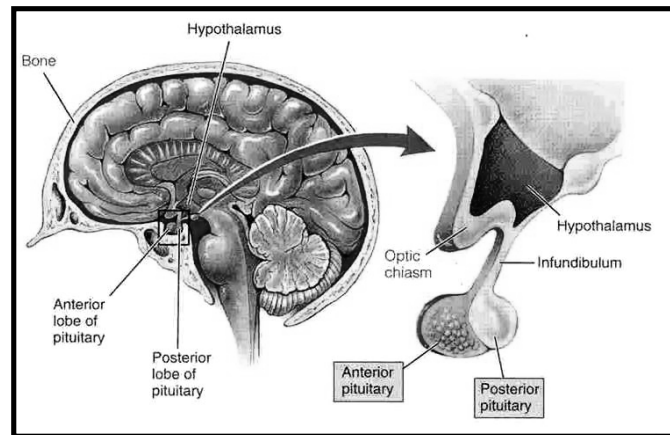
MEASUREMENT

- **Radioimmunoassay (RIA)**
- **Chemiluminescence**
- **Enzyme-linked immunosorbent assay (ELISA)**
- **Immunoradiometric assay (IRMA)**



SESSION TWO

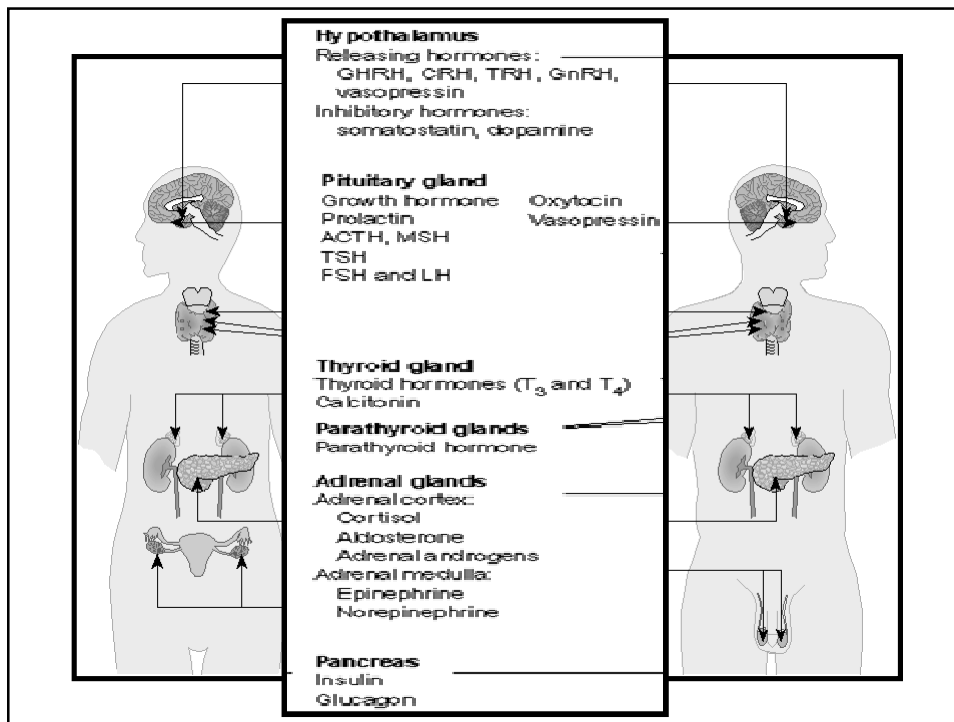
PITUITARY & HYPOTHALAMUS



OBJECTIVES

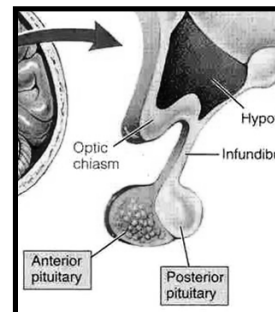
At the end of this Session you should be able to:

- *Describe the functional relationship between the pituitary and the hypothalamus.*
- *List the hormones of the anterior pituitary and explain how their secretion is regulated by the hypothalamus.*



PITUITARY

- Oval in Shape
- 8 mm anteroposteriorly
- 10-13 mm transversely
- 5 mm height
- 500 mg



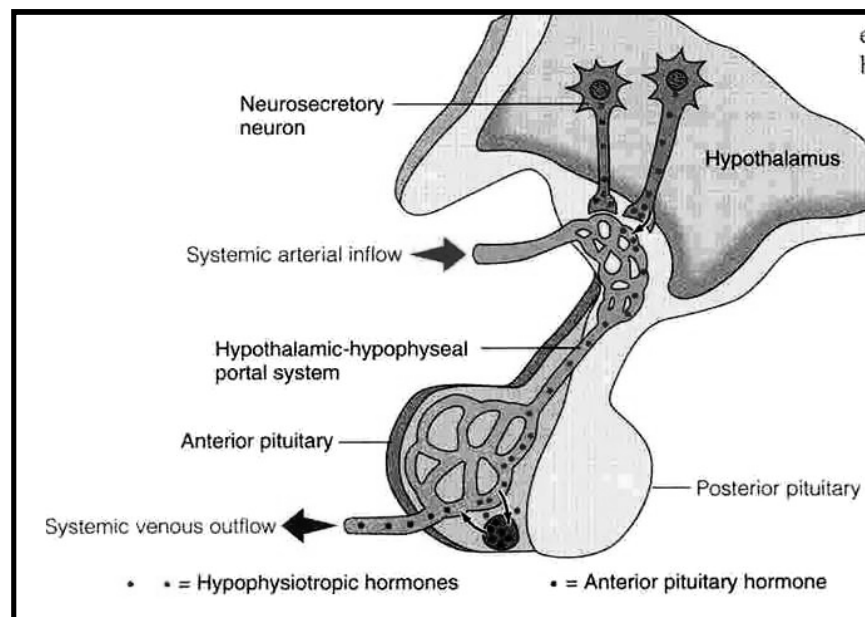
Pituitary gland consist of two lobes

Anterior (Adenohypophysis) originates from Rathke's pouch (pharyngeal epithelium)
Posterior (Neurohypophysis) originates from hypothalamus (glial-type cells)

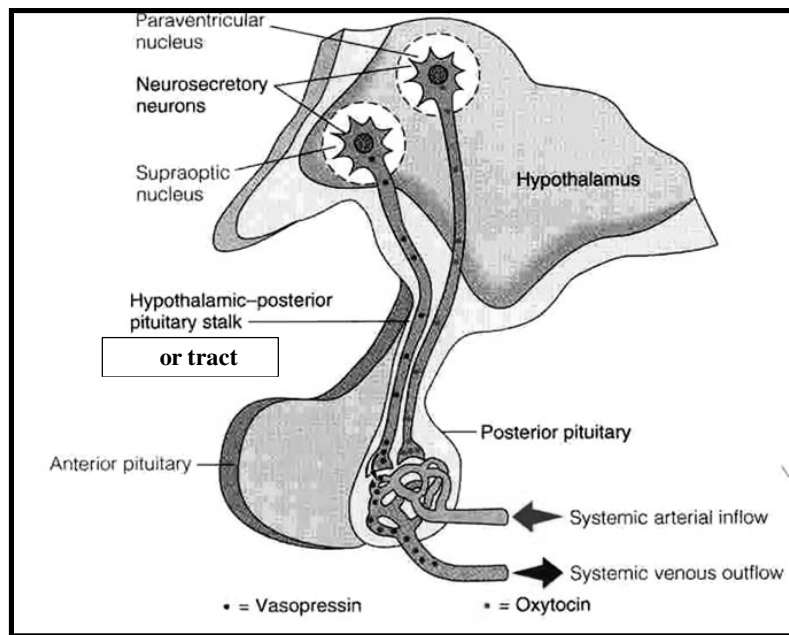
Hypothalamus Controls Pituitary Secretion

- Hypothalamic releasing and inhibitory hormones are conducted to the anterior pituitary through blood vessels called hypothalamic-hypophysial portal vessels.
- Nerve fibers carry hormones synthesized in the hypothalamus to the posterior pituitary

ANT PITUITARY & HYPOTHALAMUS



POST PITUITARY & HYPOTHALAMUS



Hormones of the Hypothalamus

- Thyrotropin-releasing hormone (TRH)
- Gonadotropin-releasing hormone (GnRH)
- Growth hormone-releasing hormone (GHRH)
- Growth hormone-inhibiting hormone (GHIH) also called Somatostatin
- Corticotropin-releasing hormone (CRH)
- Prolactin Inhibiting Hormone (PIH) Dopamine

Antidiuretic hormone (ADH) & Oxytocin are synthesized in hypothalamus and carried by neurosecretory neurons to be stored in post pituitary and released from there.

Table 75-2

Hypothalamic Releasing and Inhibitory Hormones That Control Secretion of the Anterior Pituitary Gland

Hormone	Structure	Primary Action on Anterior Pituitary
Thyrotropin-releasing hormone (TRH)	Peptide of 3 amino acids	Stimulates secretion of TSH by thyrotropes
Gonadotropin-releasing hormone (GnRH)	Single chain of 10 amino acids	Stimulates secretion of FSH and LH by gonadotropes
Corticotropin-releasing hormone (CRH)	Single chain of 41 amino acids	Stimulates secretion of ACTH by corticotropes
Growth hormone-releasing hormone (GHRH)	Single chain of 44 amino acids	Stimulates secretion of growth hormone by somatotropes
Growth hormone inhibitory hormone (somatostatin)	Single chain of 14 amino acids	Inhibits secretion of growth hormone by somatotropes
Prolactin-inhibiting hormone (PIH)	Dopamine (a catecholamine)	Inhibits secretion of prolactin by lactotropes

ANTERIOR PITUITARY HORMONES

- **Thyroid Stimulating Hormone (TSH)**
- **Gonadotropins**
 - **Follicle Stimulating Hormone (FSH)**
 - FSH in females
 - FSH in males
 - **Luteinizing Hormone (LH)**
 - LH in females
 - LH in males
- **Prolactin (PRL)**
- **Growth Hormone (GH)**
- **Adrenocorticotrophic Hormone (ACTH)**

PARS INTERMEDIA
 α β γ -MSH , γ LPH
no known effect

Hormones-secreting cells of the human anterior pituitary gland

5 Cell Type	Hormones Secreted	% of Total	Stain Affinity
Somatotrope	Growth hormone	50	Acidophilic
Lactotrope	Prolactin	(10-30)	Acidophilic
Corticotrope	ACTH, β -LPH	10	Basophilic
Thyrotrope	TSH	5	Basophilic
Gonadotrope	FSH, LH	20	Basophilic

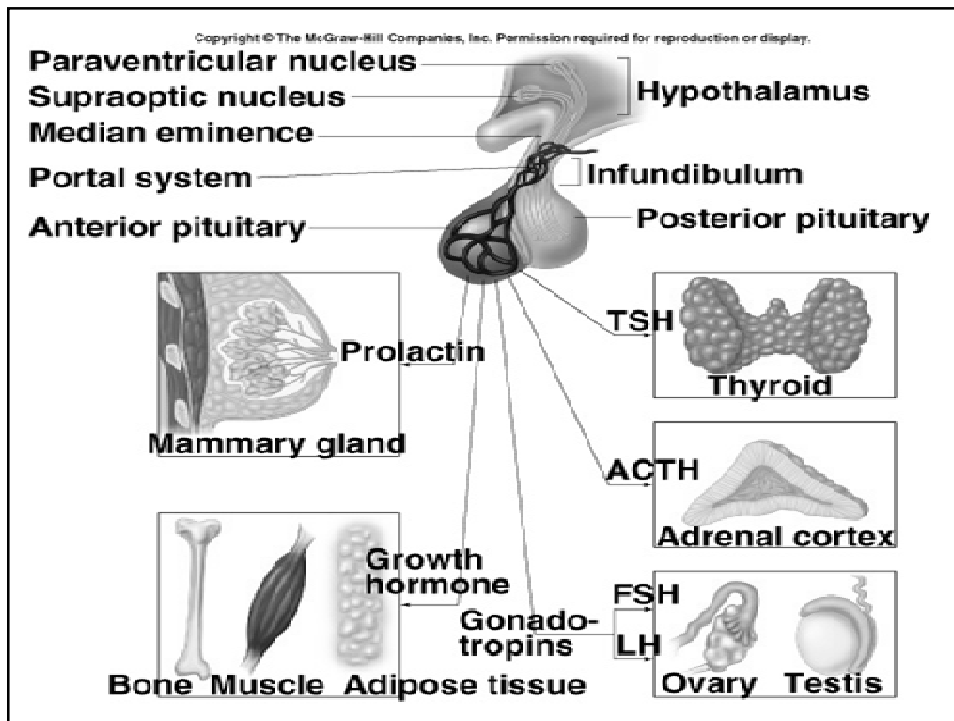
Chromophobes	<p>These are cells that have minimal or no hormonal content. may be acidophils or basophils that have degranulated may be stem cells that have not yet differentiated into hormone-producing cells.</p>
---------------------	---

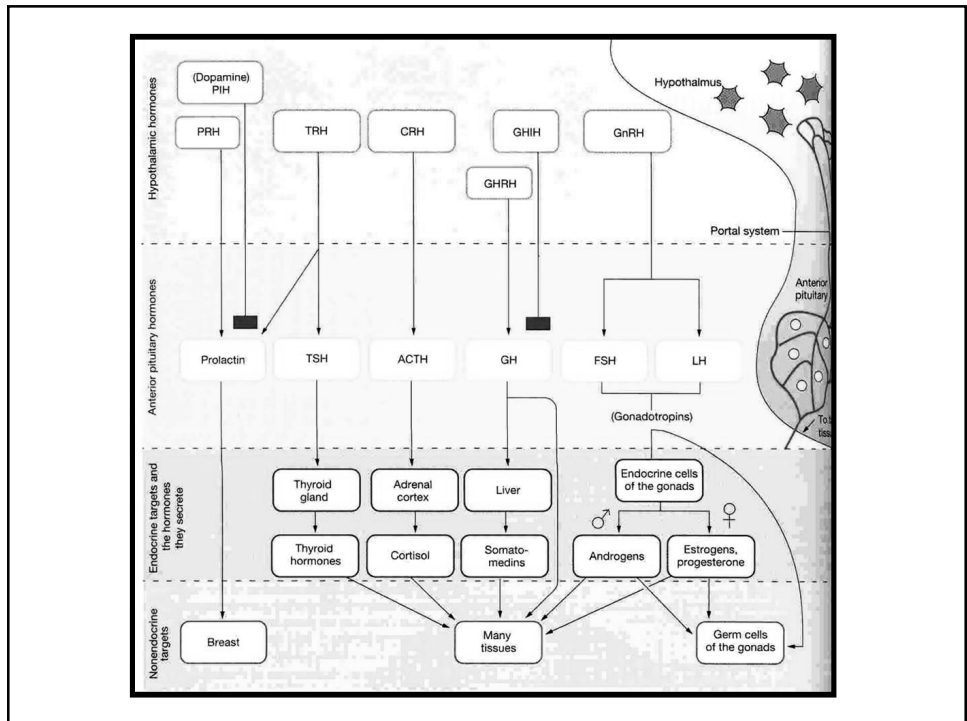
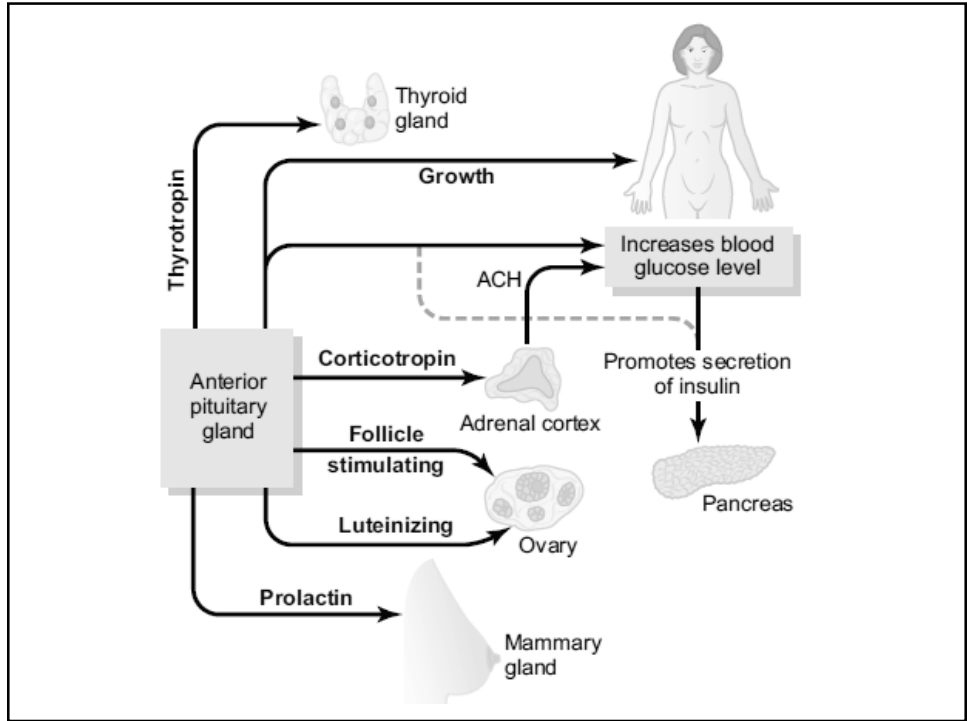
	Hormone	Major target organ(s)	Major Physiologic Effects
Anterior Pituitary	Growth hormone	Liver, adipose tissue	Promotes growth (indirectly), control of protein, lipid and carbohydrate metabolism
	Thyroid-stimulating hormone	Thyroid gland	Stimulates secretion of thyroid hormones
	Adrenocorticotrophic hormone	Adrenal gland (cortex)	Stimulates secretion of glucocorticoids
	Prolactin	Mammary gland	Milk production
	Luteinizing hormone	Ovary and testis	Control of reproductive function
	Follicle-stimulating hormone	Ovary and testis	Control of reproductive function
Posterior Pituitary	Antidiuretic hormone	Kidney, Blood Vessels	Conservation of body water
	Oxytocin	Ovary and testis	Stimulates milk ejection and uterine contractions

Table 75-1

Cells and Hormones of the Anterior Pituitary Gland and Their Physiological Functions

Cell	Hormone	Chemistry	Physiological Actions
Somatotropes	Growth hormone (GH; somatotropin)	Single chain of 191 amino acids	Stimulates body growth; stimulates secretion of IGF-1; stimulates lipolysis; inhibits actions of insulin on carbohydrate and lipid metabolism
Corticotropes	Adrenocorticotropic hormone (ACTH; corticotropin)	Single chain of 39 amino acids	Stimulates production of glucocorticoids and androgens by the adrenal cortex; maintains size of zona fasciculata and zona reticularis of cortex
Thyrotropes	Thyroid-stimulating hormone (TSH; thyrotropin)	Glycoprotein of two subunits, α (89 amino acids) and β (112 amino acids)	Stimulates production of thyroid hormones by thyroid follicular cells; maintains size of follicular cells
Gonadotropes	Follicle-stimulating hormone (FSH)	Glycoprotein of two subunits, α (89 amino acids) and β (112 amino acids)	Stimulates development of ovarian follicles; regulates spermatogenesis in the testis
	Luteinizing hormone (LH)	Glycoprotein of two subunits, α (89 amino acids) and β (115 amino acids)	Causes ovulation and formation of the corpus luteum in the ovary; stimulates production of estrogen and progesterone by the ovary; stimulates testosterone production by the testis
Lactotropes, Mammotropes	Prolactin (PRL)	Single chain of 198 amino acids	Stimulates milk secretion and production
	IGF, insulin-like growth factor		







SESSION THREE

ENDOCRINOLOGY
GROWTH HORMONE (hGH-N)
SOMATOTROPIN

OBJECTIVES

At the end of this Session you should be able to:

- *Describe the mechanism of action of GH*
- *Explain Direct and Indirect effects of Growth Hormone*
- *List factors which increase & decrease GH levels*
- *Describe regulation of GH Secretion*
- *Describe effects of hyper & hyposcretion*

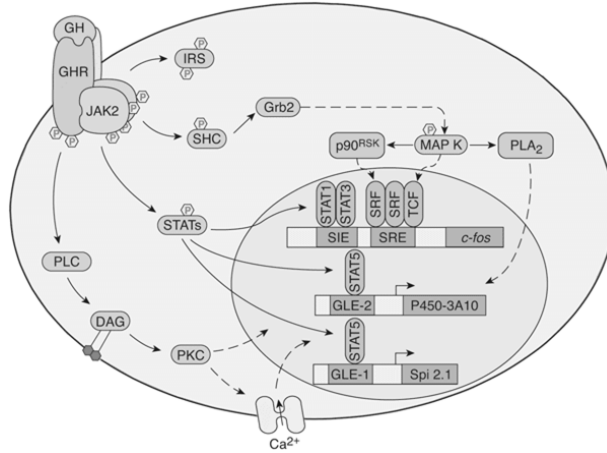
Growth Hormone (hGH-N) Somatotropin

- Source Anterior Pituitary
- Chemistry Protein 191 aa
 - hGH-N (75 %)
 - hGH-V
- Molecular Weight (22 K / 20 K)
- Half Life 6-20 min
- Daily Output 0.2-1 mg per day
- Basal Levels 3 ng/ml
- Transport Half Dissolved in Plasma and Half Protein Bound

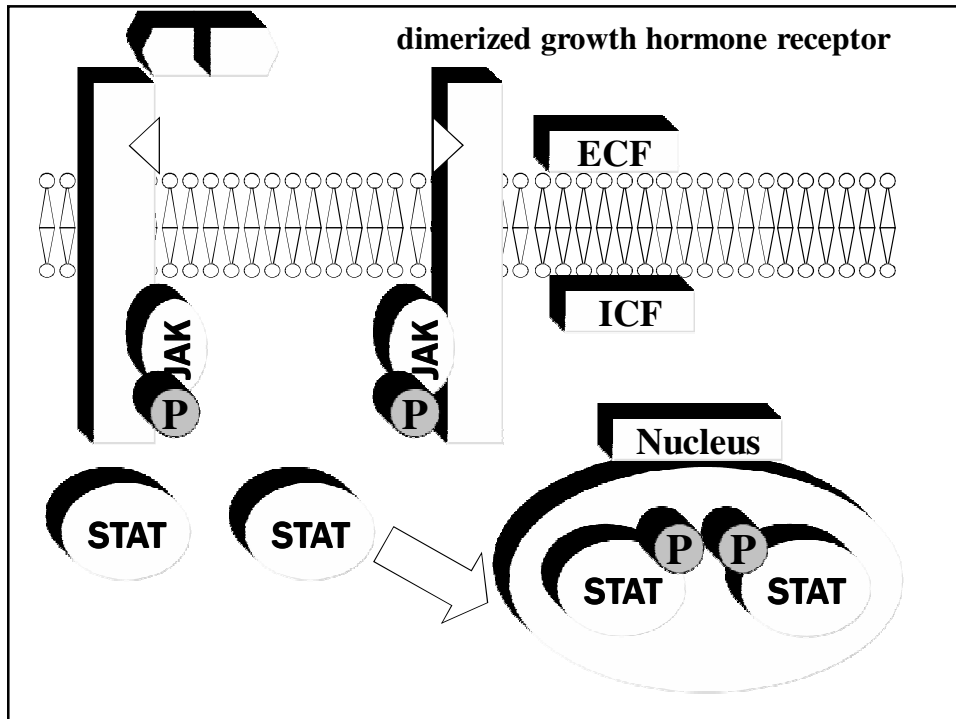
Chromosome 17

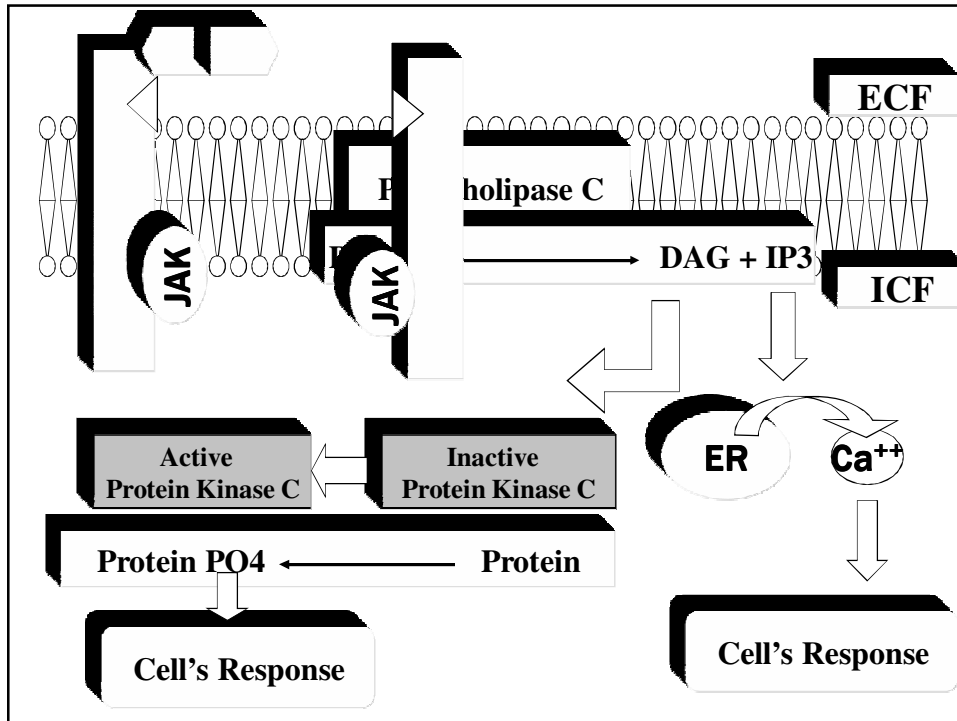


MECHANISM OF ACTION



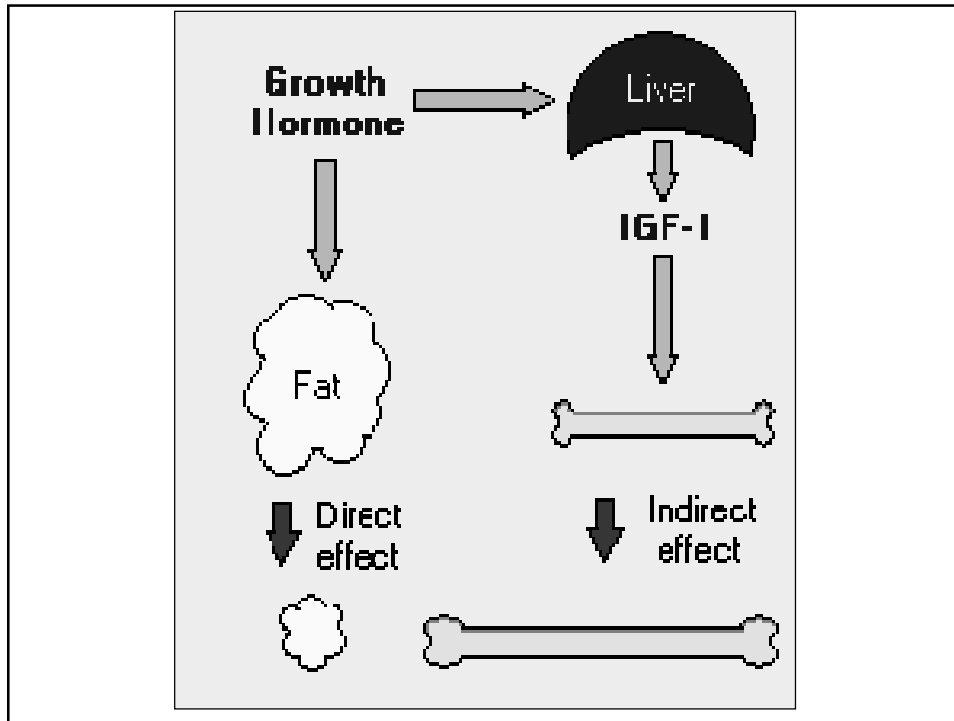
- Phospholipase C Pathway*
- JAK STAT Pathway*





Physiologic Effects of Growth Hormone

- **Direct effects are the result of growth hormone binding its receptor on target cells eg. Fats & Carbohydrates**
- **Indirect effects are mediated primarily by a insulin-like growth factor-1 (IGF-1) eg. On bones & Proteins**



GROWTH HORMONE (GH)

**binding to receptors on
the surface of liver cells**

**release insulin-like growthfactor-1
(IGF-1; also known as somatomedin)**

**IGF-1 acts on
bones, cartilage & proteins for growth**

A) Long term effects

Promotion of growth:

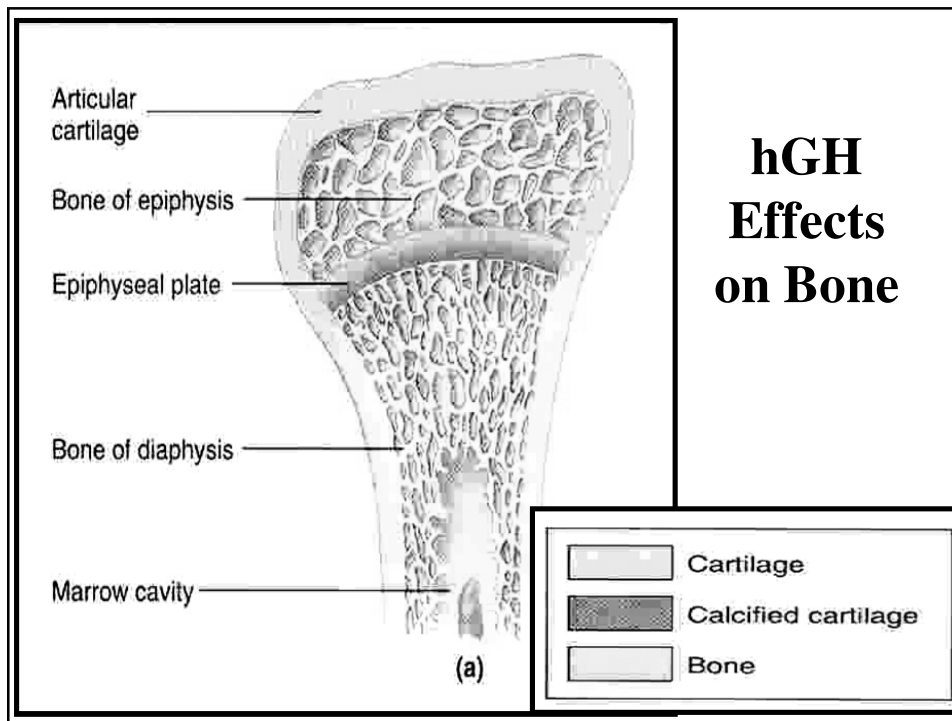
- ↑ cellular sizes & ↑ mitosis
- ↑ tissue growth & organ size

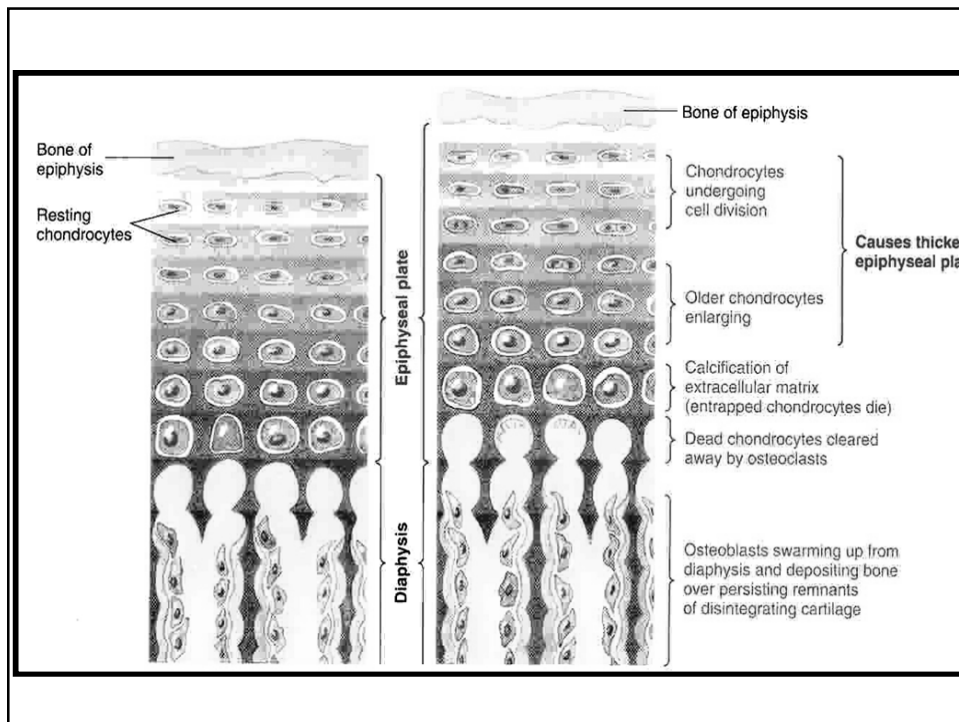
(Increased Chondrogenesis and Increased Osteoblastic activity)

Short term effects

Metabolic Effects on:

1. Carbohydrates
2. Proteins
3. Lipids





METABOLIC EFFECTS

Protein metabolism:

- Increased amino acid uptake
- Increased protein synthesis (↑ transcription & ↑ translation)
- Decreased catabolism of proteins

Protein anabolism
Positive Nitrogen and Phosphorus Balance
Increase in lean body mass

METABOLIC EFFECTS

Fat metabolism:

- **Release fatty acids from adipose tissue & conversion to acetyl CoA to provide energy**
- **Stimulate triglyceride breakdown and oxidation in adipocytes**

**Provides Fats as a Major Energy Source
Ketogenic effect**

METABOLIC EFFECTS

Carbohydrate metabolism:

- **Anti-insulin activity (\uparrow insulin resistance)**
- **Enhance hepatic glucose output (\uparrow gluconeogenesis)**
- **Decreases the number of insulin receptors**
- **Supresses uptake of glucose in peripheral tissues like skeletal muscle & fat**

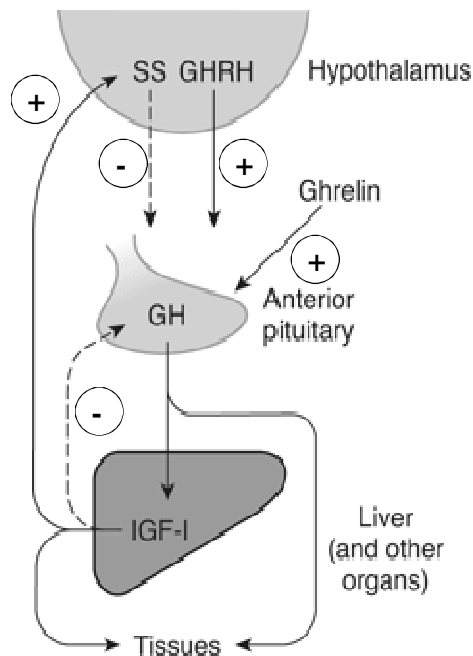
**Conservation of Glucose for Glucose dependant Tissues
Diabetogenic effect**

OTHER EFFECTS

- Increases calcium absorption from GIT
- Strengthens and increases the mineralization of bone
- Retention of Na^+ and K^+
- Increases muscle mass
- Stimulates the growth of all internal organs excluding the brain
- Contributes to the maintenance and function of pancreatic islets
- Stimulates the immune system

REGULATION & FEEDBACK

- Growth hormone-releasing hormone (GHRH)
Somatoliberin
- Growth hormone-inhibiting hormone
Somatostatin (SS)
- Ghrelin



DIURNAL RHYTHM

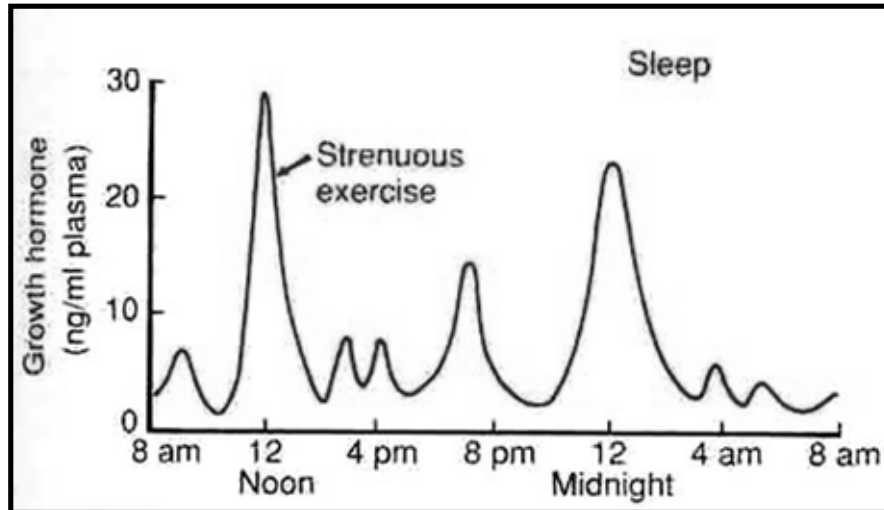


Table 75-3

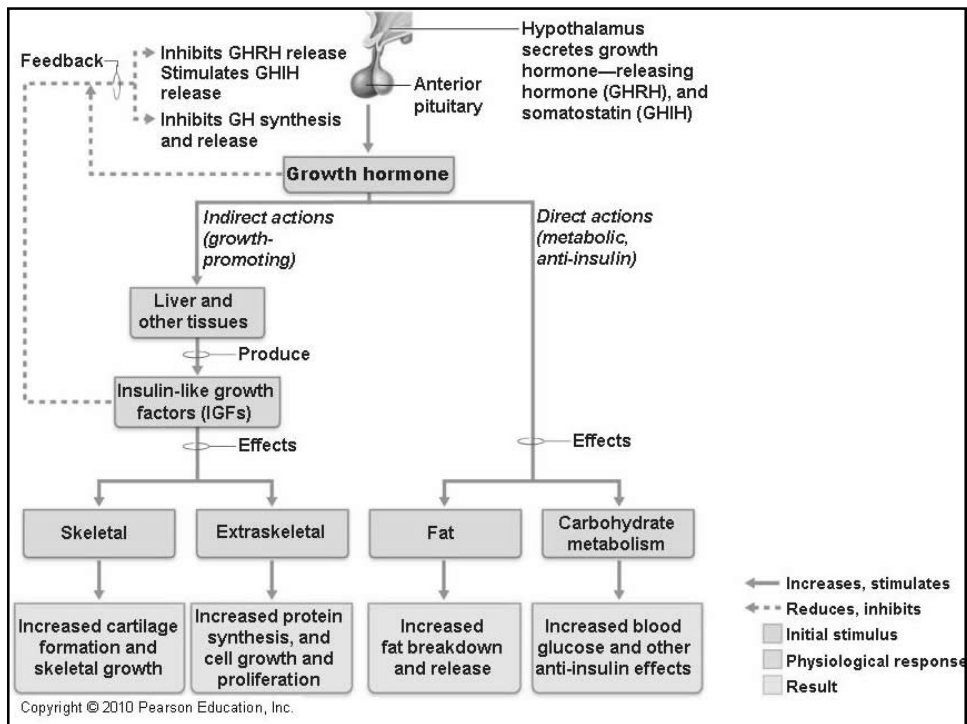
Factors That Stimulate or Inhibit Secretion of Growth Hormone

Stimulate Growth Hormone Secretion

Decreased blood glucose
 Decreased blood free fatty acids
 Starvation or fasting, protein deficiency
 Trauma, stress, excitement
 Exercise
 Testosterone, estrogen
 Deep sleep (stages II and IV)
 Growth hormone-releasing hormone

Inhibit Growth Hormone Secretion

Increased blood glucose
 Increased blood free fatty acids
 Aging
 Obesity
 Growth hormone inhibitory hormone (somatostatin)
 Growth hormone (exogenous)
 Somatomedins (insulin-like growth factors)



PHYSIOLOGY OF GROWTH

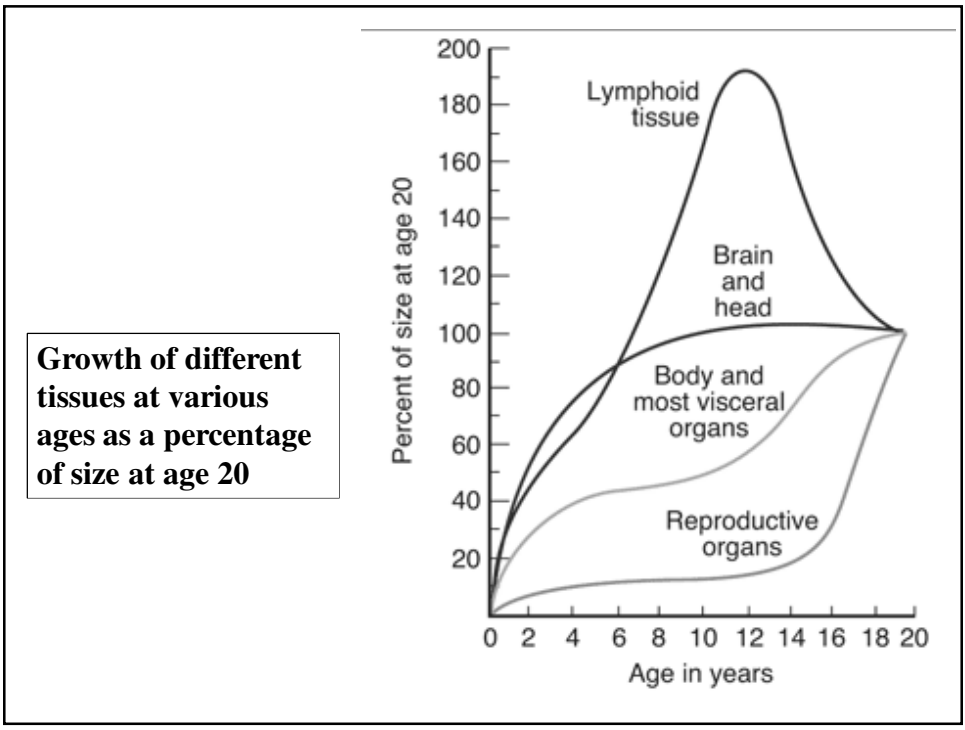
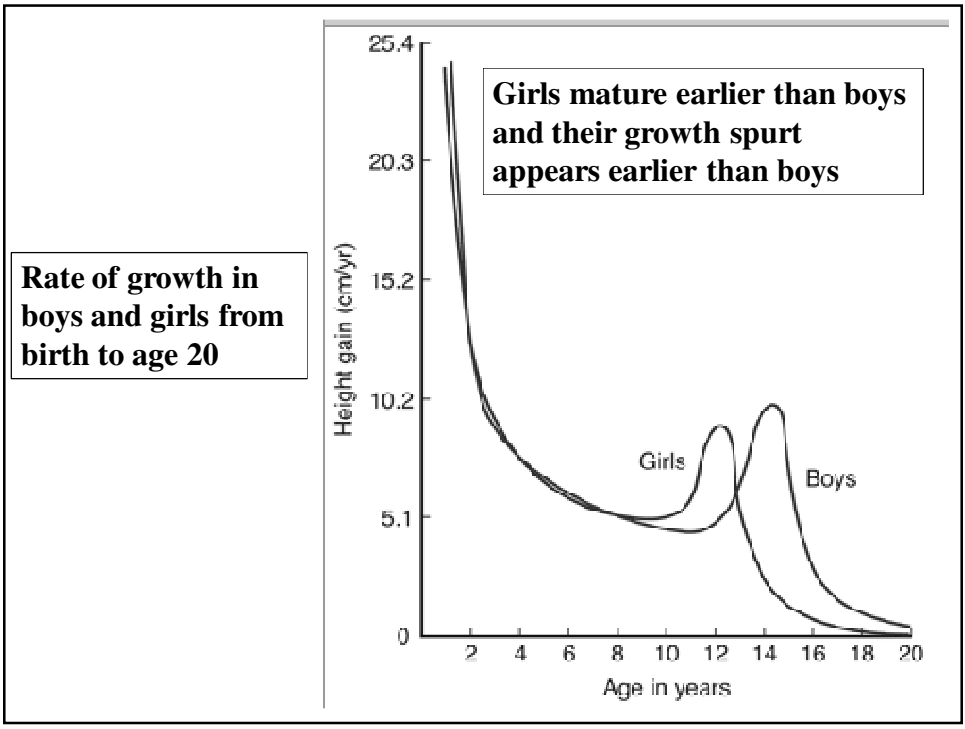
PHYSICAL

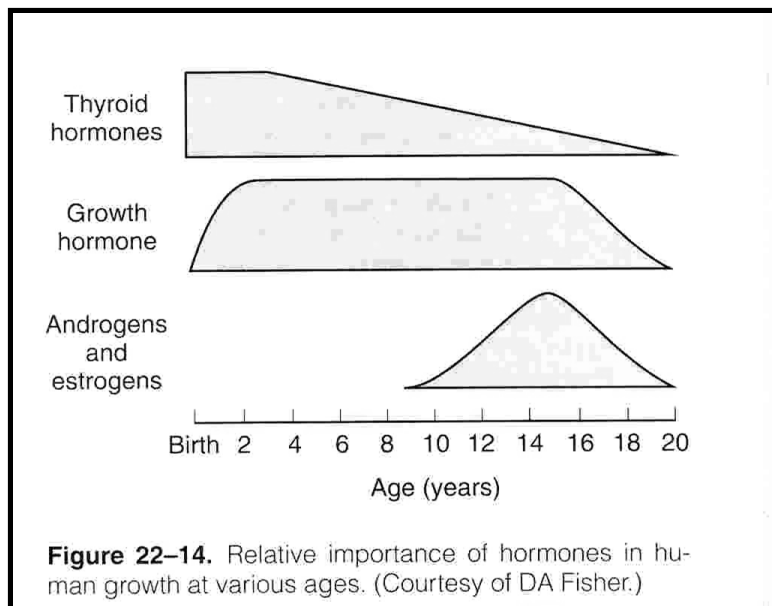
MENTAL

GONADAL

- **Genetic Determination**
- **Role of Nutrition**
- **Freedom from Chronic Diseases & Stress**
- **Hormonal Effects**
 - IGF-1 (Production depends on adequate nutrition)
 - Androgens and Estrogens
 - Thyroid Hormones
 - Insulin
 - Adrenocortical Hormones

Growth Periods & Catch-Up Growth





GROWTH HORMONE DISORDERS

- **Panhypopituitarism**
- **Dwarfism**
- **Laron dwarfism (GH Normal & IGF-I is markedly reduced)**
- **Gigantism**
- **Acromegaly**

Dwarfism

Failure to growth



Short stature

Mild obesity

Delayed puberty

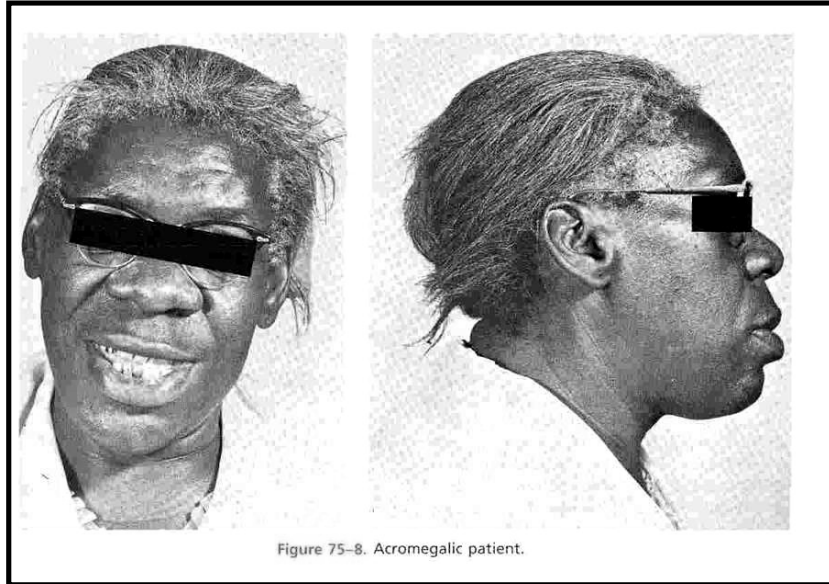


GIANTISM

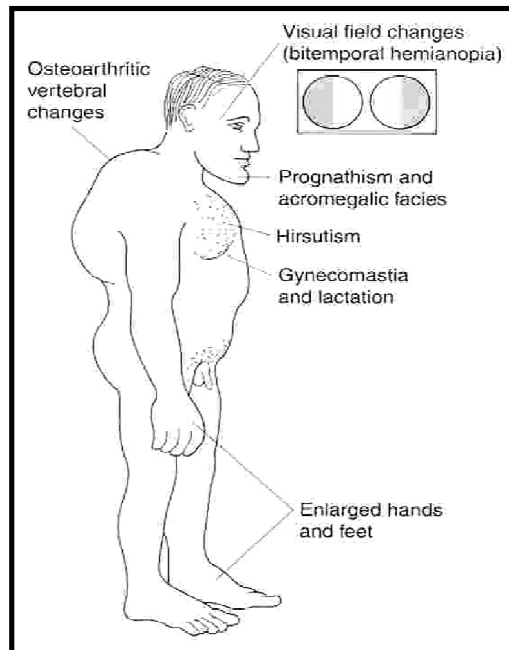
*Before
disappearance of
Epiphyseal plates*



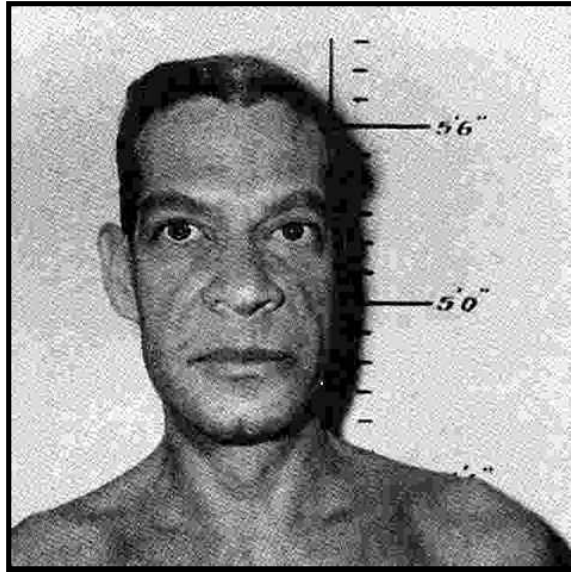
ACROMEGALY *After Adulthood*



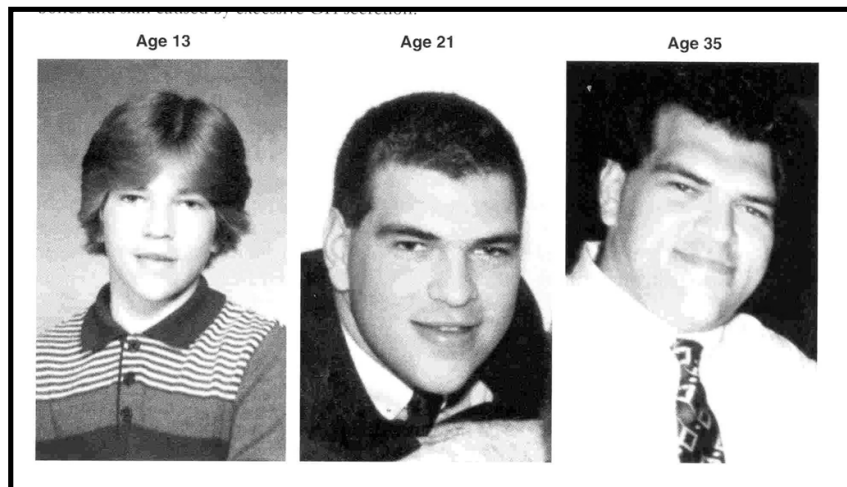
ACROMEGALY *After disappearance of Epiphyseal plates*

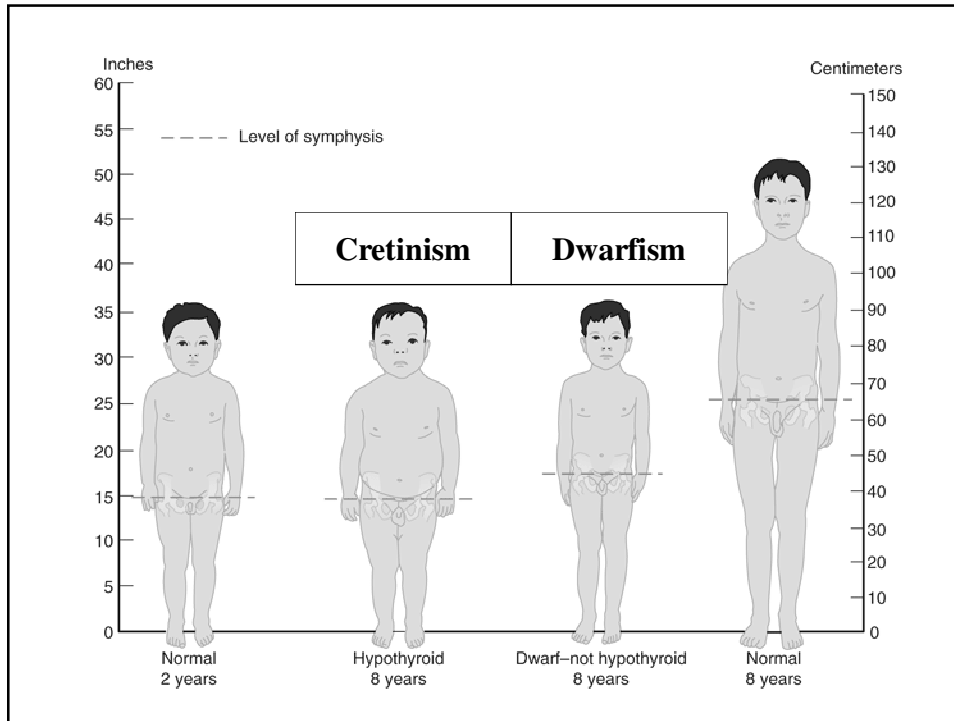


ACROMEGALY



ACROMEGALY





Prolactin

- **Source Anterior Pituitary**
- **Chemistry Protein 198 aa**
- **Effects Prolactin promotes mammary gland development and increases milk production**

