

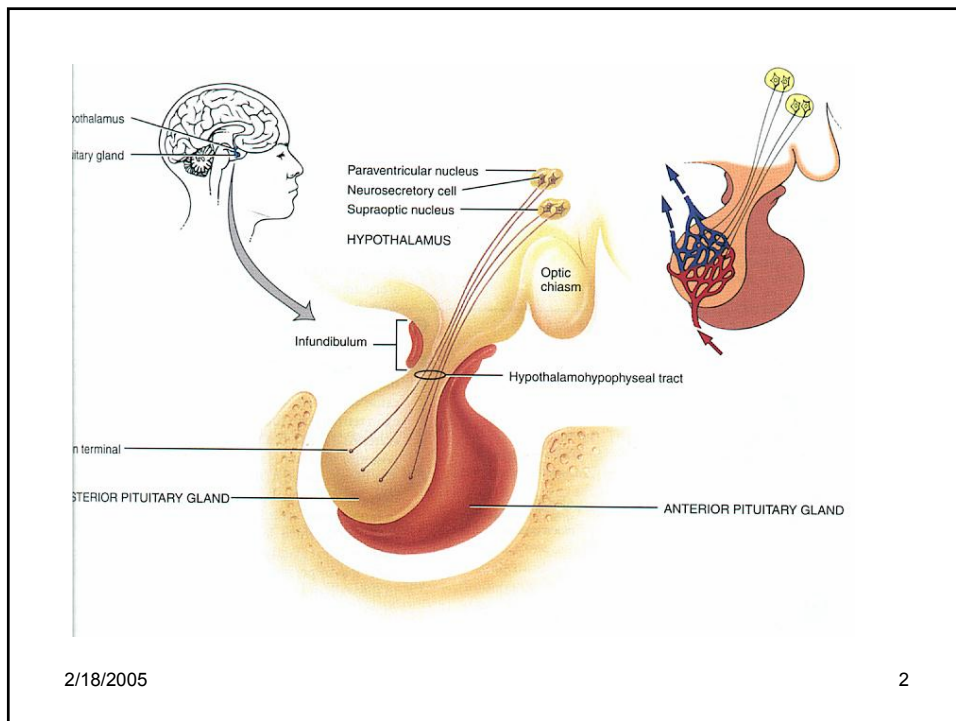
# PITUITARY GLAND

*Anterior (Adenohypophysis)*

*Rodolfo T. Rafael, MD.*

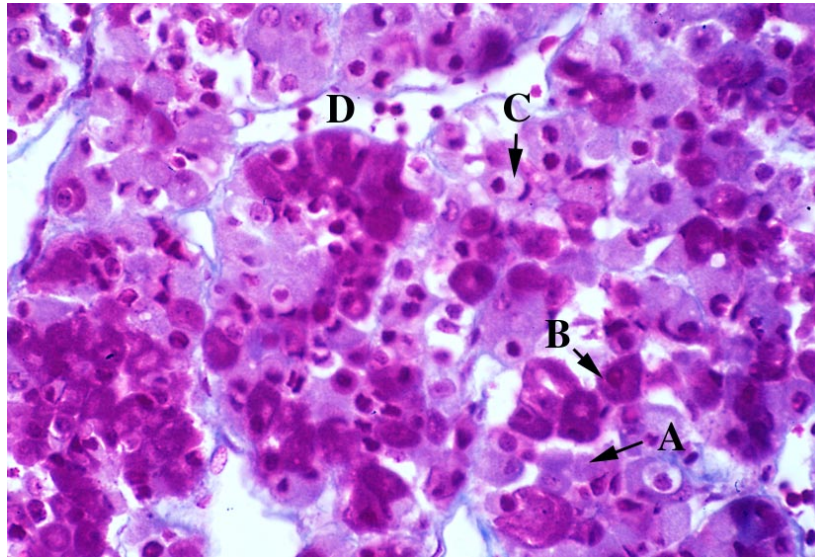
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- A basophil cell
- B acidophil cell
- C chromophobe cell
- D sinusoid

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## Eight Hormones

- Follicle Stimulating Hormone
- Luteinizing Hormone
- Prolactin
- Thyroid Stimulating Hormone
- Adrenocorticotrophic Hormone
- Growth Hormone
- Melanocyte Stimulating Hormone
- $\beta$ - lipoprotein

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# Eight Hormones

- Follicle Stimulating Hormone
  - FSH
  - regulation of follicular growth
  - spermatogenesis
  - GnRH
  - Inhibin



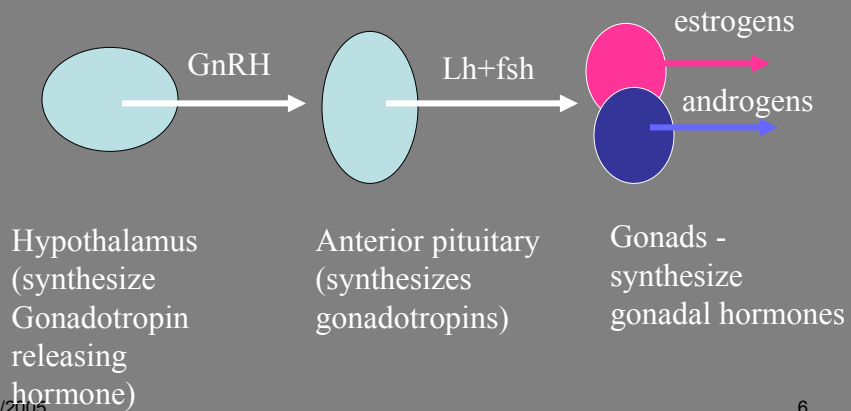
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## HORMONES AND REPRODUCTIVE PHYSIOLOGY

### HORMONAL CONTROL OVER GONADAL FUNCTION

An Overview:



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# Eight Hormones

- **Luteinizing Hormone**

- LH
- ovulation in the ovary
- androgen production



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# Eight Hormones

- **Prolactin**

- lactation
  - Estrogen
  - Progesterone
  - Oxytocin

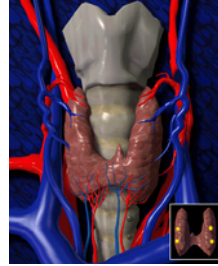


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# Eight Hormones

- Thyroid Stimulating Hormone
  - TSH
  - stimulates thyroid secretion and growth

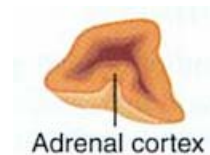


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# Eight Hormones

- Adrenocorticotrophic Hormone
  - ACTH
  - stimulates the secretion of glucocorticoids and mineralocorticoid
  - steroidogenesis

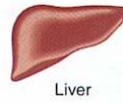


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## Eight Hormones

- Growth Hormone
  - GH
  - statural growth of many tissues



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## Eight Hormones

- Melanocyte Stimulating Hormone
  - MSH
  - involve in skin darkening



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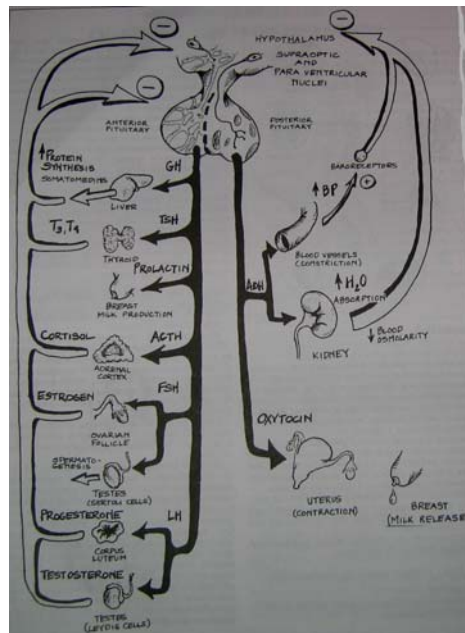
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# Eight Hormones

- $\beta$ - lipoprotein
  - latest to be discovered
  - physiologic role is not yet clearly defined.
  
- mobilizing fatty tissue
- Opiate compounds
  - B- endorphins
  - enkephalins

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# HISTOLOGY

- Adenohypophysis contains cell types responsible for the secretion of hormones.
  - Chromophils
    - Somatotrophic
    - Lactotrophic
    - Corticotrophic
    - Thyrotrophic
    - Gonadotrophic
  - Chromophobes
    - Amphophil

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# CHROMOPHILS

- granular
- Divided into
  1. Somatotrophic cells
    - rounded or ovoid, acidophilic cells
  2. Lactotrophic or Mammotrophic cells
    - larger than S, acidophilic
  3. Corticotrophic cells
    - basophilic, secretes ACTH, MSH,  $\beta$ -LP
  4. Thyrotrophic cells
    - basophilic, TSH, hypertropied
  5. Gonadotrophic cells
    - a. FSH- large rounded, basophilic
    - b. LH – smaller, scant cytoplasm, basophilic

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# CHROMOPHOBES

- Undifferentiated precursors
- Amphophil cells
  - small granules with variable staining characteristics

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# GROWTH HORMONES

- A. Species Specificity
- B. Effects on Somatic Growth
- C. Metabolic Functions
- D. Regulation of Secretion

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# GROWTH HORMONES

## A. Species Specificity

- ☀ single chain polypeptide
- ☀ 191 amino acid
- ☀ mw 22,005
- ☀ 2 disulfide bridges
- ☀ half-life 20- 30 minutes

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# GROWTH HORMONES

## Effects on Somatic Growth

### A. Deficits of Growth Hormone

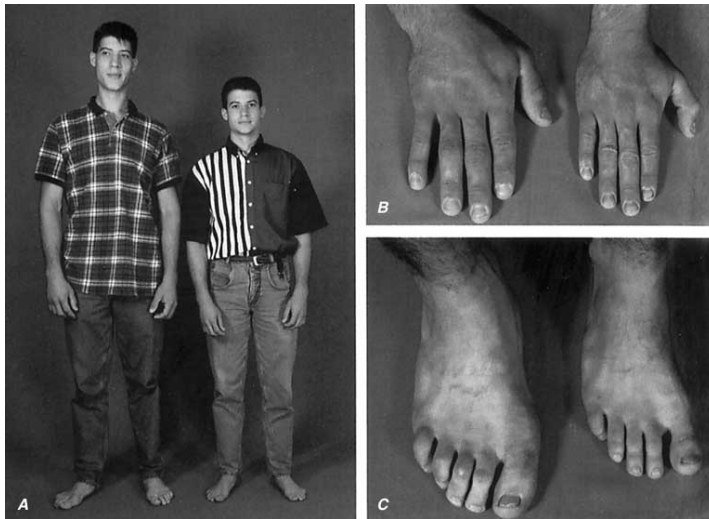
- a. Hypopituitarism or lack of growth hormones
- b. PROPORTIONAL DWARFISM

### B. Excesses of Growth Hormone

- a. GIGANTISM
  - before puberty
- b. ACROMEGALY
  - after epiphyseal closure
  - coarsening of many body features

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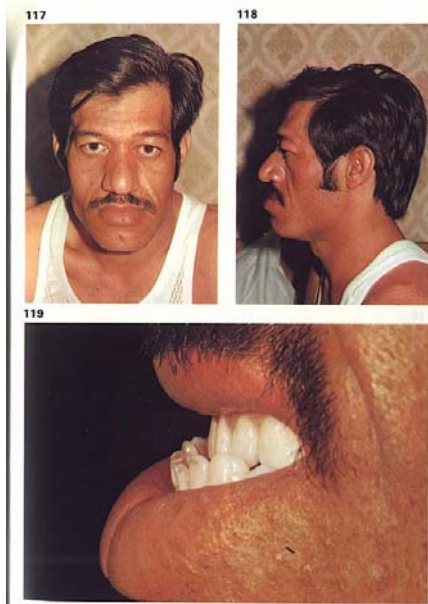
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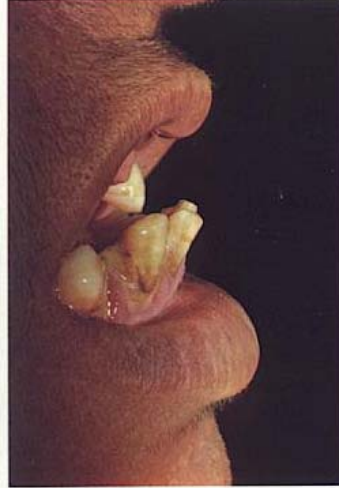
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## GROWTH HORMONES

Metabolic Functions

- A. Protein and Cartilage
- B. Carbohydrates
- C. Fats

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# GROWTH HORMONES

## Metabolic Functions

### A. Protein and Cartilage

1. Anabolic hormone
  - result in positive nitrogen balance and growth
  - + amino acid transport
  - enhance protein and nucleic acid synthesis by the ribosomes
  - increase formation of RNA
  - decrease catabolism of protein and amino acid
2. Maintenance of Calcium,  $PO_4$ , K, Na
3. Exert major effects on Cartilage and Growth of Long Bones
  - thought to be mediated by a "sulfation factor" or SOMATOMEDIN-promotes cartilage growth

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# GROWTH HORMONES

## Metabolic Functions

### B. Carbohydrates

- diabetogenic effect
  - increase hepatic glucose output
  - exerts anti- insulin effect
- raises the levels of glucose-6- phosphate

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# GROWTH HORMONES

## Metabolic Functions

### C. Fats

- increase lipolysis
- elevate levels of plasma- free fatty acid
  - ketogenesis

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# GROWTH HORMONES

## Regulation of Secretion

- Secretion of GH is controlled by 2 releasing factors
- Stimuli which will stimulate GH secretion
- Hormones that Influence GH

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# GROWTH HORMONES

## Regulation of Secretion

- *Secretion of GH is controlled by 2 releasing factors*
  1. Growth- Hormone Releasing Factor or Somatotropin Releasing Factor (SRF)
  2. Growth- Hormone Inhibitory Factor or Somatotropin Inhibitory Factor (SRIF)
- No specific feedback regulation

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# GROWTH HORMONES

## Regulation of Secretion

- Stimuli which will stimulate GH secretion
  1. Hypoglycemia
  2. Arginine
  3. Stressful stimuli (pyrogen, lysine, vasopressin, various psychological stresses)
  4. Sleep
  5. L-dopa

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# GROWTH HORMONES

## Regulation of Secretion

- Hormones that Influence GH
  1. Thyroxine
  2. Cortisol
  3. Estrogen
  4. Somatotropin
  5. SRF
    - The activity of serum response factor (SRF), an essential transcription factor
    - **Serum response factor is crucial for actin cytoskeletal organization and focal adhesion assembly in embryonic stem cells**

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# TSH

- A. Structure
- B. Half Life and Metabolism
- C. Actions
- D. Mechanism of Action
- E. Regulation of Secretion

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# TSH

## A. Structure

- Glycoprotein ( glucosamine, galactosamine and sialic acid)
- MW 28,000
- 2 chains ( $\alpha$  and  $\beta$ )
- TSH-L
- Functional specificity conferred by the beta unit

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# TSH

## B. Half Life and Metabolism

- ✓ 30 minutes
- ✓ destroyed by proteolytic enzymes (destruction in the circulation and elsewhere)

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# TSH

## C. Actions

- ❖ increases proteolysis of the thyroglobulin
- ❖ increases the activity of the iodide pump
- ❖ increases iodination of thyrosine and coupling to form thyroid hormone
- ❖ increases size and secretory activity of thyroid cells
- ❖ increases number of thyroid cells

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# TSH

## D. Mechanism of Action

- Circulating TSH binds to specific receptor sites on the thyroid cell membrane
- ® coupled to adenylyl cyclase
- intracellular cyclic AMP increase → function as the intracellular mediator of the diverse effects of TSH on the Thyroid

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# TSH

## E. Regulation of Secretion

1. The primary feedback of thyroxine is on the pituitary
  - dose related to both TRF and thyroxine levels, either is capable of breaking through the other
  - TRF shown to release TSH
  - Increasing doses of Thyroxine inhibit TRF response
2. TRF has a specific receptor site on thyrotropin cell membranes
3. The thyroxine feedback requires new DNA and protein synthesis

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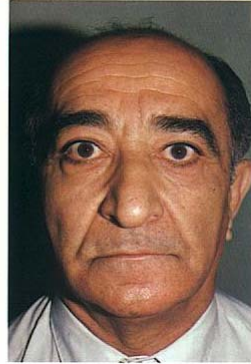
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## ACTH

- A. Structure
- B. Circadian Rhythm
- C. Regulation of Secretion
- D. Actions

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# ACTH

## A. Structure

- single open chain polypeptide
  - 39 amino acids
  - first 20-24 amino acid from the N- terminal
- $\alpha$  and  $\beta$  MSH share peptide sequences with ACTH
  - $\alpha$  MSH same with the first 13 amino acid of ACTH
  - $\beta$  MSH shares a sequence with both ACTH and  $\alpha$  MSH
  - synthetic ACTH has the ability to elicit skin darkening
- ACTH excess----- elevation of  $\beta$  MSH
- Immunological staining of pituitary cells indicate that ACTH,  $\beta$ -MSH and  $\beta$ -Lipoprotein are present in the same cell
  - $\beta$ - Lipoprotein – precursor molecule of  $\beta$ -MSH and the endorphins which interact with the opiate receptors.
  - Both ACTH and  $\beta$ - Lipoprotein secreted from the AP in response to stress
  - The  $\beta$ - endorphin  $\rightarrow$  enkephalins (morphine like activity at times of stress)
- ACTH has no blood protein carrier
- Half- life 15 minutes

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# ACTH

## Circadian Rhythm

- secretion follows diurnal pattern
  - peak occurs in the early morning hours
  - followed within few moments by a peak of cortisol from the adrenal cortex
  - progressive decline (lowest late evening)
- evaluating adrenal cortical function in health and disease and in using adrenal corticosteroids therapeutically

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# ACTH

## Regulation of Secretion

### 1. Negative Feedback Mechanism

- if plasma cortisol levels are lowered → increase in ACTH
- CRF stimulates ACTH synthesis and secretion → increase ACTH → stimulate the adrenal cortex → increase cortisol

### 2. CNS

- Circadian Rhythm
- Stress- raises ACTH levels and endogenous cortisol

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# ACTH

## Actions

### 1. On Adrenal Cortex

- regulates steroid hormone production by the adrenal cortex, including adrenal androgen
- maintains the structure of adrenal cortex, and serve as growth stimulus
- Permissive role on aldosterone

### 2. On Fat Cells

- ACTH stimulates cyclic AMP production and subsequent lipolysis from adipose tissue

### 3. On Skin

- ACTH has MSH-activity leading to hyperpigmentation

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# Prolactin

- A. Source
- B. Nature
- C. Biologic Action
- D. Regulation of Secretion

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# Prolactin

## SOURCE

1. Adenohypophysis
  - Lactotrops markedly increased during pregnancy and lactation
2. Ectopic Production
  - neoplastic origin (hyperprolactinism)

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# Prolactin

## NATURE

- single open- chain polypeptide
- high degree of overlap with GH (30%) and also with placental lactogen

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# Prolactin

## Biologic Action

- Mammatrophic and lactogenic
- Induction of binding sites for testosterone in the human prostate

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# Prolactin

## Regulation of Secretion

- The secretion of prolactin is under dual control; (PRF- PIF)
- Estrogen – via positive feedback promote prolactin secretion (dual action decrease in PIF and an increase in pituitary prolactin synthesis)
- Suckling stimulus- goes rapidly to the hypothalamus through a reflex
- Plasma prolactin level increase during sleep, after stress and exercise.

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# FSH and LH

- A. Source
- B. Nature
- C. Biological Action (Synergism)
- D. Mechanism of Action
- E. Regulation of Gonadotropin
- F. Metabolism and Excretion of Gonadotropins

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# FSH and LH

## SOURCE

- Adenohypophysis- gonadotrophins
- Postmenopausal urine
- Ectopic production

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# FSH and LH

## NATURE

- Glycoprotein containing hexose, mannose, hexosamine, fructose and sialic acid
- Both are made-up of an alpha and beta subunit

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# FSH and LH

## Biological Action (Synergism)

### 1. FSH

- follicular growth in the ovary (granulosa cell proliferation)
- Stimulates secretion of estradiol by the ovarian follicular complex
- Important in control of spermatogenesis in testicular tubules

### 2. LH

- Steroidogenesis
  - Interstitial and stroma cells
  - Ovarian follicles (maturation-synergistic- FSH)
  - Leydig cells of testis
- Luteinization (granulosa and theca cells)
- Ovulation (mature follicles)
- Corpus Luteum (function and steroidogenesis)

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# FSH and LH

## Mechanism of Action

- FSH and LH exert their action on gonadal tissue via adenylyl cyclase cyclic-AMP system.

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# FSH and LH

## Regulation of Gonadotropins

- Hypothalamic FSH-RF and LH-RF
- CNS
  - pituitary mechanisms
  - Periodic CNS signal
  - Episodic FSH-RF and LH-RF release into portal vessel catecholamine as mediator
  - Pulsatile discharge of FSH and LH by the patients
- Modulation by gonadal steroids (will be discussed in reproductive endo).

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# FSH and LH

## Metabolism and Excretion of Gonadotropins

### A. Plasma Half-life

- LH= 30 minutes
- FSH= 3 hours

### B. Survival time of glycoprotein dependent on their Sialic acid content

### C. Liver and Kidney

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# CLASSIFICATION OF PITUITARY DISEASE

## Anterior Lobe

### 1. OVERACTIVITY

- a. Gigantism
- b. Acromegaly
- c. Pituitary basophilism (Cushing's Disease)

### 2. DEFICIENCY

- a. Dwarfism
- b. Pituitary cachexia (Simmond's Diseases
- c. Acromicria

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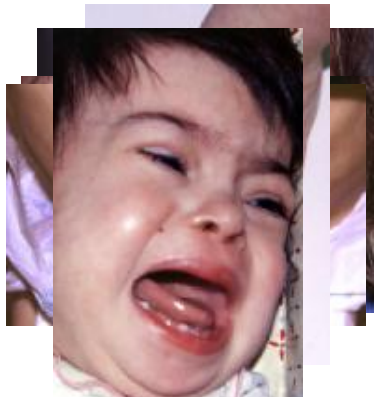


- statue of Robert V  
ever recorded. He

was the tallest person  
the time of his death.

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THANK YOU!

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