

# Pituitary Gland Disorders

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# Normal Anatomy & Function

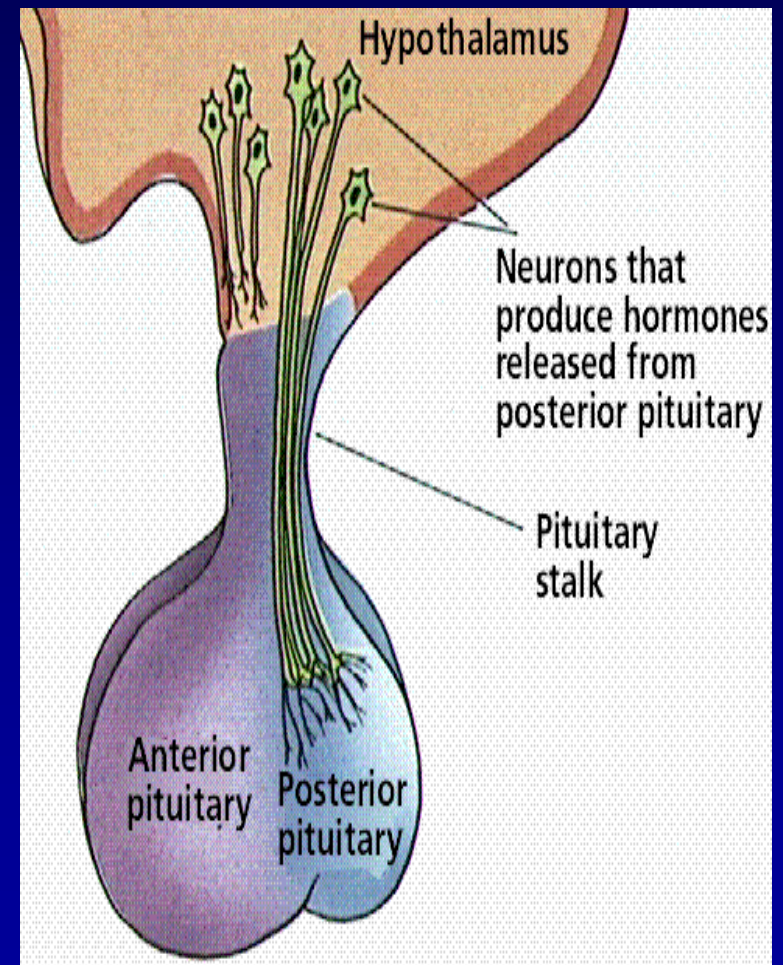
- The pituitary is located at the base of the brain, in a small depression of the sphenoid bone (sella turcica).
- Purpose: control the activity of many other endocrine glands.

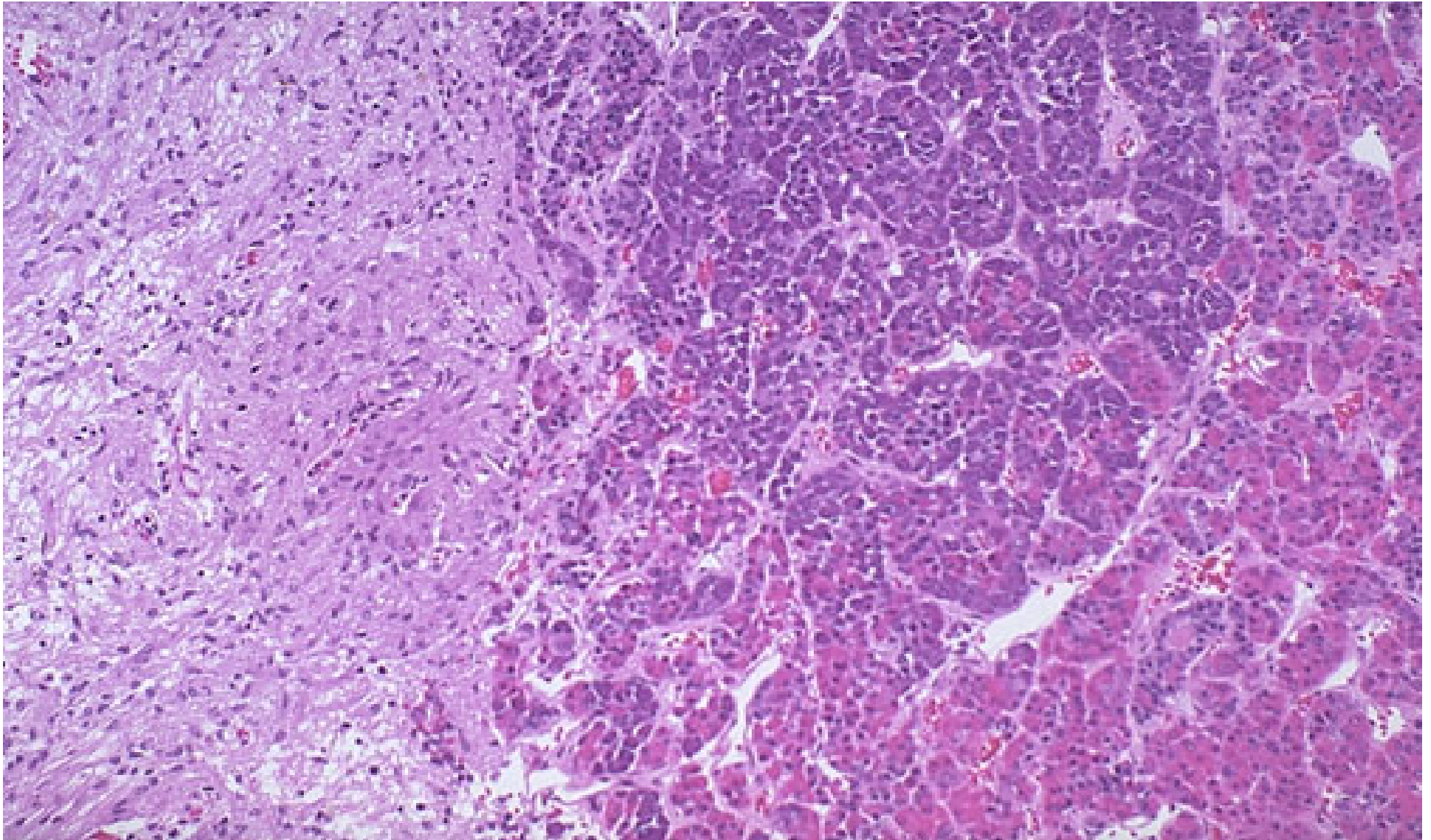
## “Master gland”

- Has two lobes, the anterior & posterior lobes.

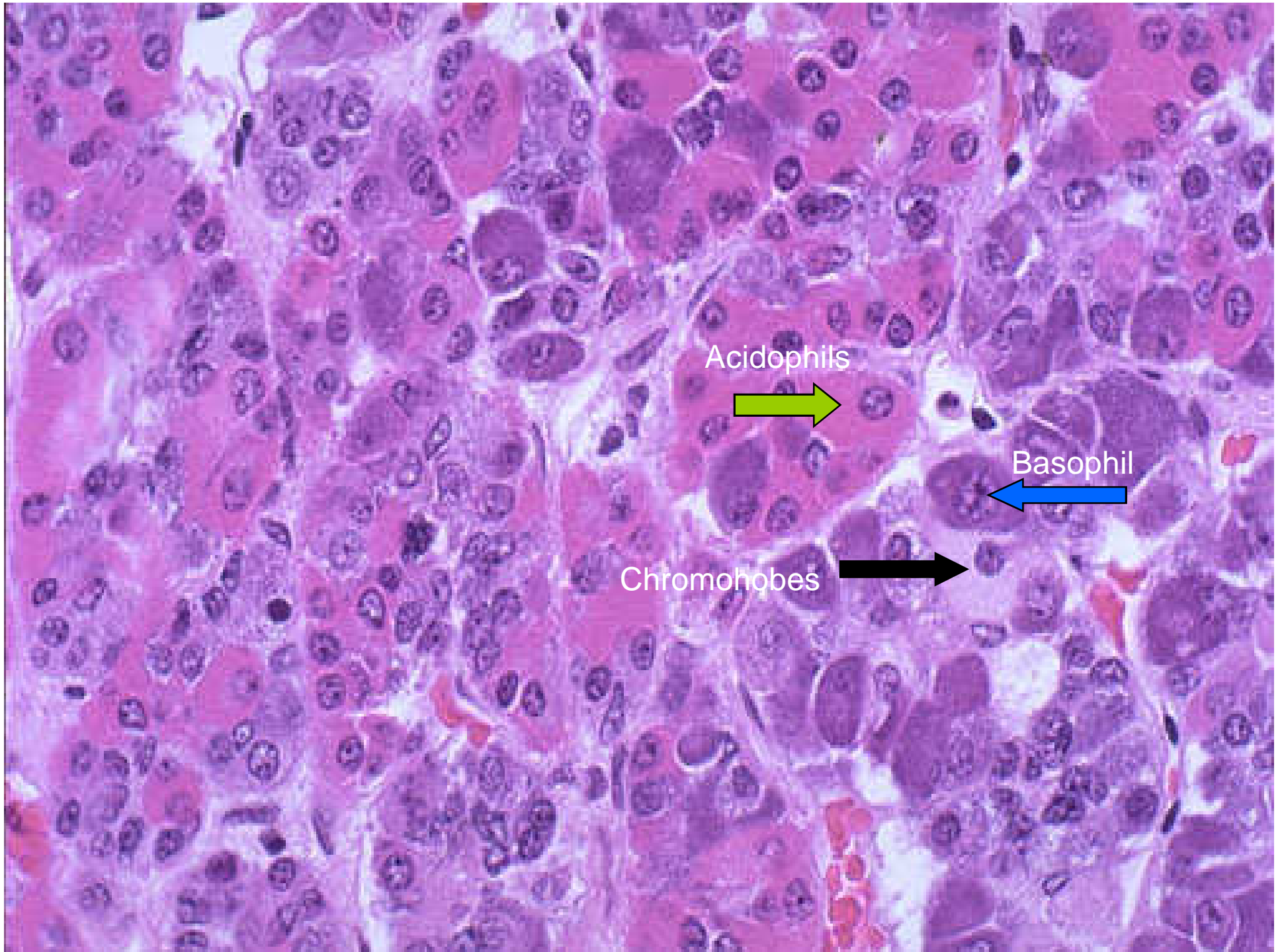
# Anatomy

- **Anterior lobe:** glandular tissue, accounts for 75% of total weight. Hormones in this lobe are controlled by **regulating** hormones from the hypothalamus (stimulate or inhibit)
- **Posterior:** nerve tissue & contains axons that originate in the hypothalamus. Therefore this lobe does not produce hormones but stores those produced by the neurosecretory cells in the hypothalamus. Release of hormones is triggered by receptors in the hypothalamus.





**The normal microscopic appearance of the pituitary gland is shown here. The adenohypophysis is at the right and the neurohypophysis is at the left.**



Acidophils

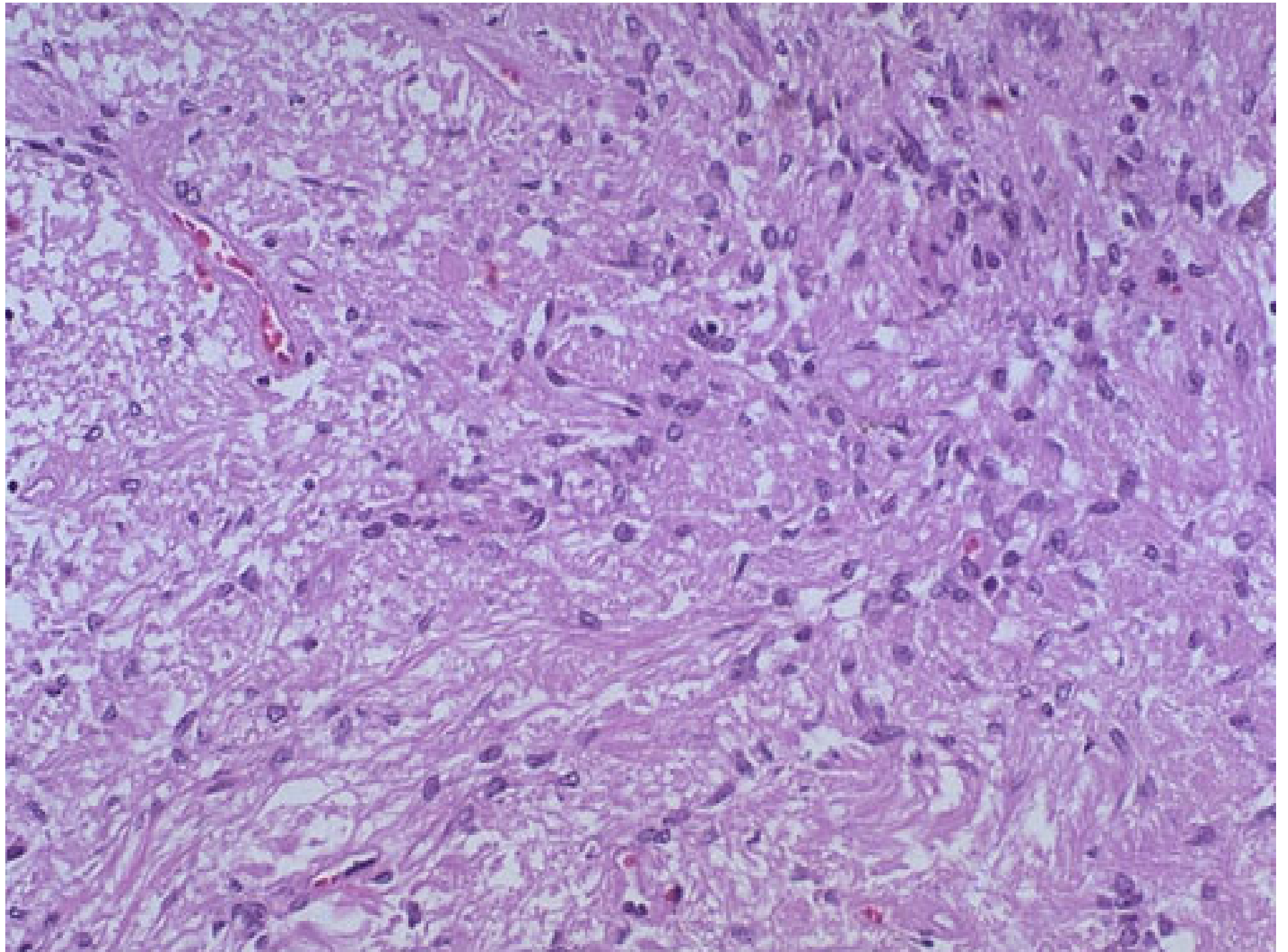


Basophil



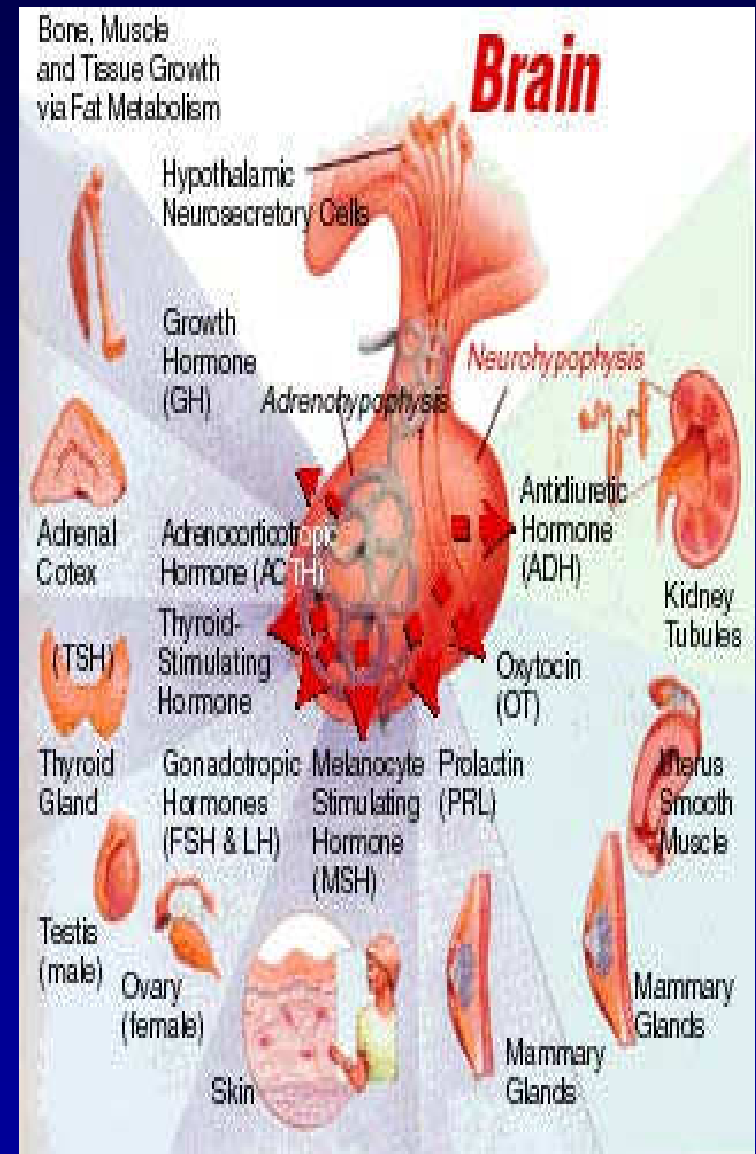
Chromophobes





# Terms

- **Trophic hormones:** hormones that control the secretion of hormones by other glands. Example: TSH stimulates the thyroid to secrete hormones.
- **Effector hormones:** produce an effect directly when secreted. Example ADH stimulates kidneys



# Review - Hormones

## Anterior Pituitary

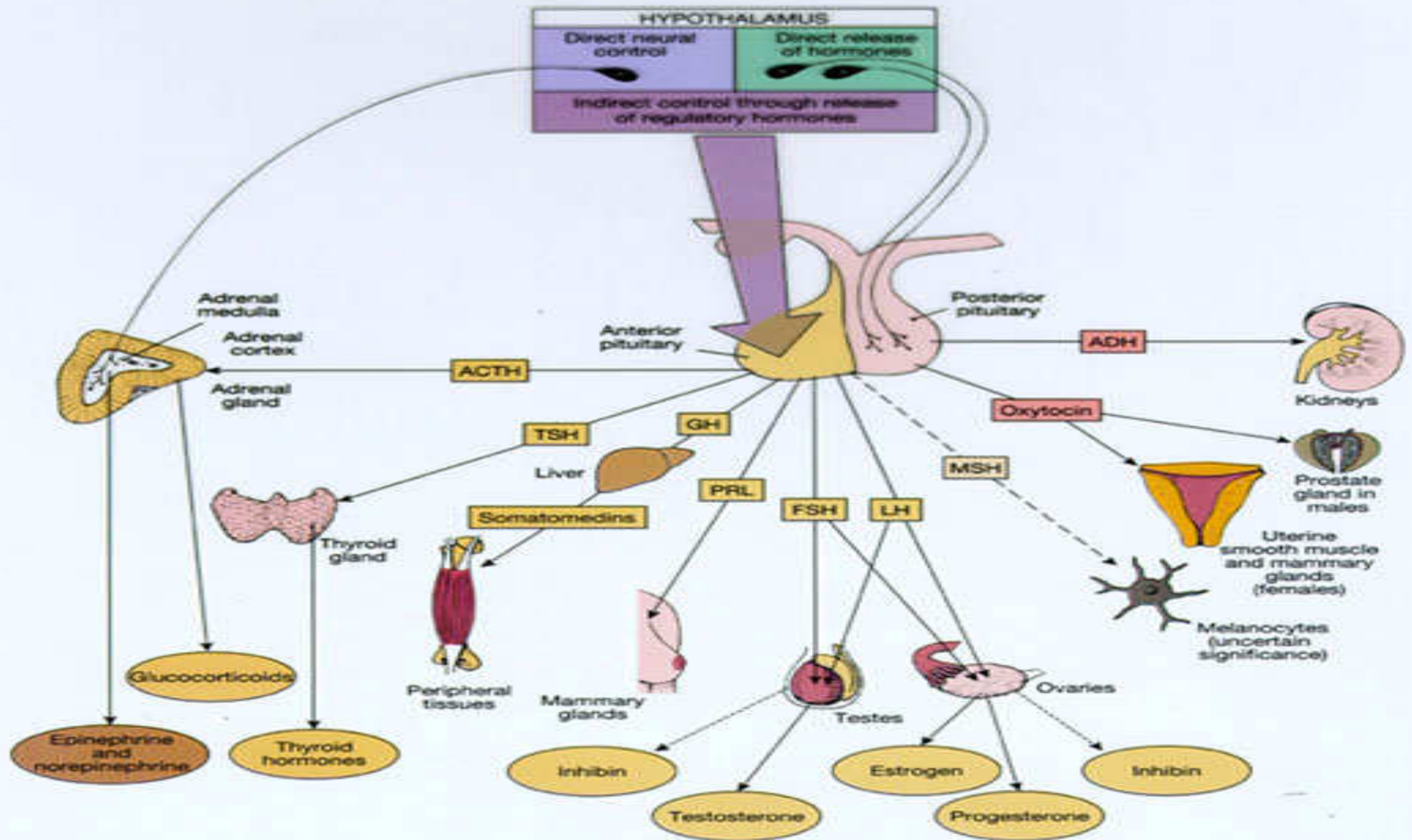
- GH: growth hormone
- ACTH: adrenocorticotrophic hormone
- TSH: thyroid-stimulating hormone
- PRL: prolactin
- FSH: follicle-stimulating hormone
- LH: luteinizing hormone
- MSH: melanocyte stimulating hormone

## Posterior Pituitary

- ADH: anti-diuretic hormone (vasopressin)
- OT: oxytocin



Fig. 11-8 Pituitary Hormones and Their Targets



ACTH Adrenocorticotropic hormone  
 TSH Thyroid-stimulating hormone  
 GH Growth hormone  
 PRL Prolactin

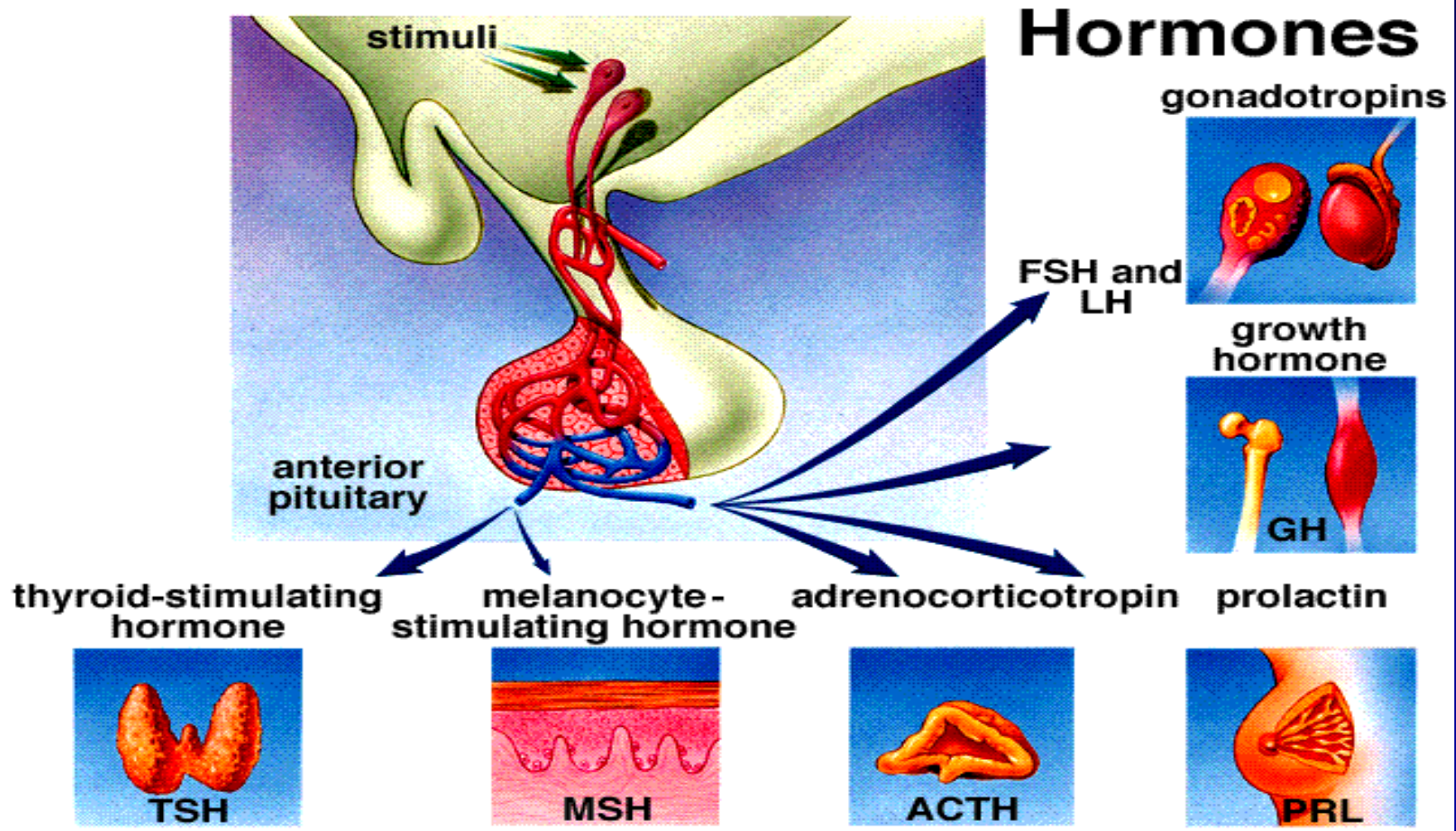
FSH Follicle-stimulating hormone  
 LH Luteinizing hormone  
 MSH Melanocyte-stimulating hormone  
 ADH Antidiuretic hormone

# Anterior Pituitary Secretes:

- **GH:** stimulates growth of bone and muscle , promotes protein synthesis and fat metabolism.
- **ACTH** (Adrenocorticotropin ): stimulates adrenal gland cortex secretion of mineralcorticoids (aldosterone) & glucocorticoids (cortisol).
- **TSH:** stimulates thyroid to increase secretion of thyroxine, its control is from regulating hormones in the hypothalamus.

# Anterior Gland Disorders

Sylvia S. Mader, Inquiry into Life, 8th edition. Copyright © 1997 The McGraw-Hill Companies, Inc. All rights reserved.



# Anterior Pituitary Cont'd

- **Prolactin:** stimulates milk production from the breasts after childbirth to enable nursing. Oxytocin from posterior lobe controls milk ejection.
- **FSH:** promotes sperm production in men and stimulates the ovaries to enable ovulation in women. LH and FSH work together to cause normal function of the ovaries and testes.
- **LH:** regulates testosterone in men and estrogen, progesterone in women.

# Posterior Pituitary

- **Antidiuretic hormone or ADH** - also called vasopressin, vasoconstricts arterioles to increase arterial pressure; increases water reabsorption in distal tubules.
- **Oxytocin**: stimulates uterus to contract at childbirth; stimulates mammary ducts to contract (milk ejection in lactation).

# Anterior Pituitary Disorders

| <b>Hormone</b> | <b>Increased level</b>                          | <b>Decreased level</b>                            |
|----------------|---|---|
| GH             | Gigantism (child)<br>Acromegaly (adult)         | Dwarfism (child)<br>Lethargy, premature aging     |
| ACTH           | Cushing's Disease                               | Addison's Disease                                 |
| TSH            | Goiter, increased BMR, HR, BP<br>Graves disease | Decreased BMR, HR, CO, BP<br>Cretinism (children) |
| Prolactin      | amenorrhea                                      | Too little milk                                   |
| FSH            |   | Late puberty, infertility                         |
| LH             | Menstrual cycle disturbance                     | Amenorrhea, impotence                             |

# Posterior Pituitary Disorders

| <b>Hormone</b>        | <b>Increased</b>  | <b>Decreased</b>  |
|-----------------------|---|---|
| Oxytocin              | Precipitates childbirth, excess milk                    | Prolonged childbirth, diminished milk                     |
| ADH<br>(vassopressin) | Increased BP, decreased urinary output, edema.<br>SIADH | Diabetes insipidus, dilute urine & increased urine output |

- Disorders occur most often in the anterior pituitary

- The anterior pituitary hormones regulates growth, metabolic activity and sexual development.

- Major causes include: tumors, pituitary infarction, genetic disorders.

- Pathologic consequences of pituitary disorders are 1) hyperpituitarism, 2) hypopituitarism, 3) local compression of brain tissue by expanding tumor



# Hyperpituitarism

# Hyperfunction

- Results in excess production and secretion of one or more hormones such as GH, PRL, ACTH.
- Most common cause is a benign adenoma.

# Pituitary Adenomas

**Table 15-1**  
Pituitary Adenomas

| <b>Tumor</b>         | <b>Incidence</b> | <b>Hormone Secreted in Excess*</b> | <b>Clinical Manifestations</b>   |
|----------------------|------------------|------------------------------------|--|
| Prolactinoma         | 30%              | Prolactin                          | Amenorrhea-galactorrhea syndrome (in women); hypotension and loss of libido (in men) |
| Corticotroph adenoma | 15%              | ACTH                               | Cushing disease  |
| Gonadotroph adenoma  | 10%              | LH, FSH                            | Menstrual disturbances (in women); loss of libido (in men)                           |
| Somatotroph adenoma  | 5%               | Growth hormone                     | Gigantism (in prepubertal children); acromegaly (in adults)                          |
| Thyrotroph adenoma   | 1%               | TSH                                | Hyperthyroidism (high serum TSH, T <sub>3</sub> , and T <sub>4</sub> levels)         |

ACTH = adrenocorticotropic hormone; FSH = follicle-stimulating hormone; LH = luteinizing hormone; T<sub>3</sub> = triiodothyronine; T<sub>4</sub> = thyroxine; TSH = thyroid-stimulating hormone.

\*Thirty percent of pituitary adenomas are nonfunctioning.

# Classification:

- According to cell staining characteristics ?  
(acidophil, basophil, chromophobe cell adenoma)
- According to size?  
(Macroadenoma  $> 1$  cm, microadenoma  $< 1$  cm)
- According to type of hormone produced?  
(functional, non-functional)

# Pituitary Hyperfunction Cell Types

**TABLE 20-1**

*Pituitary Hyperfunction*

| Hormone                       | Lesion  | Classic Staining of Tumor Cells | Manifestations  |
|-------------------------------|---|---------------------------------|---|
| Prolactin                     | Prolactinoma  | Chromophobic                    | Amenorrhea and galactorrhea in women; impotence and sometimes galactorrhea in men |
| Somatotropin (growth hormone) | Somatotropic adenoma  | Acidophilic                     | Gigantism or acromegaly   |
| Corticotropin (ACTH)          | Corticotropic adenoma or multiple corticotropic microadenomas                           | Basophilic                      | Pituitary Cushing syndrome  |
| Antidiuretic hormone (ADH)    | Nonpituitary lesions with ectopic hormone production (small cell carcinoma of the lung) |                                 | Water retention with dilutional hyponatremia                                      |

Ref: Pathology Board Review Series, 3<sup>rd</sup> Ed.

# Pituitary Adenoma

**Anterior pituitary adenoma**, a benign tumor which is classified according to size, degree of invasiveness and the hormone secreted.

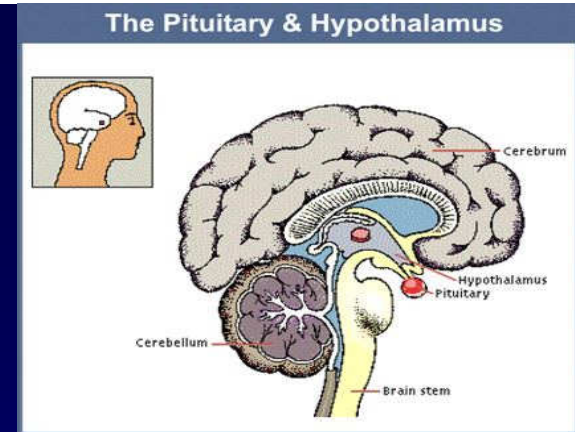
**Prolactin** and **GH** are the hormones most commonly over-produced by adenomas.

## Adenoma's Cont'd

Changes in neurological function may occur as adenomas compress surrounding tissue.

Manifestations include headaches, visual defects and increased ICP.

Treatment is surgical resection through *transphenoidal hypophysectomy*



- **Gigantism** is the result of GH hypersecretion before the closure of the epiphyseal plates (childhood).
  - Abnormally tall but body proportions are normal
- **Acromegaly** is over secretion of GH in adulthood
  - Continued growth of bone, connective tissue leads to disproportionate enlargement of tissue..





# Acromegaly

Rare condition – develops between ages 30-50

## Symptoms:

- Coarsening of facial features
- Enlarged hands & feet
- Carpel tunnel syndrome
- Excessive sweating & oily skin
- Headaches
- Vision disturbance
- Sleep apnea
- General tiredness
- Oligomenorrhea or amenorrhea
- Impotence (adult males)
- Decreased libido

# Diagnosis

- History & physical exam
- Investigation includes:
  - GH analysis (**glucose tolerance**) Normally GH concentration falls with oral glucose; in acromegaly it does not.
  - Prolactin levels as well as other pituitary function tests
  - MRI or CT & visual field tests to determine size and position of the adenoma.
  - Bone scan

# Treatment

- Surgery (primary choice)
- Radiotherapy
- Drug treatment – when surgery is not feasible
- Combinations of above

# Drug treatment of Acromegaly

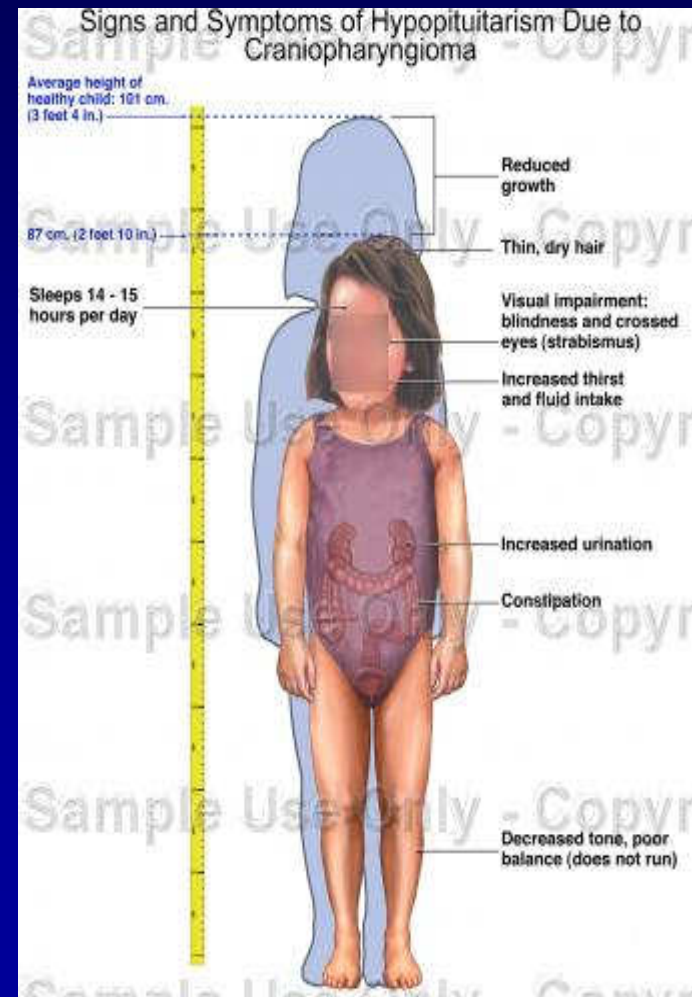
- Dopamine agonists: Dopamine agonists work on specialist markers (dopamine receptors) on the surface of the tumor to inhibit GH release from the tumour (**Parlodel**).
- Somatostatin: growth hormone receptor antagonist decreases the action of GH on target tissues. (**octreotide acetate**)
- Dopamine agonists are taken by mouth but in general are less effective than somatostatin analogues, which have to be injected.

# Hypopituitarism

# Hypopituitarism- Anterior Pituitary

## Decreased GH in child: Dwarfism

- Condition of being undersized
- There are many forms of dwarfism
- Dwarfism related to pituitary gland is the result of insufficient GH
- Pituitary dwarfism is successfully treated by administering human growth hormone



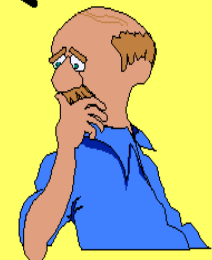
# Hypopituitarism (Adult)- GH

## Hypopituitarism

Many clinical pictures with diverse symptomology

Unrecognized

Death



- Lack of GH leads to:
  - Increased CV disease
  - Excessive tiredness
  - Anxiety
  - Depression
  - Reduced “quality of life”
  - Possible premature death

# Hyperprolactemia

- Prolactin levels are normally high during pregnancy and lactation.
- Symptoms of hyperprolactemia include;
  - discharge from breasts (galactorrhoea)
  - oligomenorrhoea or amenorrhoea in women
  - reduced libido and potency in men
  - pressure effects (e.g. headache and visual disturbance) - more commonly in men



- Treatment is surgery, radiation, or medical therapy with drugs that will suppress the production of prolactin

- Urgent: deterioration in vision

- Important:

- successful RX. results in restoration of fertility
- Patients may be predisposed to problems related to osteoporosis
- Ask about erectile function & reassure client that it is part of the disease and can be treated.

## Increased ACTH:Cushing's Disease

- Cushing's is a disorder in which the adrenal glands are producing too much cortisol (hypercortisolism).
- If the source of the problem is the pituitary gland, then the correct name is **Cushing's Disease** whereas, if it originates anywhere else (adrenal tumors, long term steroid administration) then the correct name is **Cushing's Syndrome**.
- **Cushing's Disease** is caused by pituitary hypersecretion of ACTH.

# Etiology - Hypercortisolism

- Iatrogenic hypercortisolism resulting from medical intervention is most common cause of Cushing Syndrome.
- Pituitary hypersecretion and pituitary tumors account for 70% of Cushing's Disease. Adrenal tumors account for 30%.
- Ectopic secretion of ACTH by tumors located outside the pituitary gland are rare cause of the syndrome and associated with increased morbidity/mortality (ie oat cell ca).

# Symptoms: hypercortisolism

- **Neurological:** Psychosis, emotional lability, loss of memory, depression
- **Musculoskeletal:** muscle weakness (proximal myopathy, muscle wasting, osteoporosis, buffalo hump, truncal obesity
- **Integumentary:** ecchymosis (tendency to bruise), purple striae on abdomen, poor wound healing, skin infections, thin skin, acne.

## Symptoms Cont'd

- **CV:** HTN
- **GI:** peptic ulcers
- **Metabolic:** hypokalemia, hypernatremia, edema, moon face, weight gain.
- **Classic symptoms of Cushing's:** moon face, buffalo hump, purple striae, truncal obesity.

# Diagnosis

- 24 hr urine cortisol levels ↑
- Serum sodium levels ↑
- Serum potassium levels ↓
- Serum glucose ↑
- Serum ACTH ↑ in Cushing Disease
- ACTH suppression test to identify cause
- Dexamethasone suppression test: cause pituitary or adrenal
- Radiological exam to reveal pituitary or adrenal tumor

# Treatment

- Transphenoidal surgery if the condition is due to a pituitary tumor
- Where surgery is contraindicated or fails to reduce cortisol levels, adrenalectomy and/or pituitary radiation may be necessary.
- Adrenocortical Inhibitors: (metapyrone, aminogluthimide) are only effective short-term.
- Diet: low calorie, carbohydrate & salt. High potassium.

# Posterior Pituitary Disorders



# Deficiency or excess of ADH

- Diabetes insipidus
- SIADH

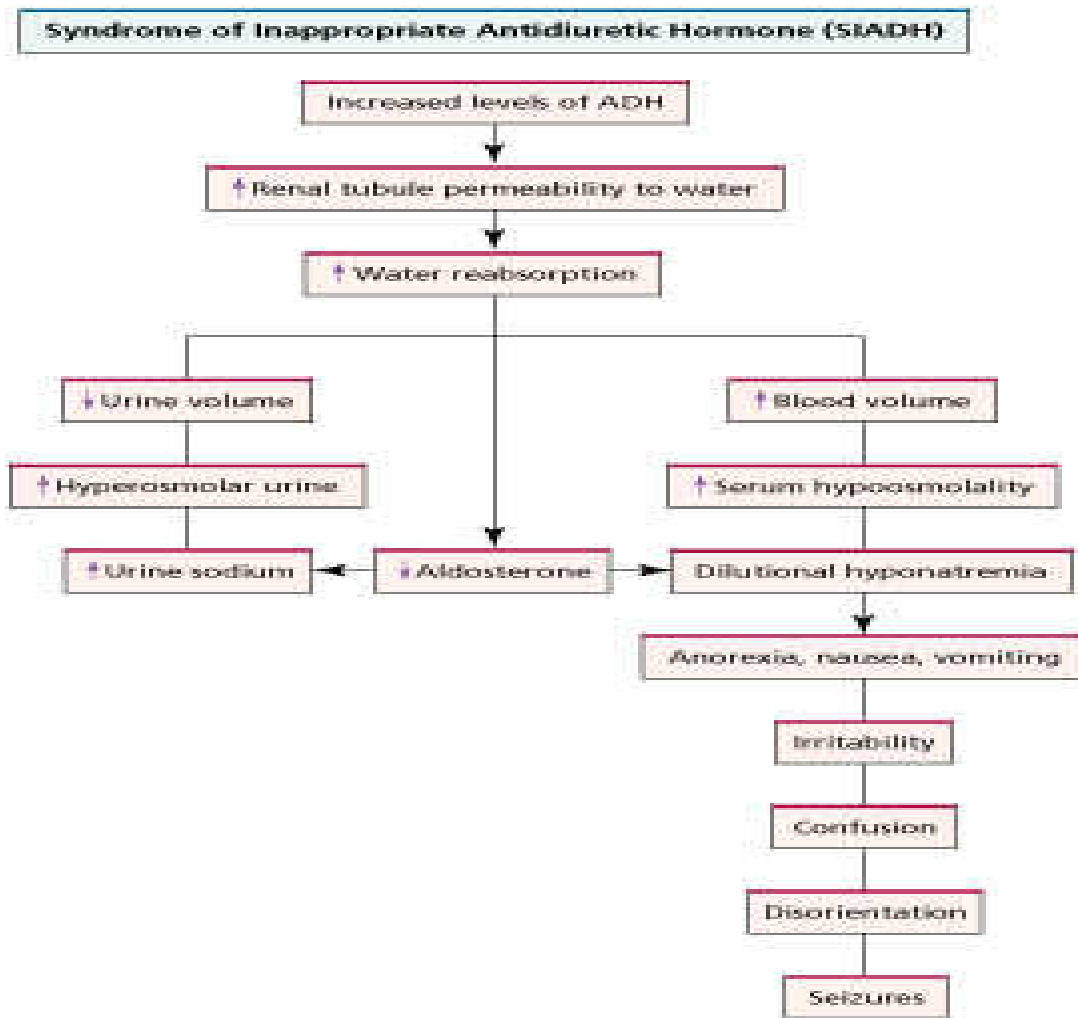
# Posterior Lobe Disorders

- SIADH & diabetes insipidus are major disorders of the posterior pituitary.....however
- Even if posterior lobe becomes damaged, hormonal deficiencies usually do not develop

# Hyper – Posterior Pituitary

# SIADH

- Syndrome of Inappropriate Anti-Diuretic Hormone
- Too much ADH produced or secreted.
- SIADH commonly results from malignancies, CHF, trauma, CNS infections (e.g. meningitis) & CVA - resulting in damage to the hypothalamus or pituitary which causes failure of the feedback loop that regulates ADH.
- Patient retains water causing dilutional hyponatremia & decreased osmolality.
- Decreased serum osmolality cause water to move into cells



**Figure 47-4** Pathophysiology of syndrome of inappropriate antidiuretic hormone (SIADH).

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# Signs and Symptoms

- Lethargy & weakness
- Confusion or changes in neurological status
- Cerebral edema
- Muscle cramps
- Decreased urine output
- Weight gain without edema
- Hypertension

# Assessment

- Serum sodium low
- Serum osmolality low
- Urine osmolality disproportionately elevated in relation to the serum osmolality
- Urine specific gravity elevated
- Plasma ADH elevated

# Treatment of SIADH

- Treat underlying cause
- Hypertonic or isotonic IV solution
- Monitor for signs of fluid and electrolyte imbalance
- Monitor for neurological effects
- Monitor in and out
- Weigh
- Restrict fluid intake
- Lithium inhibits action of ADH to promote water excretion.

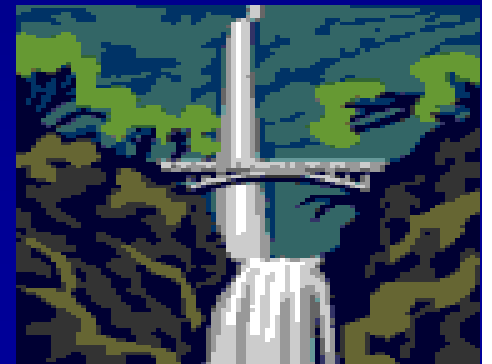


# Hypofunction – Posterior pituitary



# Diabetes Insipidus (DI)

- DI is usually insidious but can occur with damage to the hypothalamus or the pituitary. (Neurogenic DI)
- May be a result of defect in renal tubules, do not respond to ADH (Nephrogenic DI)
- Decreased production or release of ADH results in massive water loss
- Leads to hypovolemic & dehydration.



# Clinical Manifestations

- Polyuria of more than 3 litres per 24 hours in adults (may be up to 20!)
- Urine specific gravity low
- Polydipsia (excessive drinking)
- Weight loss
- Dry skin & mucous membranes
- Possible hypovolemia, hypotension, electrolyte imbalance

# Diagnostic Tests

- Serum sodium
- Urine specific gravity
- Serum osmolality
- Urine osmolality
- Serum ADH levels
- Vasopressin test and water deprivation test:  
increased hyperosmolality is diagnostic for DI.

# Management

- Medical management includes
  - Rehydration IV fluids (hypotonic)
  - Symptom management
  - ADH replacement (vasopressin)
  - For nephrogenic DI: thiazide diuretics, mild salt depletion, prostaglandin inhibitors (i.e. ibuprophen)

# Panhypopituitarism

- When both the anterior and posterior fail to secrete hormones, the condition is called *panhypopituitarism*.
- Causes include tumors, infection, injury, iatrogenic (radiation, surgery), infarction
- Manifestations don't occur until 75% of pituitary has been obliterated.
- Treatment involves removal of cause and hormone replacement (adrenocortical insufficiency, thyroid hormone, sex hormones)

# FUNCTIONS OF THE Pituitary Gland with Symptoms of Deficiencies

## SYMPTOMS OF PITUITARY DEFICIENCIES IN THE ADULT FEMALE

PITUITARY GLAND

FACIAL WRINKLING

MYXEDEMA FACIES (UNDERACTIVE THYROID)

PALLOR

THYROID GLAND

SEVERE FATIGUE

WATER RETENTION AND WEIGHT GAIN

DRY SKIN

CONSTIPATION

JOINT AND MUSCLE ACHES AND PAINS

FLABBY MUSCLES

MAMMARY GLANDS (BREASTS)

BREAST ATROPHY AND LOSS OF LACTATION

ADRENAL GLANDS

LOW BLOOD SUGAR

LOW BLOOD PRESSURE

OVARIES

AMENORRHEA

GENITAL AND DONALAD ATROPHY WITH DECREASED SEX DRIVE

LOSS OF PUBIC AND AXILLARY HAIR

TSH- THYROID-STIMULATING HORMONES

MSH- MELANOCYTE STIMULATING HORMONES (SKIN)

GH- GROWTH HORMONES (AFFECTING MANY BODY TISSUES INCLUDING THE LIVER)

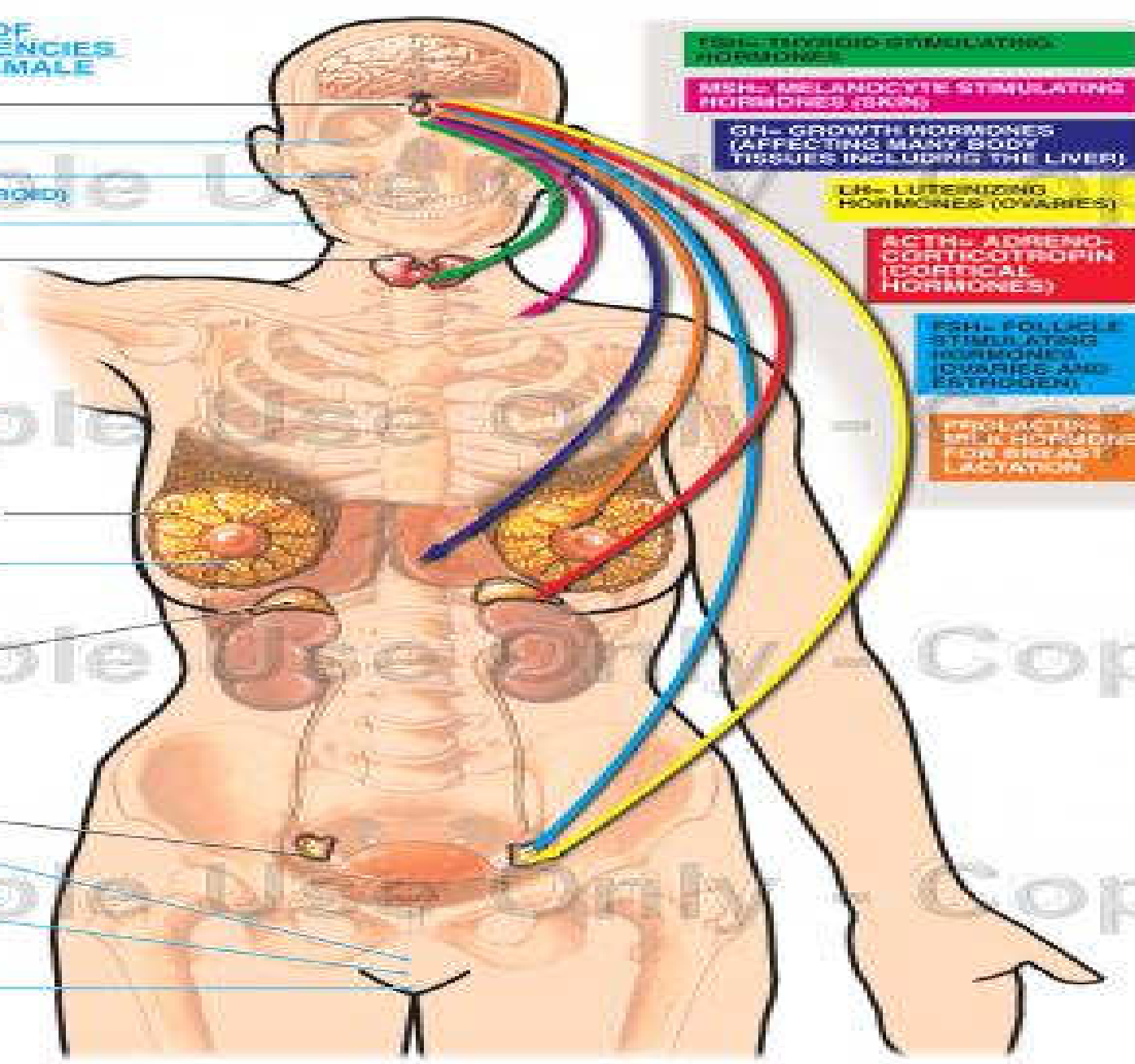
LH- LUTENIZING HORMONES (OVARIES)

ACTH- ADRENO-CORTICOTROPIN (CORTICAL HORMONES)

FSH- FOLLICLE STIMULATING HORMONES (OVARIES AND ESTROGEN)

PROLACTIN- PRL- STIMULATE LOW BREAST LACTATION

ANTERIOR VIEW





# References

- Robins Pathological Basis of Diseases, 6<sup>th</sup> Edition, Chapter 26 – Pituitary.

Download seminar notes: [www.pathologyatsmhs.wordpress.com](http://www.pathologyatsmhs.wordpress.com)

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