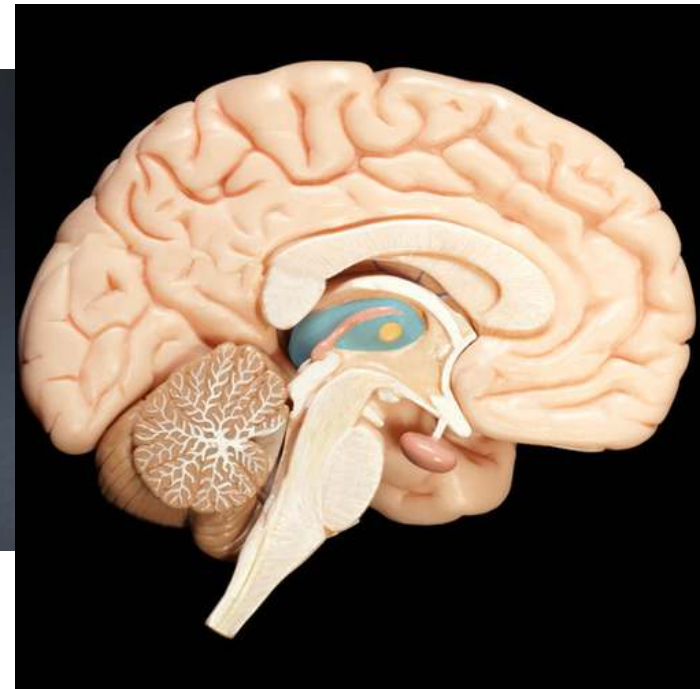
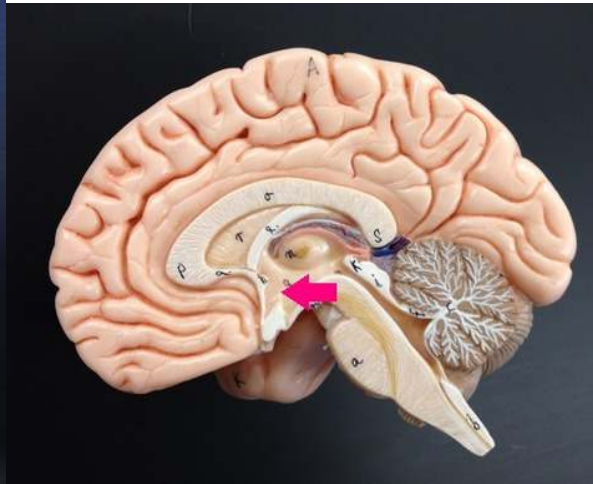
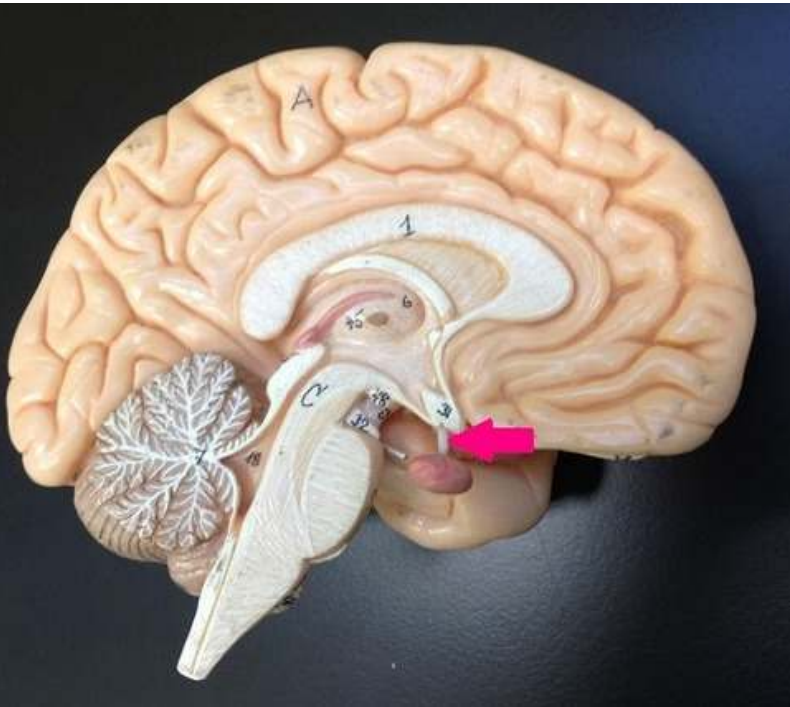


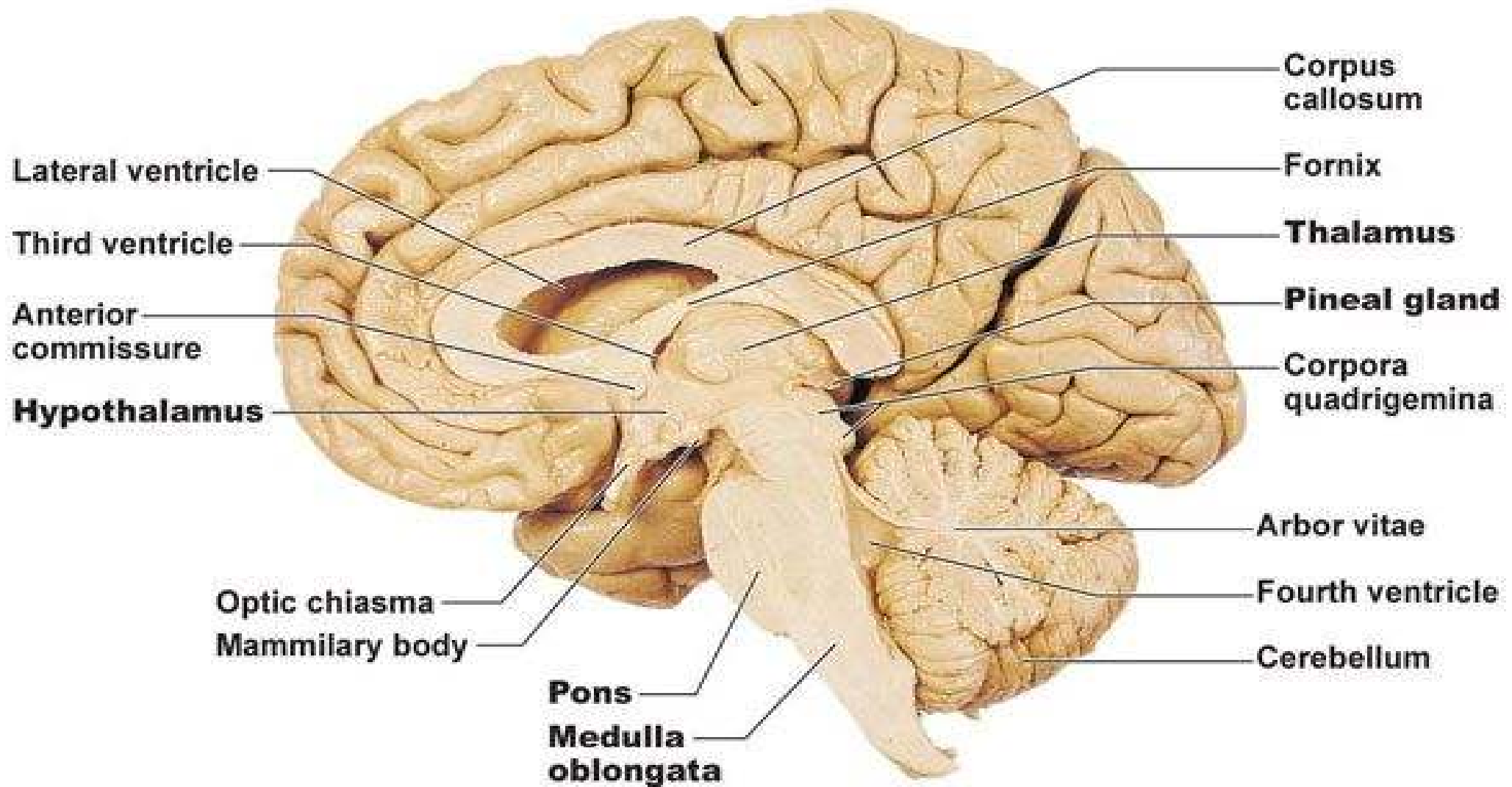
# Neuro- endocrine.

D.HAMMOUDI. MD



# NEURO- ENDOCRINE



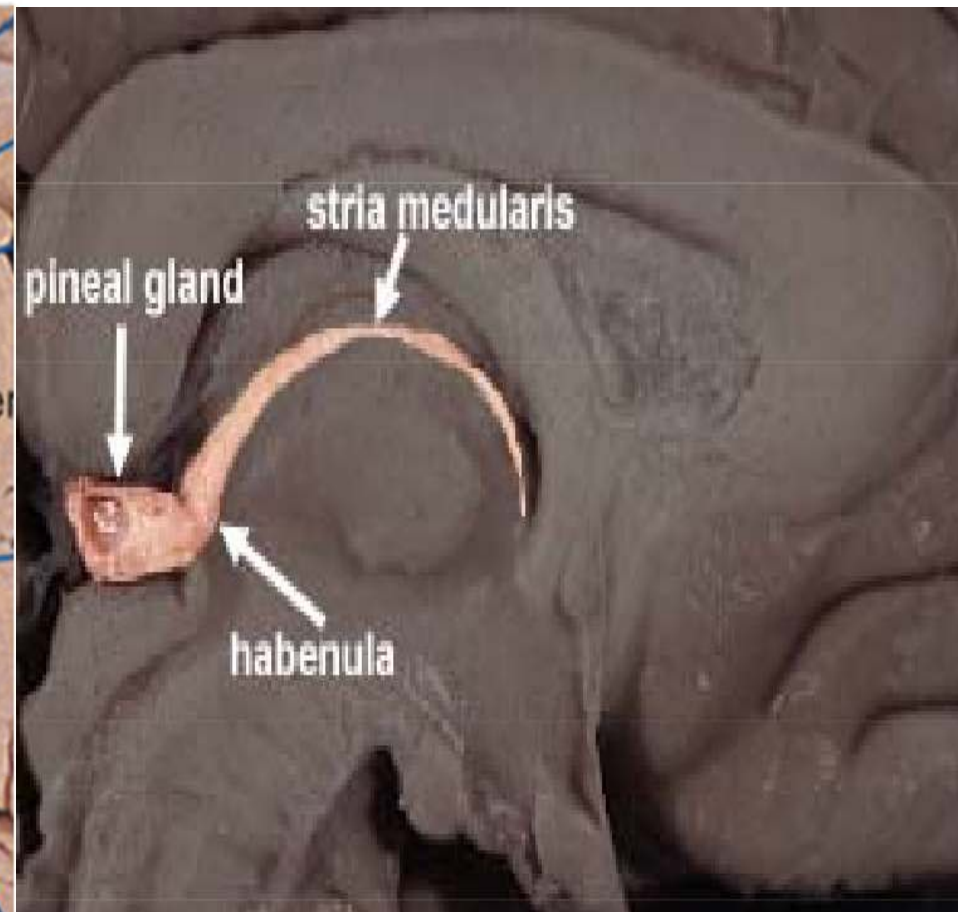
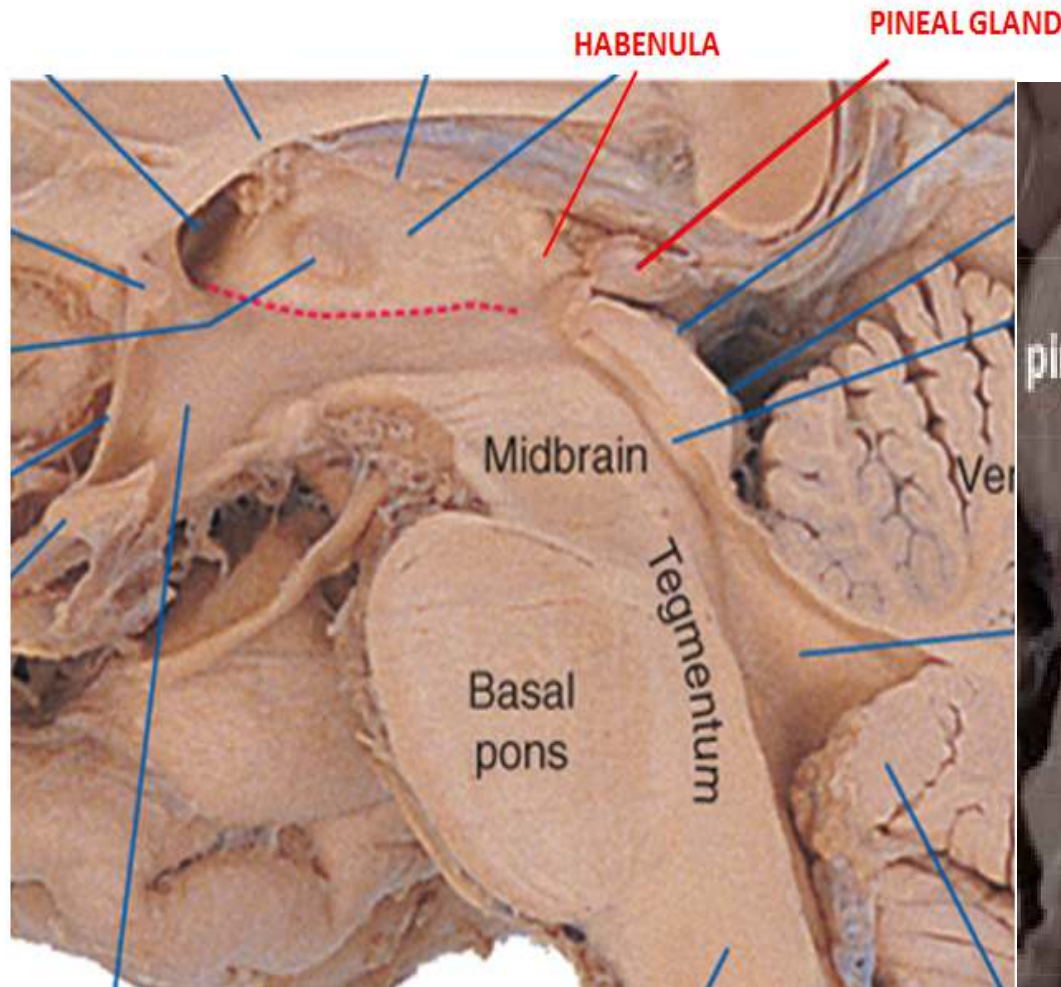




# EPITHALAMUS

MADE UP OF PINEAL GLAND AND HABENULA

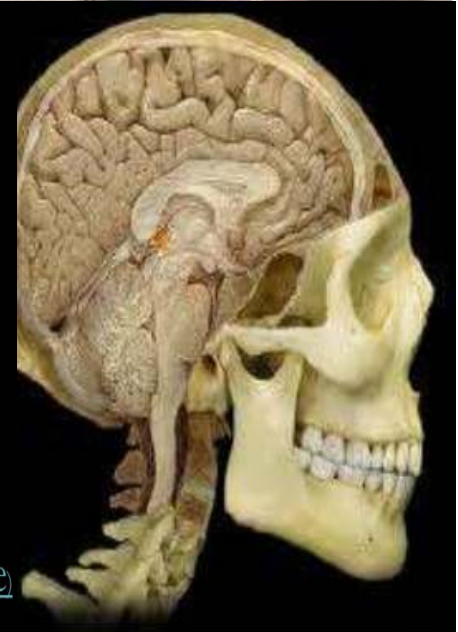
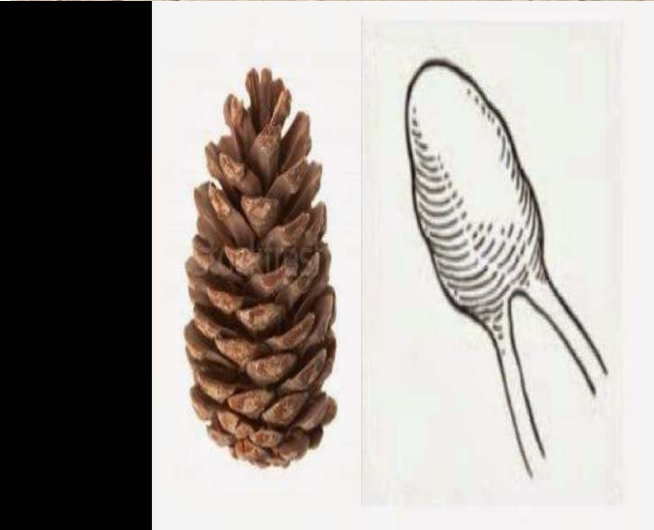
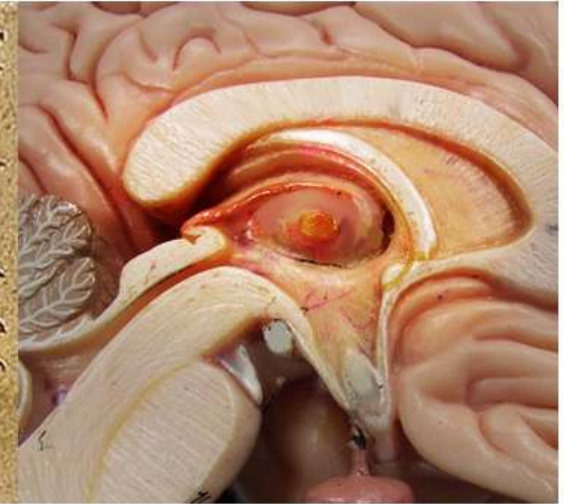
- Habenula involved in food and water intake



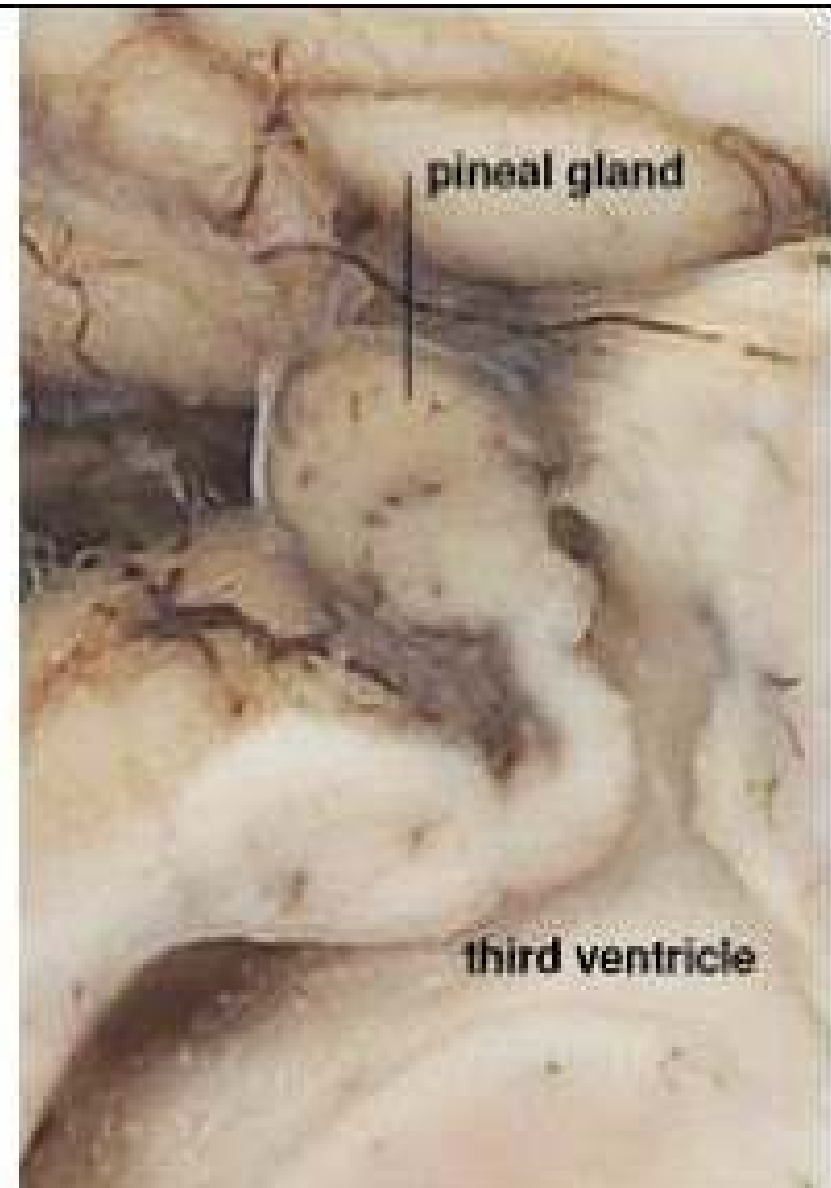
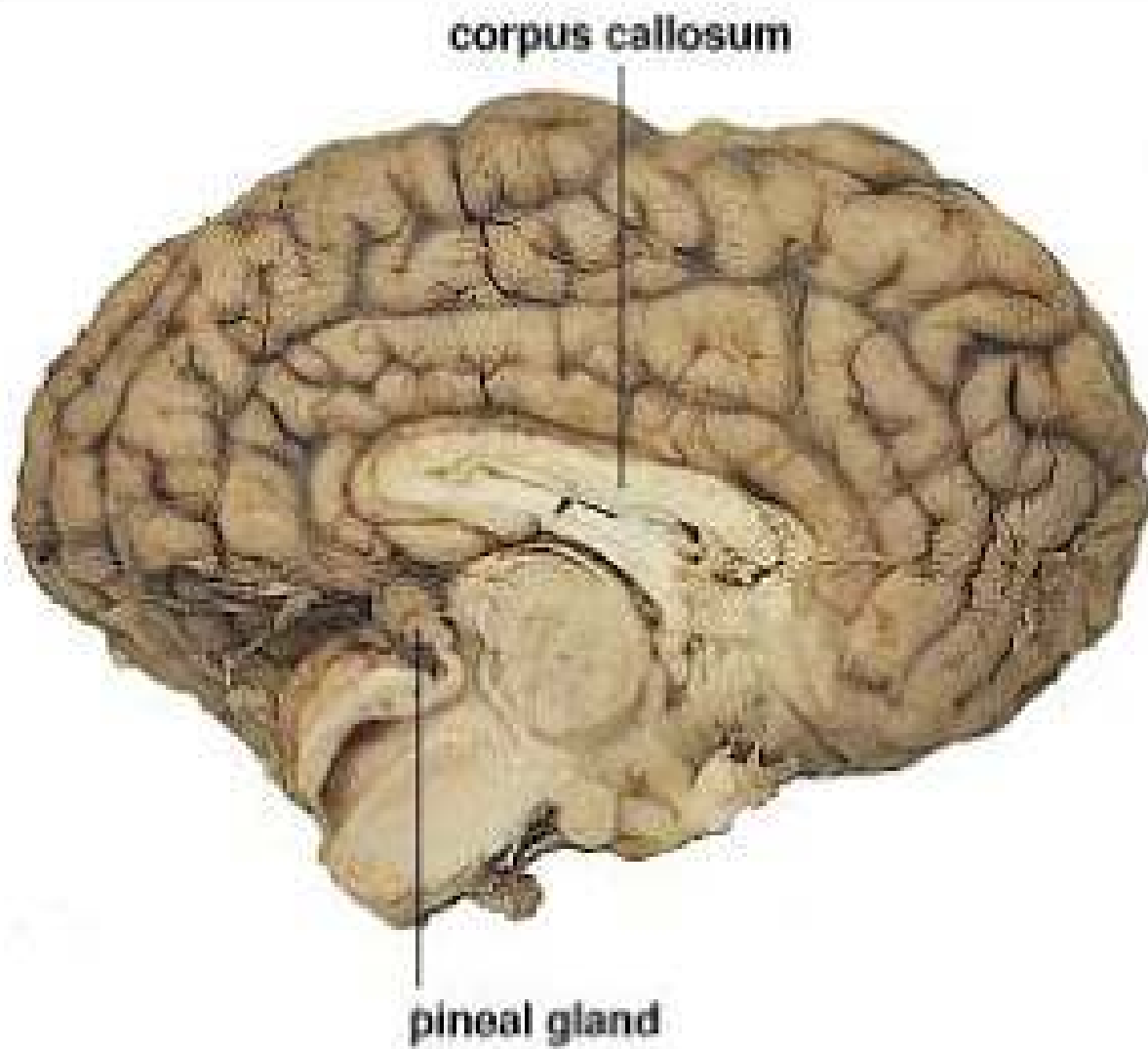
# Pineal Gland

The 3<sup>rd</sup> eye of anubis

- AKA epiphysis cerebi
- **Pinealocytes secrete melatonin**
  - Involved in diurnal rhythms
  - Innervated by neurons of the ANS
- Brain Sand
  - Crystallized deposits of calcium carbonates and calcium phosphates



Its shape resembles a tiny pine cone (hence its name)



- The pineal body is **surrounded by pia mater**, which functions as its capsule and which sends connective tissue septa into the pineal body, subdividing it into lobules.
- **In the pineal we find two cell types:**
  - **pinealocytes** (about 95% of the cells; large, light and round nuclei)
  - **astrocytes** (glial cells; dark, elongated nuclei).
- Aside from the cells the pineal gland also contains ..... sand - well - **brain sand (or acervuli cerebri or - just for good measure - corpora arenacea)**. These are calcium-containing concretions in the pineal parenchyma, which increase in size and number with age.
- The most prominent secretory product of the pineal body is **melatonin**.
  - they may **"delay" puberty through anti-gonadotrophic effects**.
- blocks the secretion of gonadotropins (LH & FSH) from anterior pituitary gland. inhibit ovarian activity
- • These hormones aid in the proper development and functioning of the ovaries and testes
- Secretory activity in the pineal gland is stimulated by **darkness and inhibited by light**.
- Via the effects of pineal hormones on the adenohipophysis and sex hormones it is likely that the pineal body is involved in phenomena associated with **the circadian rhythm and seasonal phenomena** (e.g. seasonal affective disorder, SAD).
- The pineal body is innervated by **postganglionic sympathetic fibres derived from the superior cervical ganglion**.
- **serotonin** serotonin -neuro transmitter , vasoconstrictor
  - stimulates smooth muscles and inhibits gastric secretion



### **Melatonin effects :**

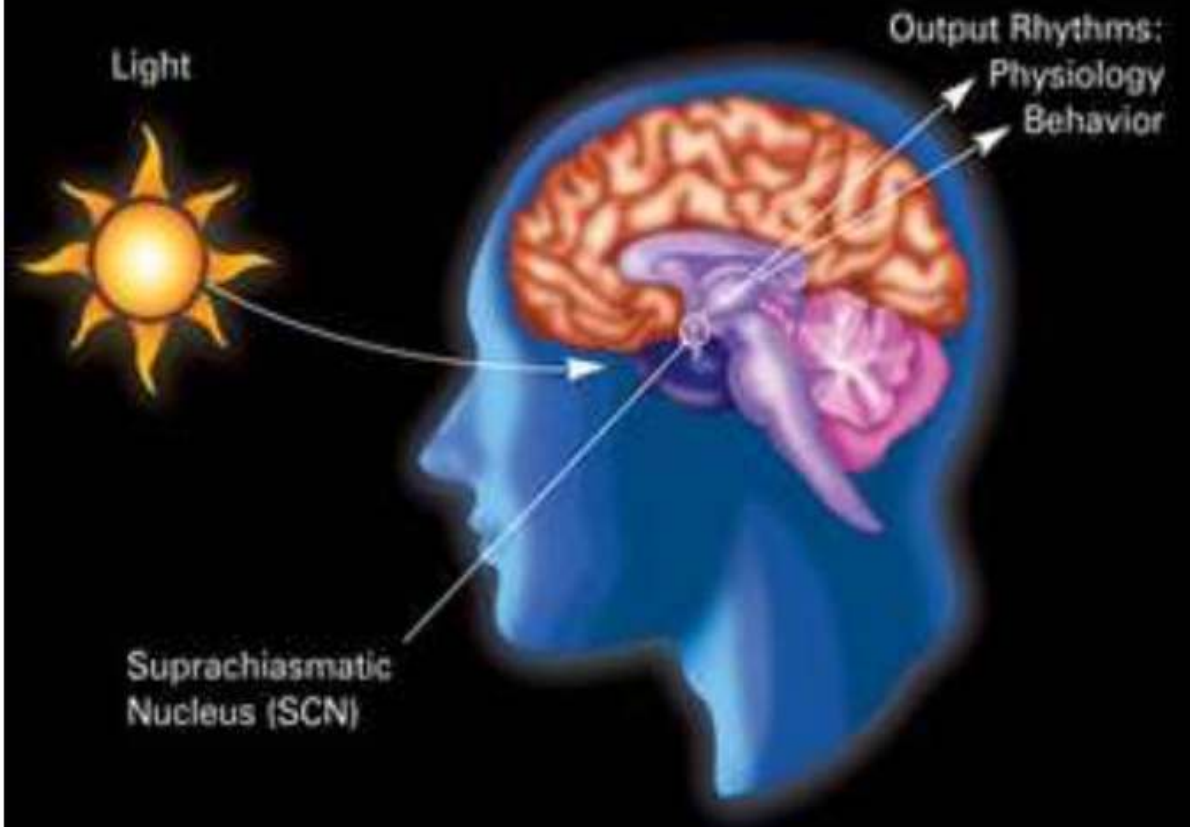
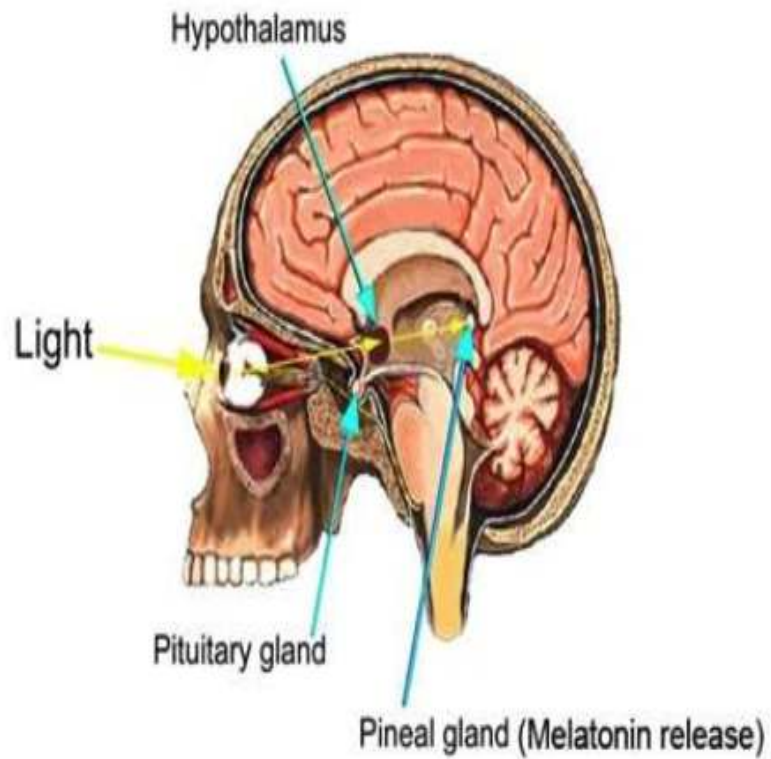
▣ **Dreaming:** Some supplemental melatonin users report an increase in vivid dreaming .

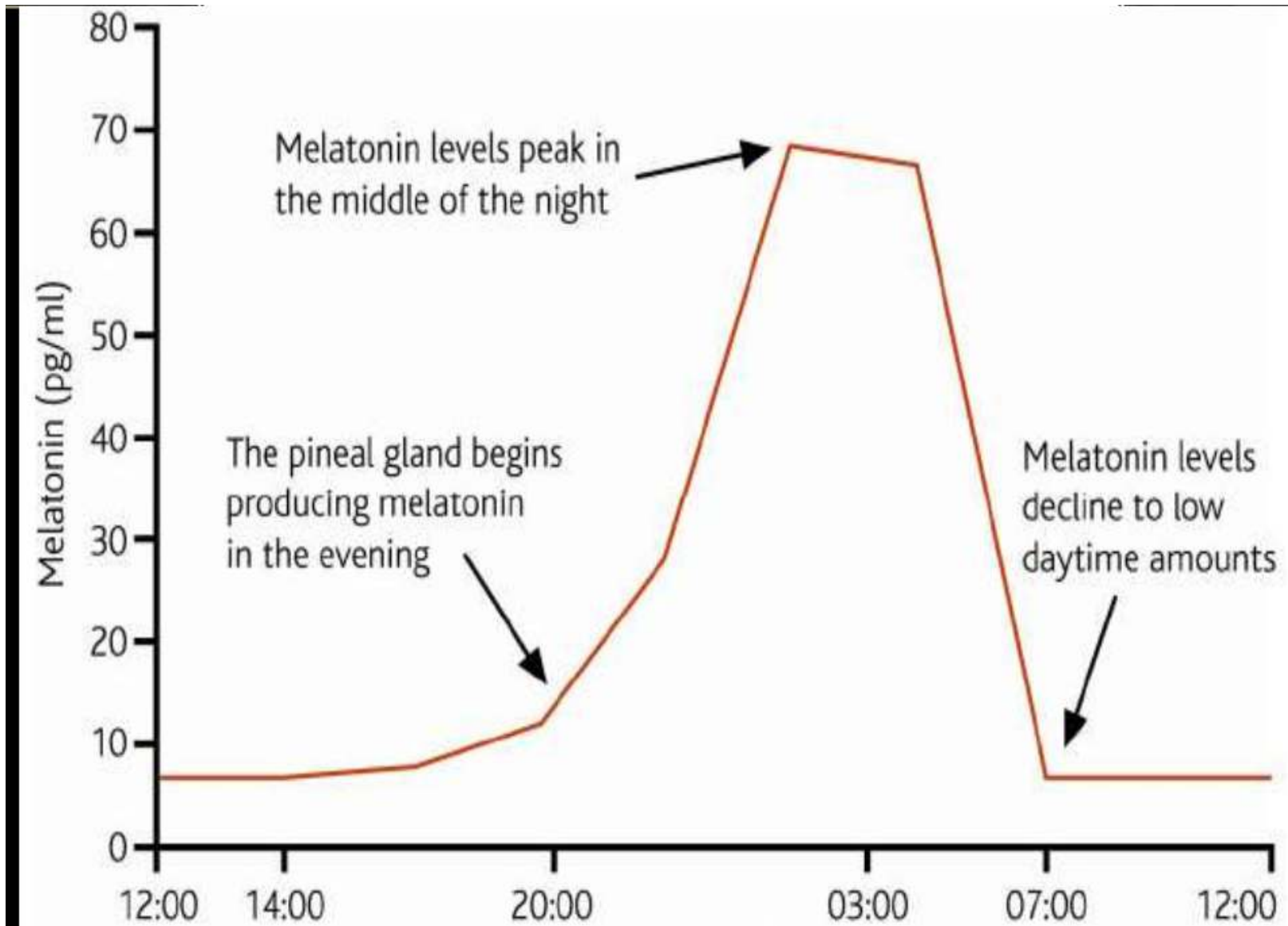
Extremely high doses of melatonin (50mg) dramatically increased REM sleep time and dream activity in both people with and people without narcolepsy .

▣ **Autism** Individuals with autism spectrum disorders (ASD) may have lower than normal levels of melatonin

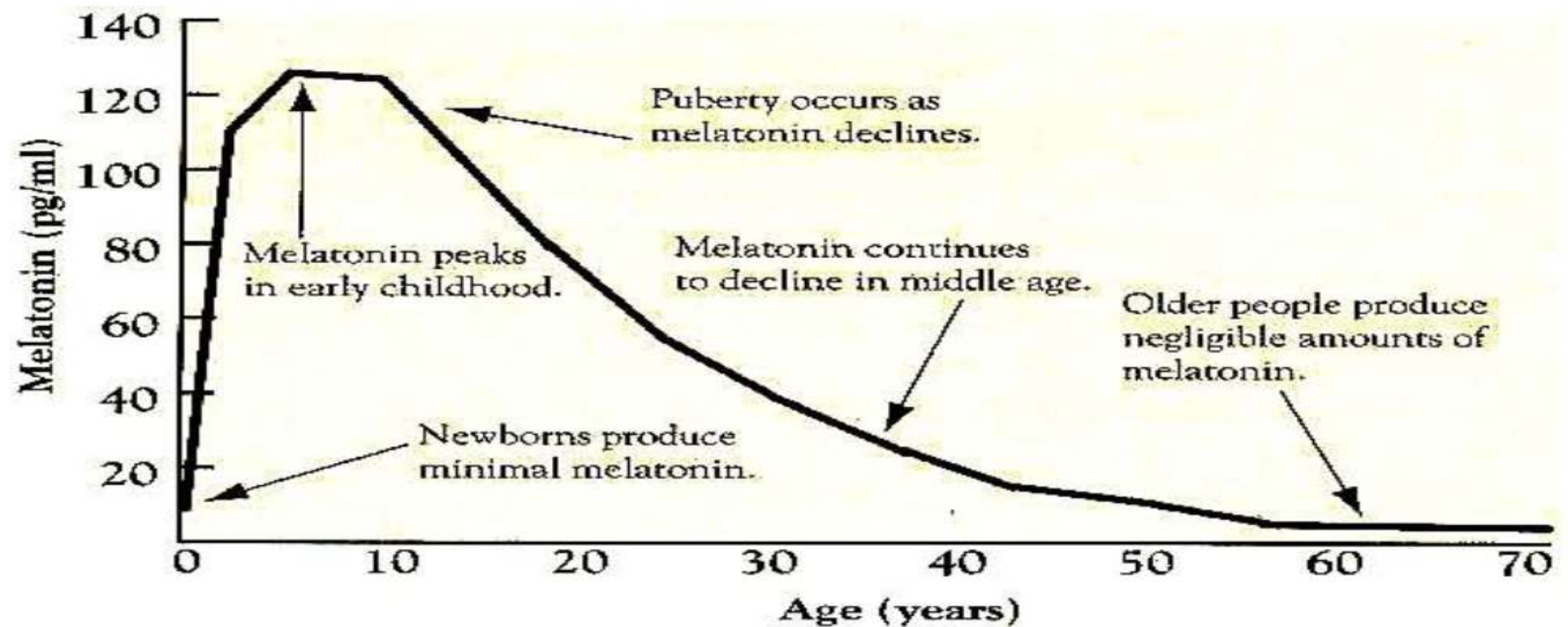


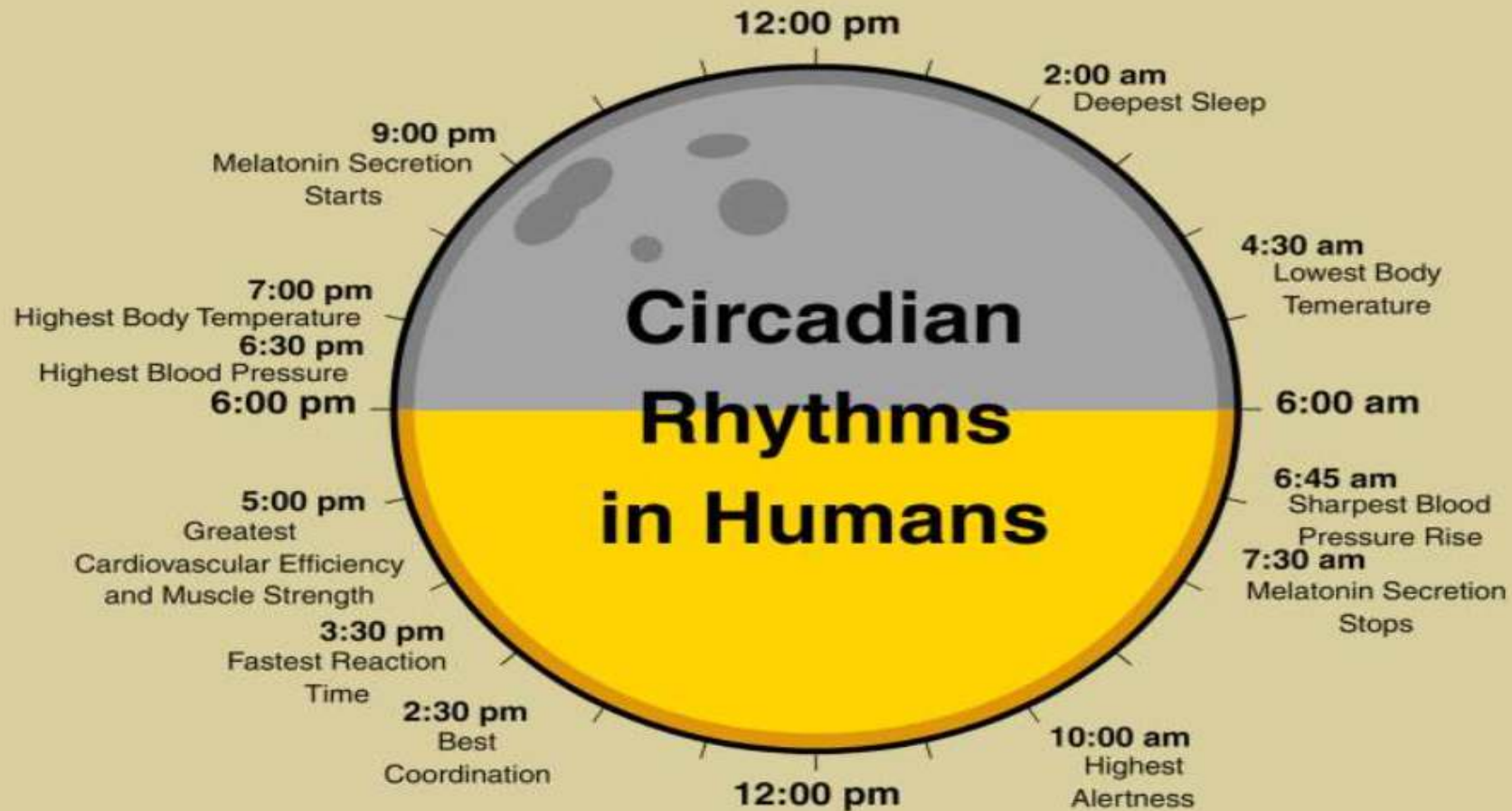
- Natural Sleeping Tablet





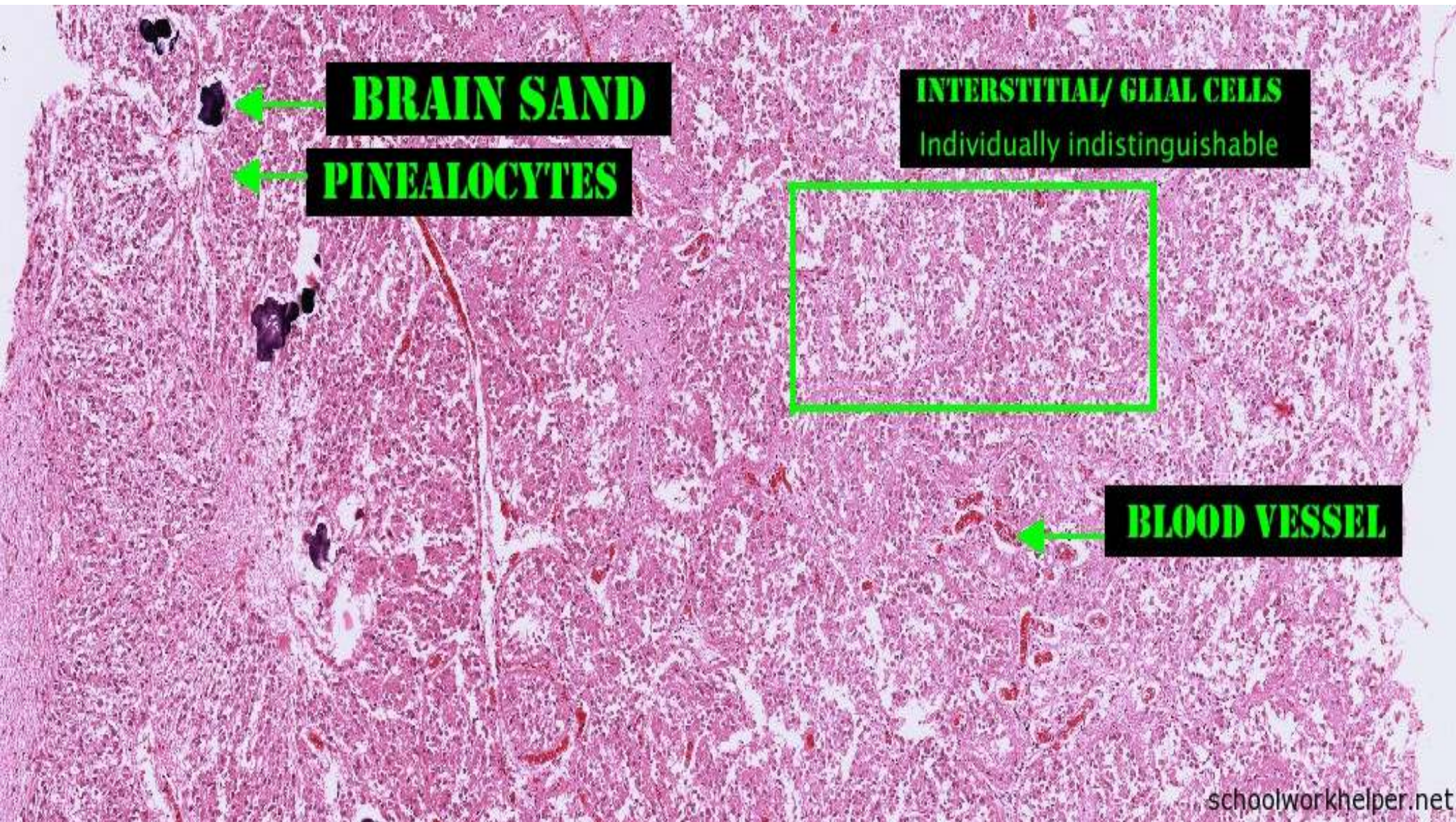
# MELATONIN VS AGE





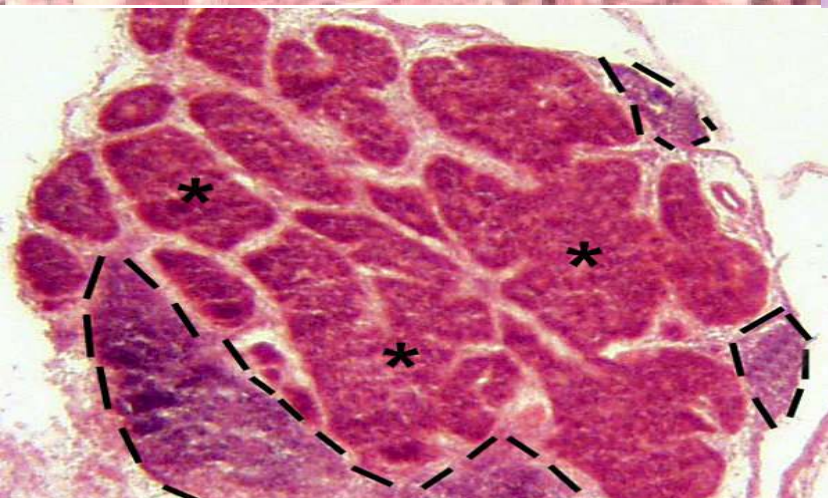
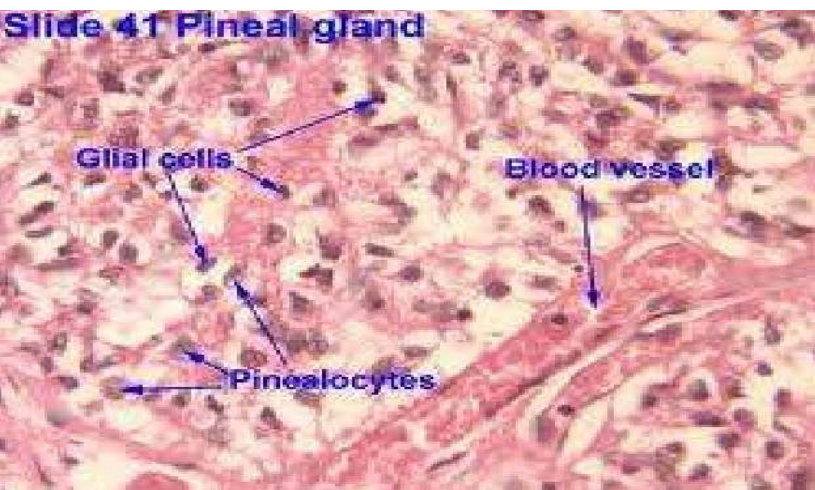
Circadian rhythms are physical, mental and behavioral changes that follow a roughly 24-hour cycle, responding primarily to light and darkness in an organism's environment.





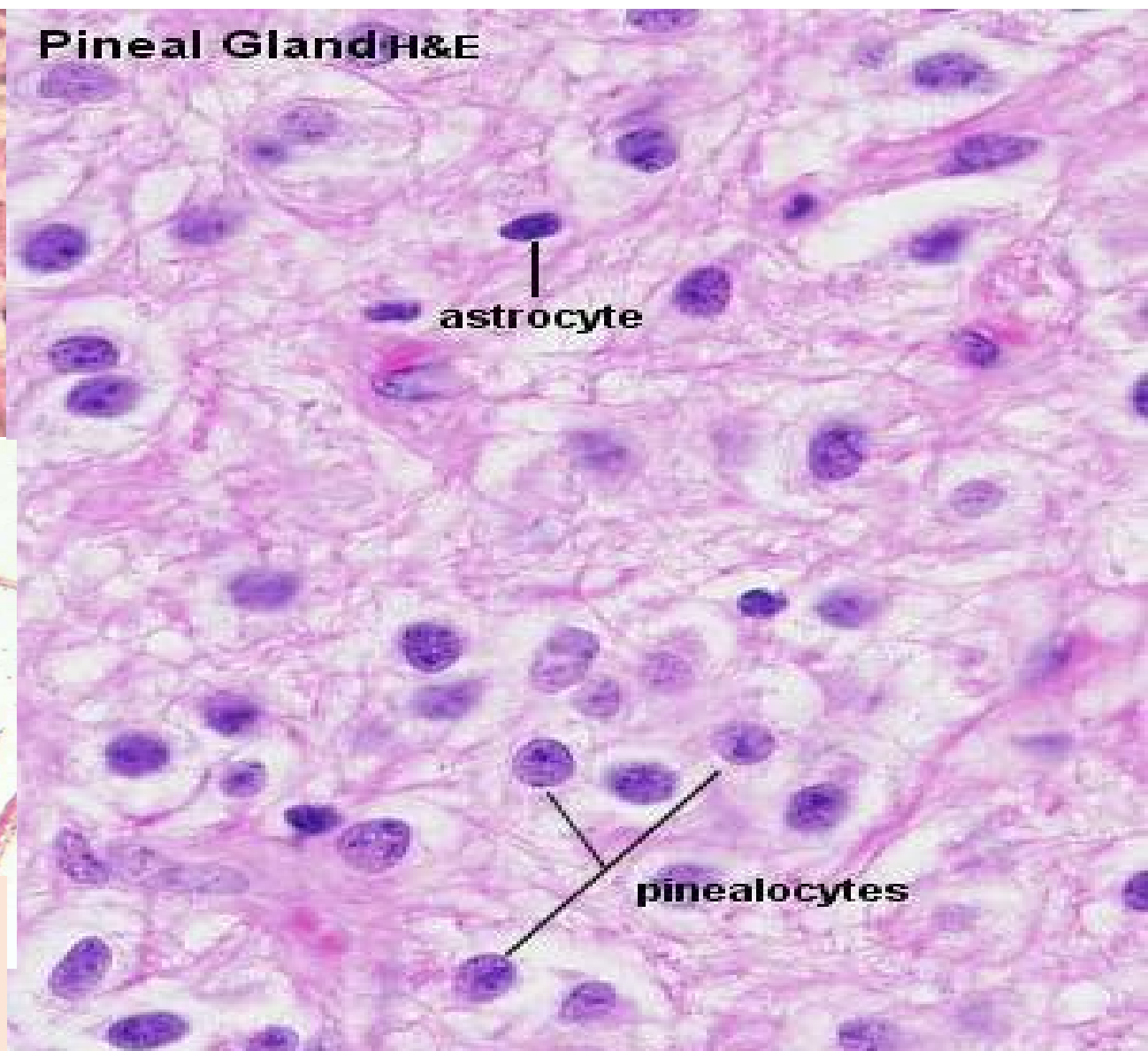


Slide 41 Pineal gland



The pineal follicles (\*) comprise pinealocytes and supportive cells arranged as epithelium. Prominent interstitial septa separate individual follicles.

Pineal Gland H&E



## **FUNCTIONS OF THE NEUROENDOCRINE SYSTEM**

Along with the nervous system, hormones provide the necessary communication between all the cells that constitute a multicellular animal

**Nervous system**-Is involved in rapid transfer of short-term events and coordination of short-term events. Electrochemical information involving neurons.

**Neurosecretory cells**-Neurons have electrical activity but involved in the production and release of neurosecretion that produces their effect as chemicals.

**Endocrine system**-Is involved in the integration and coordination of long-term events through chemicals called hormones.

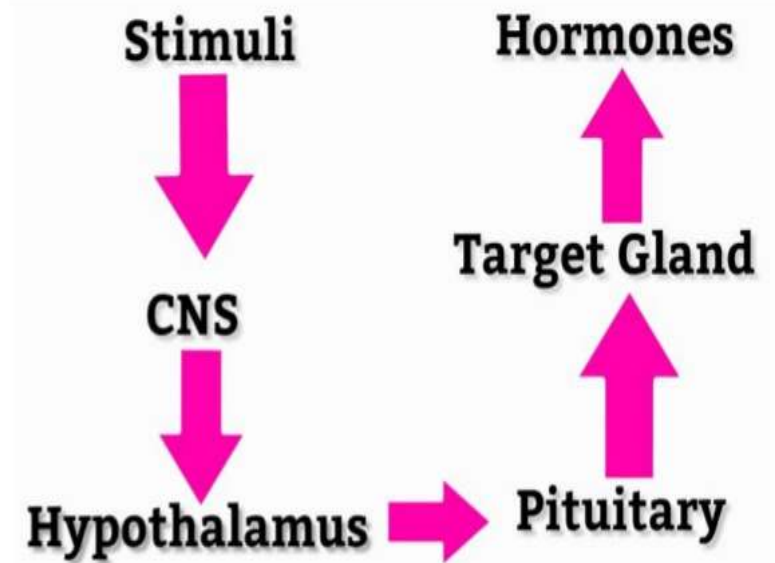
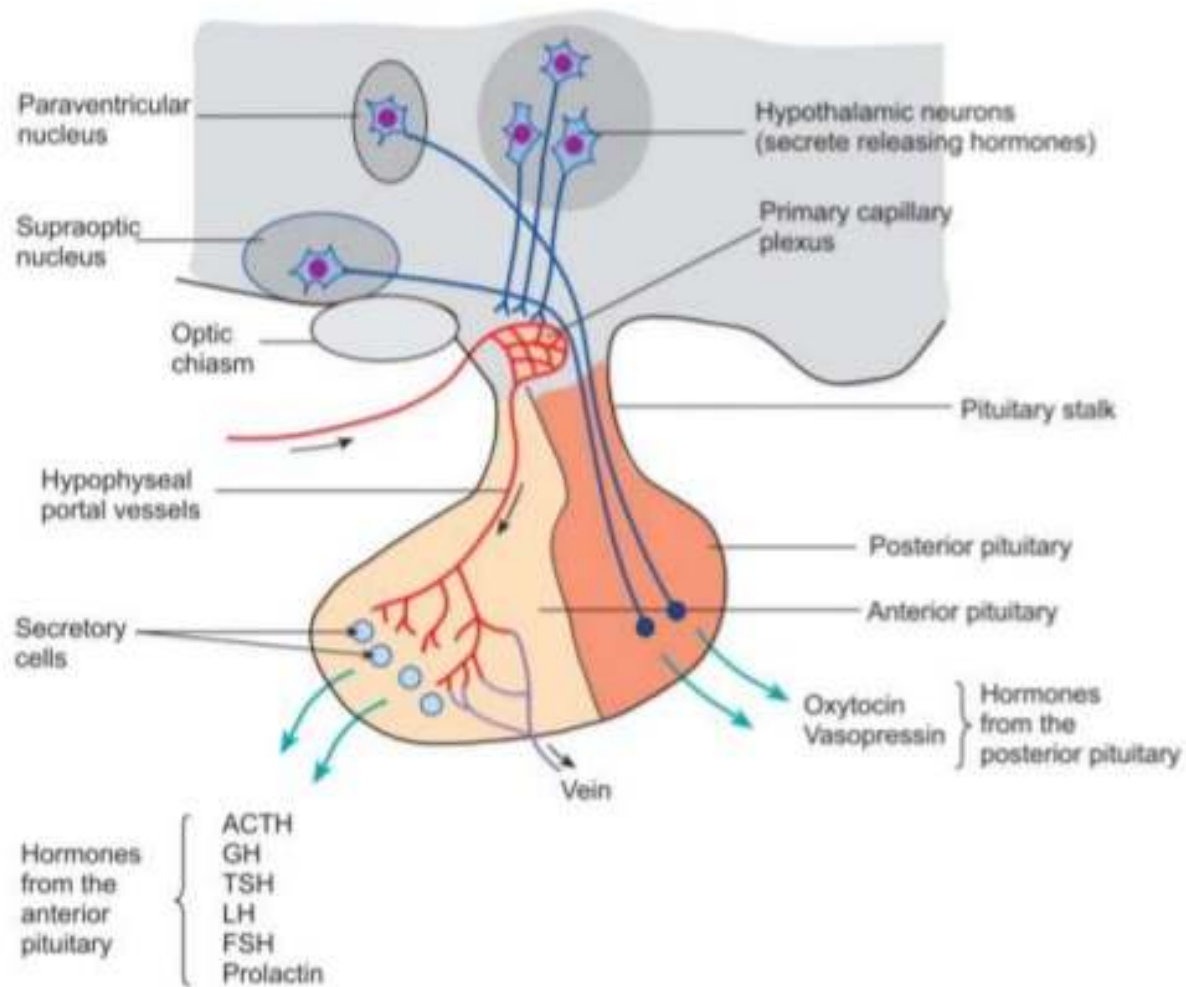
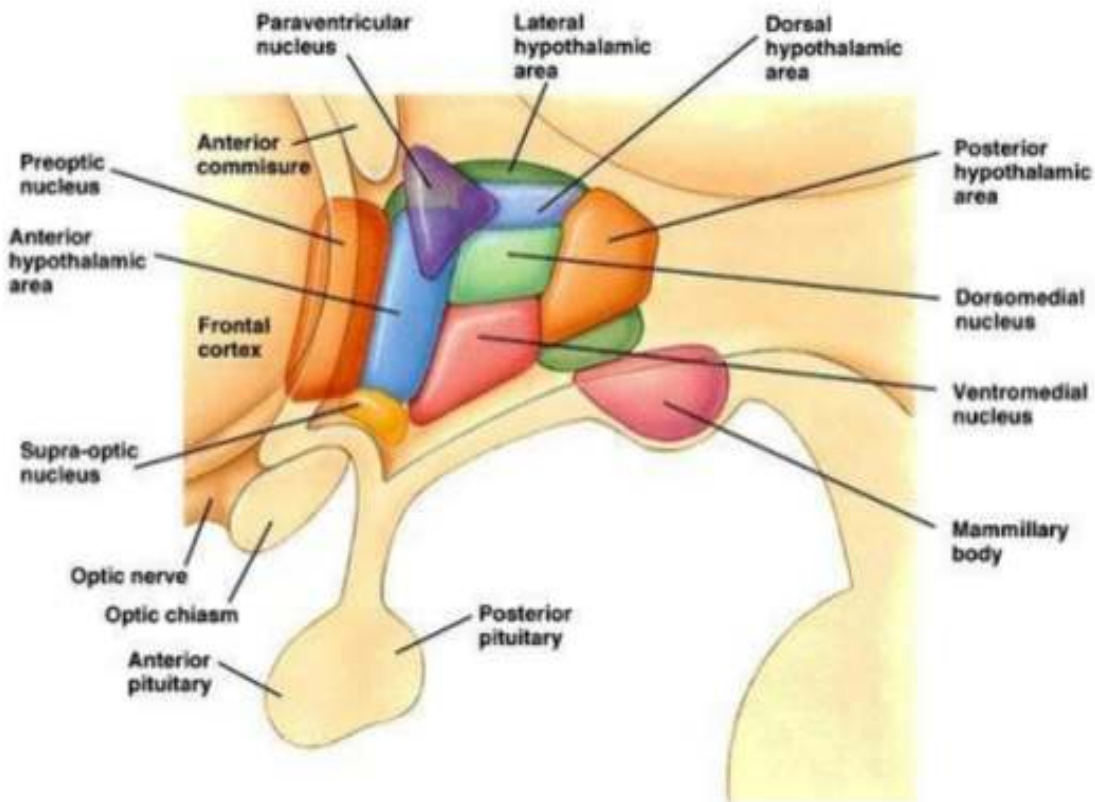


Fig. Showing ,The secretory activity of many endocrine glands is controlled by the nervous system.



# Hypothalamus

Nuclei of the Hypothalamus



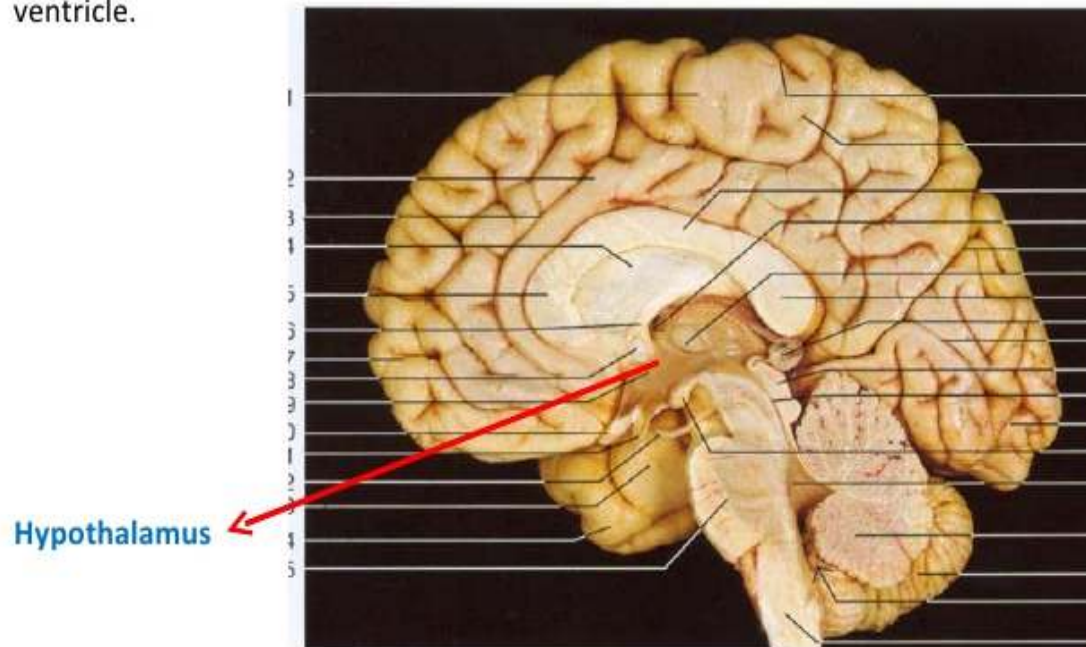
## Functions of Hypothalamus. (AS-RESPECT)

- Autonomic functions.
- Sleep –wake cycle.
- Reward & punishment centre.
- Endocrinal functions.
- Sexual behaviour & reproduction.
- Ph(F)ood intake regulation.
- Emotional & Instinctual behaviour.
- Circadian Rhythm control.
- Temperature regulation.

## Hypothalamus

The hypothalamus consists of only 4 cm<sup>3</sup> of neural tissue, or 0.3% of the total brain.

The hypothalamus extends from the lamina terminalis to a vertical plane posterior to the mammillary bodies, and from the hypothalamic sulcus to the base of the brain beneath the third ventricle.



- The hypothalamus contains neurons that control releases from the anterior pituitary.
- Seven hypothalamic hormones are released into a **portal system** connecting the hypothalamus and pituitary, and cause targets in the pituitary to release eight hormones.

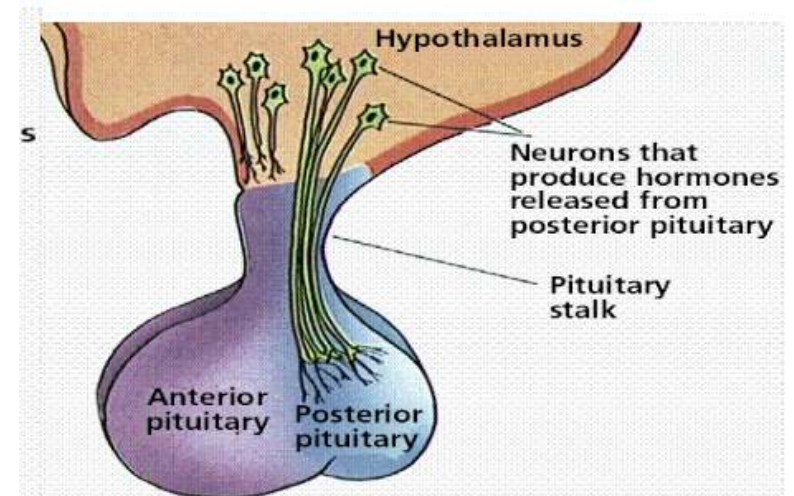
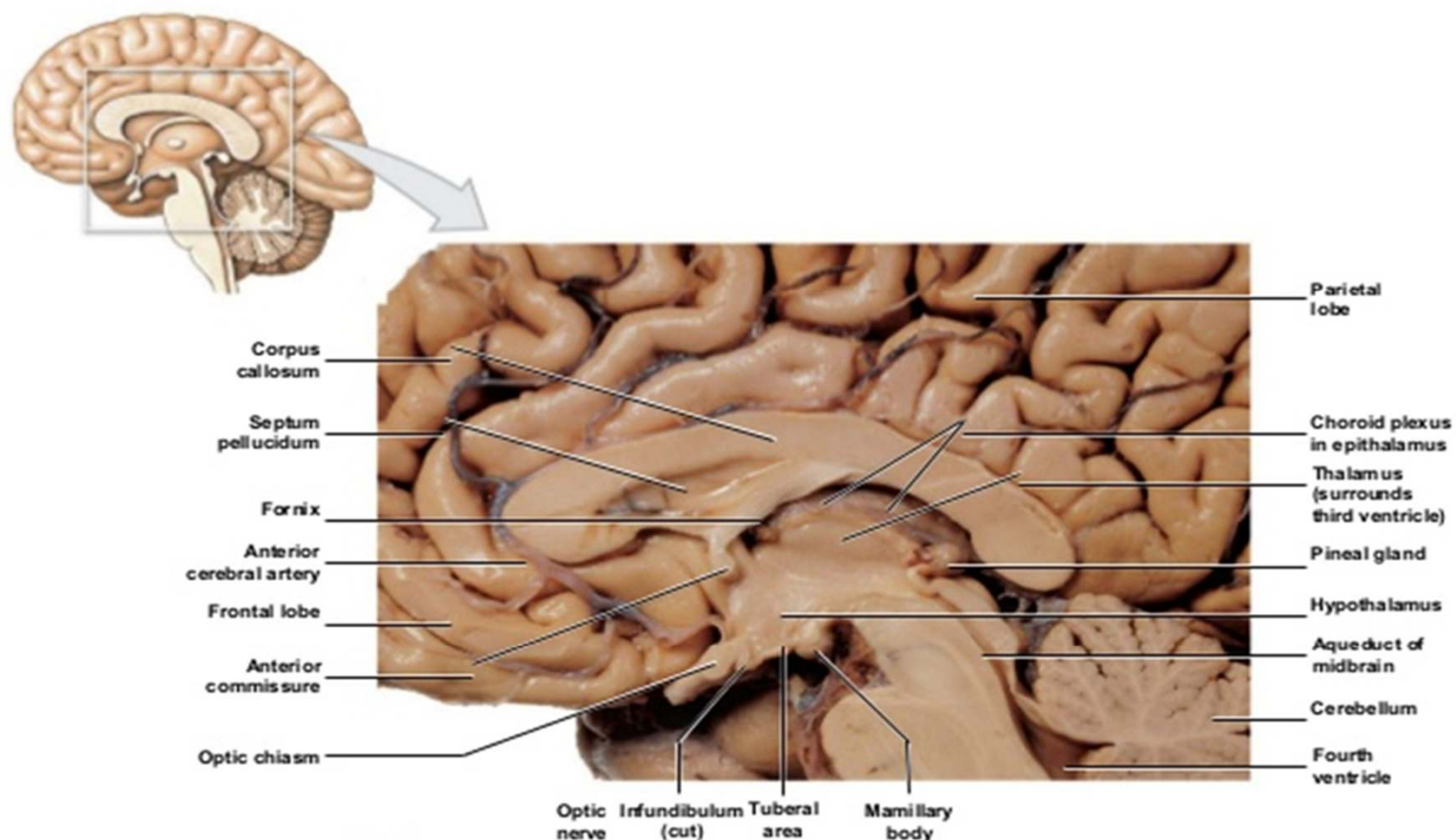


Figure 16.12a The Hypothalamus



**Midsagittal section through the brain.** This view shows the major features of the diencephalon and adjacent portions of the brain stem.

# PRINCIPAL HYPOTHALAMIC POLYPEPTIDE.

## ■ Food intake increased by

- Neuropeptide Y.
- Orexin – A
- Orexin – B
- Melanin concentrating hormone. (MCH)
- Ghrelin.

## ■ Food intake decreased by

- Cocaine & amphetamine regulated transcript. (CART)
- CRH.



## **Endocrinal functions.**

---

- Anterior Pituitary.(through Tubero-infundibular tract & hypophyseal portal system)
- Controls Thyroid G.
- Controls Metabolism through adrenal gland.
- Keep gonads inhibited.
- Control formation of milk by prolactin secretion.
- Posterior Pituitary regulate water balance through ADH.
- Regulation Of Uterine Contractility & regulation of Milk Ejection from breast through oxytocin.

# RAGE

- **Rage** – violent & aggressive emotional state by strong stimulation of **Punishment Centre**.
- Kept in check by counterbalancing activity of Ventromedial N of hypothalamus, hippocampus, amygdala & ant portion of limbic cortex.
- **Characterized by** –
  - Development of defense posture.
  - Extension of limbs
  - Lifting of tail.
  - Hissing & splitting
  - Piloerection.
  - Wide openings of eye.
  - Pupil dilation.

## Hypothalamic control of Anterior pituitary gland secretion

- Hypothalamus controls the hormonal secretions of the anterior pituitary, which in turn regulates other endocrine glands.
- Neurons in the hypothalamus **secrete releasing hormones and inhibiting hormones** into blood capillaries at the base of the hypothalamus.
- Releasing & inhibiting hormones released by **Paravocellular Neurosecretory cells of the hypothalamus**.

### **Releasing and Inhibiting hormones**

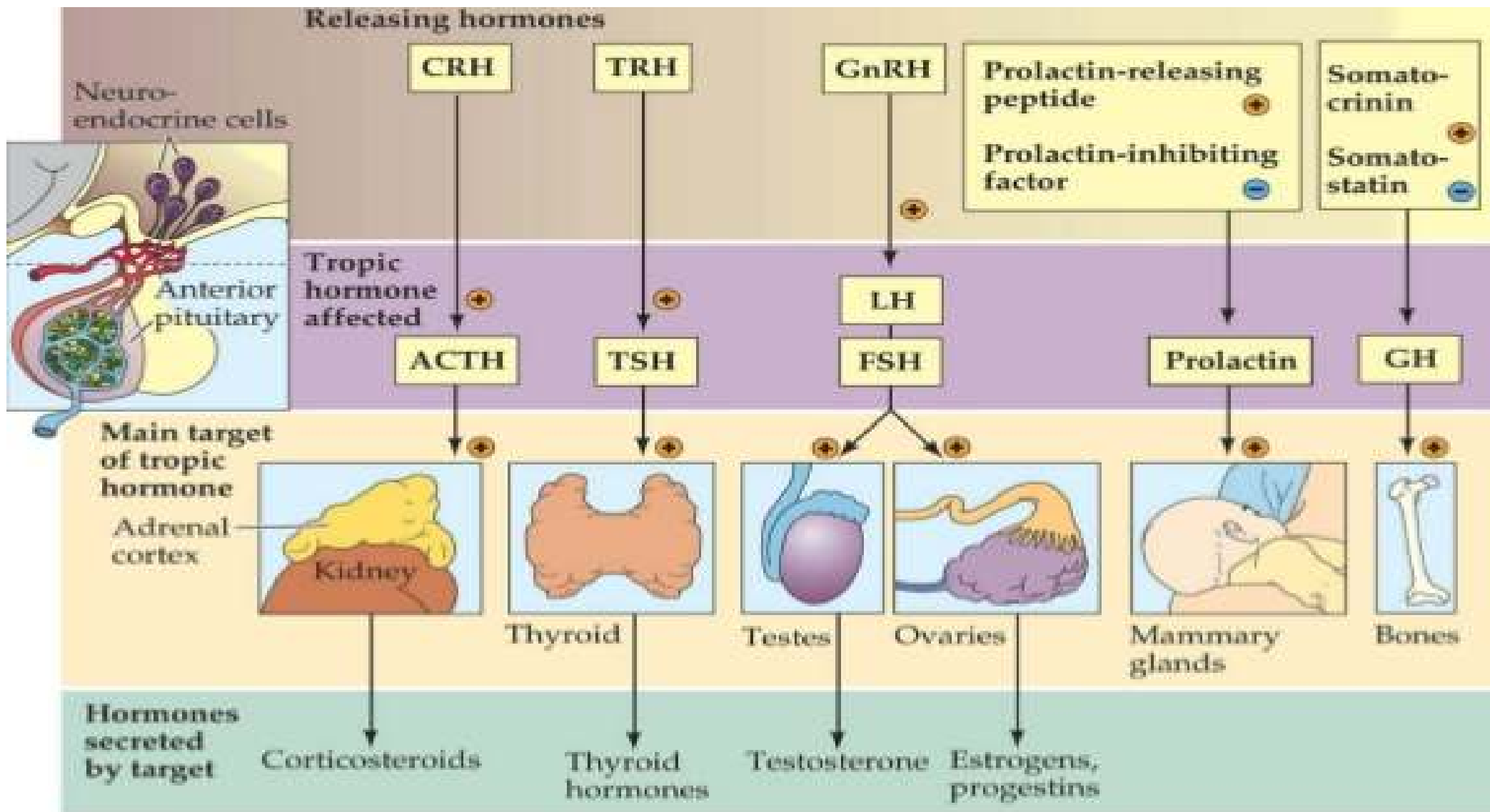
#### Hypothalamic -Releasing hormones :

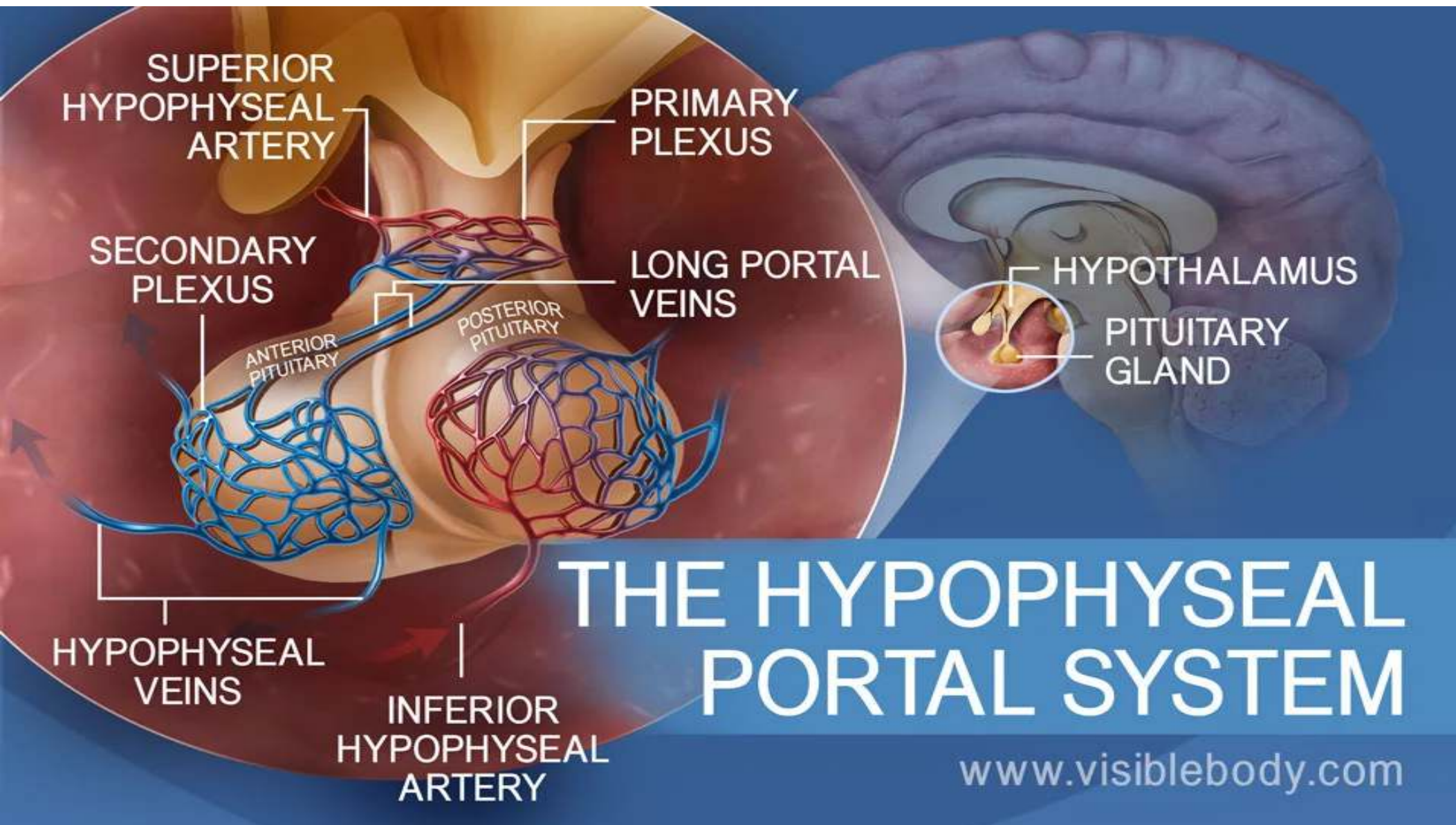
- CRH (Corticotropin releasing Hormone) ==> Stimulates the release of ACTH
- TRH (Thyrotropin-Releasing Hormone) ==> Stimulates the release of TSH
- GnRH (Gonadotropin-Releasing Hormone ) ==> stimulates the release of FSH& LH
- GHRH (Growth Hormone Releasing Hormone) ==> Stimulates the release of GH

# Hypothalamic releasing hormones

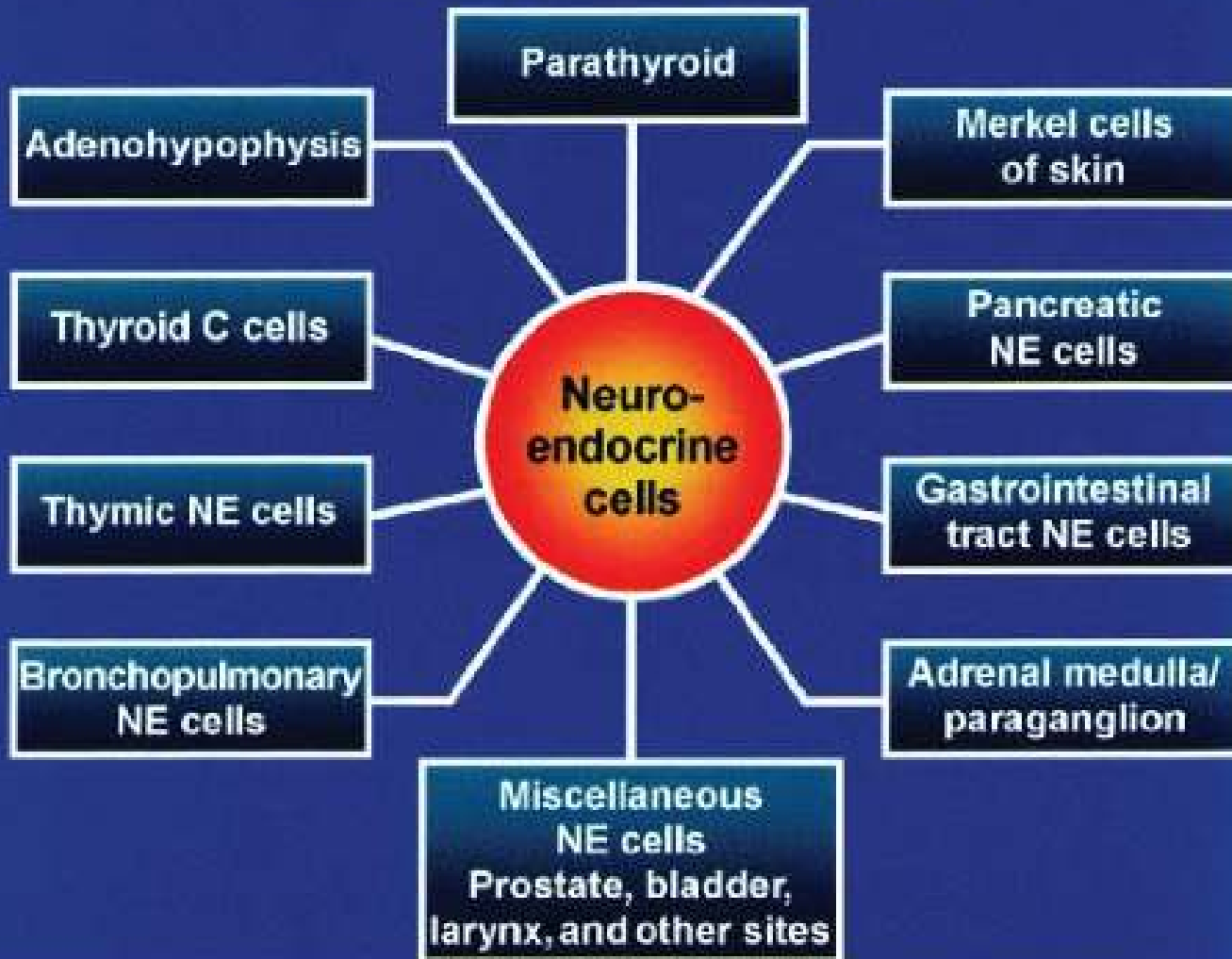
Hypothalamic releasing hormone	Effect on pituitary
Corticotropin releasing hormone (CRH)	Stimulates ACTH secretion
Thyrotropin releasing hormone (TRH)	Stimulates TSH and Prolactin secretion
Growth hormone releasing hormone (GHRH)	Stimulates GH secretion
Somatostatin	Inhibits GH (and other hormone) secretion
Gonadotropin releasing hormone (GnRH)	Stimulates LH and FSH secretion
Prolactin releasing hormone (PRH)	Stimulates PRL secretion
Prolactin inhibiting hormone (dopamine)	Inhibits PRL secretion







## Diffuse Neuroendocrine System



diffuse neuroendocrine system, which is composed of classic endocrine organs as well as scattered neuroendocrine cells in various organs and tissues.

- **Neurohypophysis**- It shows presence of axons of neuron , cell bodies of which are situated in hypothalamus. Interspersed among the nerve fibre few neuroglial cells called as pituicytes.

## Pituitary Gland

### MASTER GLAND

- Also known as Hypophysis Cerebri
- Situated in the hypophyseal fossa in middle cranial fossa
- Histologically it shows two parts-  
Adenohypophysis and Neurohypophysis  
**Adenohypophysis** shows presence of chromophobes & chromophils  
Chromophils are of two types- Acidophils & Basophils.

## Anterior Pituitary: Hormones

### •Anterior pituitary hormones

- FLAT PiG
  - FSH (follicle-stimulating hormone)
  - LH (luteinizing hormone)
  - ACTH (adrenocorticotrophic hormone)
  - TSH (thyroid-stimulating hormone)
  - Prolactin
  - Growth hormone (somatotropin)
- categories of hormones
  - corticolipotropins
    - ACTH and MSH (melanocyte-stimulating hormone)
  - glycoprotein hormones
    - FSH, LH, TSH
  - somatomammotropins
    - prolactin and growth hormone

### •Corticolipotropins

#### •synthesis

- corticolipotropins are derived from a single precursor, POMC

•POMC = pro-opiomelanocortin

- pathway details

#### •MSH

- corticolipotropin synthesis products (aka fragments) contain MSH
- increased MSH levels → skin pigmentation
- e.g., Addison's disease
- ↑ ACTH → ↑ MSH → skin pigmentation

### •Glycoprotein hormones

- subunits of peptide hormones
  - glycoprotein hormones contain 2 subunits: **α and β subunit**
    - α subunits identical, β subunits non-identical
    - hormone specificity determined by β subunit
- human chorionic gonadotropin (hCG) structurally related to glycoprotein hormone
  - hCG contains identical α subunit

### ACIDOPHILS (growth)

- GROWTH HORMONE
- PROLACTIN

### BASOPHILS (trophy)

- TSH
- ACTH
- LH, FSH



- Somatomammotropins

- prolactin

- growth hormone

- secretion

- pulsatile secretory pattern

- secretory **bursts approximately every 2 hours**

- ↑ in secretory bursts during exercise and sleep

- functions

- ↑ linear growth and muscle mass

- growth mediated by production of somatomedins

- aka insulin-like growth factors (IGFs)

- diabetogenic effect

- insulin resistance

- decreases glucose uptake and utilization

- "diabetogenic"

- growth hormone produces increases in blood glucose

# Hormones secreted by anterior pituitary

1. **FSH** (follicle stimulating hormone)

1. **LH** (luteinizing hormone)

The above two are called **gonadotropins**

**Hormones from basophils** :go to other endocrine glands, thyroid, adrenal cortex, ovary, testis. Cells from acidophils do NOT.

**Acidophils make GROWTH related hormones. Basophils make hormones which STIMULATE OTHER endocrine glands.**

**Chromophobes make NOTHING.**

3. **TSH** (thyroid stimulating hormone, thyrotropin)

4. **ACTH** (adrenocorticotrophic hormone)

5. **GH** (growth hormone; somatotropin or somatotrophic hormone)

6. **PRL** (prolactin)

- When stained with the PAS reaction all three types of basophils appear reddish

• **Tropic (trophic) hormones--** target other endocrine glands to release their own hormones.

## **Chromophobe cells**

**anterior pituitary cells that lack granules and that do not react with acidophilic/basophilic stains**

**e.g., stromal cells and degranulated chromophils**

- **Chromophobe cells are unstained or weakly stained cells. appears relatively pale under the microscope**
- EM and immunocytochemistry are used.
- They are now thought to represent acidophil and basophilic cells in a dormant or recently degranulated stage (degranulation = release of most of the secretory vesicles), but may also include stem cells of the secretory cells.

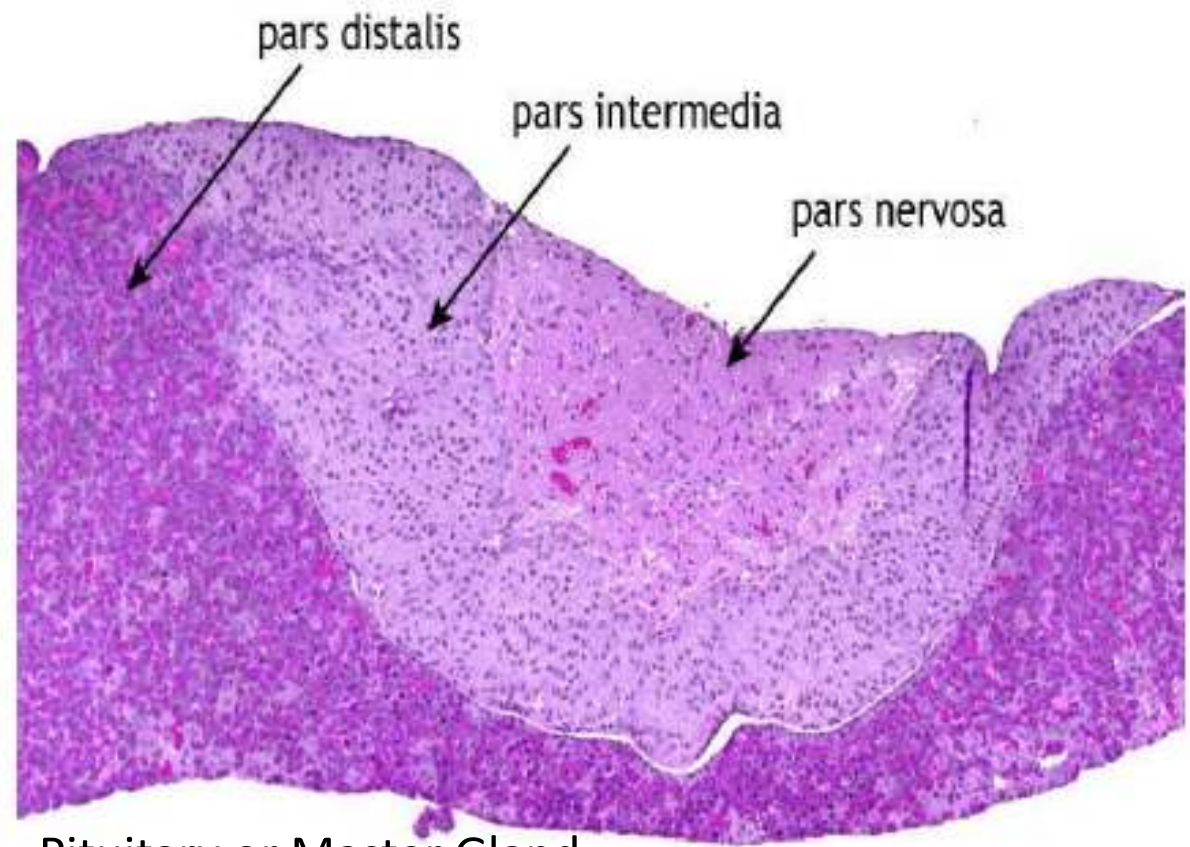
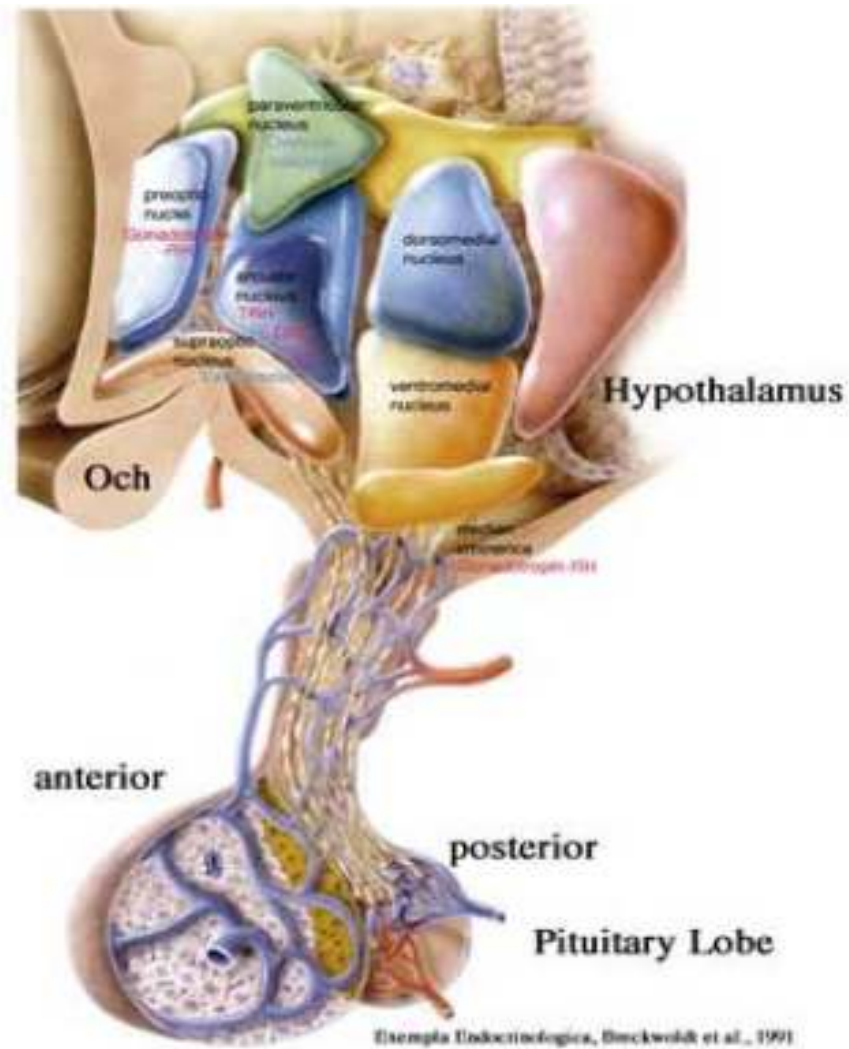
One type of chromophobe cell is known as amphophils.

- **Amphophils** are epithelial cells found in the anterior and intermediate lobes of the pituitary.
  - Together, these epithelial cells are responsible for producing the hormones of the anterior pituitary and releasing them into the bloodstream.
- **Melanotrophs** (also, Melanotropes) are another type of chromophobe which secrete melanocyte stimulating hormone (MSH).

Chromophobe" also refers to a type of renal cell carcinoma (distinct from "clear cell")  
30% of patients with Birt-Hogg-Dubé syndrome will also develop chromophobe renal cancer.

Table 20.3 Pituitary Gland Hormones		
Hormone	Target Cells	Effects of Hormone
<b>HORMONES OF THE ANTERIOR PITUITARY</b>		
Adrenocorticotropic hormone (ACTH)	Adrenal cortex	Stimulates production of corticosteroid hormones
Follicle-stimulating hormone (FSH)	Female: Ovaries Male: Testes	Female: Stimulates growth of ovarian follicles Male: Stimulates sperm production
Luteinizing hormone (LH)	Female: Ovaries Male: Testes	Female: Stimulates ovulation, estrogen and progesterone synthesis in ovary Male: Stimulates androgen synthesis in testes
Thyroid-stimulating hormone (TSH)	Thyroid gland	Stimulates thyroid hormone synthesis and secretion
Prolactin (PRL)	Female: Mammary glands Male: Not known	Female: Stimulates milk production in mammary glands Male: May play a role in the sensitivity of the testes' interstitial cells to LH
Growth hormone (GH)	Almost every cell in the body	Increased growth and metabolism in target cells; synthesis of somatomedin in the liver to stimulate growth at epiphyseal plate
Melanocyte-stimulating hormone (MSH)	Melanocytes	Stimulates synthesis of melanin and dispersion of melanin granules in epidermal cells
<b>HORMONES STORED IN THE POSTERIOR PITUITARY</b>		
Antidiuretic hormone (ADH) (also called vasopressin)	Kidney Smooth muscle in arteriole walls	Stimulates reabsorption of water from urine in kidneys Stimulates vasoconstriction in arterioles of body, thereby raising blood pressure
Oxytocin (OT)	Female: Uterus, mammary glands Male: Smooth muscle of male reproductive tract	Female: Stimulates smooth muscle contraction in uterine wall; stimulates milk ejection from mammary glands Male: Stimulates contraction of smooth muscle of male reproductive tract





Pituitary or Master Gland

posterior lobe

neurohypophysis

anterior lobe

adenohypophysis

### Acidophil cells (or acidophils)

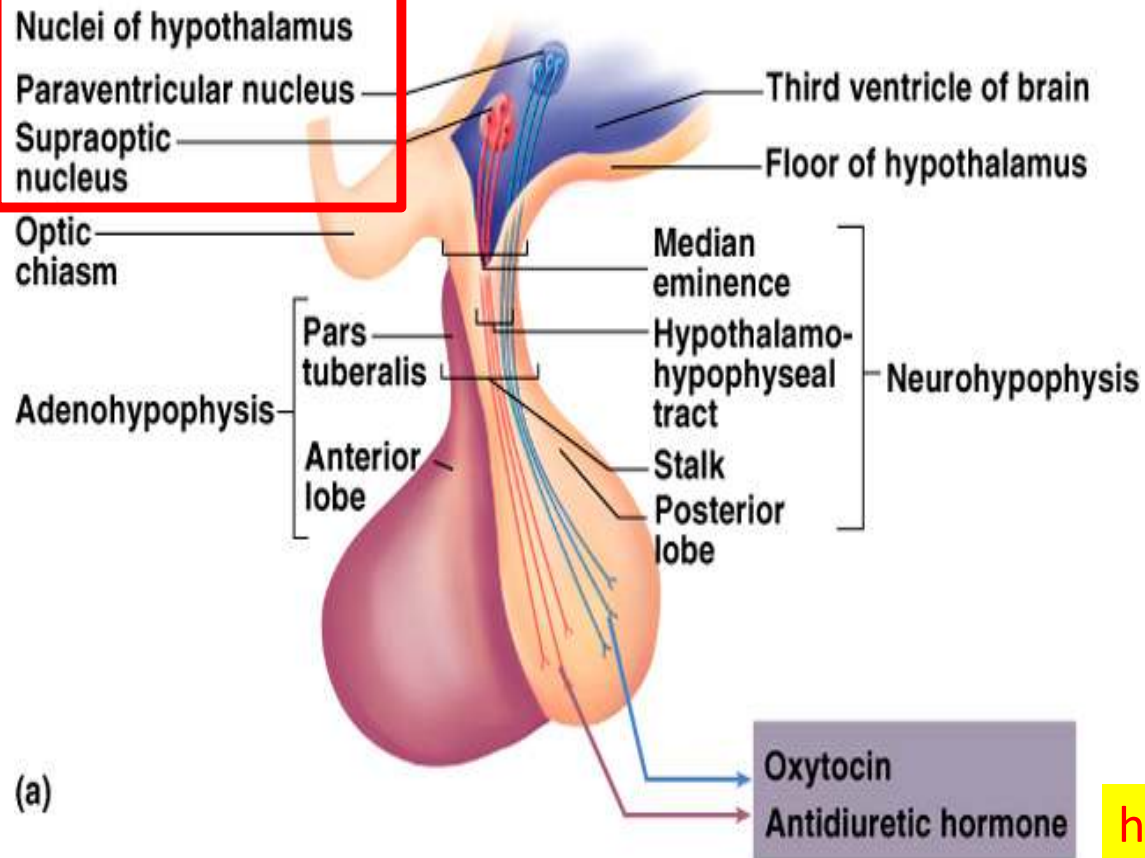
- Acidophils are rounded cells and typically smaller than basophil cells.
- Acidophils account for roughly 65% of the cells in the adenohypophysis.
- **The most frequent subtype of acidophils are the somatotrophs (which can be stained with the dye orange G).**
- **Somatotrophs produce growth hormone (GH or somatotropin)**, which e.g. stimulates liver cells to produce polypeptide growth factors which stimulate growth (e.g. somatomedin which stimulates epiphyseal cartilage - overproduction of this hormone may result in gigantism or acromegaly).
- **Mammotrophs (or lactotrophs)**, the second group of acidophils, secrete prolactin.
  - Their number increases significantly in late pregnancy and the early months of lactation.

### Basophil cells (or basophils)

Based on their hormone products basophils are divided into three subtypes.

- **Thyrotrophs produce thyroid stimulating hormone (TSH or thyrotropin).**
- **Gonadotrophs**
  - **produce follicle stimulating hormone (FSH), which stimulates the seminiferous epithelium in males in addition to early follicular growth in females.**
  - **Gonadotrophs also produce luteinizing hormone (LH), which stimulates production of testosterone by Leydig cells in males in addition to late follicular maturation, oestrogen secretion and formation of corpus luteum in females.**
- **Corticotrophs (or adrenocorticolipotrophs)**
  - **secrete adrenocorticotrophic hormone (ACTH or corticotropin) and lipotropin (LPH, no known function in humans).**
  - Corticotropes are the most frequent cell type in the pars intermedia.
  - In the pars intermedia, the precursor of ACTH and LPH undergoes further hydrolysis into melanocyte stimulating hormone (MSH, increased pigmentation in patients with Addison's disease) and a number of other peptides (among them endogenous opioids).

# The Posterior Pituitary



• **posterior pituitary, or neurohypophysis** = is the **neural portion of the pituitary**

- a **collection of unmyelinated axons**
  - axons **extend from cell bodies in hypothalamus**

• consists of:

- **pars nervosa,**
  - **infundibular stalk,**
  - **median eminence**
- **neurophysins** carry hormones made in the hypothalamus (ADH and oxytocin) from the hypothalamus to the posterior pituitary

• **embryological origin**

- **neural ectoderm**
  - **downgrowth of neural ectoderm (diencephalon)**

hormones are secreted by magnocellular neurons located in the supraoptic and paraventricular nucleus of hypothalamus

## Antidiuretic hormone (ADH; vasopressin)

- synthesis

- hypothalamic supraoptic nucleus neuronal cell bodies synthesize ADH pro-hormone
  - **ADH pro-hormone contains ADH and neurophysin II**

- ADH pro-hormones are packaged in secretory vesicles

- secretory vesicles are transported via axonal transport to nerve terminals
  - **nerve terminals** in pars nervosa of posterior pituitary

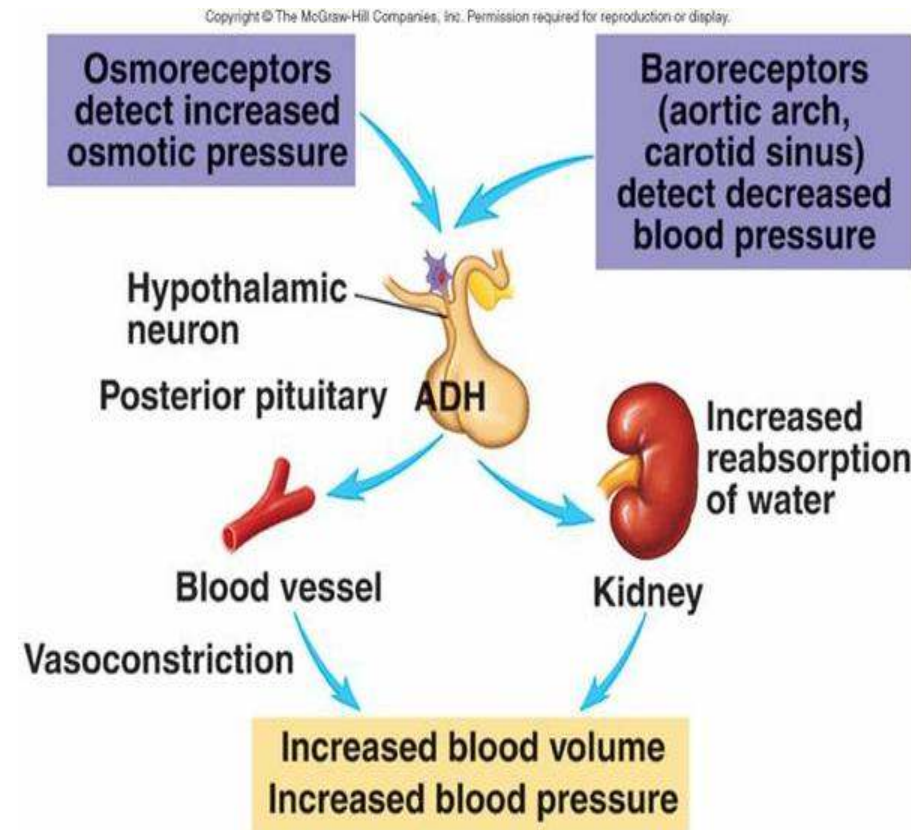
- ADH pro-hormone processing occurs in secretory vesicles during axonal transport

- cleavage of neurophysin II and release of ADH hormone

- secretion

- action potential depolarizes nerve terminals
  - neurosecretory vesicles fuse with plasma membrane
    - releases ADH and neurophysin II into perivascular space of highly fenestrated capillaries by which ADH enters systemic circulation

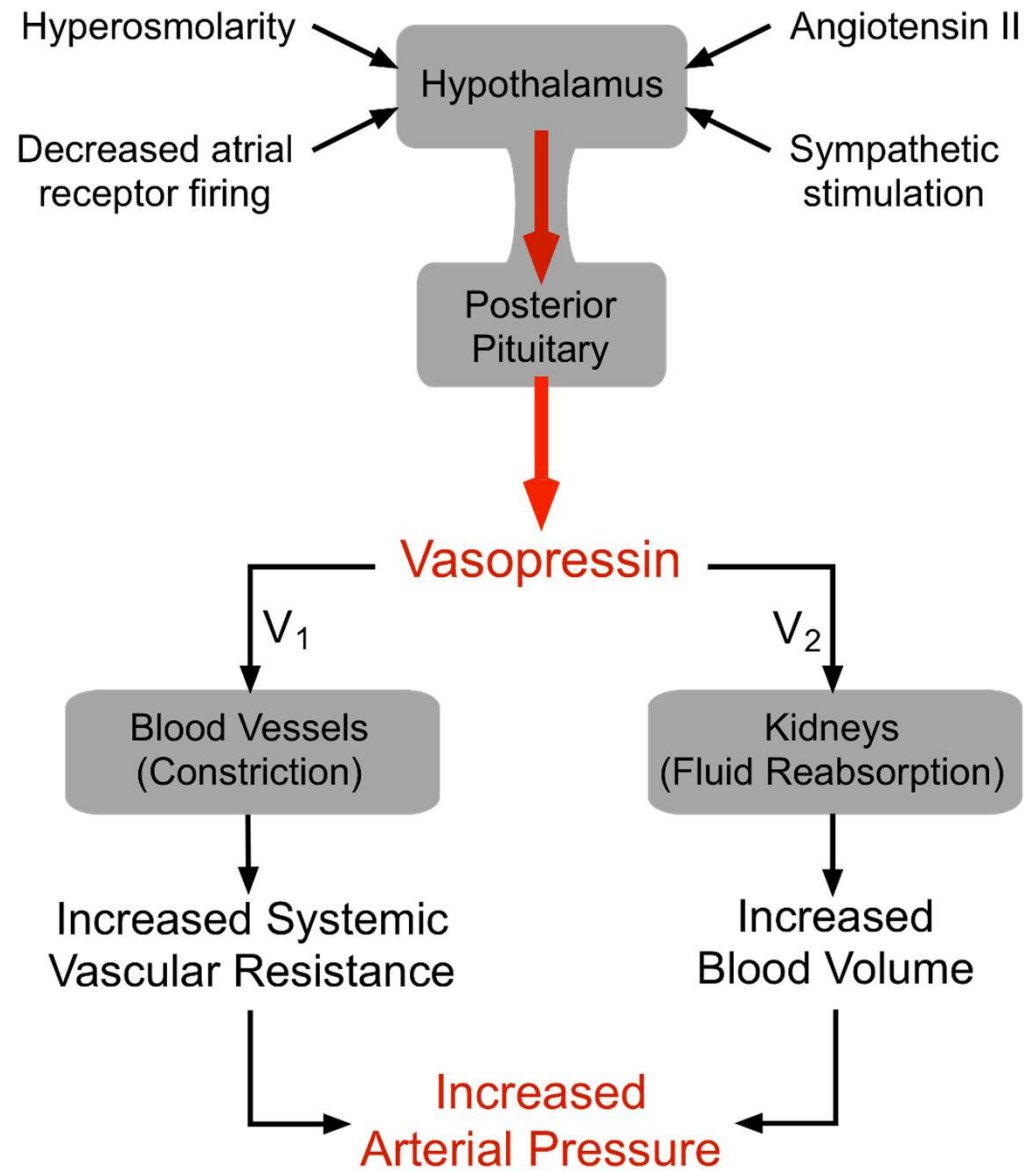
## The Posterior Pituitary

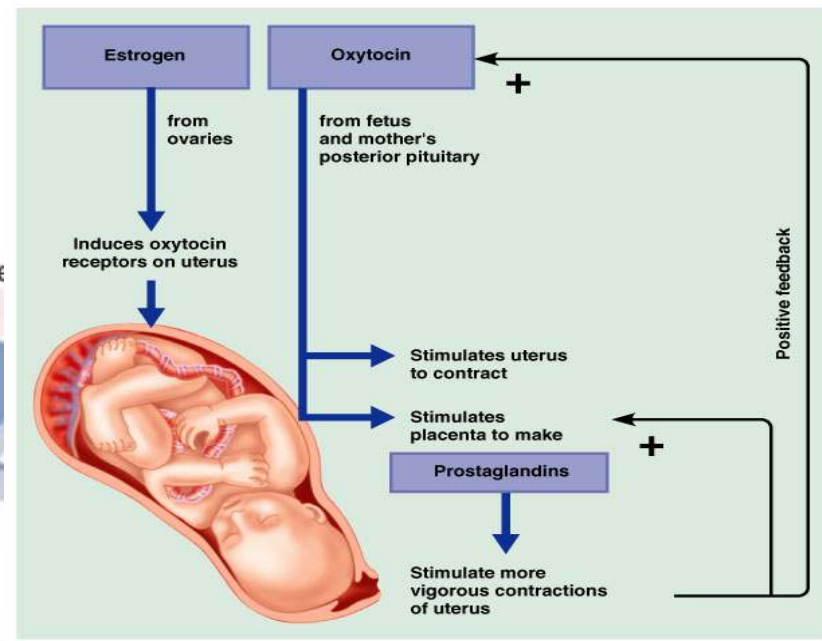
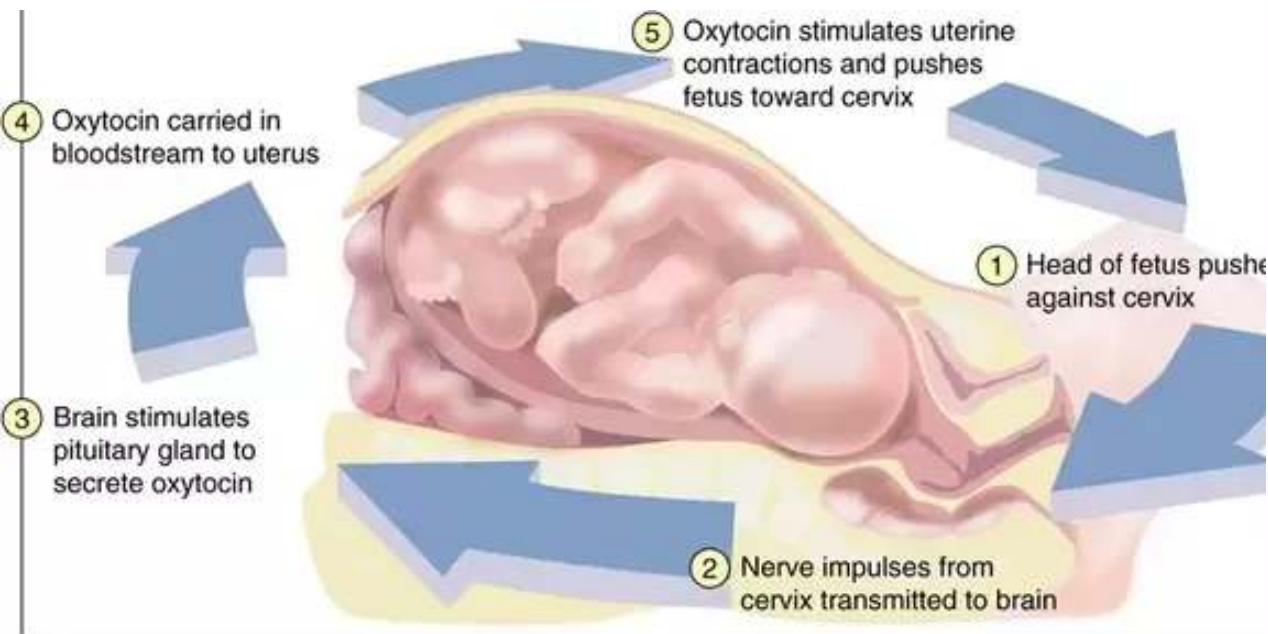




# POSTERIOR PITUITARY

- OXYTOCIN (contracts uterine smooth muscle)
- VASOPRESSIN (ADH)
  - vasoconstriction,
  - gluconeogenesis,
  - platelet aggregation,
  - release of Factor-VIII and vWb factor,
  - concentrates urine, main effects on kidney and brain)
- The posterior pituitary does not make these hormones, it just releases them.
- The hypothalamus actually makes the hormones and transfers it down the stalk to the neurohypophysis.





Copyright © 2004 Pearson Education, Inc., publishing as Benjamin Cummings.

## INCREASING OXYTOCIN

- LIGHT TOUCH
- SUCKING
- FOOD INTAKE
- WARMTH
- LIGHT PRESSURE
- MASSAGE-LIKE STROKING
- SEXUAL STIMULATION
- CALM & SUPPORTIVE ENVIRONMENT

Increases Oxytocin Release	Inhibits Oxytocin Release
<ul style="list-style-type: none"> <li>feeling secure</li> <li>privacy</li> <li>dim lighting</li> <li>people you know</li> <li>touch</li> <li>comfortable environment</li> <li>relaxation</li> </ul>	<ul style="list-style-type: none"> <li>feeling frightened</li> <li>feeling watched</li> <li>bright lights</li> <li>strangers</li> <li>questions</li> <li>uncomfortable environment</li> <li>thinking</li> </ul>

# BAHS\* of Posterior Pituitary Hormones

Hormone	Stimulates
Antidiuretic hormone	Water reabsorption in the kidney
Oxytocin	Contraction of uterine smooth muscle in labor. Contraction of breast cells to allow milk let down.

\* Boring as heck summary



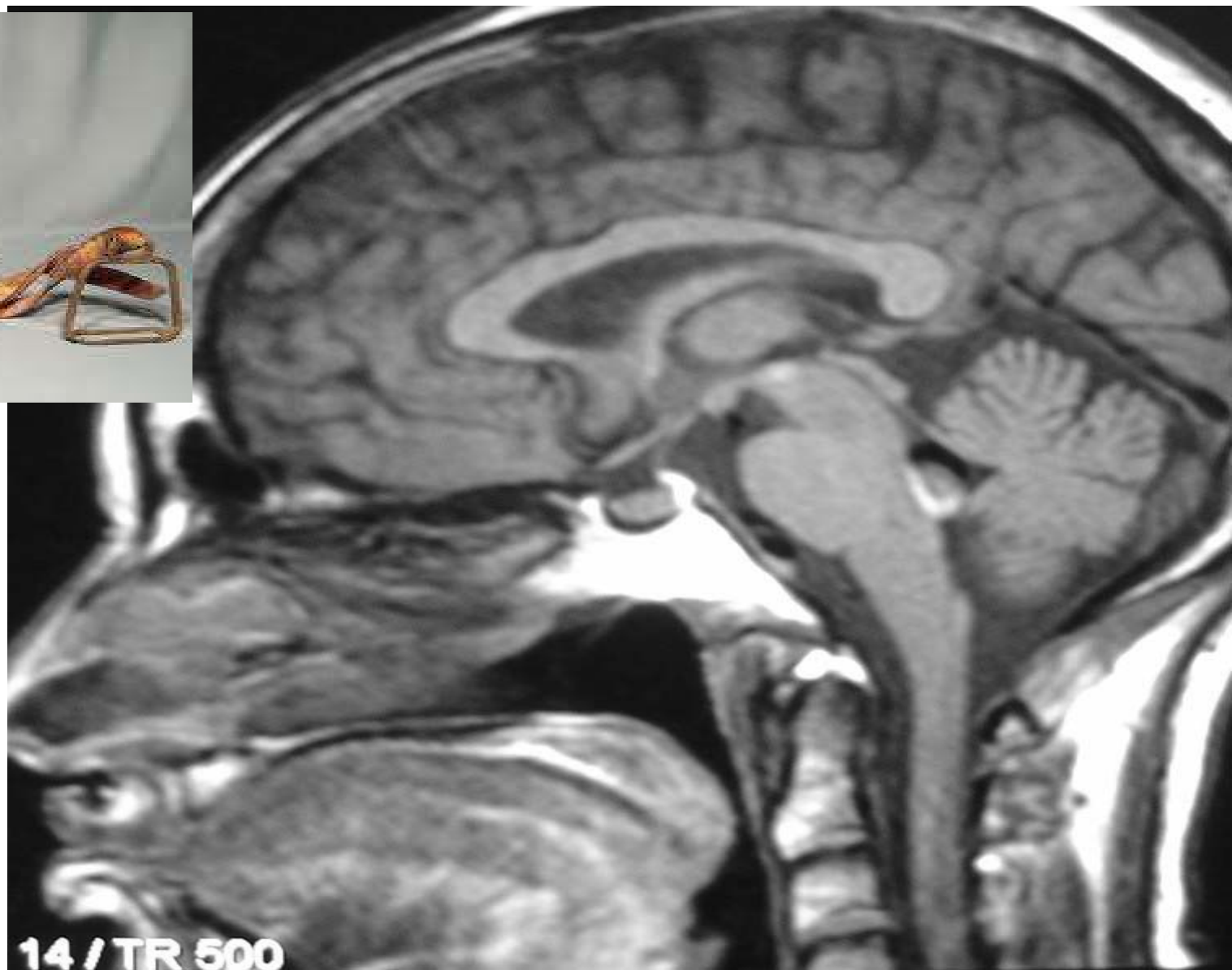
## VIS\* of Oxytocin

Situation	Stimulates
Interpersonal connection	Trust
Orgasm	Pleasure AND connection with that particular person
Intimate relationship	Monogamy
Sports teams	Better performance

\* Very interesting summary



Normal pituitary.  
With Turkish saddle,  
i.e., sella turcica.



# Pituitary Pathology

## □ Growth Hormone GH

- dwarfism -hyposecretion
- gigantism, acromegaly-hypersecretion

## □ Thyroid Stimulating Hormone TSH

- cretinism (infants) -hyposecretion
- myxedema( adults ) -hyposecretion
- Toxic goiter (adults -hypersecretion

## ■ exophthalmos

