



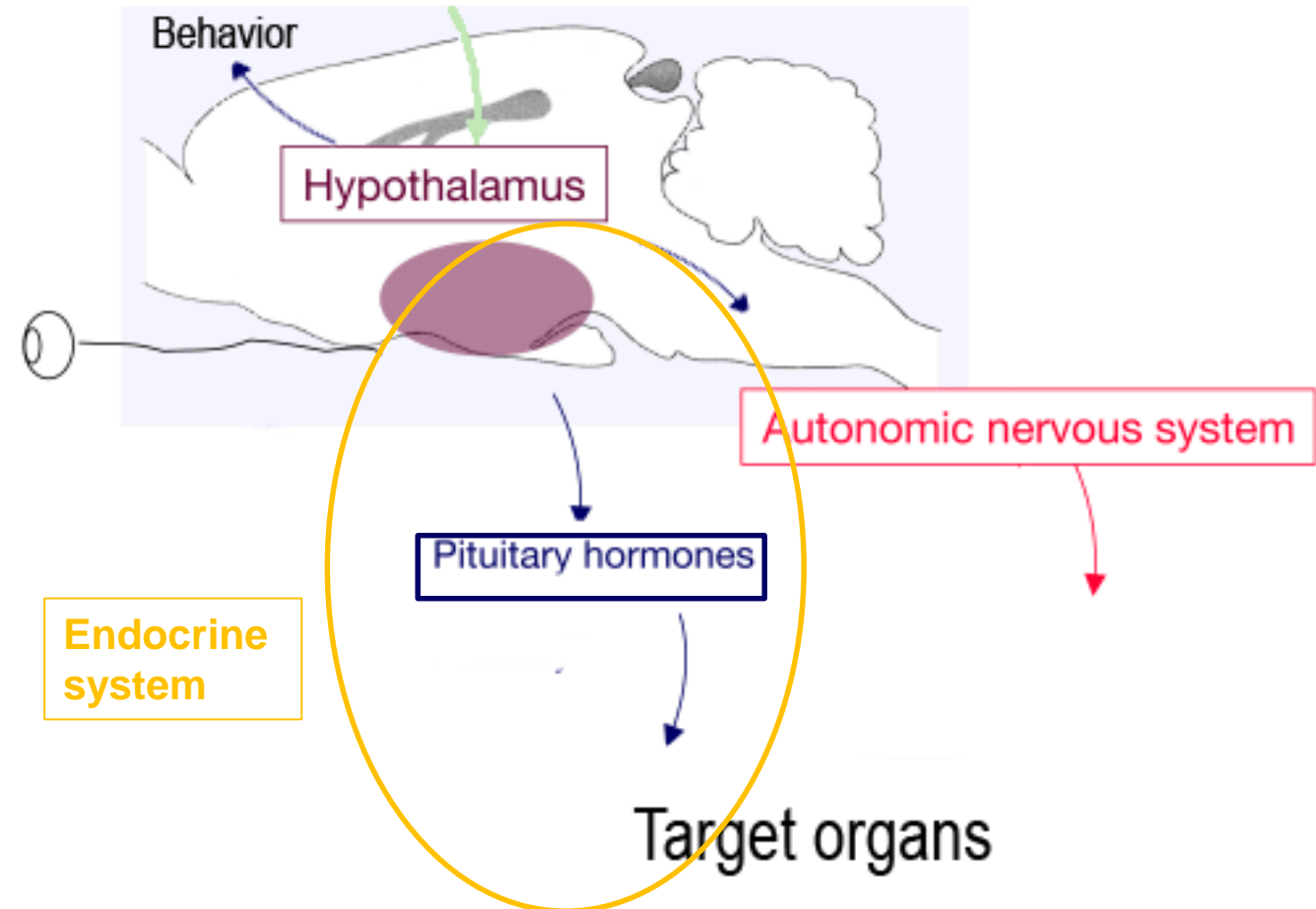
# The hypothalamo-hypophyseal system and the pituitary gland

Dr. Zsuzsanna Tóth

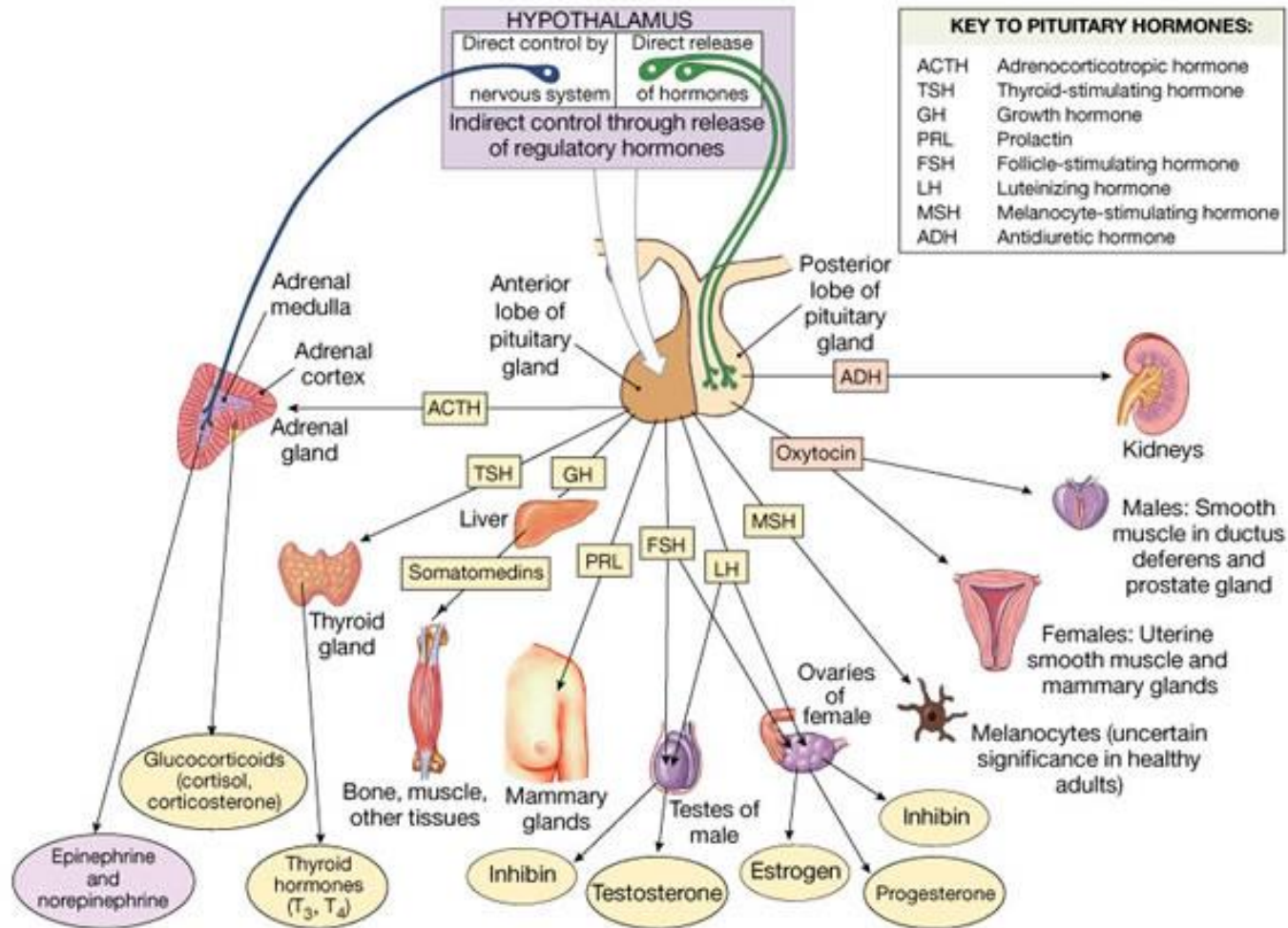
Semmelweis University, Dept. of Anatomy, Histology and Embryology

# Homeostatic integration within the hypothalamus

Environmental factors: light, temperature, stress  
Internal factors: emotions, satiety, nutritional status, water balance



# The hypothalamo-hypophyseal system- neuroendocrine system

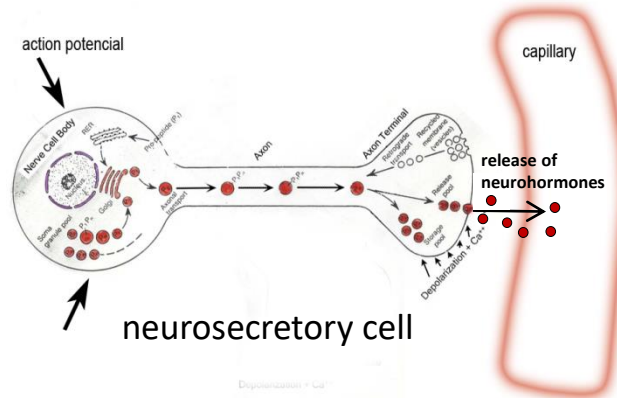




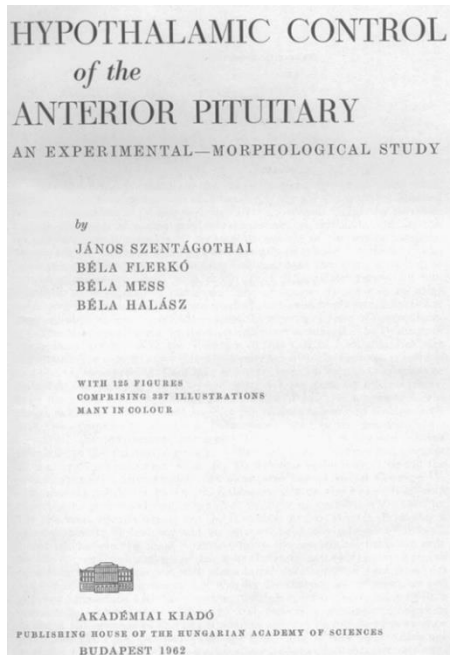
# Neurosecretion is a special feature in the hypothalamo-hypophyseal system



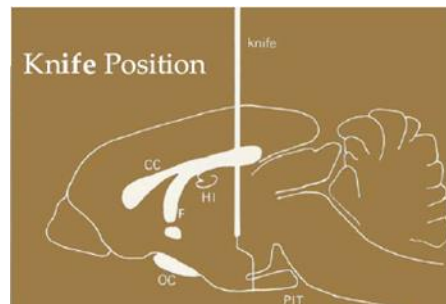
Ernst and Berta Scharrer, 1928



Béla Halász

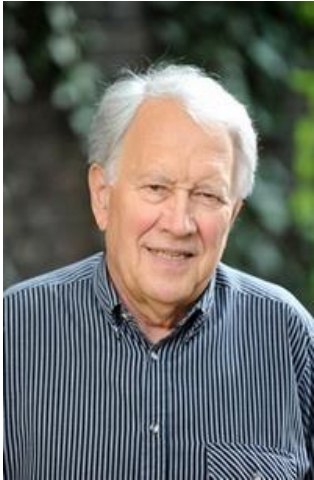


Halasz-knife

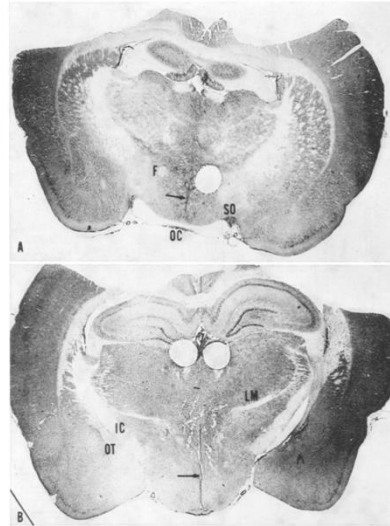


János Szentágothai

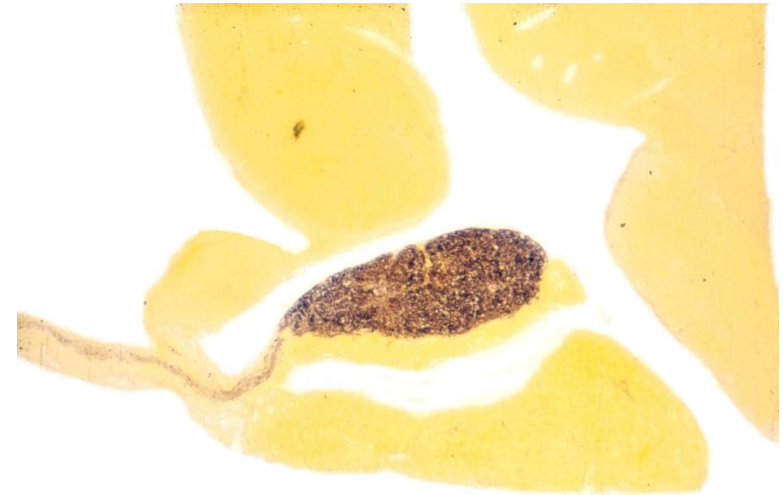
# Identification of different neurohormones and the specific nuclei where they are produced



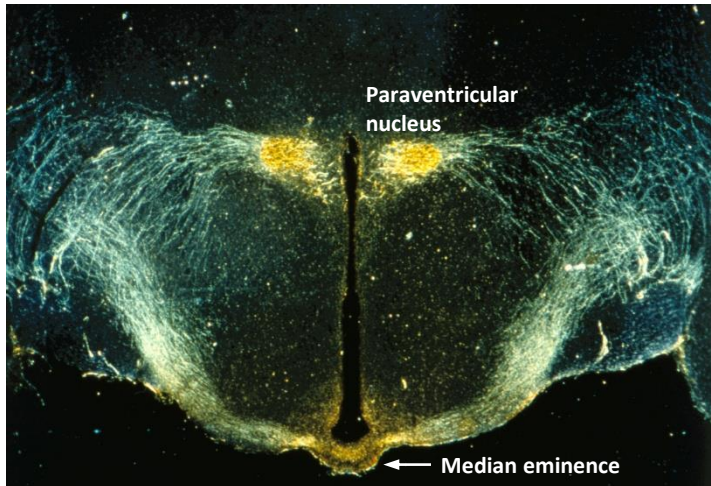
Miklós Palkovits



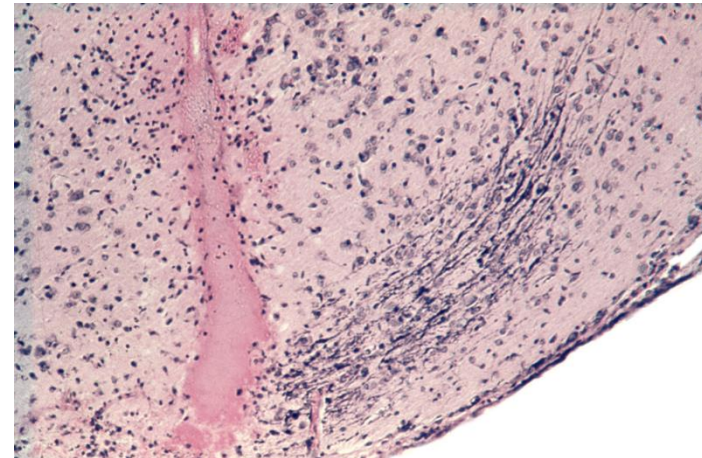
Palkovits M: Isolated removal of hypothalamic or other brain nuclei of the rat. Brain Res 59:449-450 (1973)



ADH containing fibers and accumulation of ADH in the posterior pituitary, sagittal section



ADH immunohistochemistry, rat hypothalamus coronal section



ADH accumulation right to the knife cut demonstrates the direction of the transport



# Hypothalamic nuclei and areas

## Anterior region

- n. anterior
- n. preopticus med. and lat.
- n. paraventricularis
- n. supraopticus
- n. suprachiasmaticus

## Medial region

- **Periventricular zone**

### Medial zone

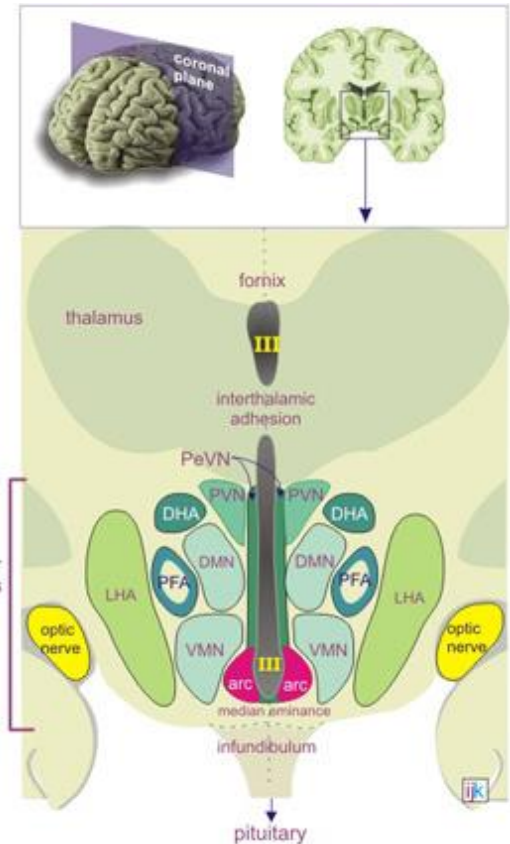
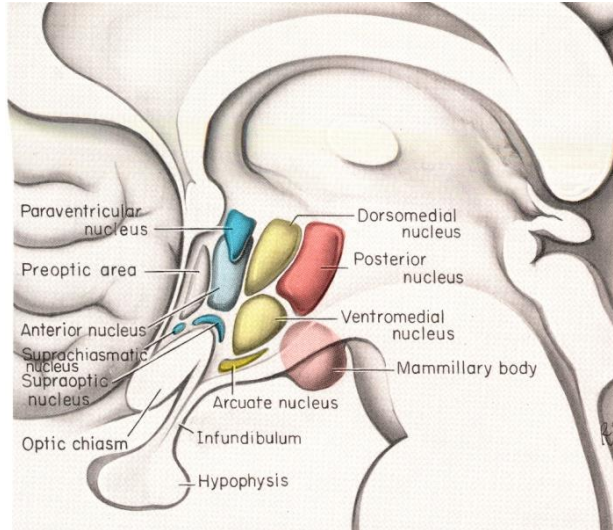
- n. ventro- and dorsomedialis
- n. infundibularis (arcuatus)

### Lateral zone

dorsolateral hypothalamic area  
medial forebrain bundle

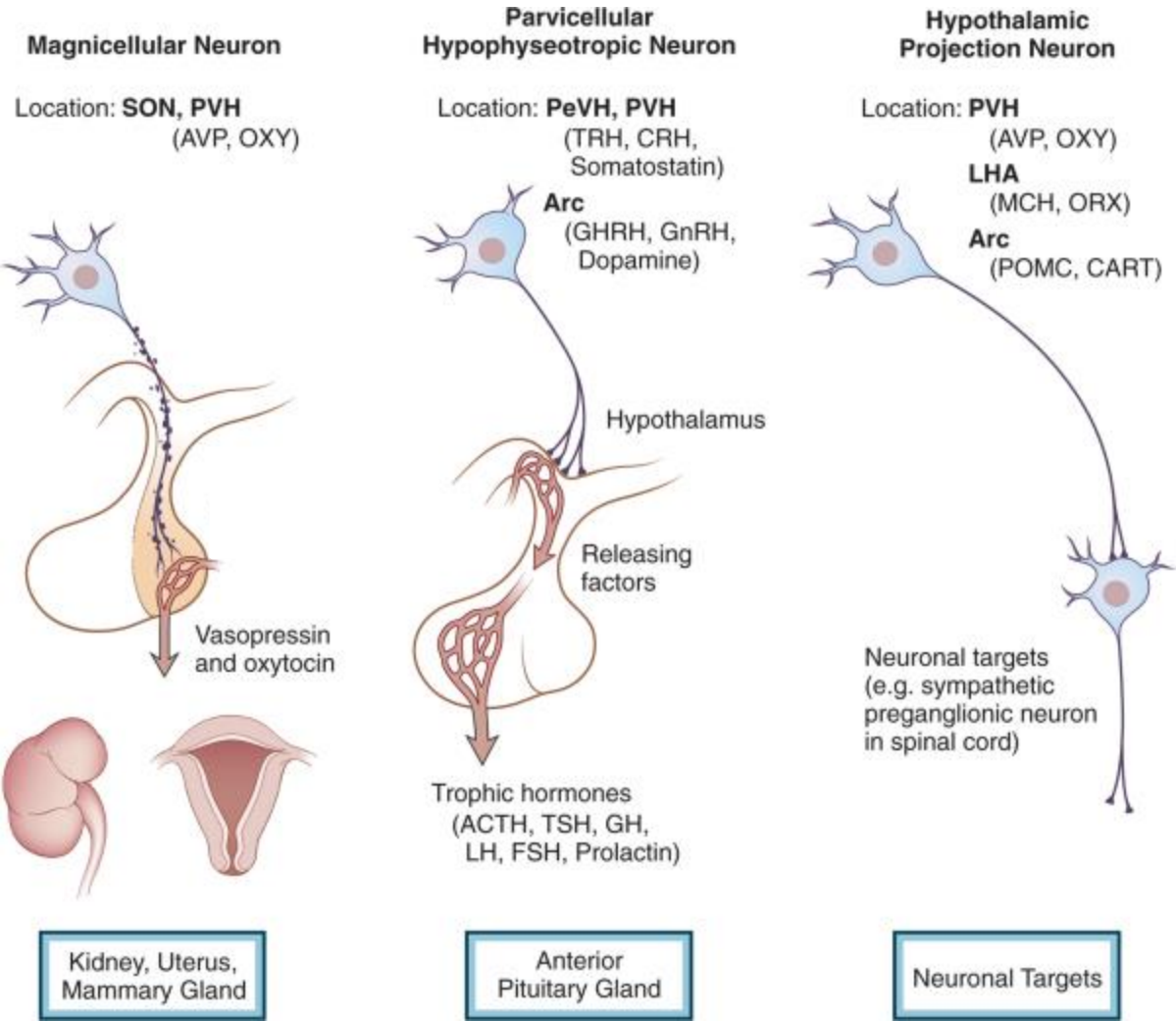
## Posterior region

n. hypothalamicus posterior  
corpus mamillare

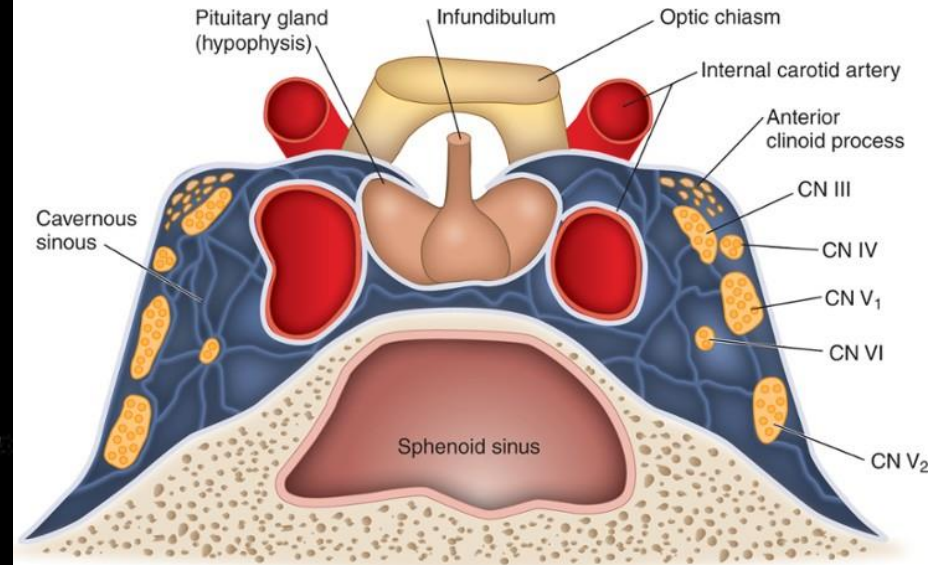
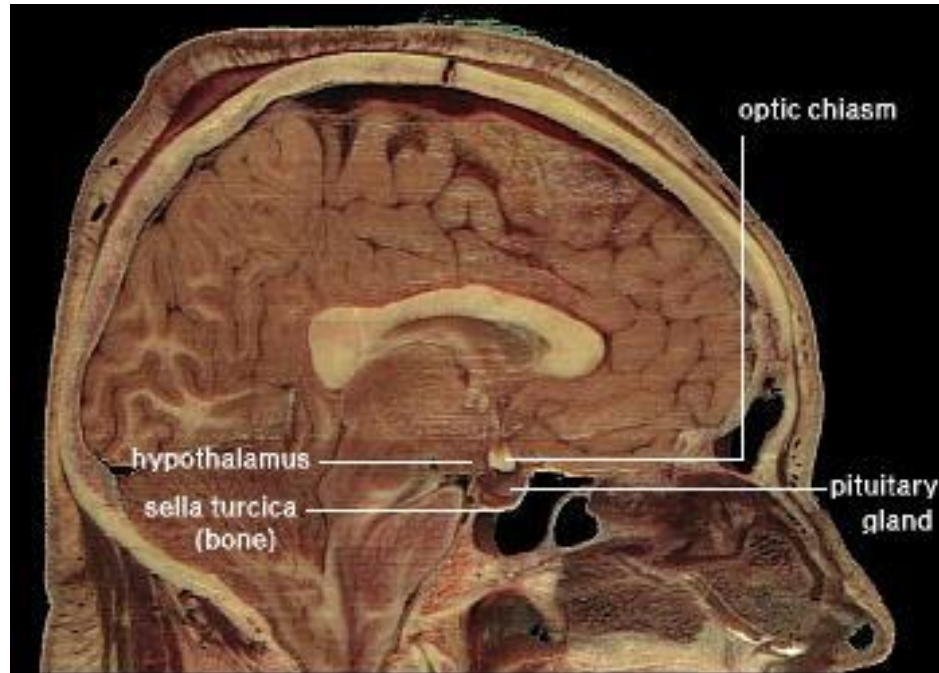


contributes to the HTH system

# Neurosecretory cells are the magno- and parvocellular neurons in the hypothalamus



# The pituitary is connected with the hypothalamus via the infundibulum



## Blood supply:

Superior hypophyseal artery – internal carotid artery

Inferior hypophyseal artery - circulus arteriosus

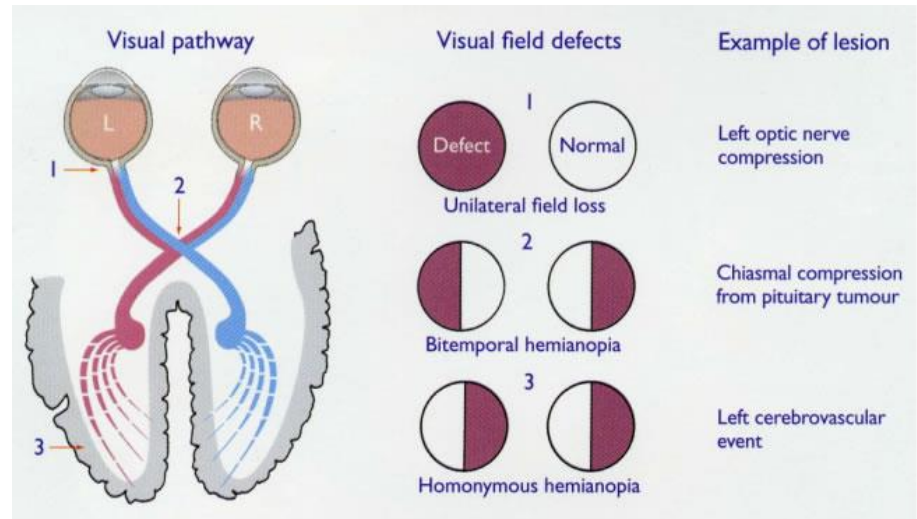


# Pituitary tumors may cause visual disturbances

normal:

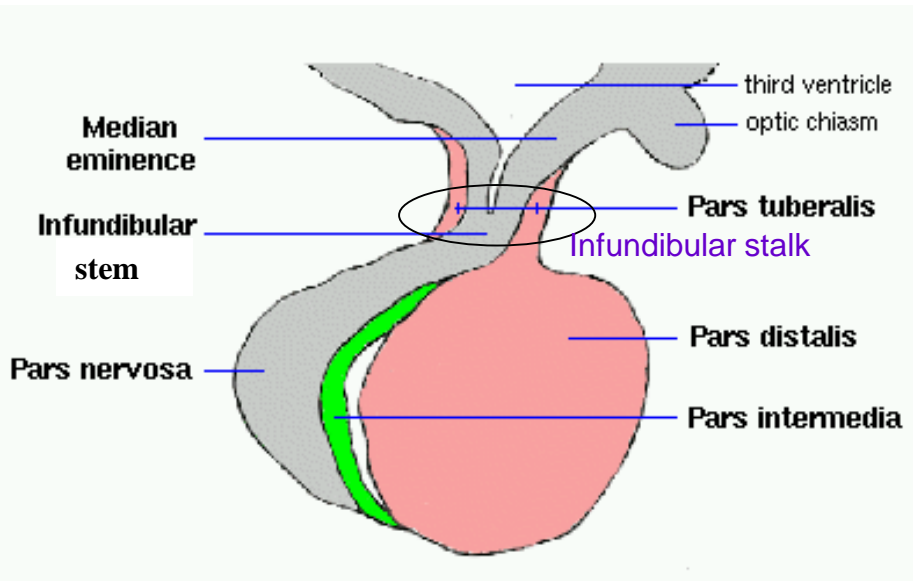


**Bitemporal Hemianopia:**  
**chiasma lesion**

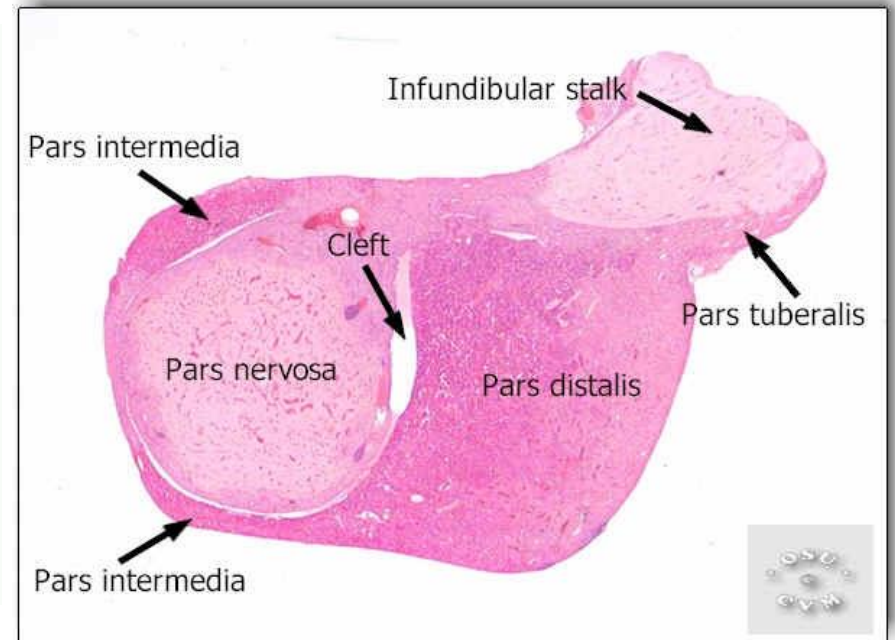


# Adeno- and neurohypophysis are the main parts of the pituitary

## Neurohypophysis:

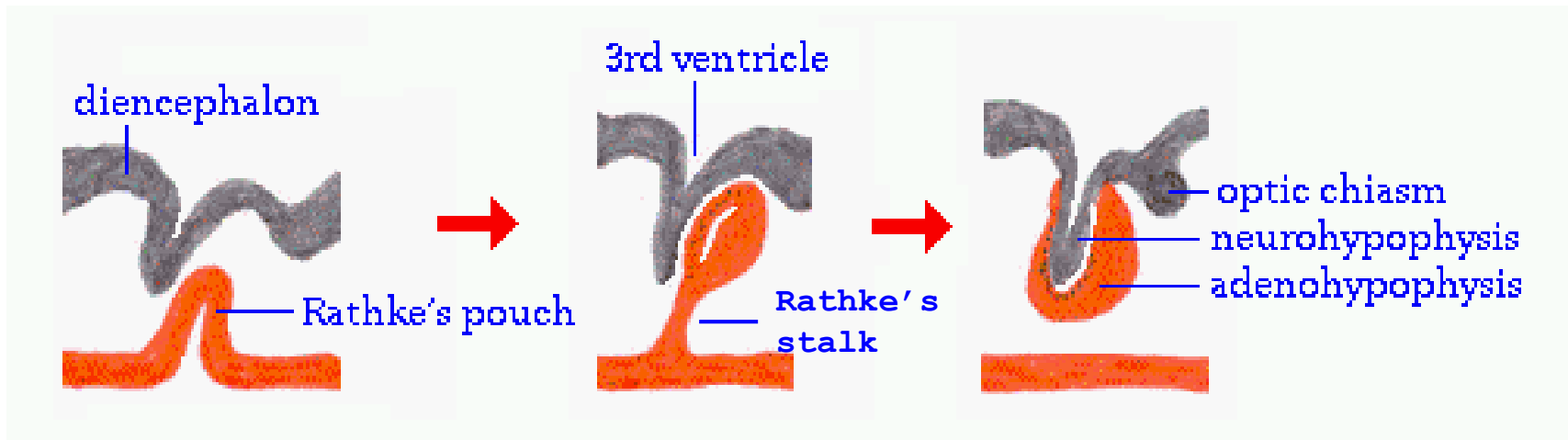


## Adenohypophysis:



- The adenohypophysis is a glandular, the neurohypophysis is a neuronal tissue.
- Neurohypophysis = posterior pituitary: does not produce hormones
- Adenohypophysis = anterior pituitary: produces its own hormones
- Hypophyseal cleft: between the pars intermedia and pars distalis

# The adeno- and neurohypophysis are both ectodermal, but have different embryological origin



Rathke's pouch is a depression in the roof of the developing mouth (stomodeum) in front of the buccopharyngeal membrane.

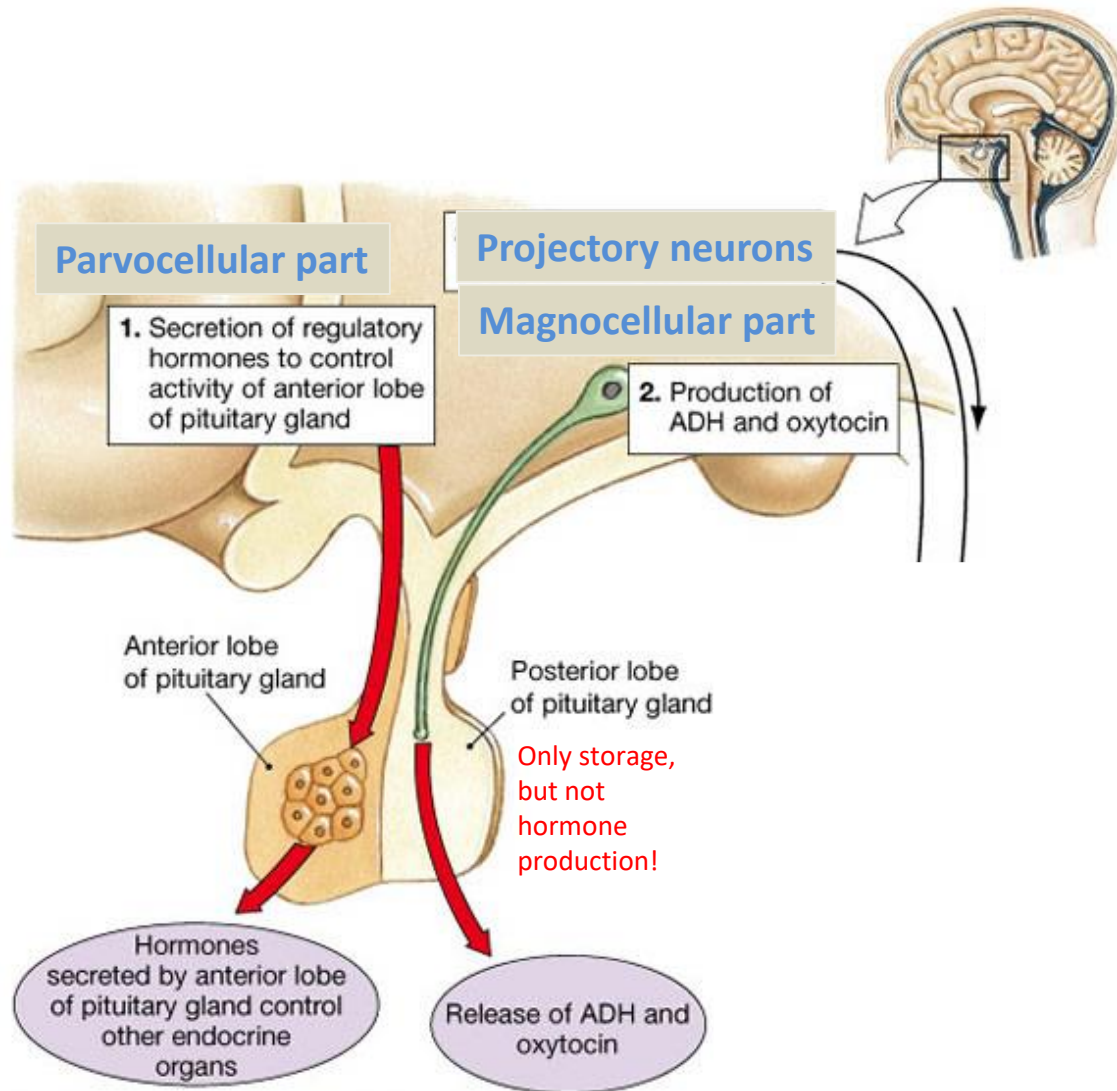
- Neurohypophysis: neuroectodermal
- Adenohypophysis: ectodermal



# Development of the Hypophysis



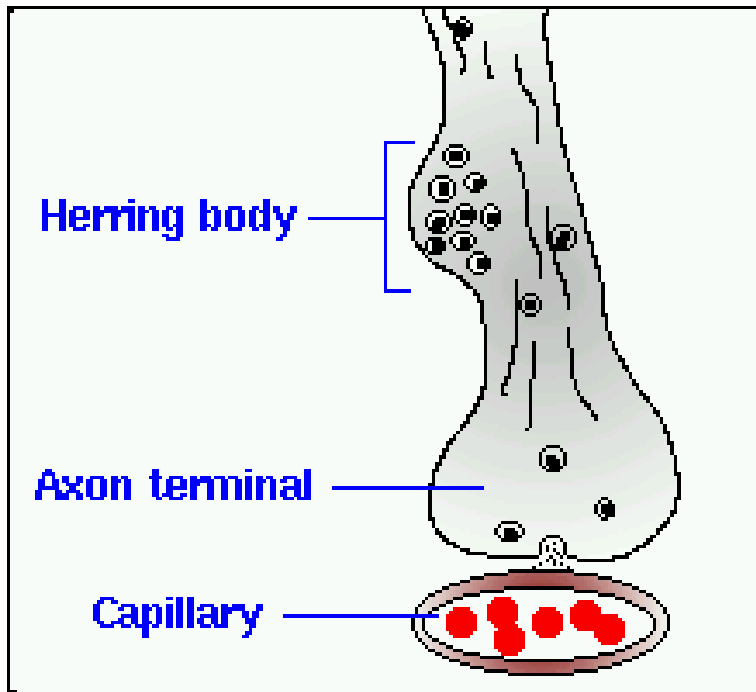
# The adeno- and neurohypophysis have different functions







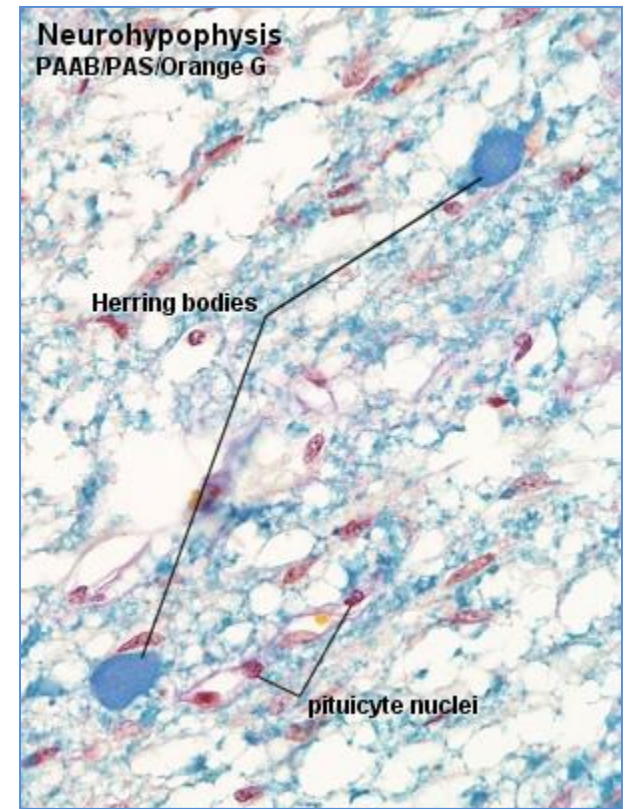
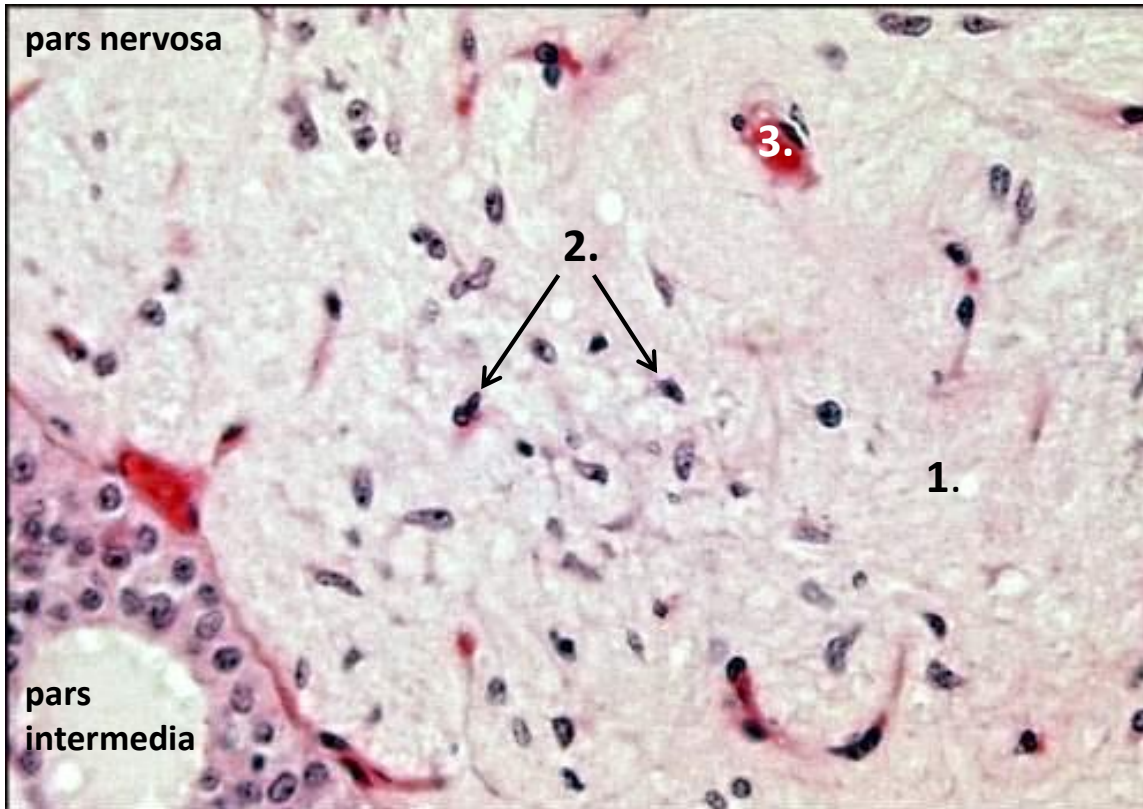
# Oxytocin and vasopressin are transported via the axons connected to carrier molecules called neurophysins



## Herring bodies:

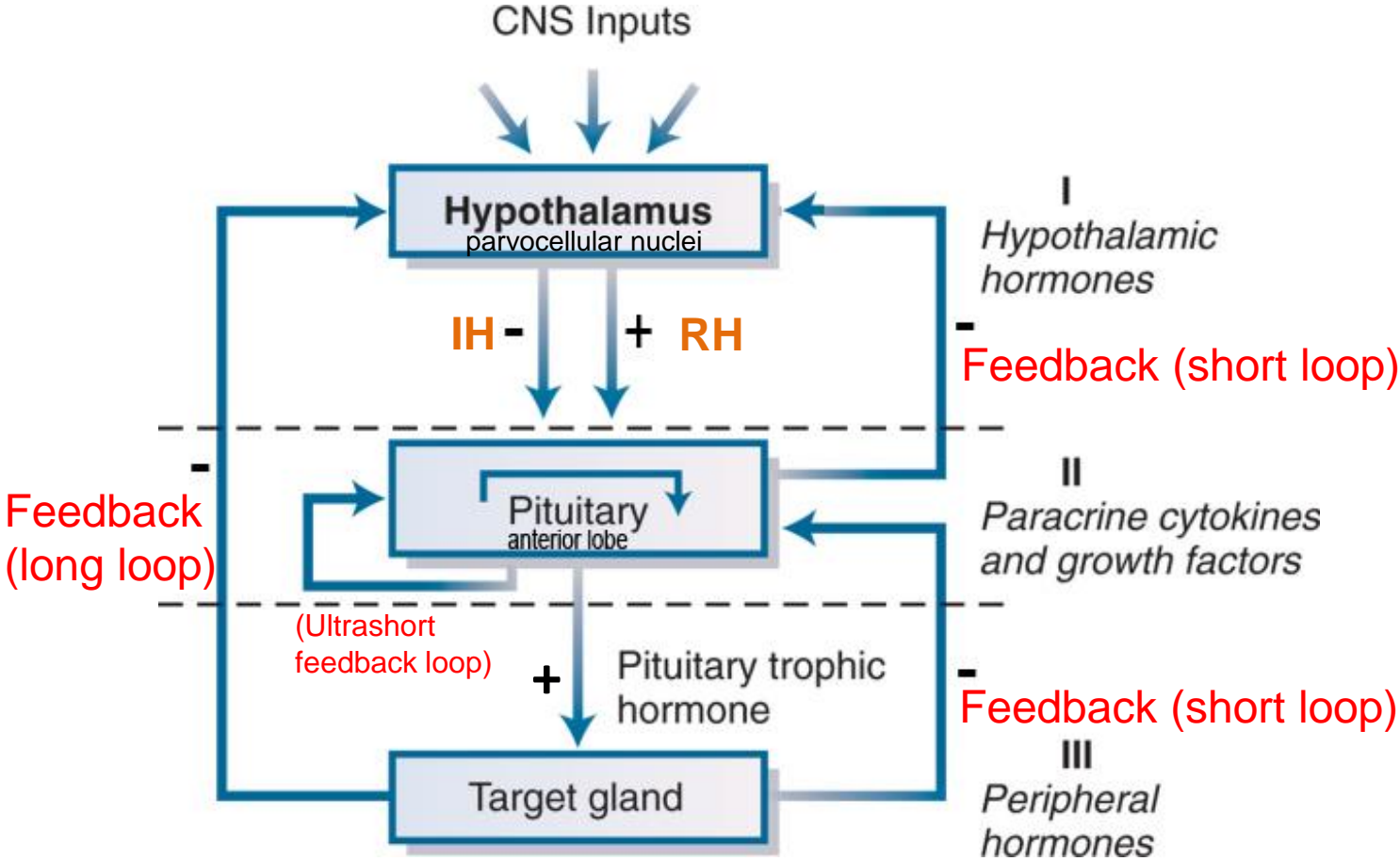
- large clusters of neurosecretory granules at the terminal portion of the axons
- oxytocin+neurophysin1 or ADH+neurophysin2 is stored in different terminals
- they can be seen at light microscopic level

# Histology of the pars nervosa



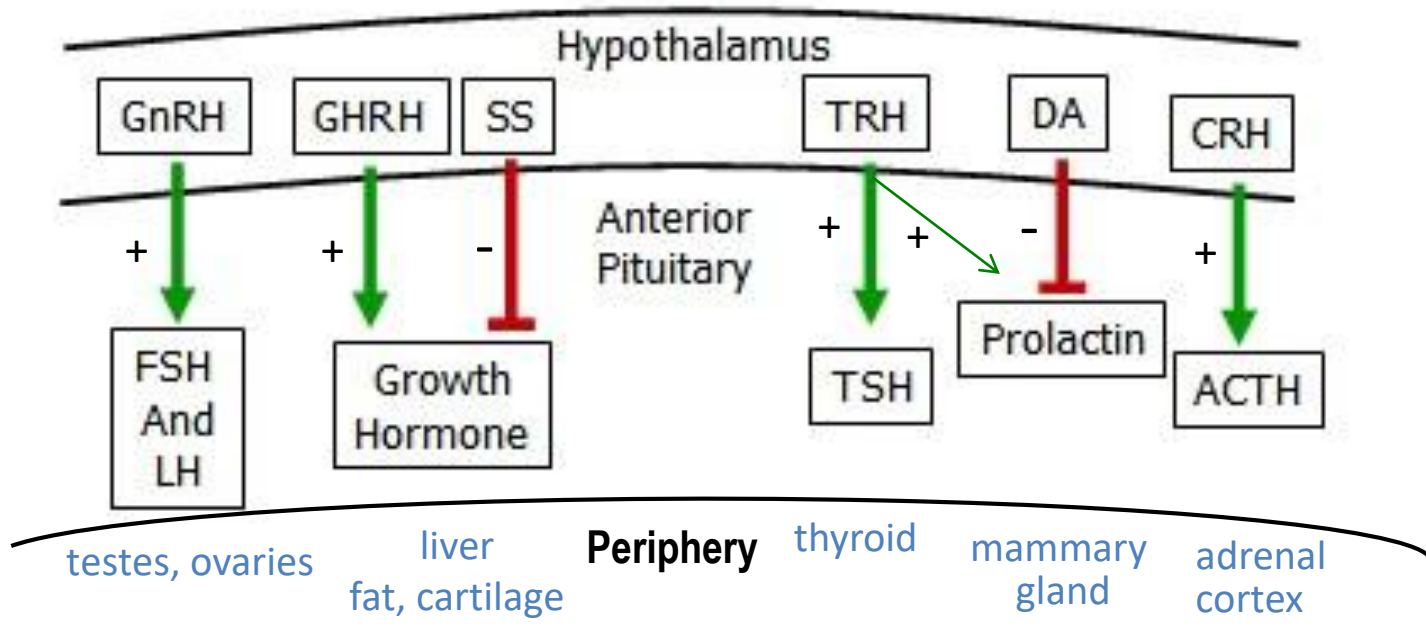
1. unmyelinated axons
2. special glial cells - pituicytes, oval nucleus
3. fenestrated capillaries

# Parvocellular neurons of the hypothalamus regulate hormone production of the adenohypophysis: **tuberoinfundibular neurosecretory system**





# Releasing and inhibiting hormones and their target in the anterior pituitary



GnRH: gonadotropin releasing hormone or luteinizing-hormone-releasing hormone (LHRH)

GHRH: growth hormone releasing hormone

SS: somatostatin

TRH: thyrotropin-releasing hormone

DA: dopamine

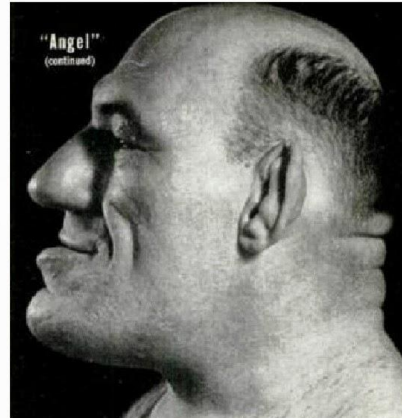
CRH: corticotropin-releasing hormone or factor (CRF)

# Growth hormone overproduction

## Gigantism

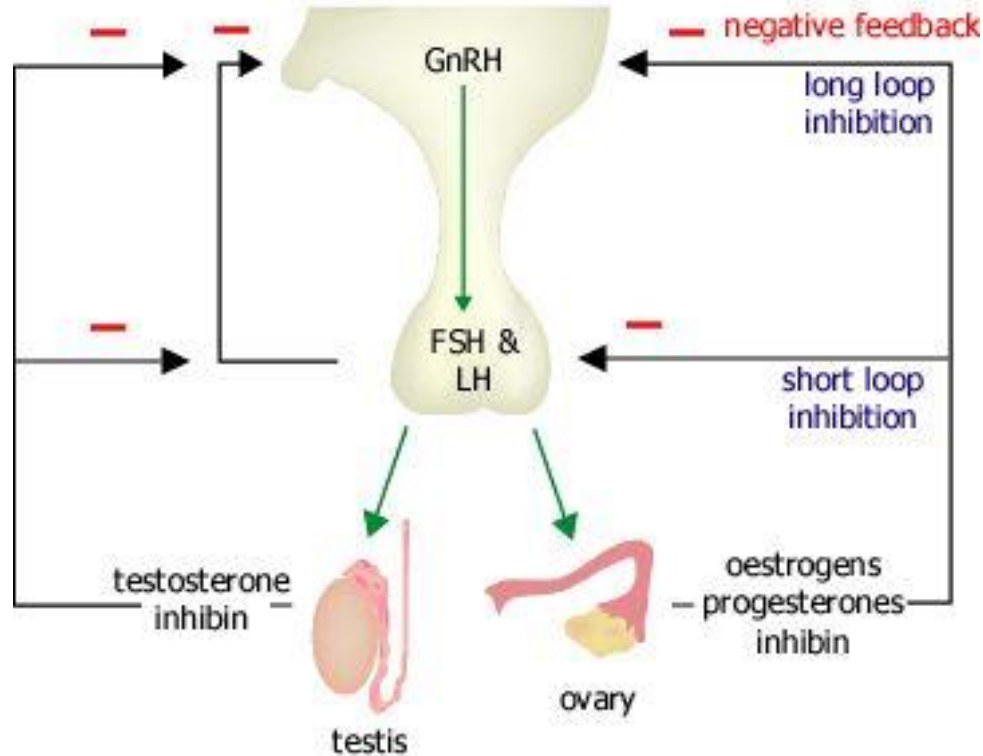


## Acromegaly

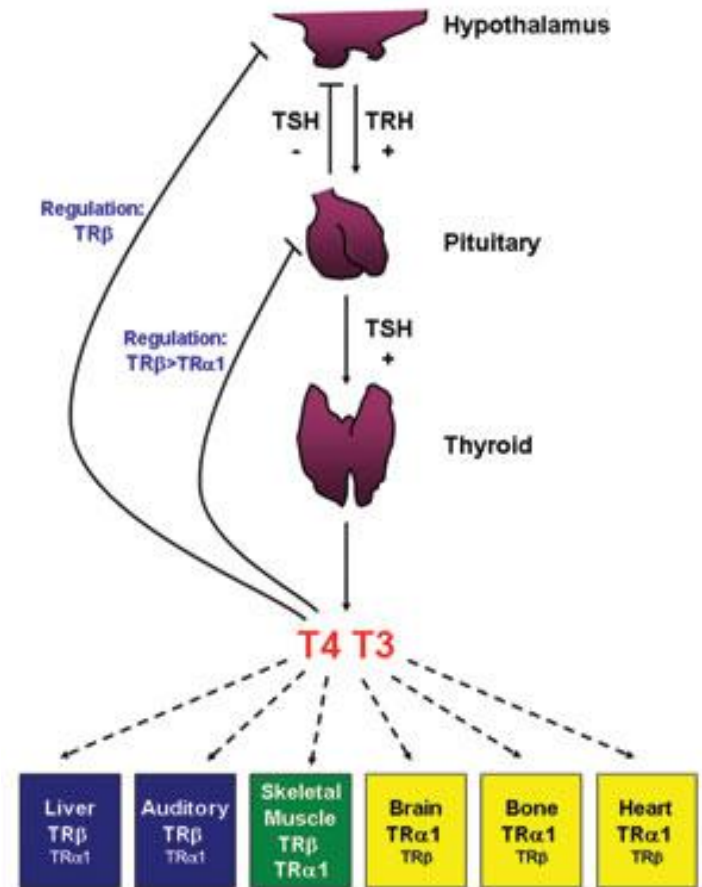


Maurice Tillet, the „French Angel“ 1940.

# Hypotamalic-pituitary-gonadal (HPG) and -thyroid (HPT) axes



HPG axis



HPT axis

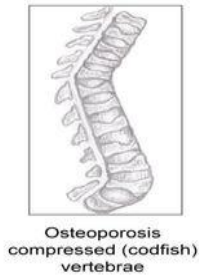
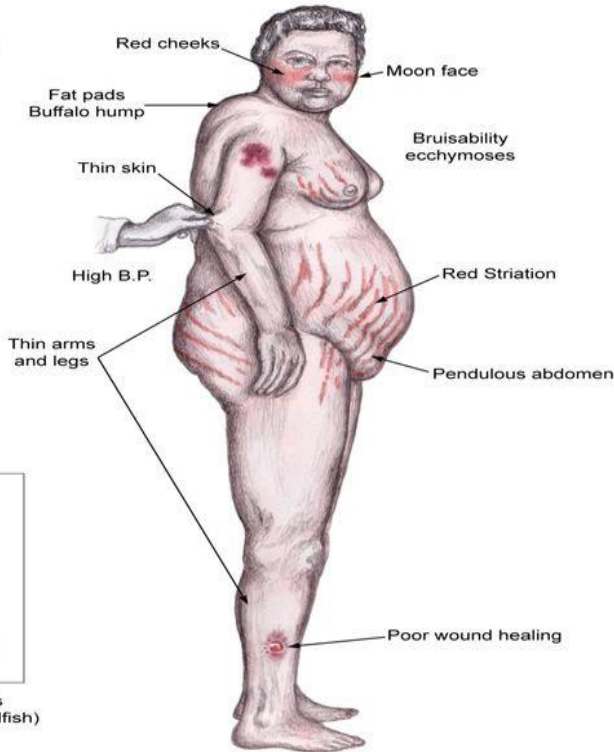


# Hypotlamic-pituitary-adrenal (HPA) axis

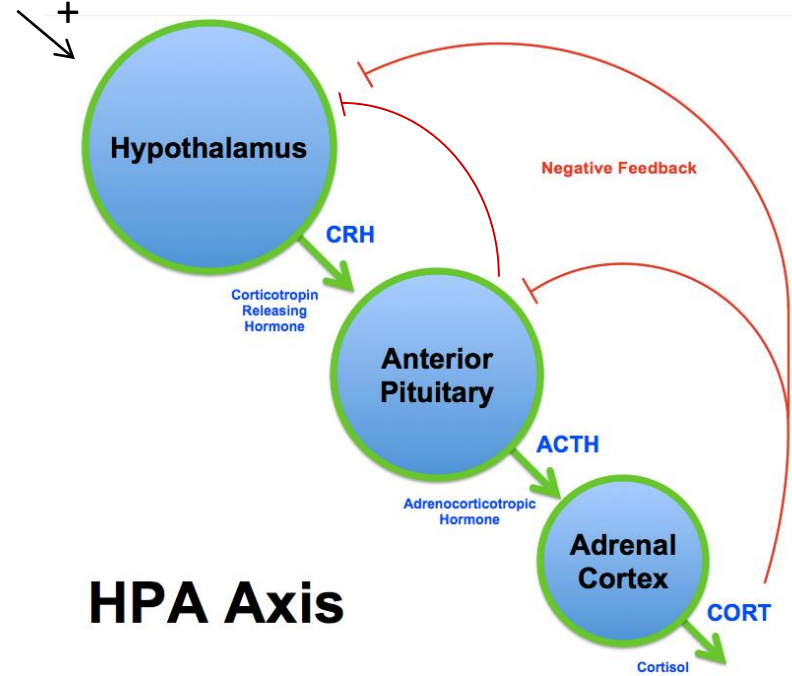
## CUSHING Syndrome

### Background

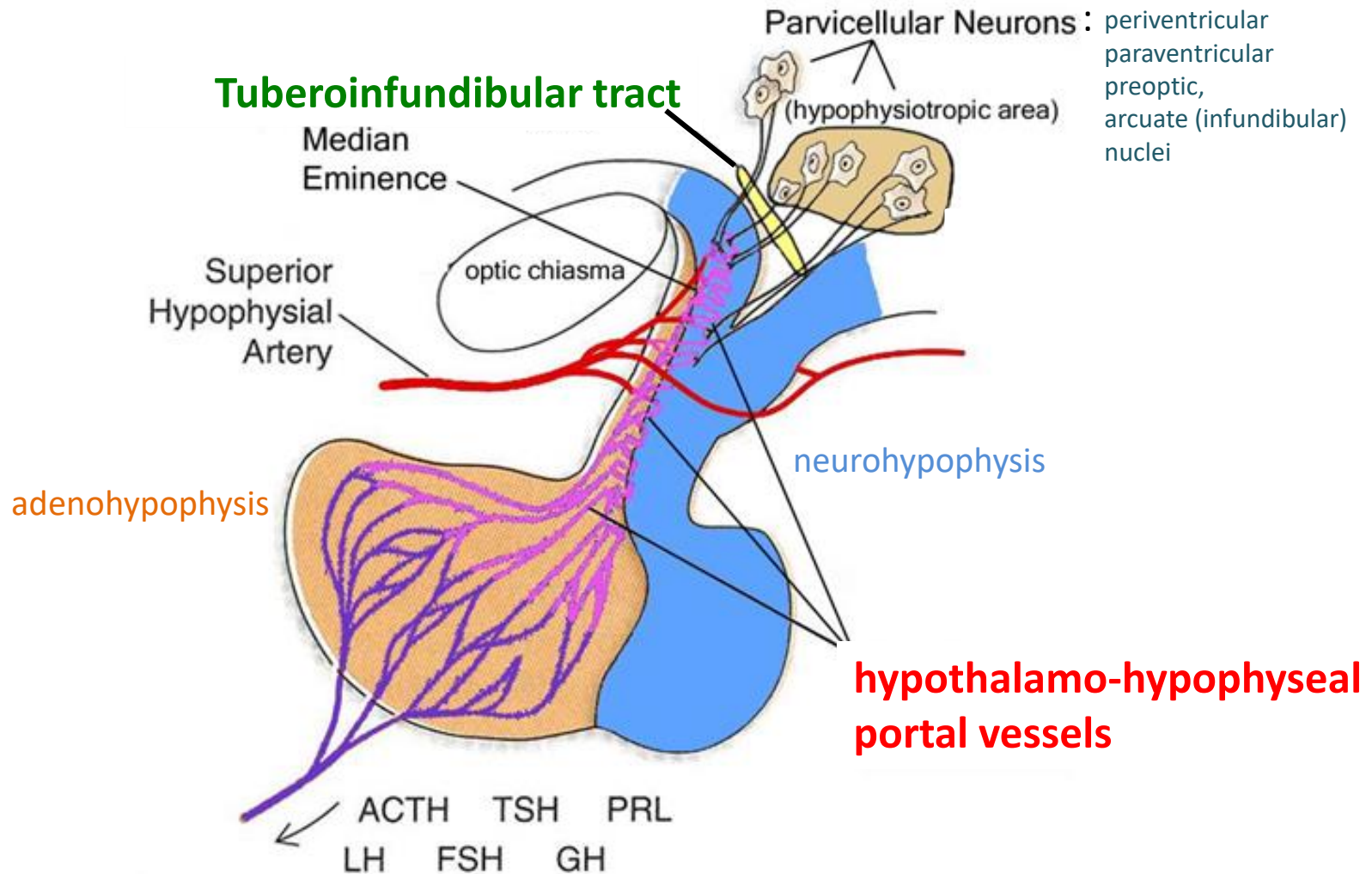
Cushing syndrome is caused by prolonged exposure to elevated levels of either endogenous glucocorticoids or exogenous glucocorticoids



(Stress)



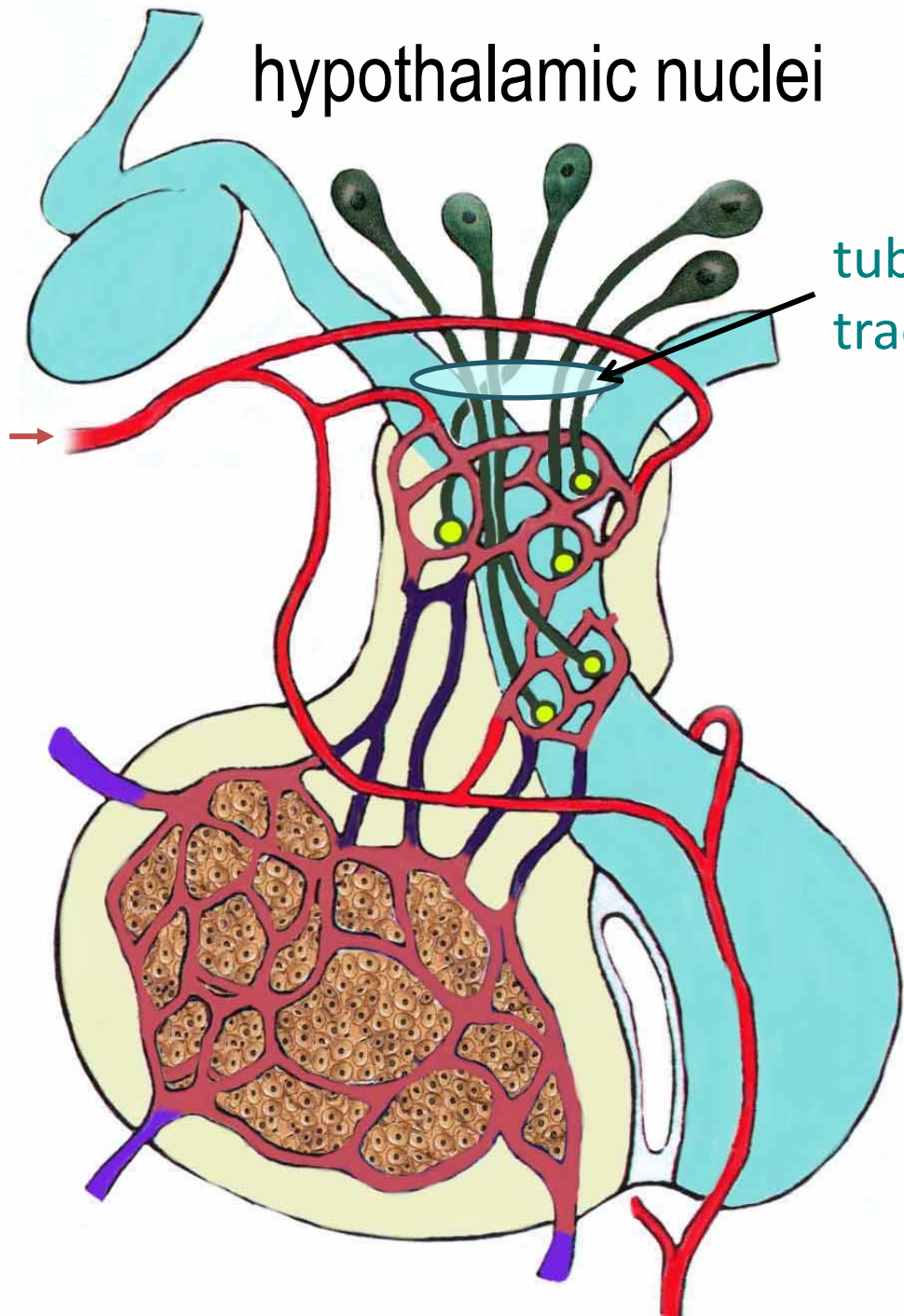
# Parvocellular neurons project to the median eminence and release hormones into the portal circulation



hypothalamic nuclei

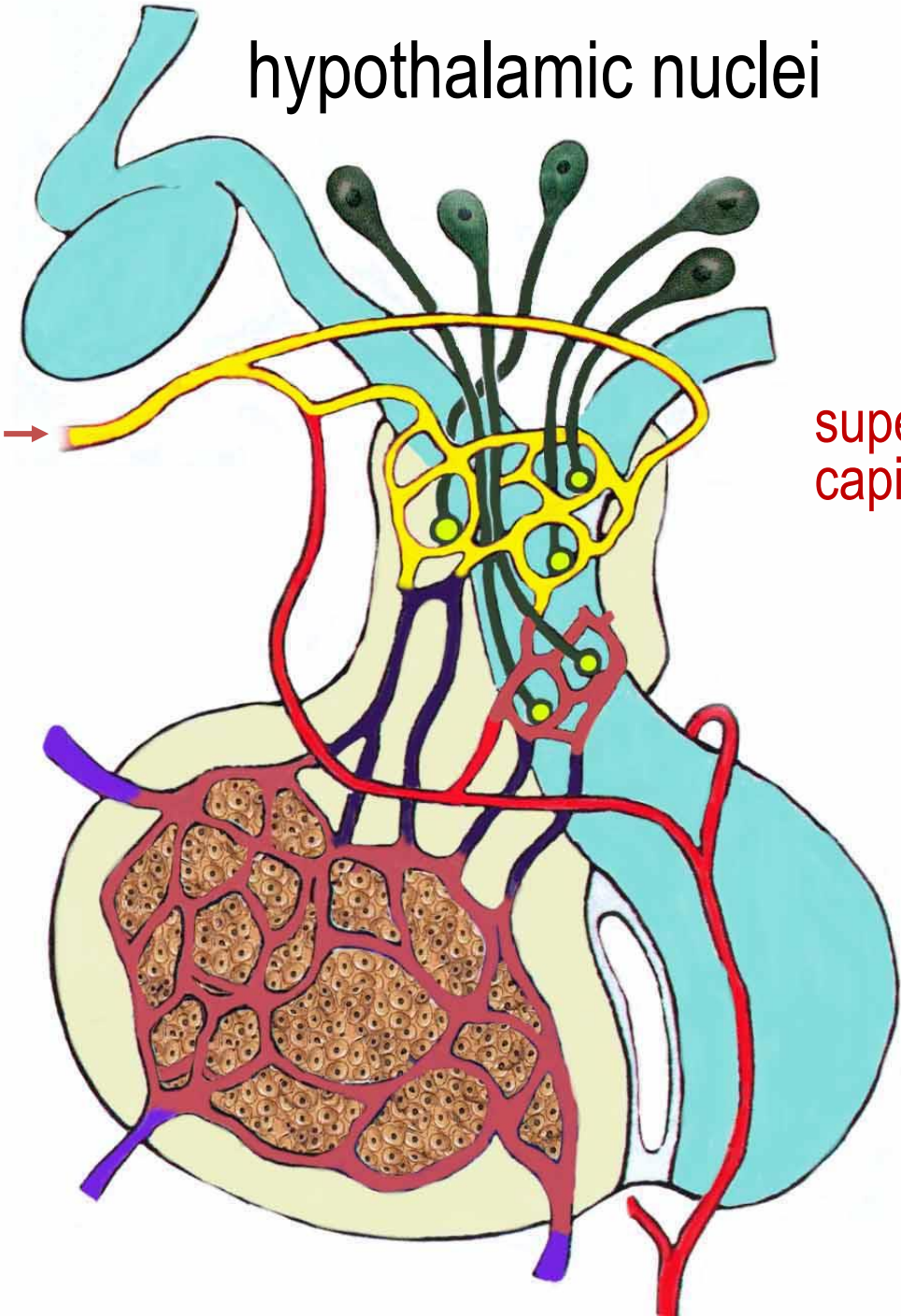
tuberoinfundibular tract

superior hypophyseal artery



# hypothalamic nuclei

superior hypophyseal artery



superficial capillary plexus

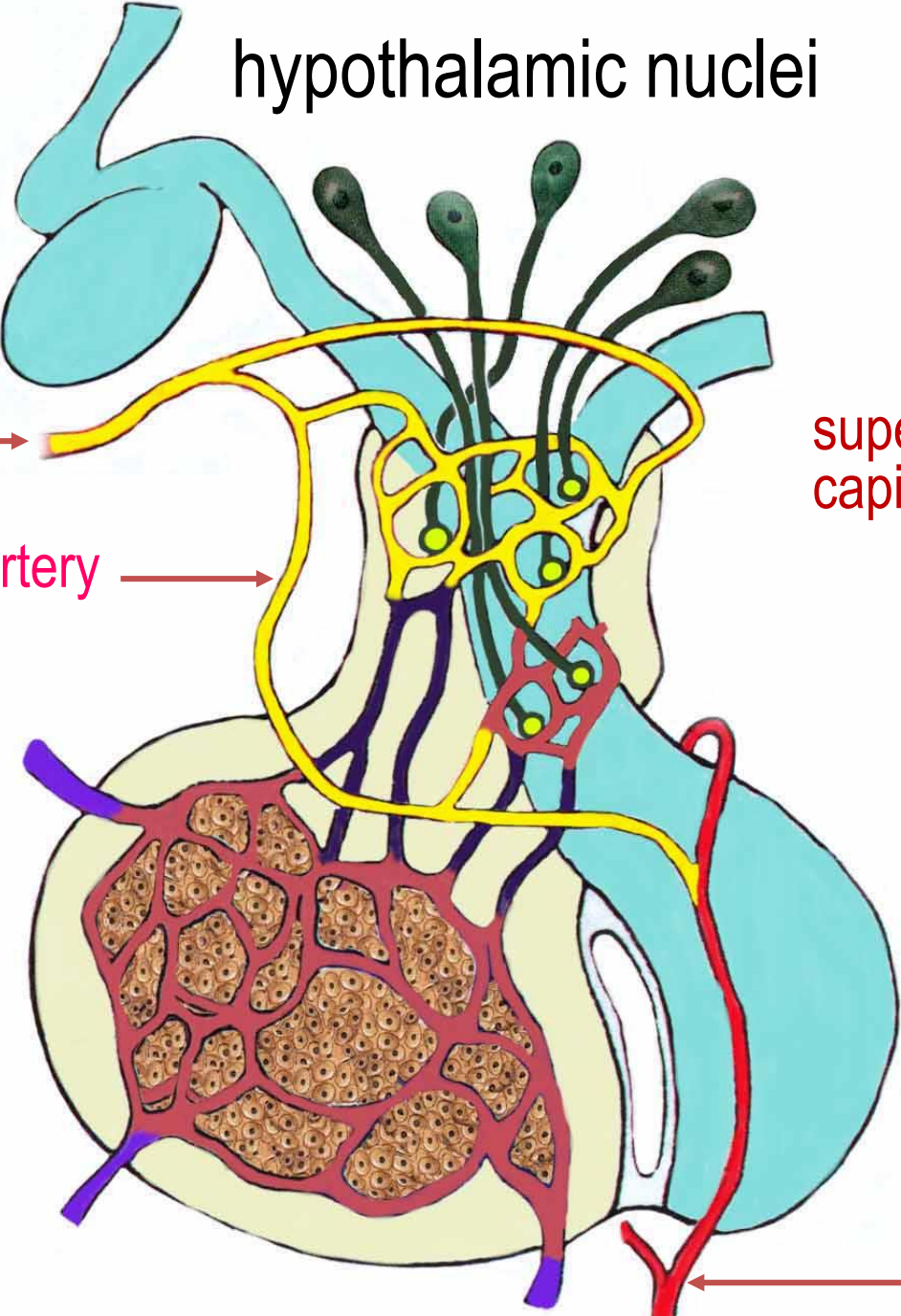


# hypothalamic nuclei

superior hypophyseal artery →

trabecular artery →

superficial capillary plexus



inferior hypophyseal artery →

# hypothalamic nuclei

primary capillary plexus

superficial capillary plexus

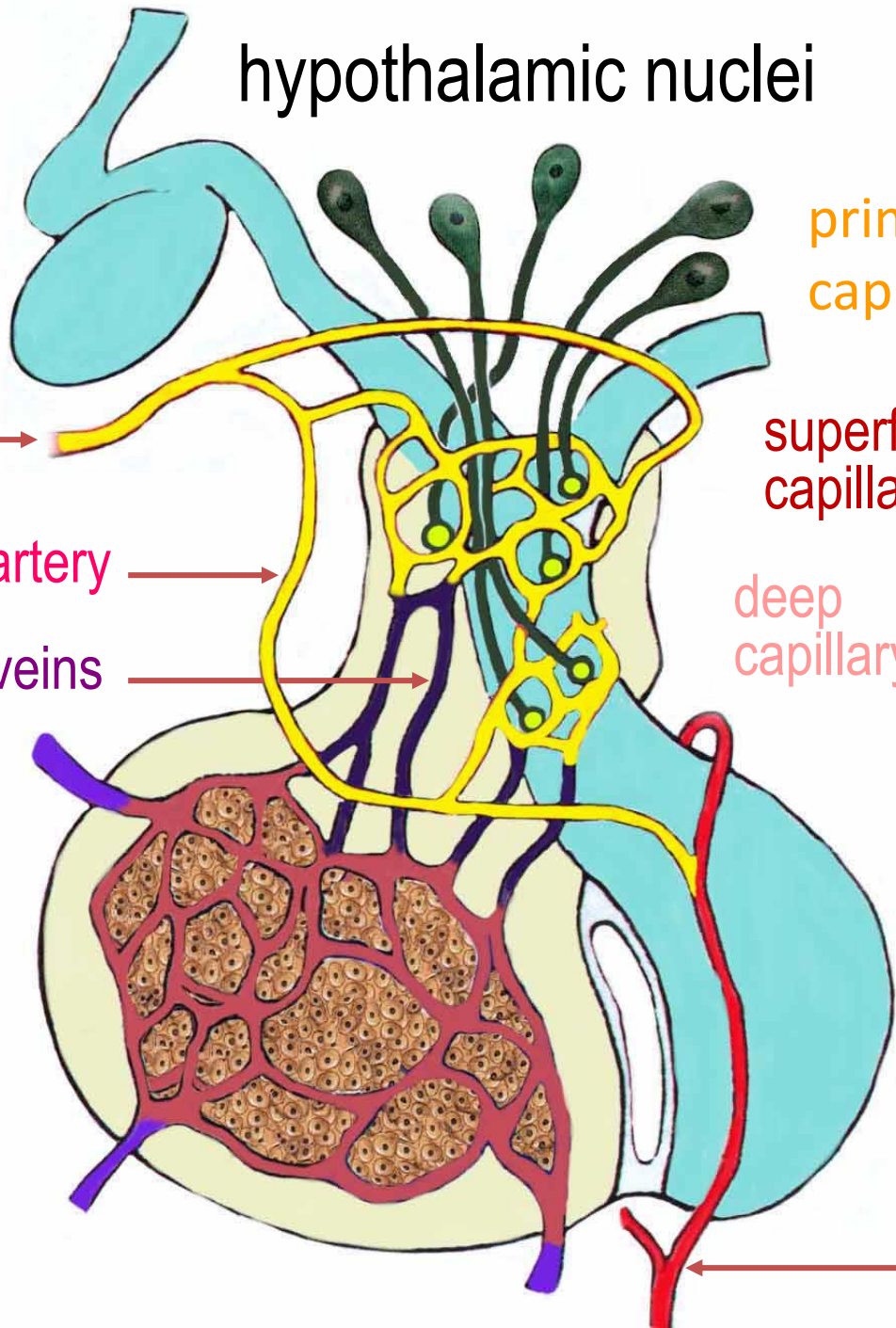
deep capillary plexus

superior hypophyseal artery

trabecular artery

long portal veins

inferior hypophyseal artery



# hypothalamic nuclei

superior hypophyseal artery

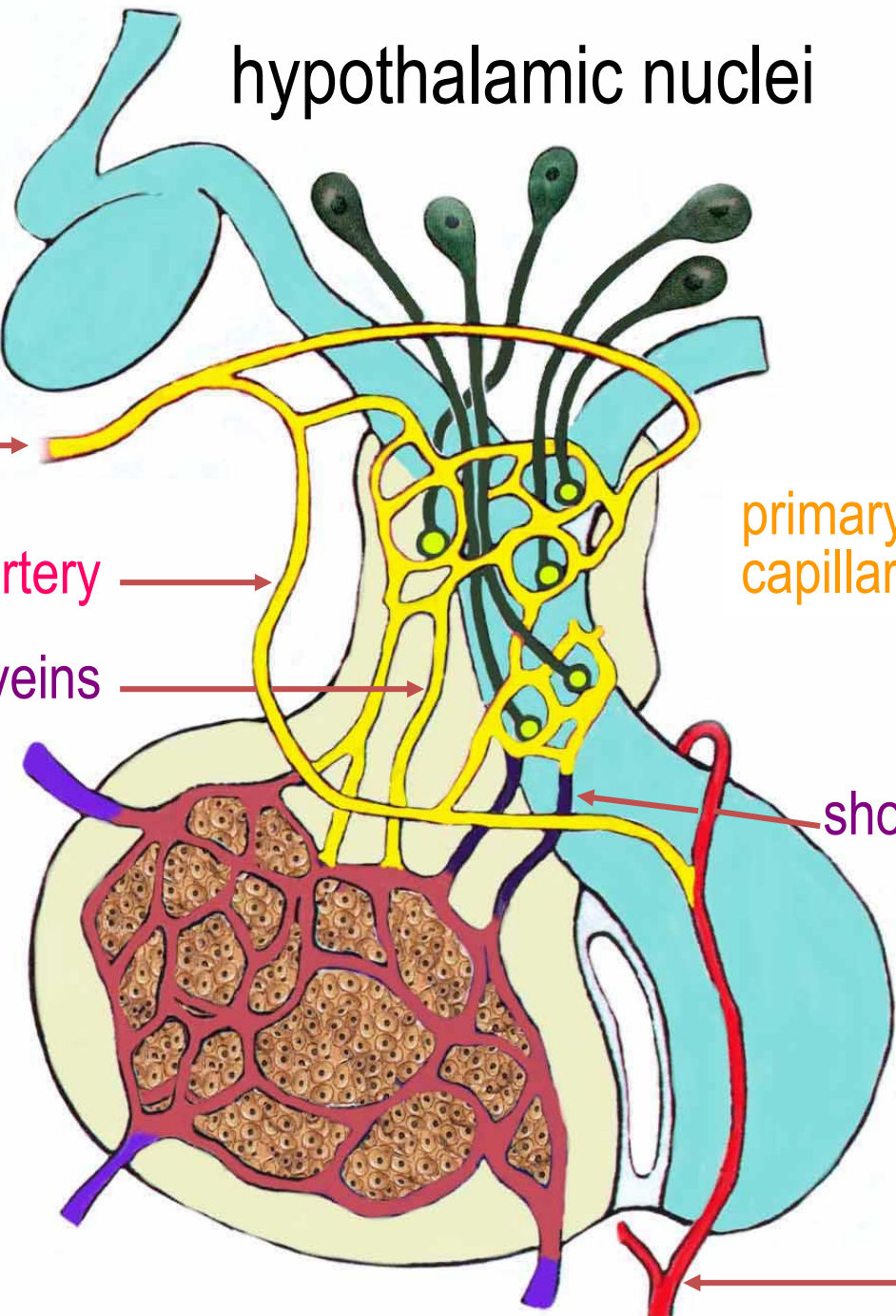
trabecular artery

long portal veins

primary capillary plexus

short portal veins

inferior hypophyseal artery





# hypothalamic nuclei

superior hypophyseal artery

trabecular artery

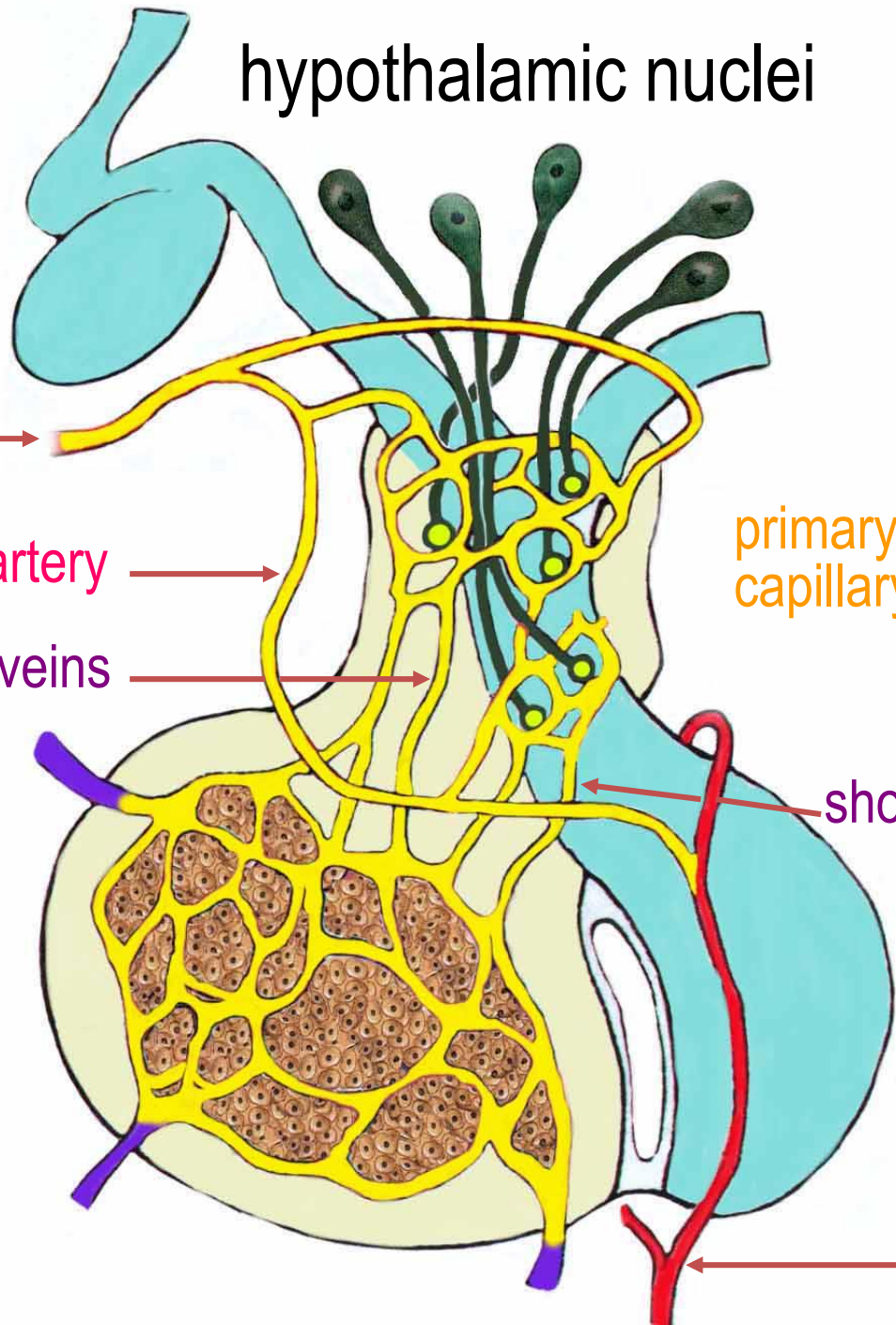
long portal veins

secondary, or adeno-hypophyseal capillary plexus

primary capillary plexus

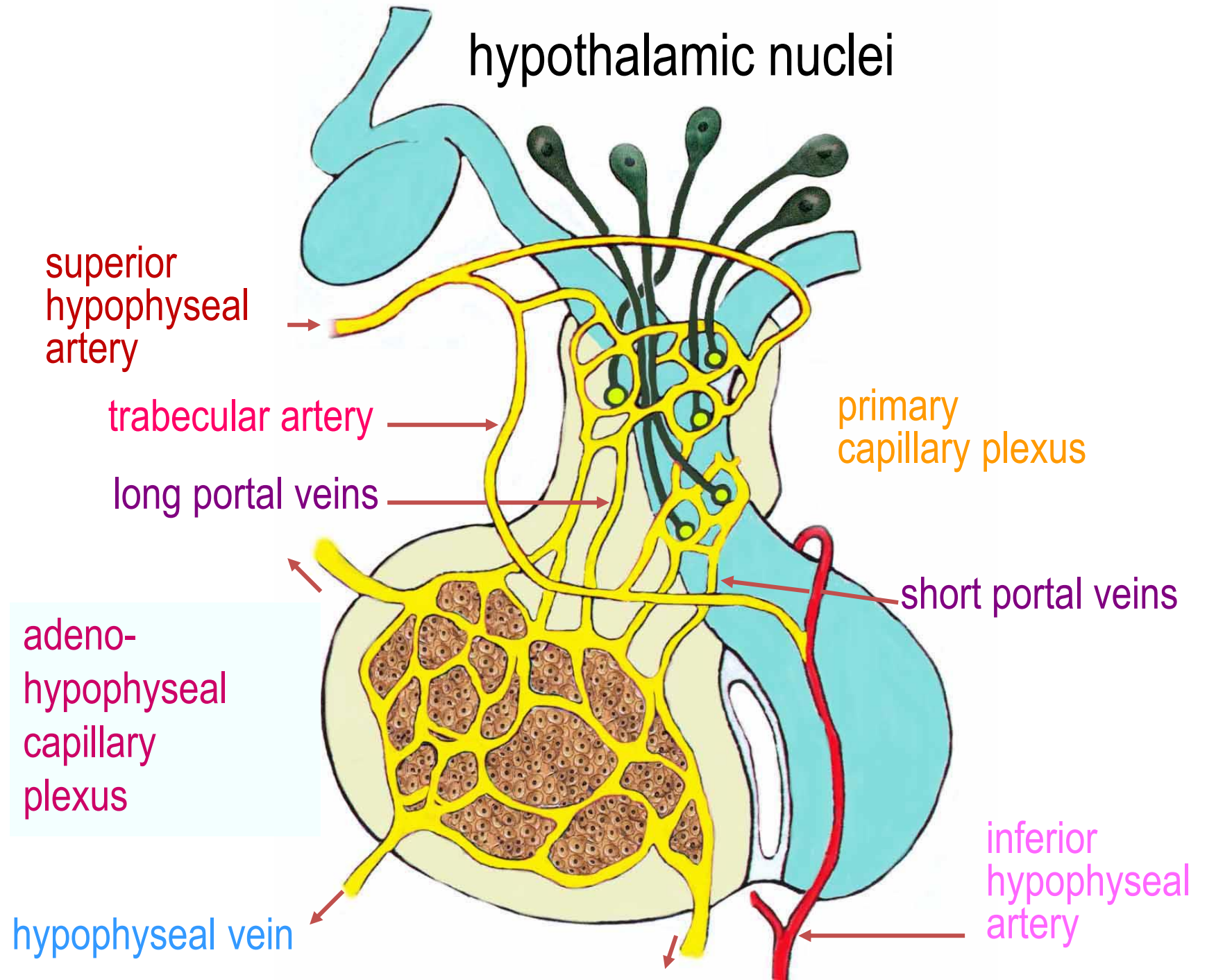
short portal veins

inferior hypophyseal artery

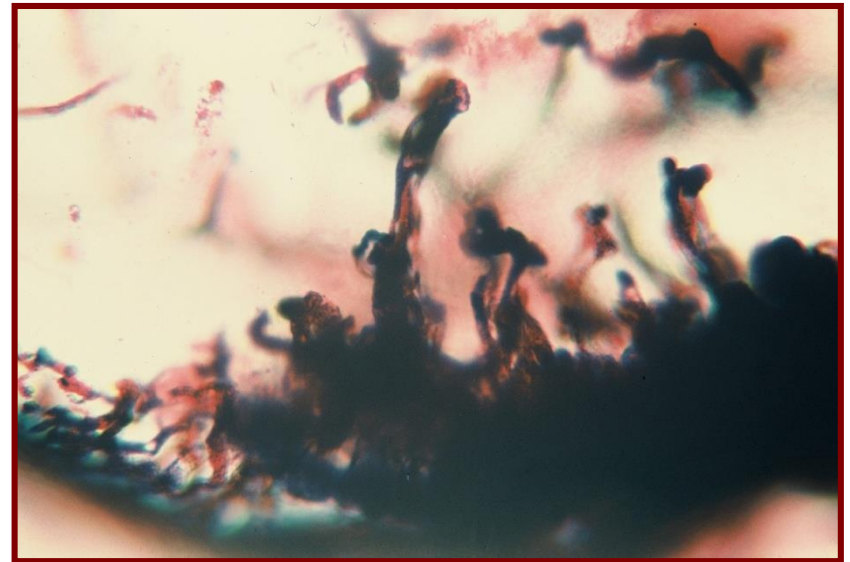
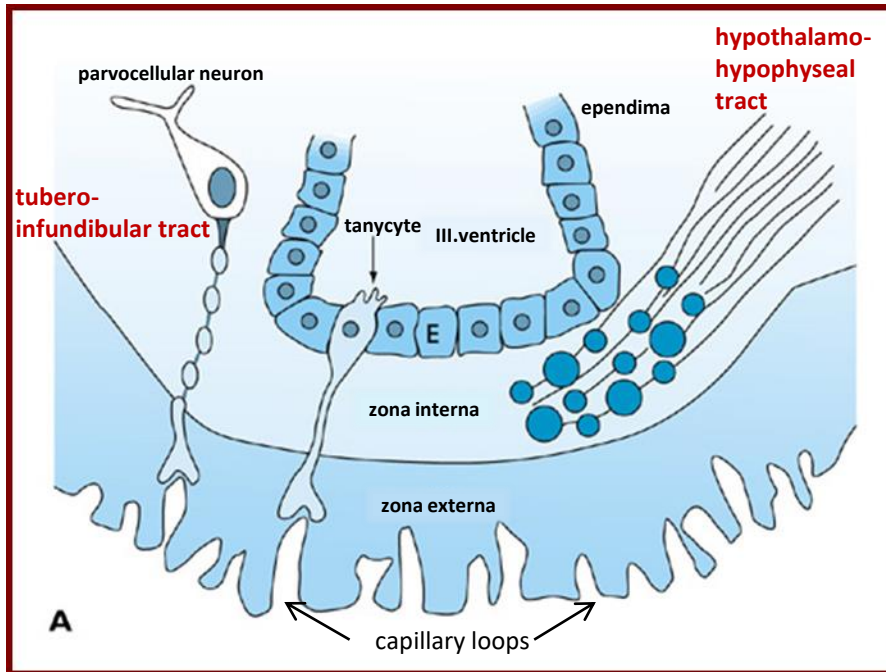




# hypothalamic nuclei



# The hypothalamo-hypophyseal and the tuberoinfundibular tracts are separated in the median eminence

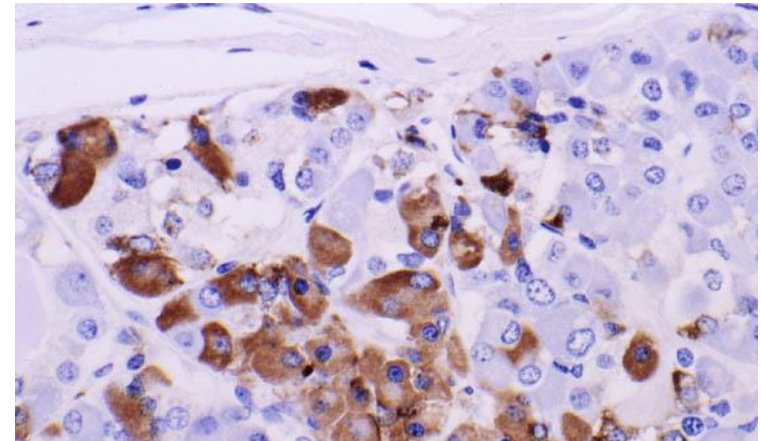
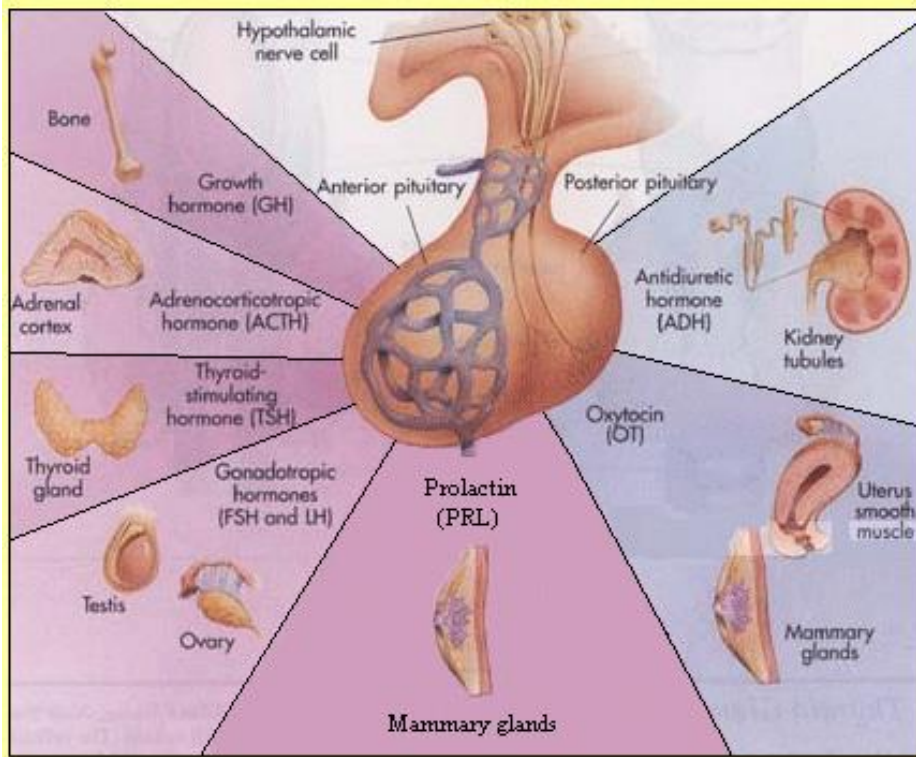


Capillary loops in the external zone of the median eminence, blood-brain barrier is missing here

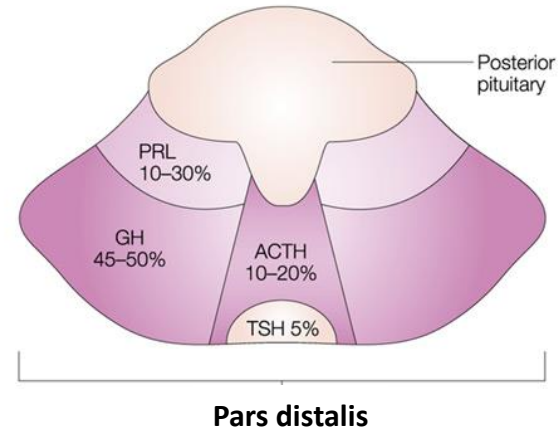
## Tanycytes:

- are radial glial – like cells, some of them are stem cells,
- are in contact with the cerebrospinal fluid and/or with hypothalamic neurons and also with the median eminence,
- are able to regulate hormone release into the perivascular space,
- are glucose sensitive.

# Hormone producing cells of the anterior pituitary can be identified by immunohistochemistry



Lactotroph cells (brown)-prolactin immunostaining



Gonadotropes (LH and FSH coexpressing cells):

- comprise 10–15% of anterior pituitary cells and are scattered throughout the anterior pituitary.



# Pituitary cell types in hematoxylin-eosin stained section

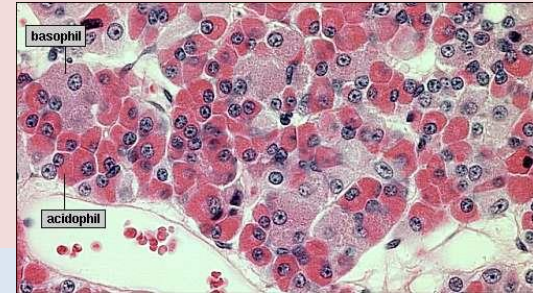
## Acidophils

- Somatotrophes produce [growth hormone](#)
- Lactotrophes produce [prolactin](#)

↑  
chromophil  
↓

## Basophils

- Thyrotrophes produce [thyroid stimulating hormone](#)
- Gonadotrophes produce [luteinizing hormone](#) or [follicle-stimulating hormone](#)
- Corticotrophes produce [adrenocorticotrophic hormone](#)

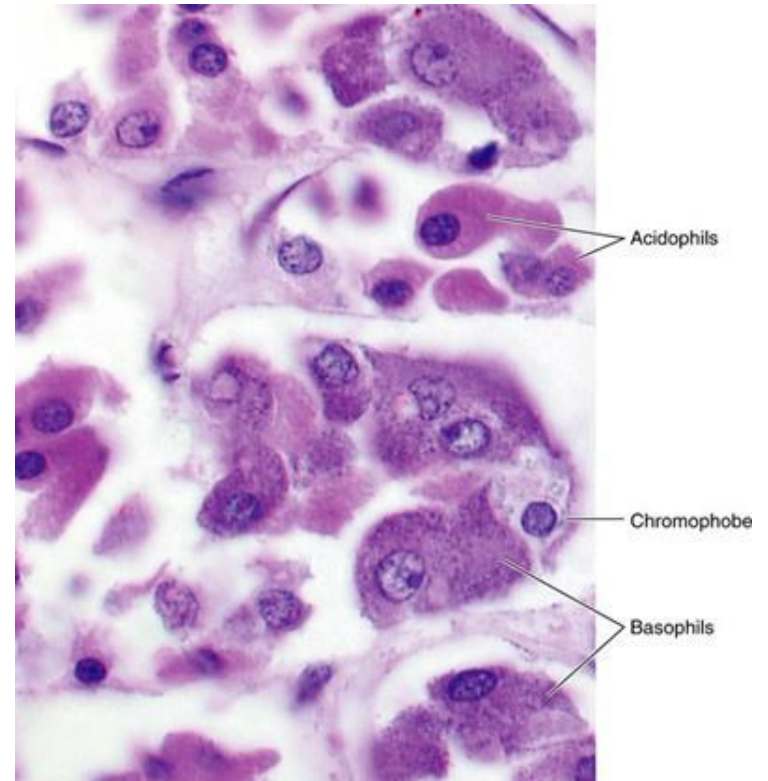
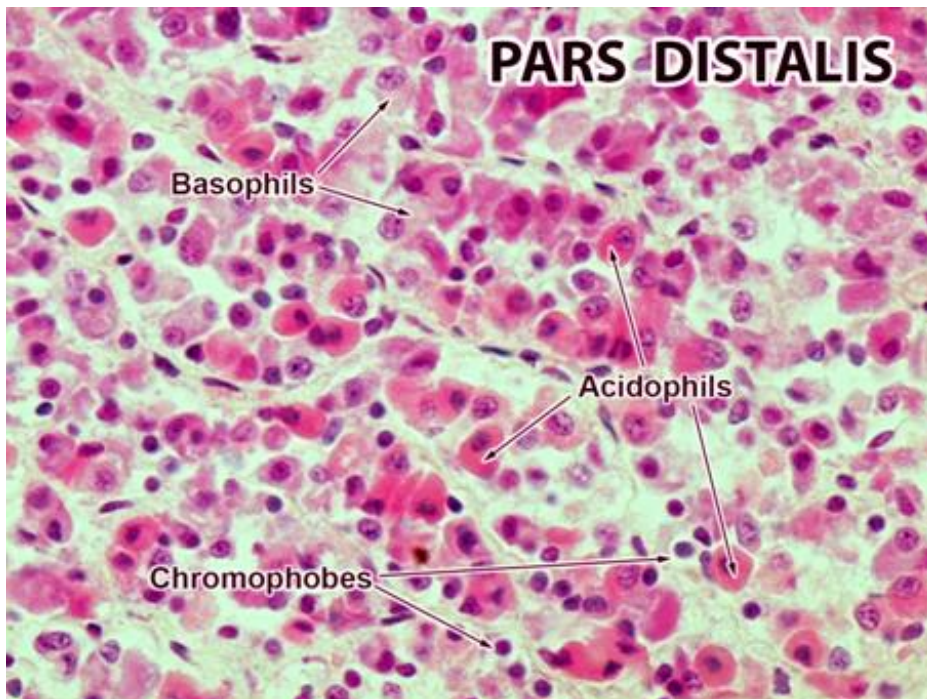
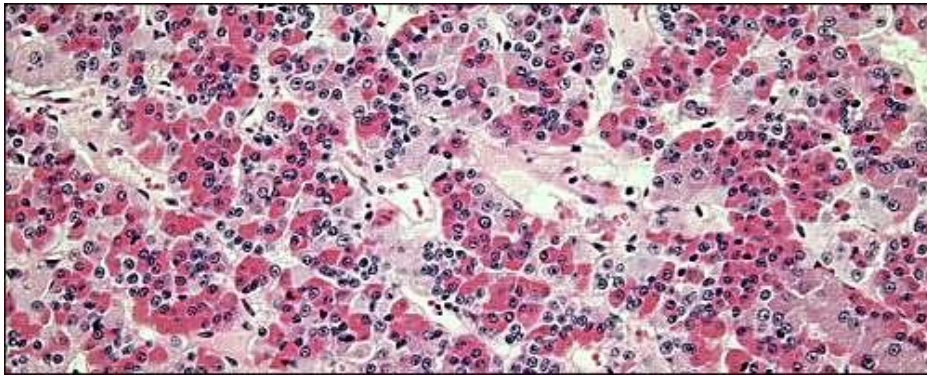


## Chromophobes

These are cells that have minimal or no hormonal content. Many of the chromophobes may be acidophils or basophils that have degranulated and thereby are depleted of hormone. Some chromophobes may also represent stem cells that have not yet differentiated into hormone-producing cells.



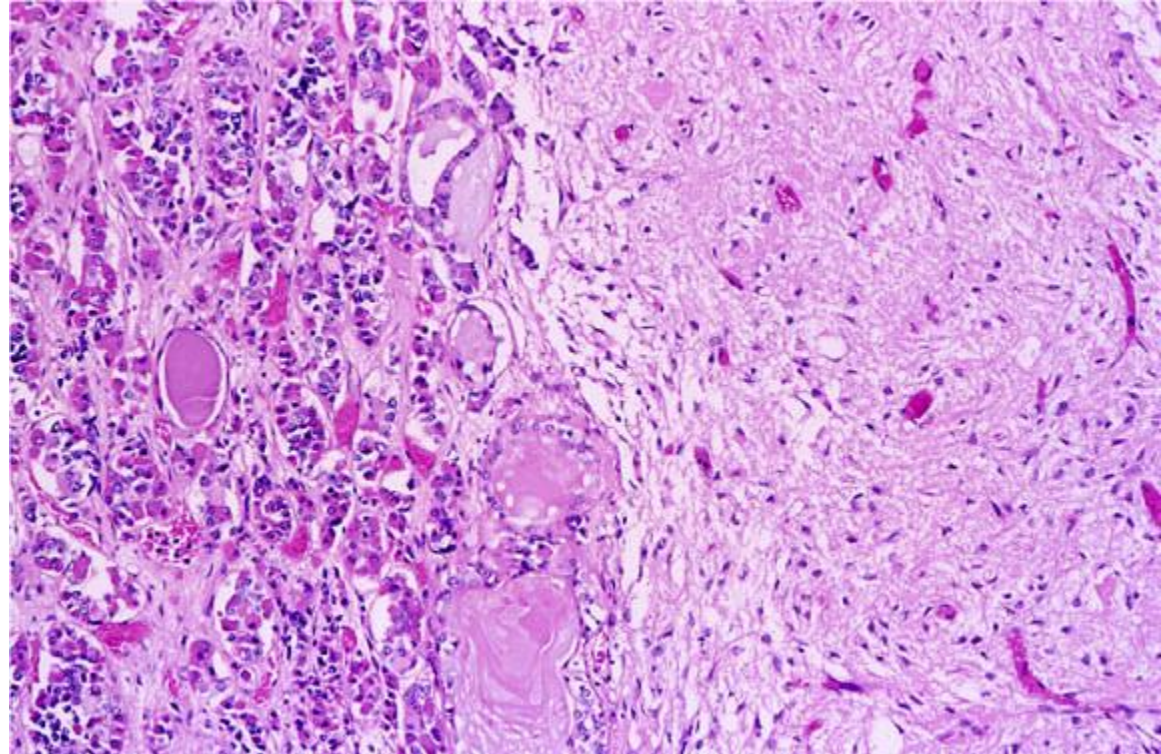
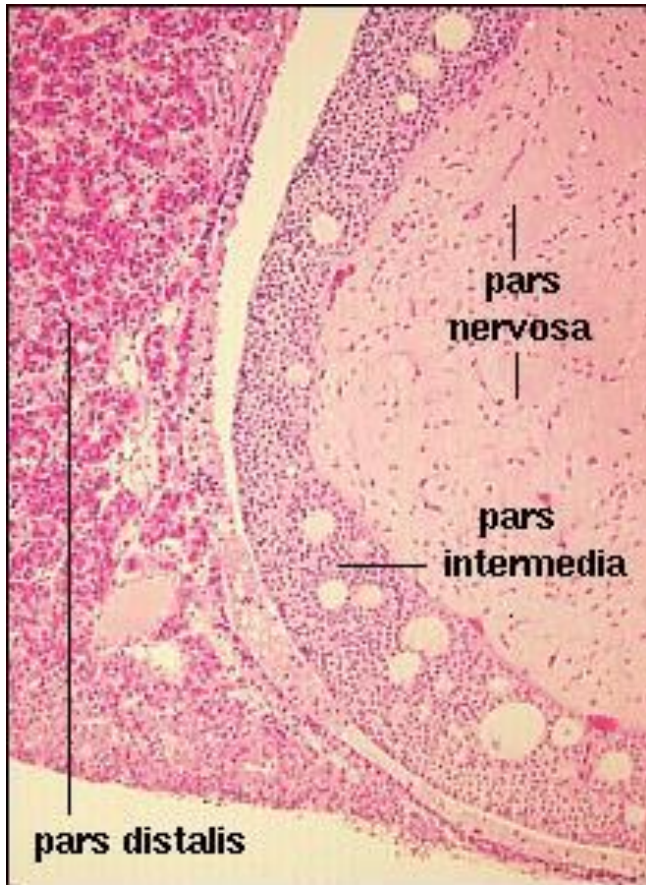
# Acidophil, basophil and chromophobe cells at light microscopic level



- cells arranged in cords
- pars distalis: all type of cells
- pars tuberalis: basophil cells

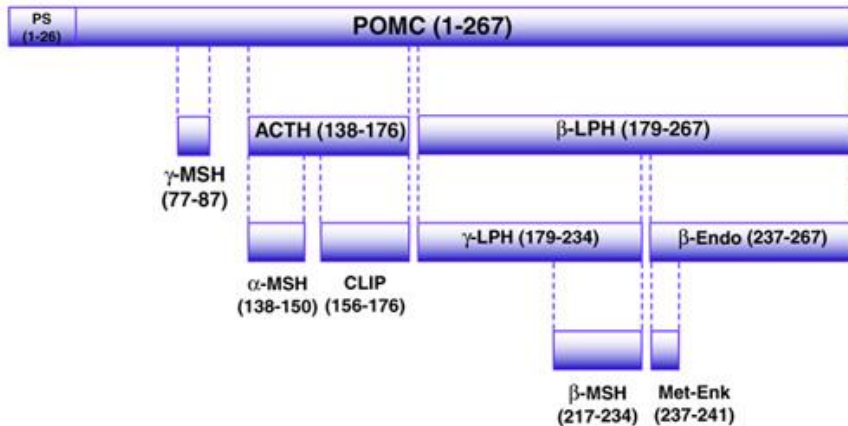


# The pars intermedia is very small in adults and may contain colloid-filled cysts

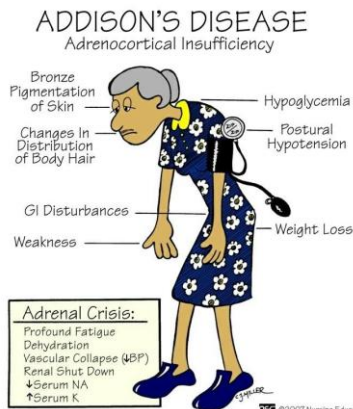


- Cysts filled with colloid, lined with cuboidal cells, remainders of the Rathke's pouch
- Small basophils-hormone production (MSH), more active during fetal life
- Chromophobes

# Proopiomelanocortin (POMC)



- Common precursor of ACTH and MSH.
- POMC cells: pars distalis and intermedia of pituitary, arcuate nucleus of the hypothalamus, epidermis.
- MSH stimulates melanin production of the skin (suntan).



## Hyperpigmentation (high MSH):

- Addison disease – adrenal cortex insufficiency: low cortisol , lack of feedback.
- Cushing disease - high ACTH and cortisol levels - pituitary adenoma.
- Pregnancy – melasma.

**SUMMARY TABLE 18-2 THE PITUITARY HORMONES**

Region/Area	Hormone(s)	Target(s)	Hormonal Effect(s)	Hypothalamic Regulatory Hormone
<b>ANTERIOR LOBE (ADENOHYPHYSIS)</b>				
Pars distalis	Thyroid-stimulating hormone (TSH)	Thyroid gland	Secretion of thyroid hormones ( $T_3$ , $T_4$ )	Thyrotropin-releasing hormone (TRH)
	Adrenocorticotropic hormone (ACTH)	Adrenal cortex (zona fasciculata)	Secretion of glucocorticoids (cortisol, corticosterone)	Corticotropin-releasing hormone (CRH)
	<i>Gonadotropins:</i>			
	Follicle-stimulating hormone (FSH)	Follicle cells of ovaries Sustentacular cells of testes	Secretion of estrogen, follicle development Stimulation of sperm maturation	Gonadotropin-releasing hormone (GnRH) As above
	Luteinizing hormone (LH)	Follicle cells of ovaries  Interstitial cells of testes	Ovulation, formation of corpus luteum, secretion of progesterone	As above
			Secretion of testosterone	As above
Prolactin (PRL)	Mammary glands	Production of milk	Prolactin-releasing factor (PRF) Prolactin-inhibiting hormone (PIH)	
Growth hormone (GH)	All cells	Growth, protein synthesis, lipid mobilization and catabolism	Growth-hormone-releasing hormone (GH-RH)	
			Growth hormone-inhibiting hormone (GH-IH)	
Pars intermedia (not active in normal adults)	Melanocyte-stimulating hormone (MSH)	Melanocytes	Increased melanin synthesis in epidermis	Melanocyte-stimulating hormone-inhibiting hormone (MSH-IH)
<b>POSTERIOR LOBE (NEUROHYPHYSIS OR PARS NERVOSA)</b>				
	Antidiuretic hormone (ADH)	Kidneys	Reabsorption of water, elevation of blood volume and pressure	None: Transported along axons from supraoptic nucleus to posterior lobe of the pituitary gland
	Oxytocin (OT)	Uterus, mammary glands (females) Ductus deferens and prostate gland (males)	Labor contractions, milk ejection Contractions of ductus deferens and prostate gland	None: Transported along axons from paraventricular nucleus to posterior lobe of the pituitary gland



# Take home message

Hypothalamus	Transport to the pituitary	Target within the pituitary	Action in the pituitary
Magnocellular nuclei (supraoptic, paraventricular)	axonal projection	neurohypophysis	storage and release into the systematic circulation
Parvocellular nuclei, regulatory hormones	portal circulation	adenohypophysis	regulation of anterior pituitary's hormone secretion

