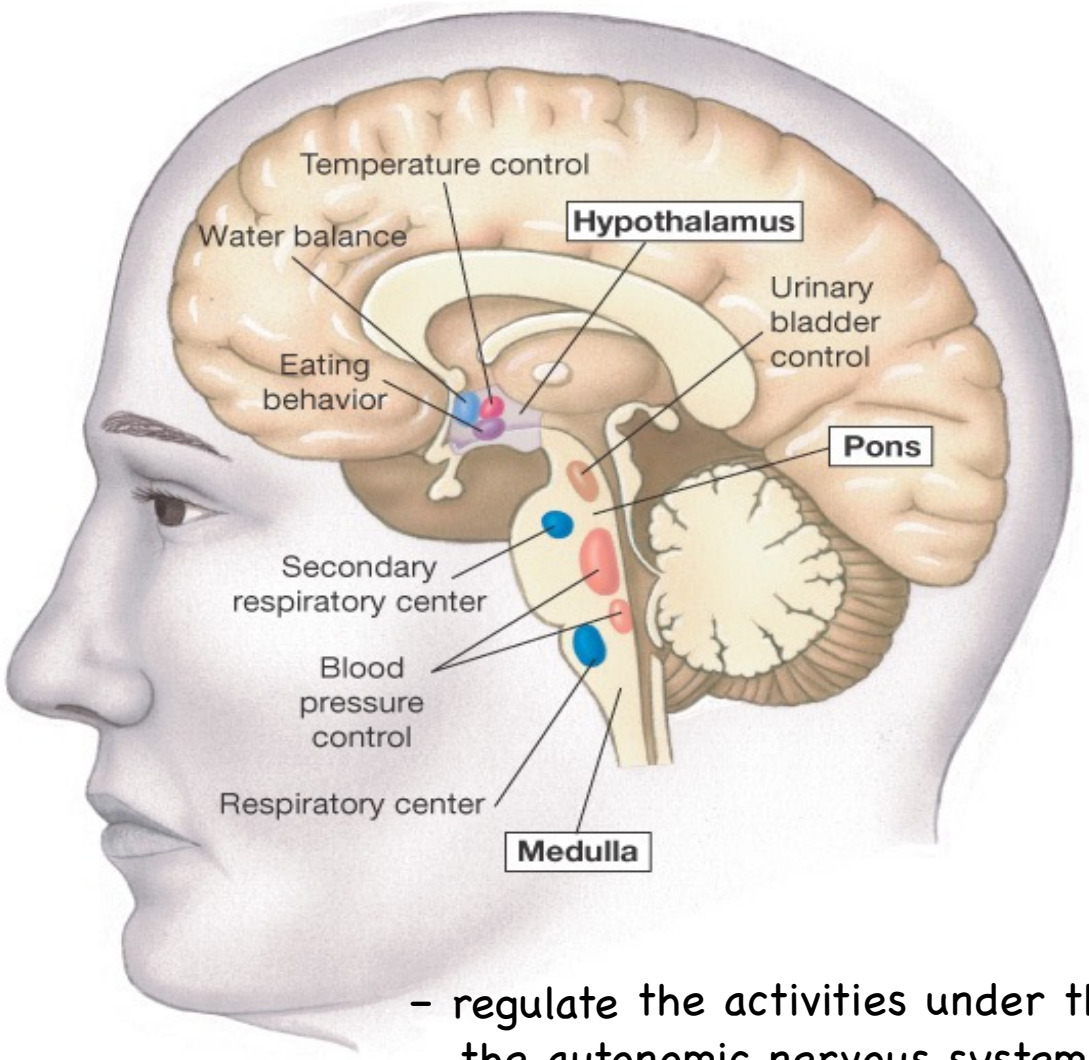
Hypothalamus and Pituitary gland

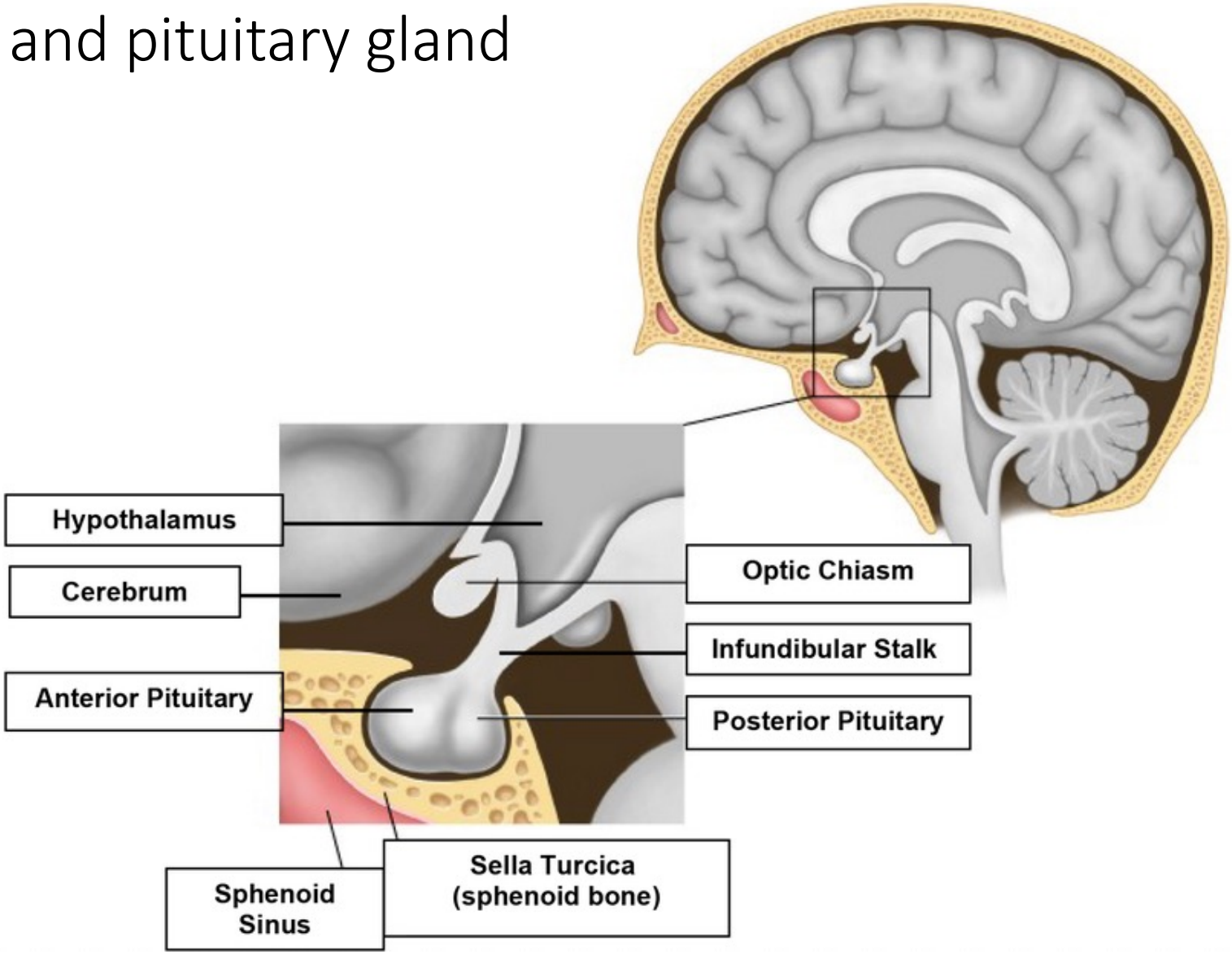
The endocrine system and the autonomic nervous system

Autonomic Control Centers in the Brain



- regulate the activities under the control of the autonomic nervous system

Hypothalamus and pituitary gland -localization-



Paraventricular and supraoptic nuclei
- regulate water balance
- produce ADH and oxytocin
- destruction causes diabetes insipidus
- paraventricular nucleus projects to autonomic nuclei of brainstem and spinal cord

Anterior nucleus
- thermal regulation (dissipation of heat)
- stimulates parasympathetic NS
- destruction results in hyperthermia

Preoptic area
- contains sexually dimorphic nucleus
- regulates release of gonadotropic hormones

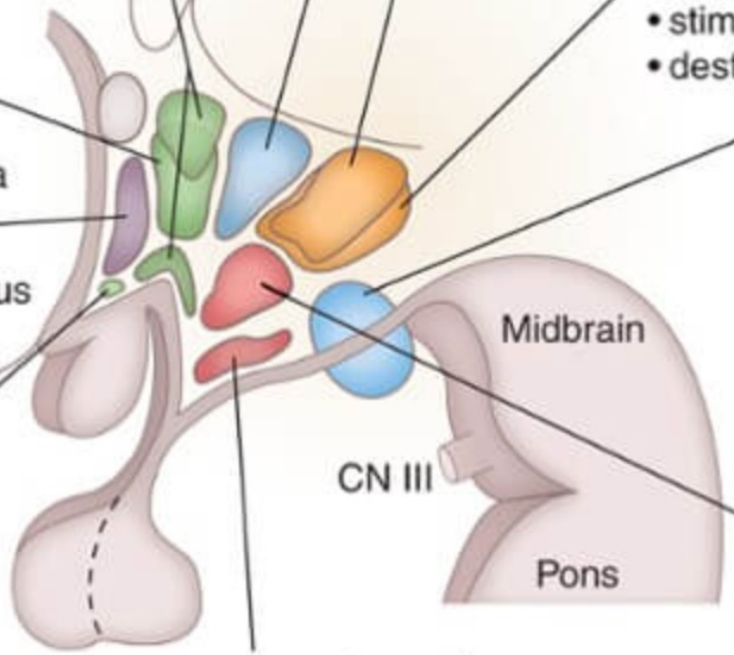
Suprachiasmatic nucleus
- receives input from retina
- controls circadian rhythms

Dorsomedial nucleus
- stimulation results in obesity and savage behavior

Posterior nucleus
- thermal regulation (conservation of heat)
- destruction results in inability to thermoregulate
- stimulates the sympathetic NS

Lateral nucleus
- stimulation induces eating
- destruction results in starvation

Mammillary body
- receives input from hippocampal formation via fornix
- projects to anterior nucleus of thalamus
- contains hemorrhagic lesions in Wernicke's encephalopathy



Ventromedial nucleus
- satiety center
- destruction results in obesity and savage behavior

Arcuate nucleus
- produces hypothalamic releasing factors
- contains DOPA-ergic neurons that inhibit prolactin release

Input to the hypothalamus-1

- nucleus of the solitary tract:

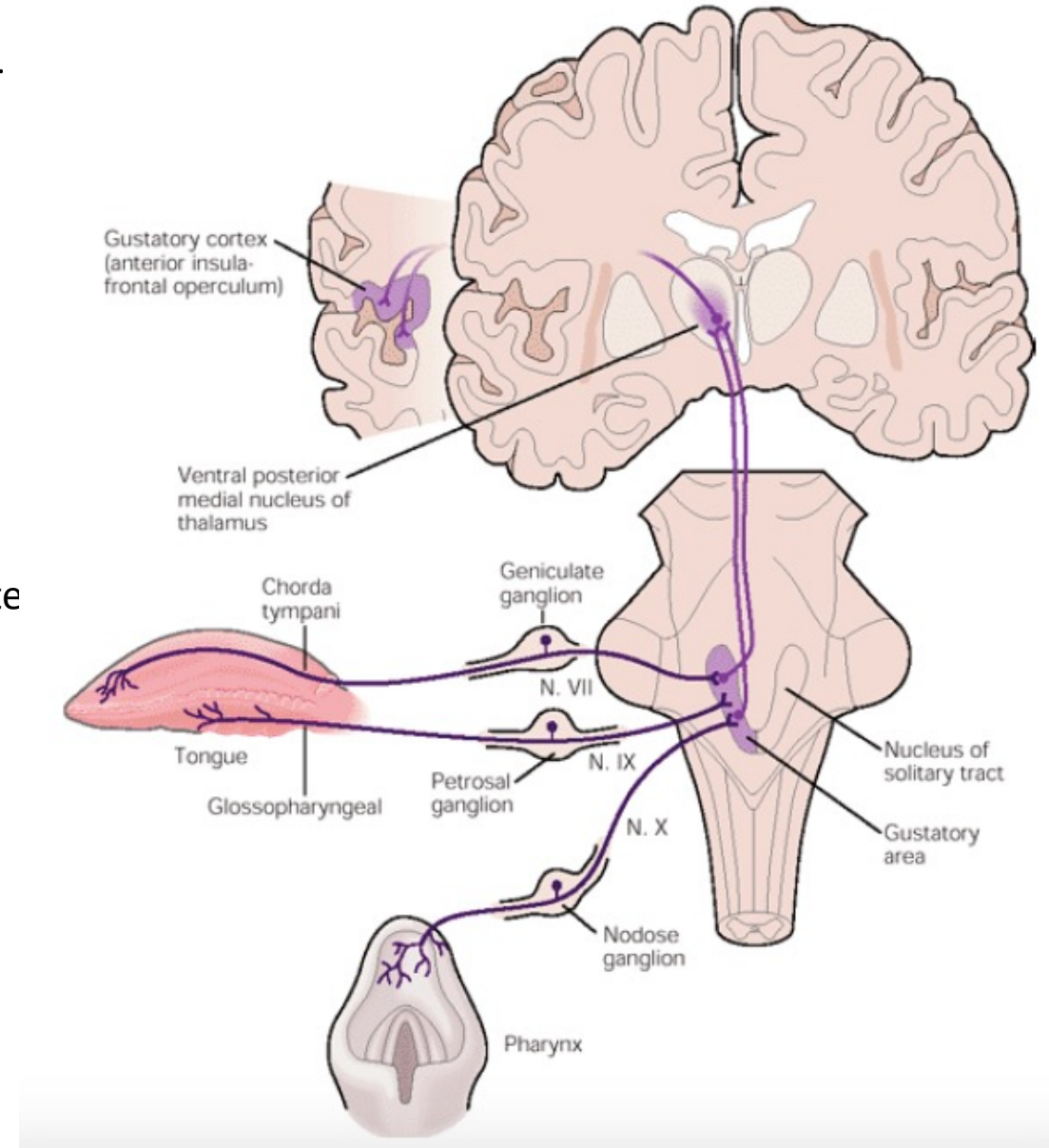
  collects all of the visceral sensory information f.i. blood pressure and gut distension

- limbic and olfactory systems:

  structures such as amygdala, hippocampus, and olfactory cortex project to the hypothalamus, and probably help to regulate behaviors such as eating and reproduction.

- hypothalamus intrinsic receptors:

  thermoreceptors and osmoreceptors to monitor temperature and ionic balance, respectively



Input to the hypothalamus-2

- reticular formation:

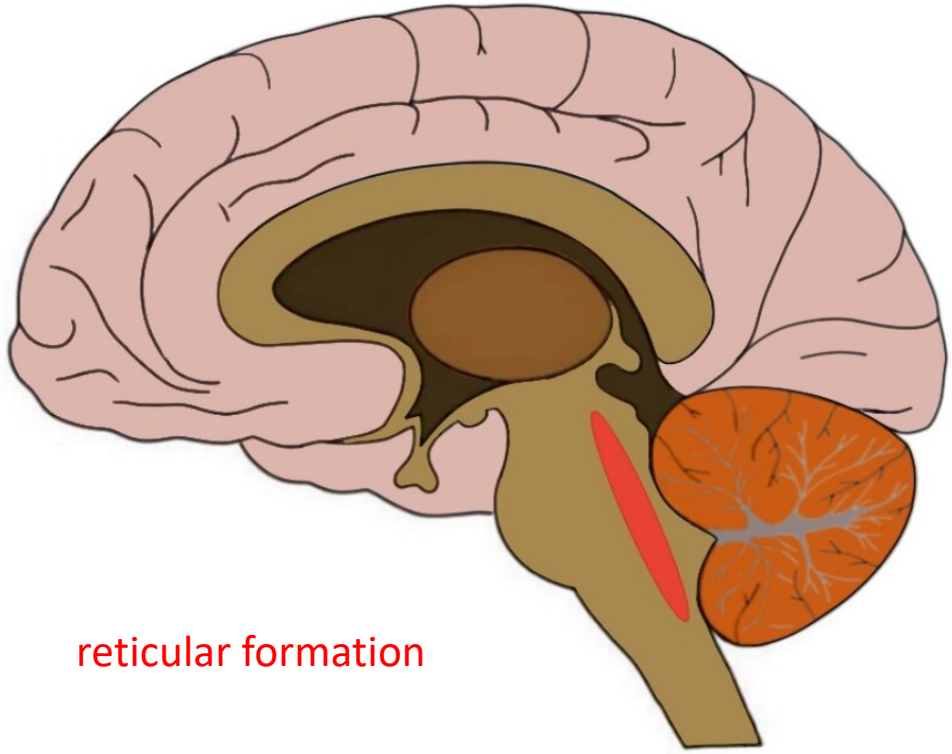
  nucleus in the brainstem, receives a variety of inputs via spinal cord f.i. skin temperature

- limbic and olfactory systems:

  structures such as amygdala, hippocampus, and olfactory cortex project to the hypothalamus, and probably help to regulate behaviors such as eating and reproduction

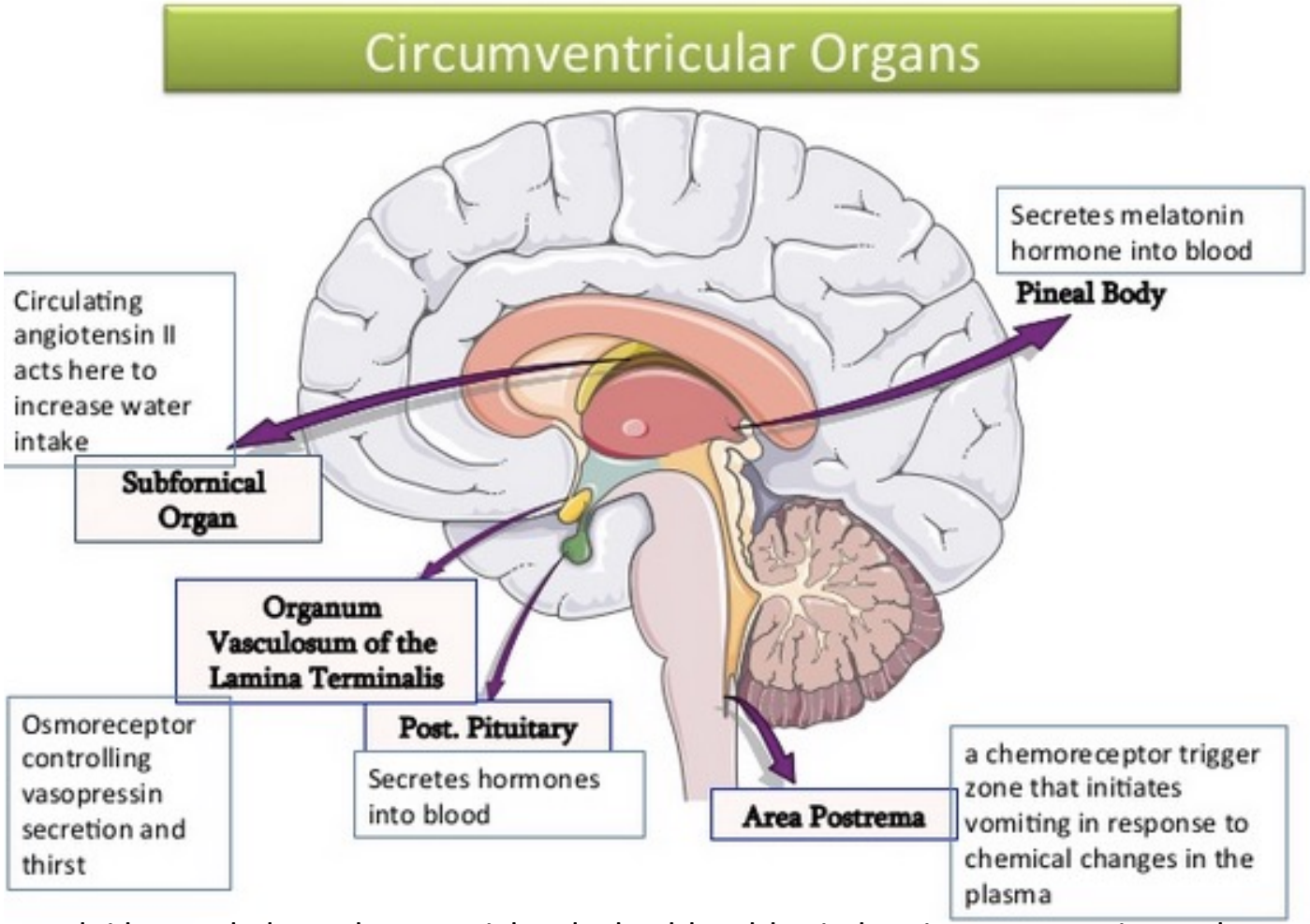
- hypothalamus intrinsic receptors:

  thermoreceptors and osmoreceptors to monitor temperature and ionic balance, respectively



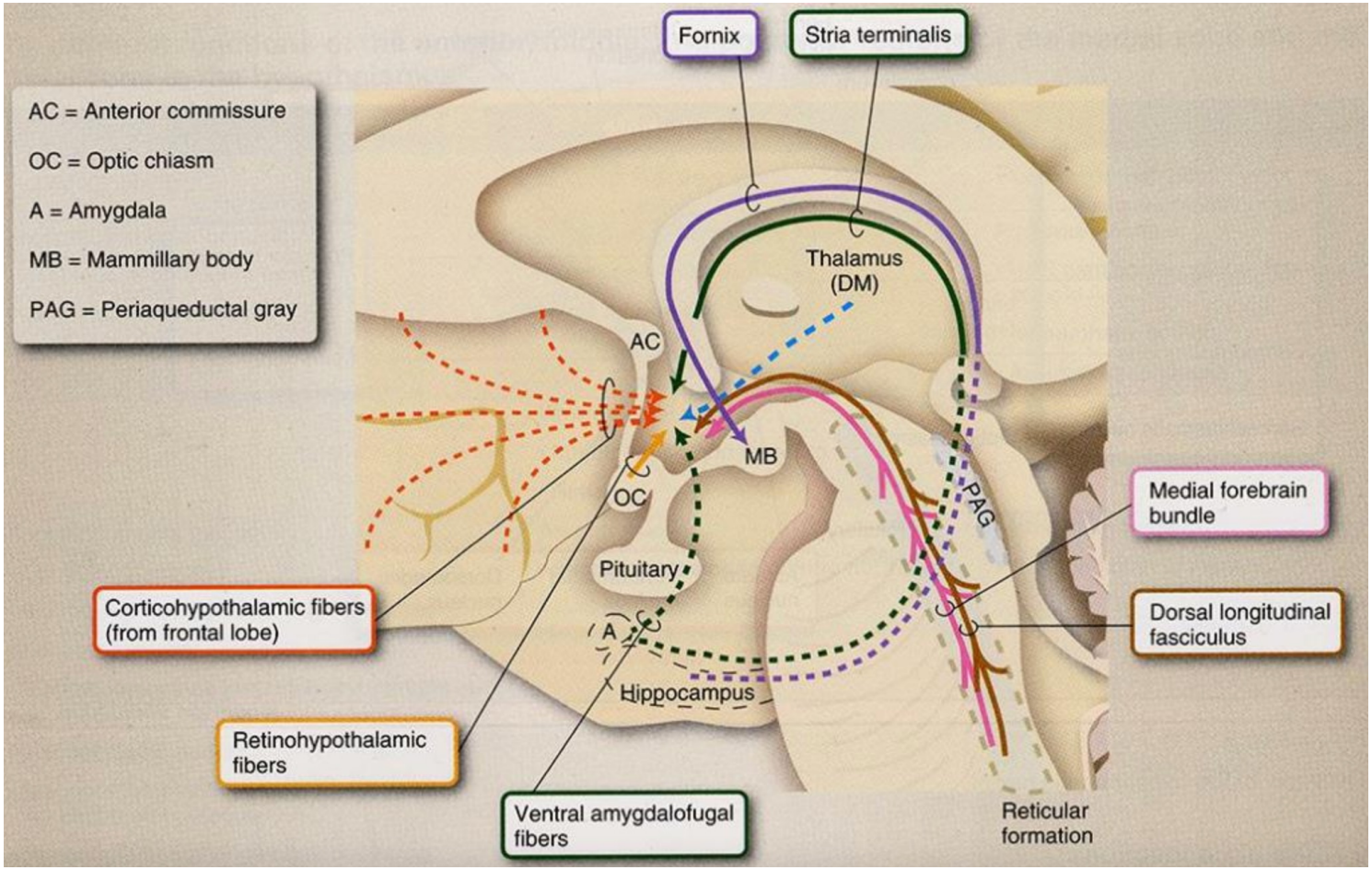
reticular formation

Input to the hypothalamus-3



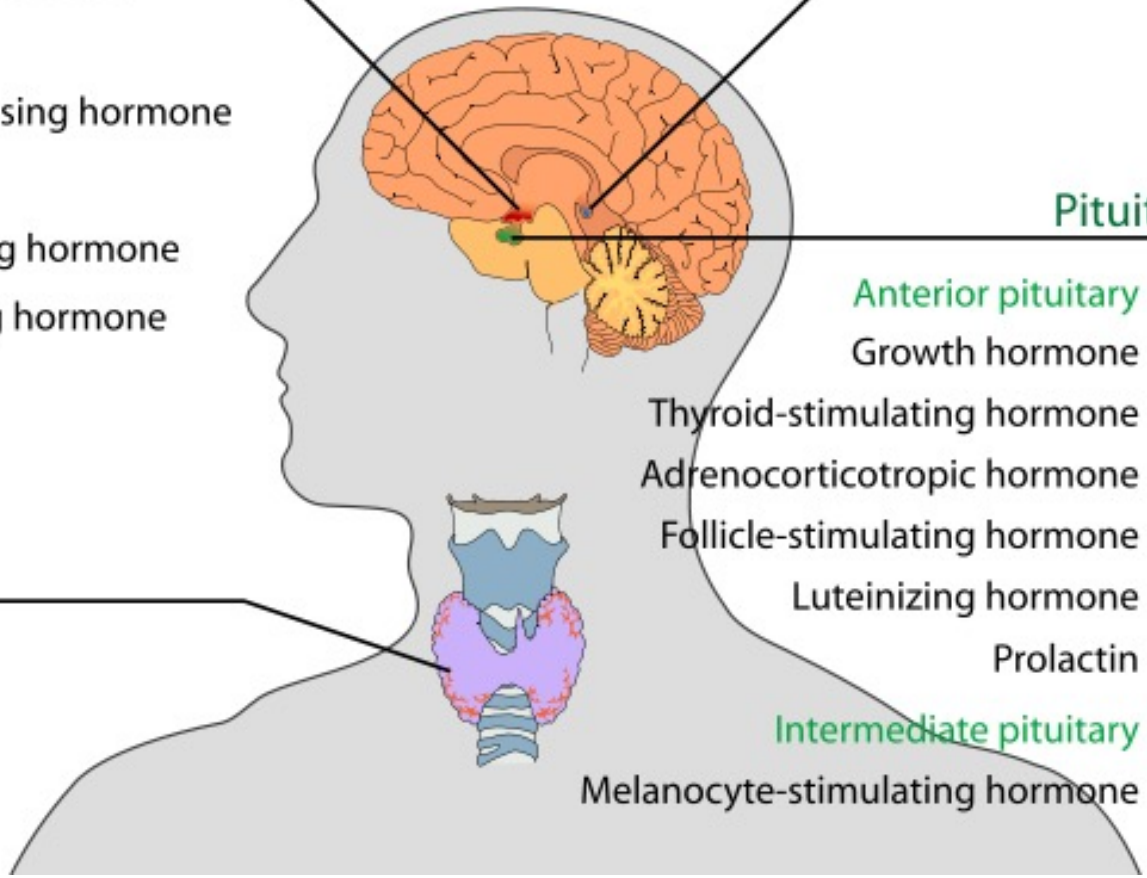
nuclei located along the ventricles, lack a blood-brain barrier: can monitor substances in the blood that would normally be shielded from neural tissue. F.I. area postrema, which is sensitive to toxins in the blood and can induce vomiting

Input to the hypothalamus-4



retina:
some fibers from the optic nerve go directly to a small nucleus within the hypothalamus called the suprachiasmatic nucleus. This nucleus regulates circadian rhythms, and couples the rhythms to the light/dark cycles.

Hormones of the Hypothalamus



Hypothalamus

Thyrotropin-releasing hormone

Dopamine

Growth hormone-releasing hormone

Somatostatin

Gonadotropin-releasing hormone

Corticotropin-releasing hormone

Oxytocin

Vasopressin

Thyroid

Triiodothyronine

Thyroxine

Pineal gland

Melatonin

Pituitary Gland

Anterior pituitary

Growth hormone

Thyroid-stimulating hormone

Adrenocorticotropic hormone

Follicle-stimulating hormone

Luteinizing hormone

Prolactin

Intermediate pituitary

Melanocyte-stimulating hormone

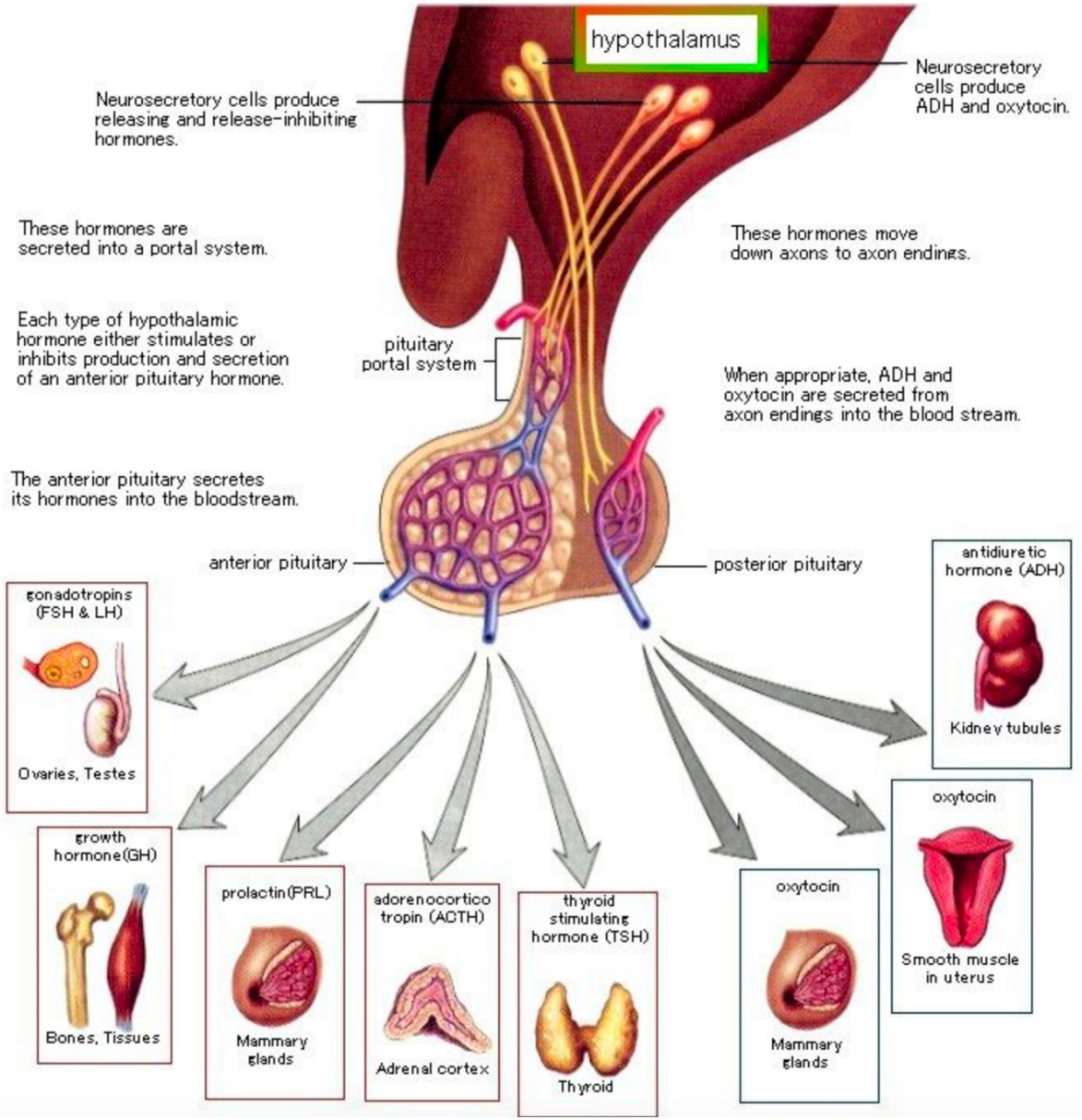
Posterior pituitary

Oxytocin

Vasopressin

Oxytocin (stored)

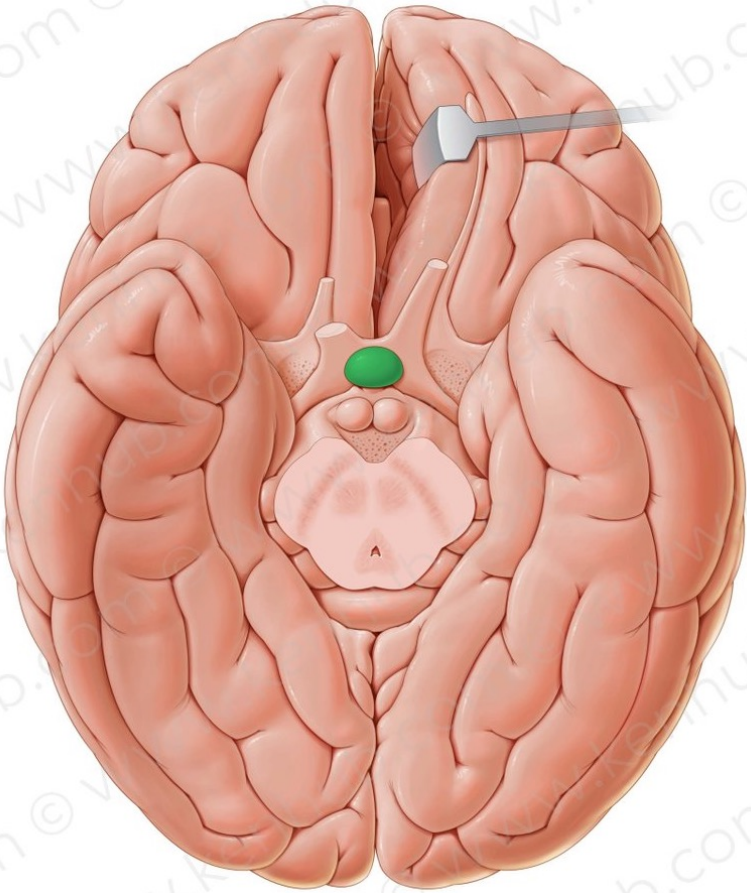
Anti-diuretic hormone (stored)

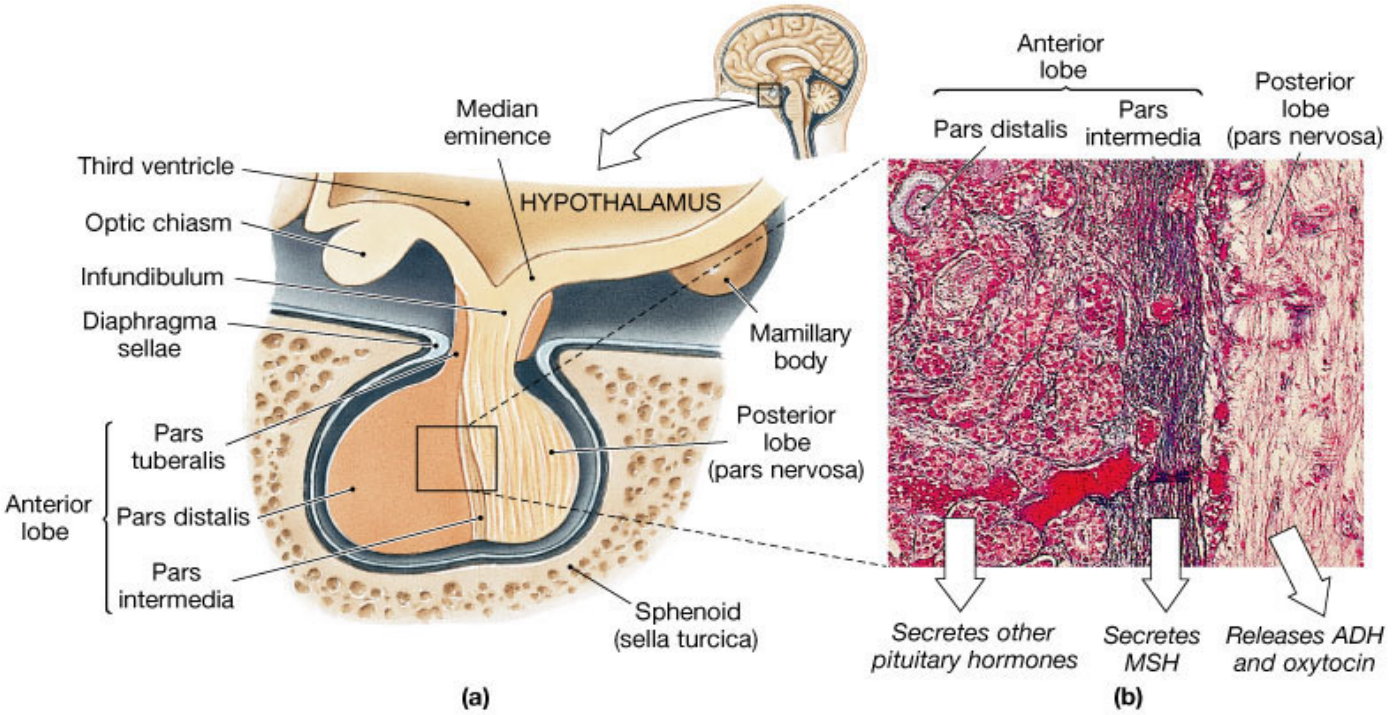

hypothalamus
Neurosecretory cells produce releasing and release-inhibiting hormones.
Neurosecretory cells produce ADH and oxytocin.
These hormones are secreted into a portal system.
These hormones move down axons to axon endings.
Each type of hypothalamic hormone either stimulates or inhibits production and secretion of an anterior pituitary hormone.
pituitary portal system
When appropriate, ADH and oxytocin are secreted from axon endings into the blood stream.
The anterior pituitary secretes its hormones into the bloodstream.
anterior pituitary
posterior pituitary
gonadotropins (FSH & LH)
Ovaries, Testes
growth hormone(GH)
Bones, Tissues
prolactin(PRL)
Mammary glands
adrenocortico tropin (ACTH)
Adrenal cortex
thyroid stimulating hormone (TSH)
Thyroid
oxytocin
Mammary glands
antidiuretic hormone (ADH)
Kidney tubules
oxytocin
Smooth muscle in uterus

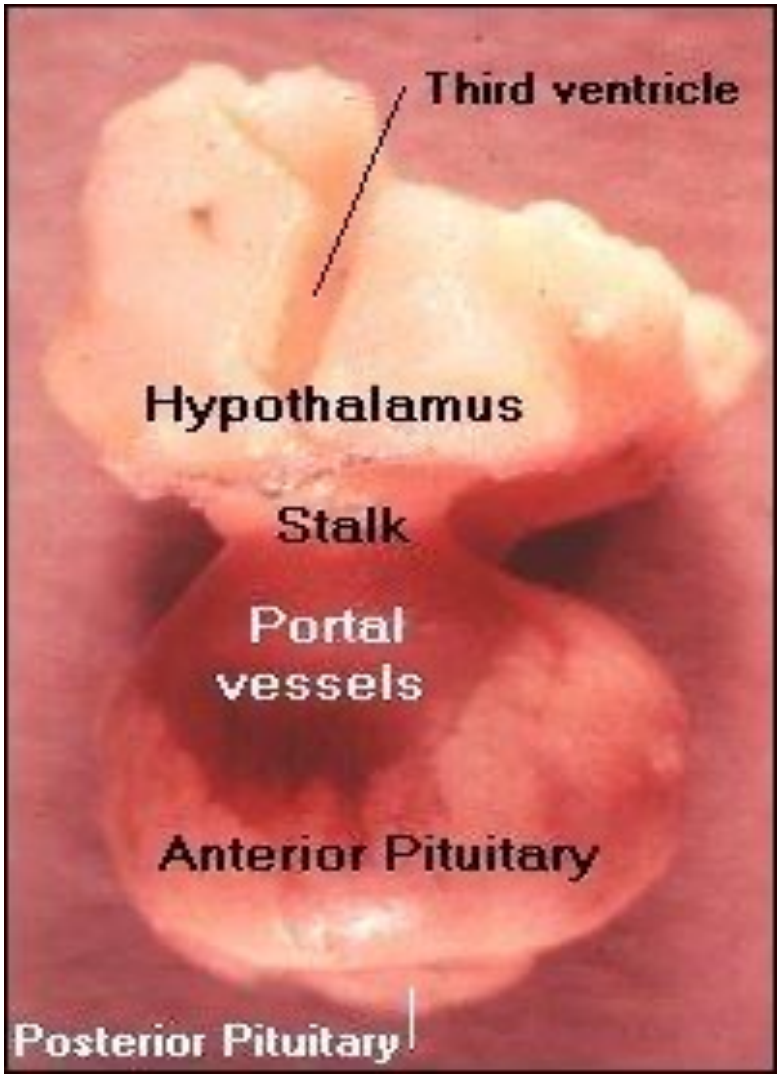
Pituitary Gland
-Hypophysis-

- 0.5-1g, enlarges during pregnancy
- is composed of :
  - adenohypophysis (glandular or epithelial hypophysis)
  - Neurohypophysis
- releases nine important peptide hormones
- all nine bind to membrane receptors and use cyclic AMP as a second messenger

The Anatomy and Orientation of the Pituitary Gland







- A**nterior pituitary or *adenohypophysis:***

-a classical gland
-composed of cells that secrete protein hormones

.• P**osterior pituitary or neurohypophysis**
-not really an organ, but an extension of the hypothalamus.

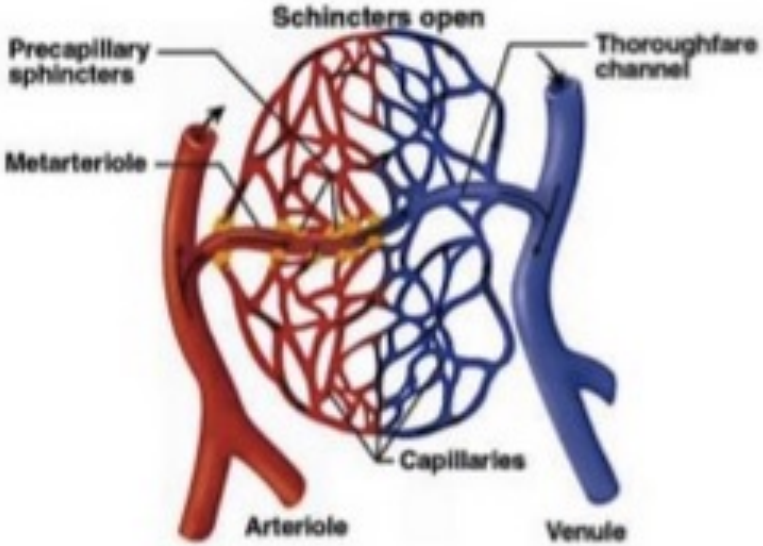
-composed largely of the axons of hypothalamic neurons which extend downward as a large bundle behind the anterior pituitary and form the **pituitary stalk**, which appears to suspend the anterior gland from the hypothalamus.

neurons of the paraventricular nucleus secrete oxytocin
Stimulates contractile cells in mammary gland
Stimulates smooth muscle cells in the uterus
neurons of the supraoptic nucleus manufacture antidiuretic hormone (ADH)
decreases the amount of water lost in the kidneys; elevates blood pressure

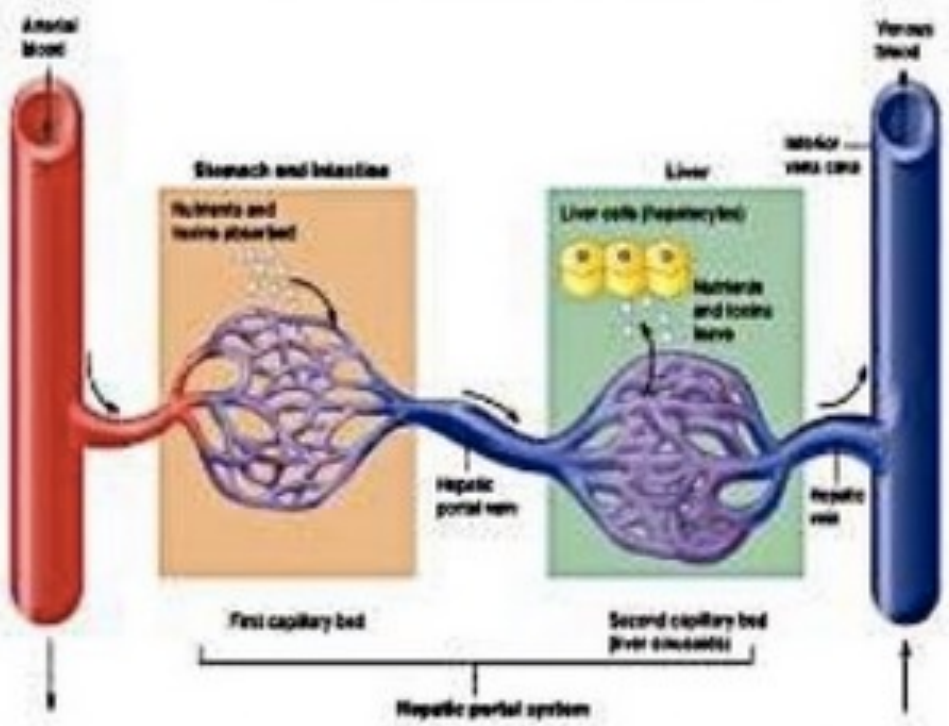
In many mammals, there is also an **intermediate lobe** (pars intermedia) between the anterior and posterior pituitary.

Portal System

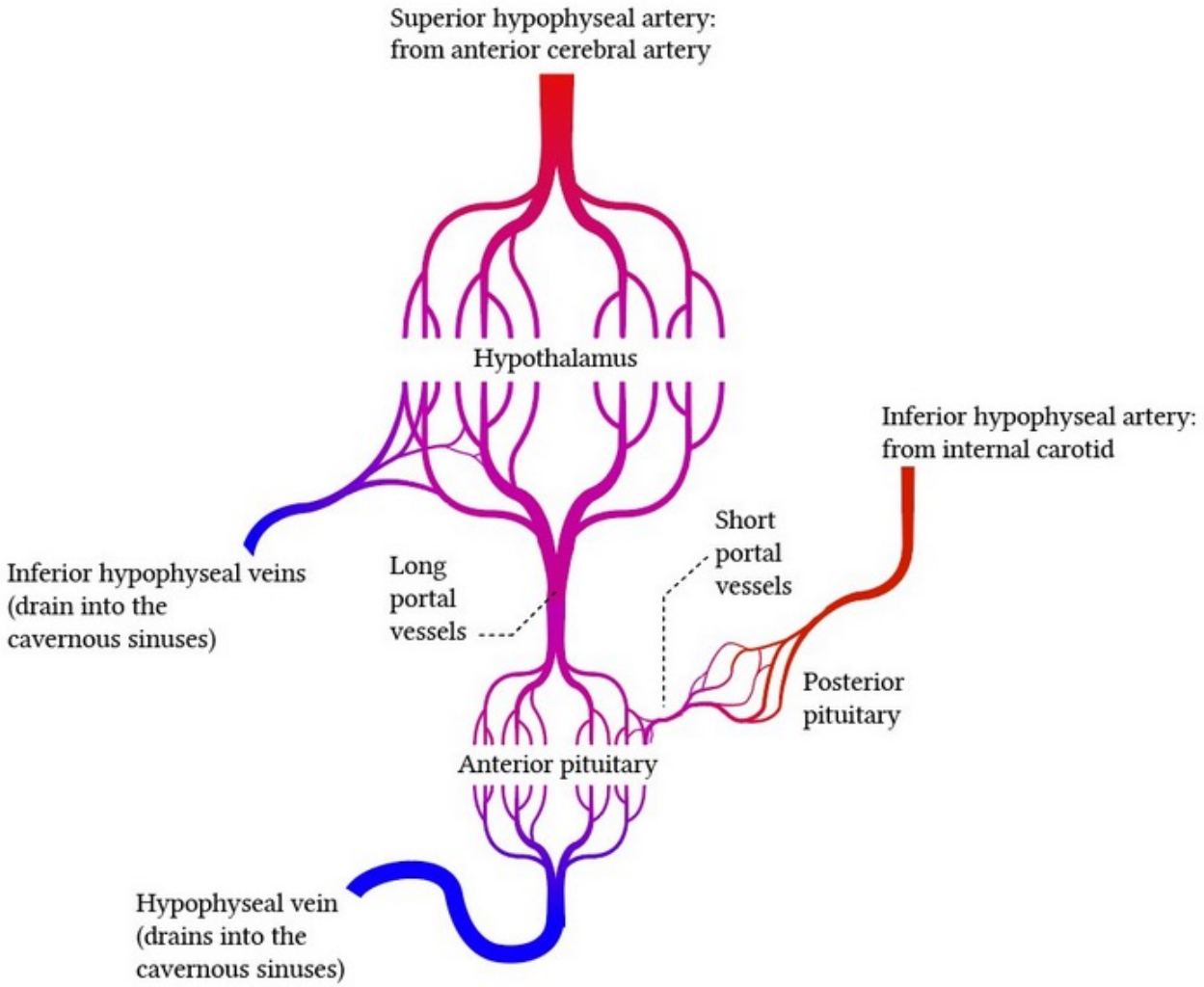
Usual circulation



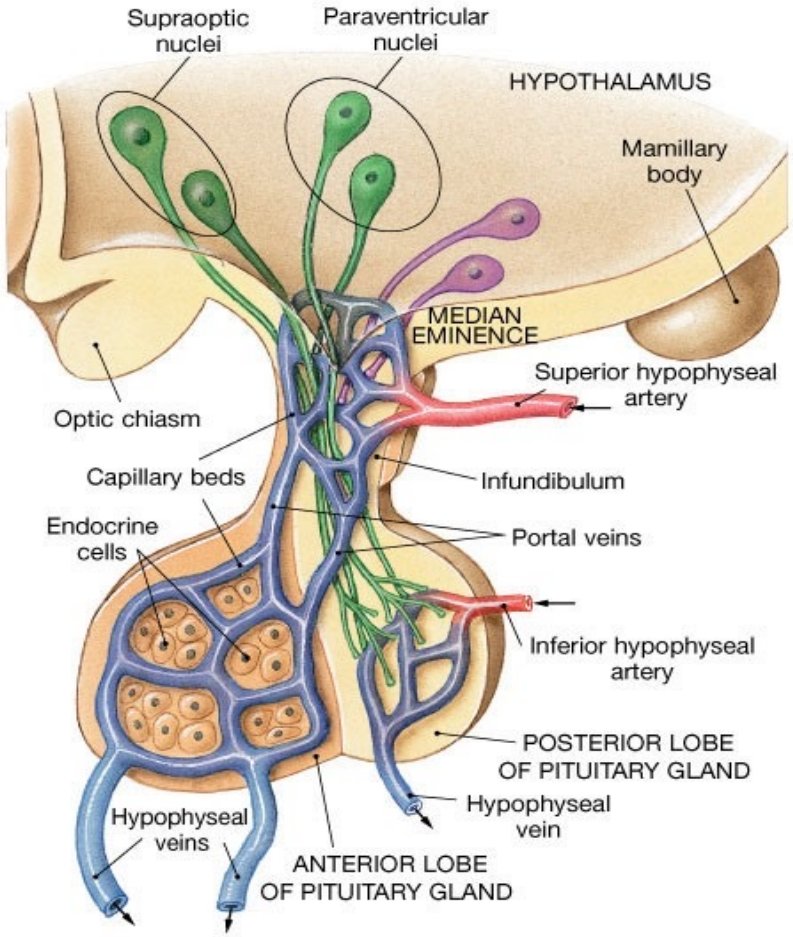
Portal circulation



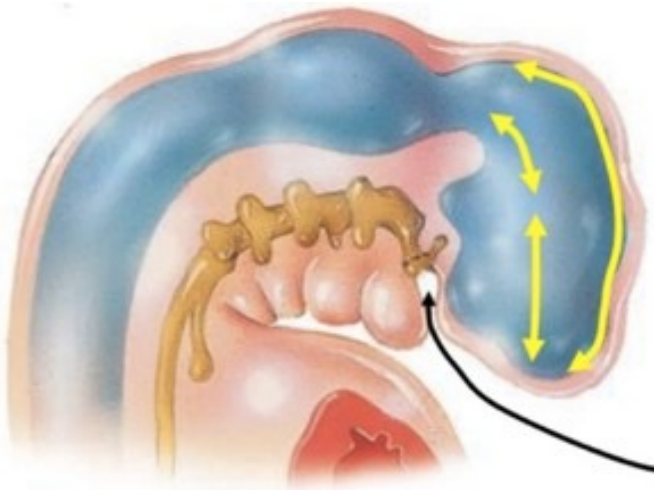
Pituitary portal circulation



The Hypophyseal Portal System



Embryonic development of the pituitary gland



Prosencephalon (Forebrain)

1. Diencephalon
2. Telencephalon

Primitive oral cavity (stomodeum)

Floor of diencephalon

Neuroectodermal diverticulum

Rathke's pouch

Roof of stomodeum

Infundibulum

Neurohypophysis

Adenohypophysis

Ant pituitary

Intermediate pituitary

Pituitary Gland:

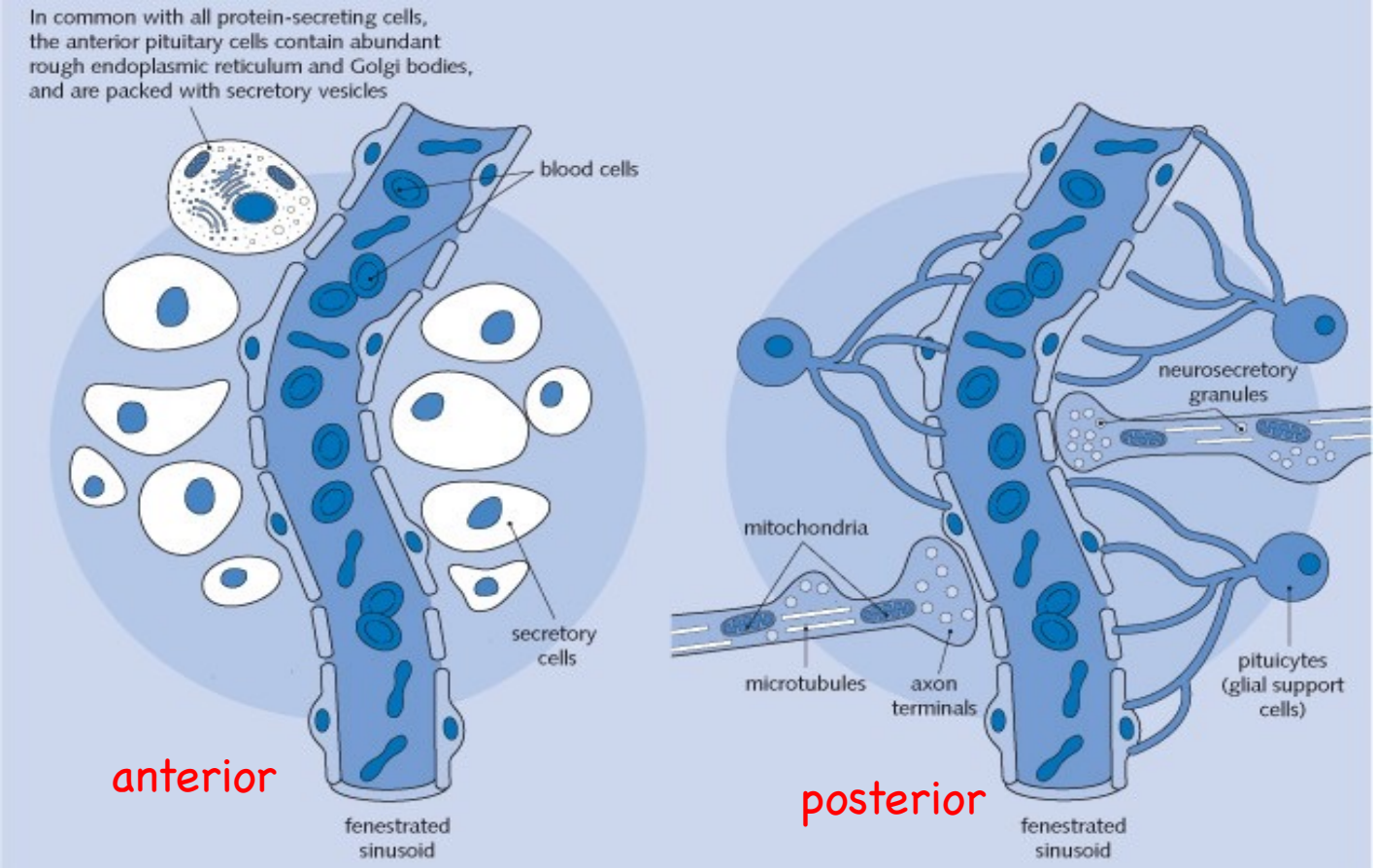
- **Posterior pituitary "gland", neurohypophysis**
  - part of the endocrine system
  - collection of axonal projections from the hypothalamus
  - octapeptides: oxytocin, vasopressin

- **Anterior pituitary, Adenohypophysis** ἀδήν, *adên* (« gland »), ἀδένος, *adénos* (« de la glande)
  - Rathke's pouch
  - no direct nerve supply
  - chemical hypophyseal-portal system
  - ACTH, TSH, FSH, LH, GH, prolactin

Size of the pituitary varies between species

- Size of the pituitary varies between different species:
  - animals that rapidly change their colors may have a relatively large pars intermedia
  - birds lack a pars intermedia
  - aquatic species may have a small pars nervosa whereas land- dwelling species, particularly those in arid climate may have relatively large pars nervosa

Histology of the anterior and posterior pituitary gland



1901 Magnus and Schafer demonstrate the oxytocic, pressor and antidiuretic activities of posterior pituitary extracts

Rudolf Magnus
1873-1927
Brunswig-Pontresina

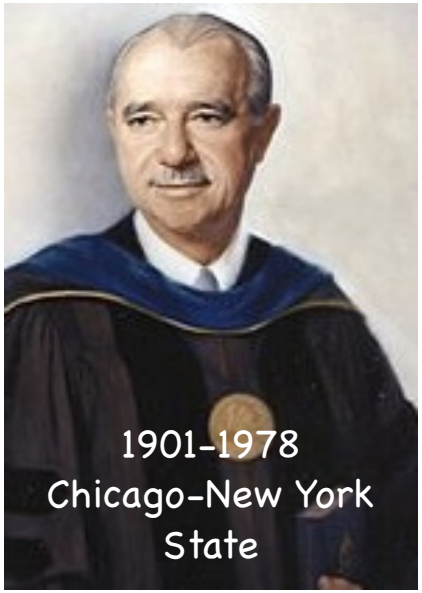
Magnus, R. & Schafer, E. A. Effects of post-pituitary extracts. J. Physiol. 12, 32–38 (1901).

1939 LM Pickford demonstrated that acetylcholine releases ADH

First female professor of Medicine in Edinburgh

Lilian Mary Pickford 1902-2002
Jabalpur, India-Hampshire, UK

Vincent Du Vigneaud



- sequenced and synthesized oxytocin and vasopressin in 1953
- Lasker Award 1948, Nobel Prize Chemistry 1955

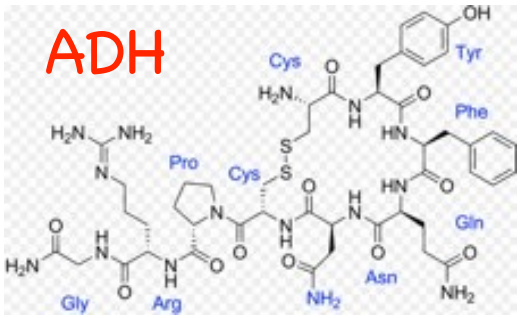
"A trail of sulfa research: from insulin to oxytocin"

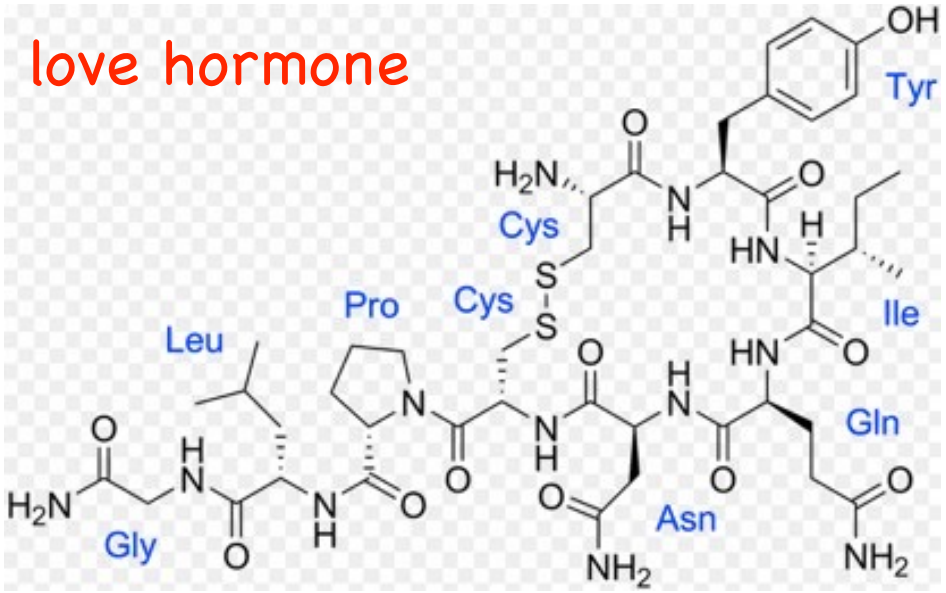
Oxytocin

1 2 3 4 5 6 7 8 9
Cys-Tyr-**Ile**-Gln-Asn-Cys-Pro-**Leu**-Gly-NH_2
S–S

ADH (Vasopressin)

1 2 3 4 5 6 7 8 9
Cys-Tyr-**Phe**-Gln-Asn-Cys-Pro-**Arg**-Gly-NH_2
S–S



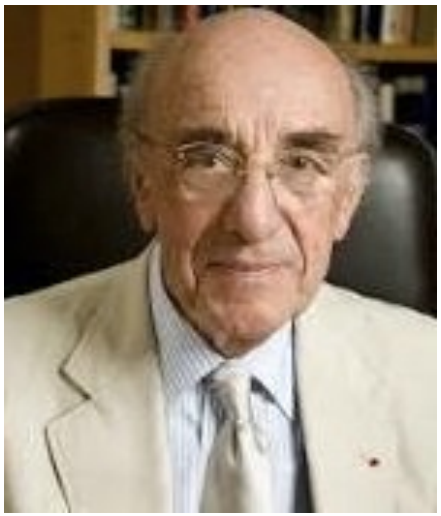


Discovery of neurohormones

1971 Purification of hypothalamic hormones

1977 Nobel Prize Medicine and Physiology

Roger Guillemin
Dijon; Baylor, Salk
1924-



Andrzej Wiktor Schally
Vilnius, McGill, Tulane, Baylor
1926-

Rosalyn Yalow: RIA
Bronx, Urbana Champaigne,
Mount Sinai
1921-2011

Hypothalamic Releasing Hormones

- 1. Thyrotropin-releasing hormone (TRH)
- 2. Corticotropin-releasing hormone (CRH)
- 3. Gonadotropin-releasing hormone (GnRH)
- 4. Growth hormone-releasing hormone (GHRH)
- 5. Growth hormone-release inhibiting hormone (GHIH)
- 6. Prolactin-releasing factor (PRF)
- 7. Prolactin-inhibiting hormone (PIH)

Secretion

Is influenced by emotions
Can be influenced by the metabolic state of the individual
Delivered to the anterior pituitary via the hypothalamic-hypophyseal portal system
Usually initiates a three-hormone sequence

Endocrine Control: Three Levels of Integration

- Hypothalamic stimulation <- CNS
- Pituitary stimulation <- hypothalamic trophic hormones
- Endocrine gland stimulation <-pituitary trophic hormones

Endocrine Control:
3 Levels of Integration

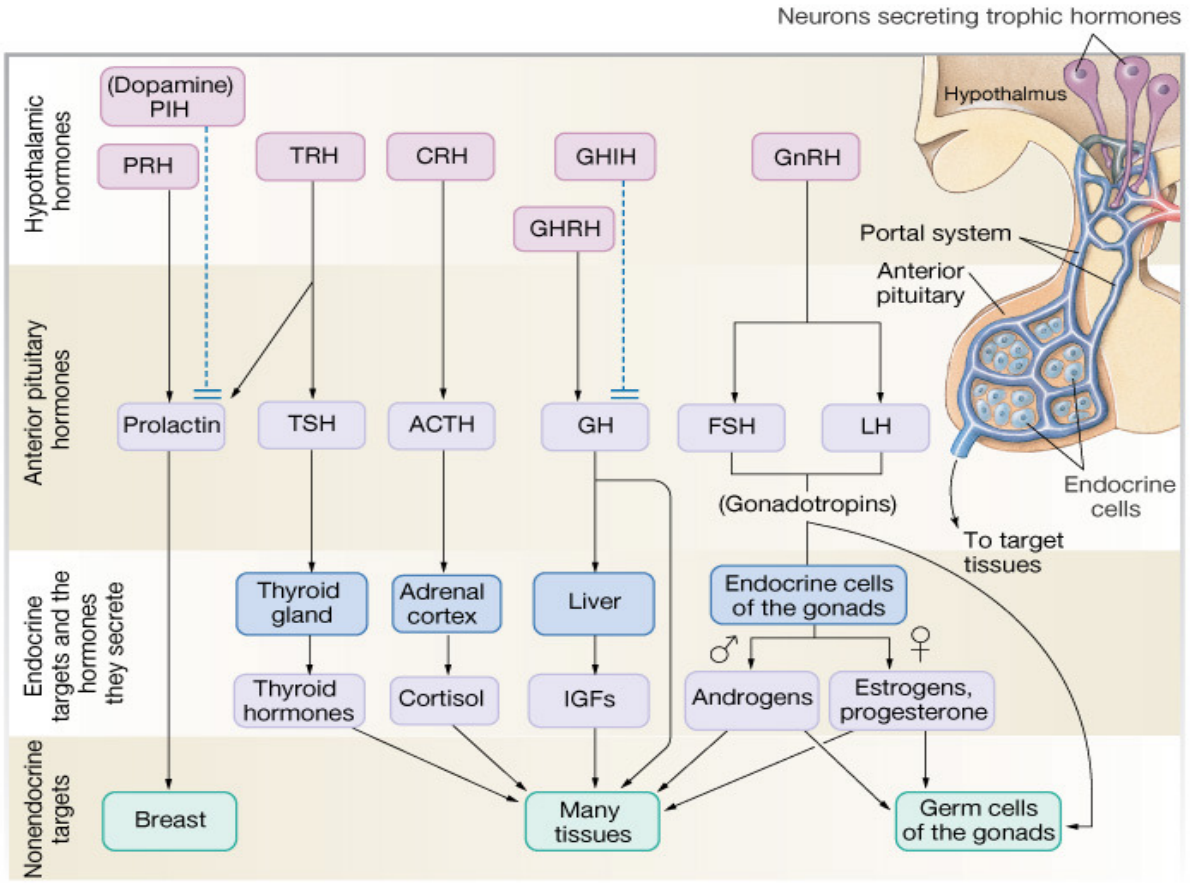


Figure 7-13: Hormones of the hypothalamic-anterior pituitary pathway

Disorders of the hypothalamus and the pituitary

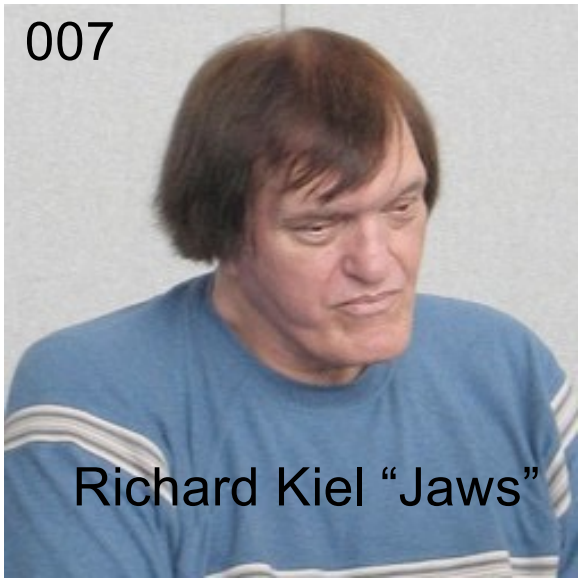
Akhenaten reign: 1353-1336 BC

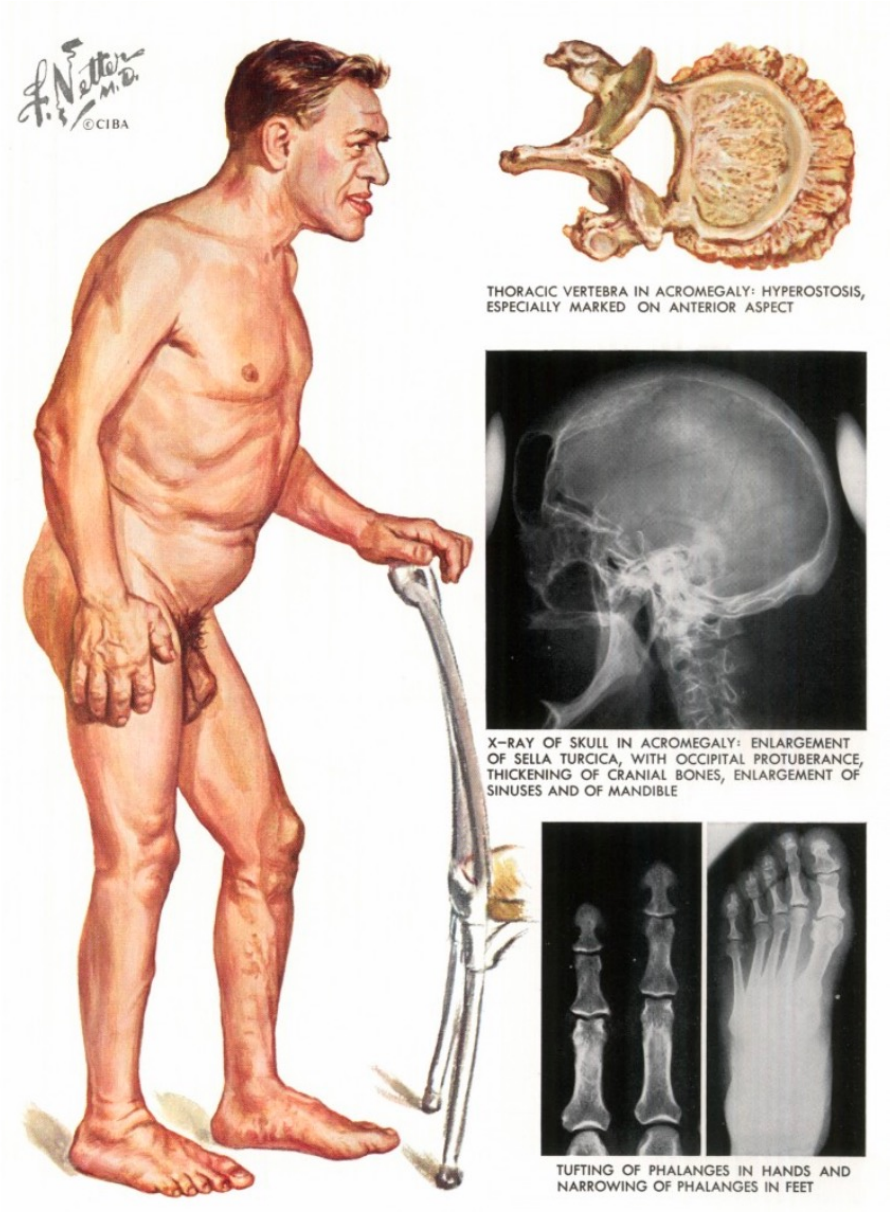
André le géant

1946-1993

- Wrestler and actor
- 2.36 m, 235 kg
- not expected to live past 40
- He chose not to be treated

Acromegaly

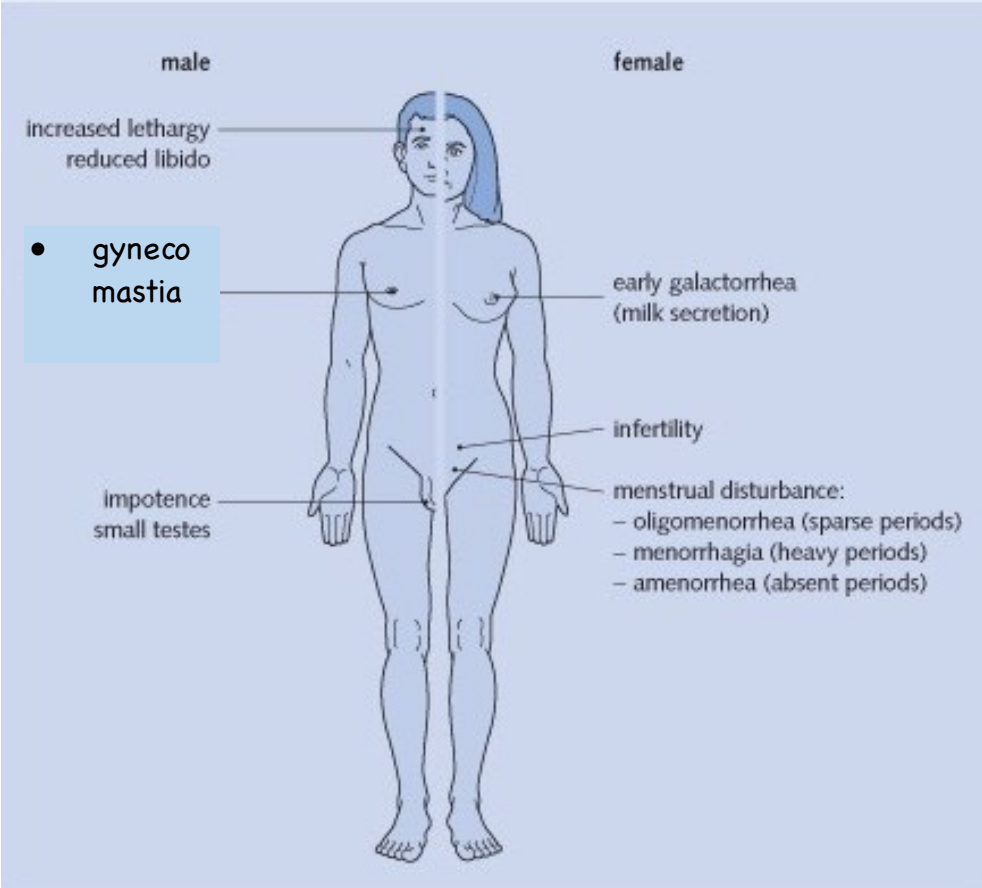

007
Richard Kiel “Jaws”


F. Netter M.D.
©CIBA
THORACIC VERTEBRA IN ACROMEGALY: HYPEROSTOSIS, ESPECIALLY MARKED ON ANTERIOR ASPECT
X-RAY OF SKULL IN ACROMEGALY: ENLARGEMENT OF SELLA TURCICA, WITH OCCIPITAL PROTUBERANCE, THICKENING OF CRANIAL BONES, ENLARGEMENT OF SINUSES AND OF MANDIBLE
TUFTING OF PHALANGES IN HANDS AND NARROWING OF PHALANGES IN FEET

Anterior pituitary hormones and the disorders caused by their deficiency and excess

Hormone	Deficiency	Excess
GH	Dwarfism in children GH deficiency syndrome	Gigantism in childrem Acromegaly in adults
LH and FSH	Gonadal insufficiency (decreased sex steroids)	rare: infertility
ACTH	Adrenocortical insufficiency (decreased cortisol and adrenal androgens)	Cusshing's disease (increased cortisol and adrenal androgens)
TSH	Hypothyroidism	Hyperthyroidism (rare)
Prolactin	Hyperprolactinemia (failure in postpartum lactation)	Hyperprolactinemia (impotence in males, amenorrhea in females, and decreased libido)

Symptoms and signs of hyperprolactinemia



Posterior pituitary hormones and the disorders caused by their deficiency and excess

Hormone	Deficiency	Excess
ADH	Diabetes insipidus	Syndrome of inappropriate ADH secretion (SIADH)
Oxytocin	Failure to progress in labor and difficulty with breastfeeding	No effect

SIADH

syndrome of inapropriate diuretic hormone (excessive secretion of ADH)

- diagnostic criteria
  - hyptonicity of plasma
  - hyponatremia
  - naturesis
  - exclusion of other causes

- symptoms
  - muscle cramps
  - nausea and vomiting
  - loss of balance
  - seizures

treatment

- water restriction 600-800 ml/day
- demeclocycline 900-1200 mg/day- blocks vasopressin at distal collecting tubule (kidney)
- hypertonic saline if sodium < 115 mEq/L

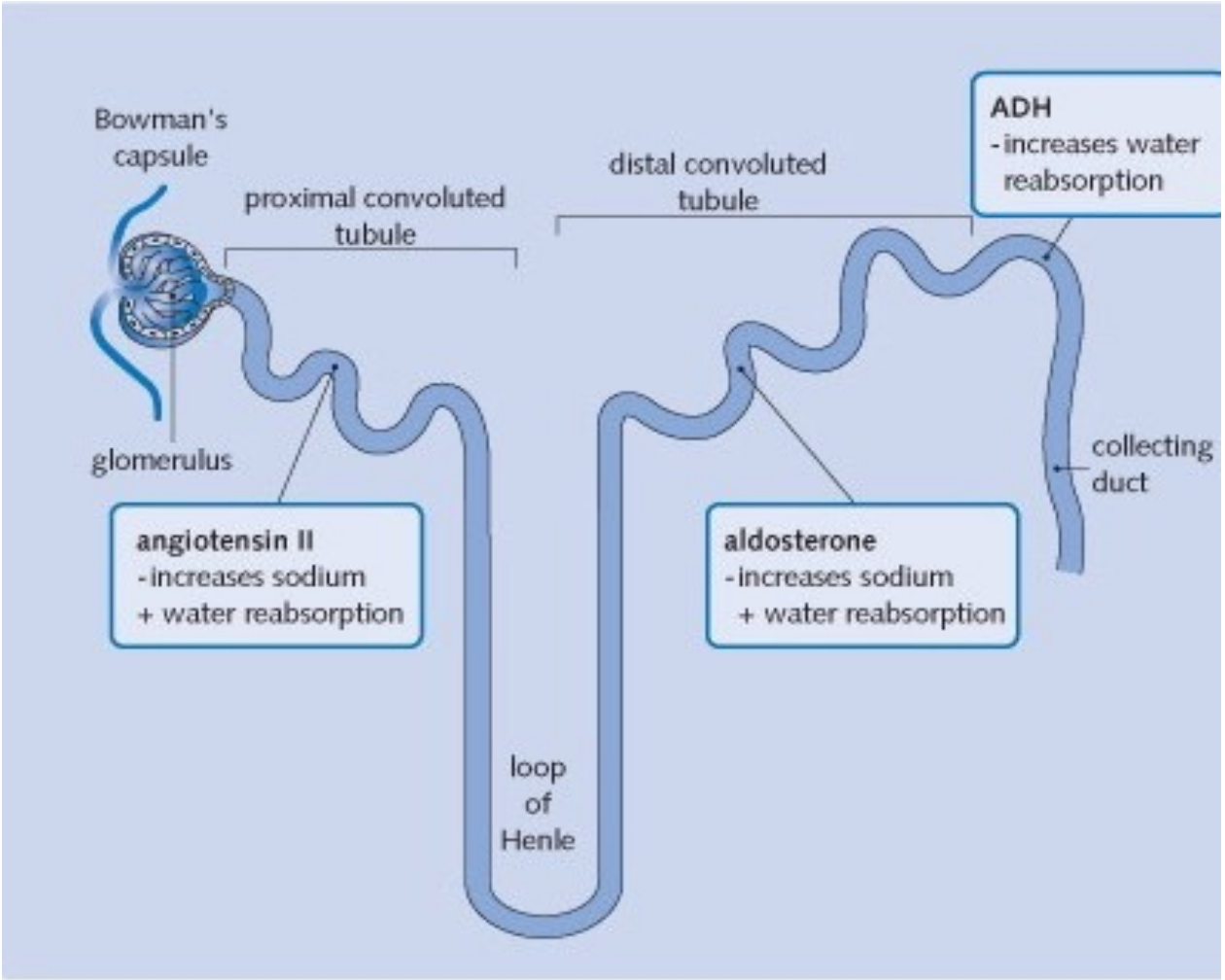
Pituitary - antidiuretic hormone (ADH)/ vasopressin

- CNS osmoreceptors supraoptic, periventricular nuclei hypothalamus
  - plasma osmolality changes
- baroreceptors, aortic arch, carotid sinus, left atrium
  - Cervical nerves IX, X
- renal action
  - ADH increases water permeability of the distal convoluted tubule and the collecting duct

Expected intake and output of water over a 24-hour period

Water intake (mL)	**Water loss (mL)**
Drinking: 1500 Food: 500 Metabolism: 400	Urine: 1500 Respiration: 500 Skin evaporation: 400 Feces: 100
Total 2400	Total 2400

Kidney: sites of hormone action



Pituitary - Diabetes Insipidus

- partial or complete absence of vasopressin
- Causes: tumor, inflammation, granuloma, trauma, vascular
- clinical features
  - polyuria- 3-15 L/day
  - urine osmolality drops to <200 mOsm/kg
  - plasma osmolality, normally maintained between 285-290 mOsm/kg may raise to >330 mOsm/kg
  - polydypsia- compensatory mechanism,
  - center destruction disastrous
  - associated features:

    visual field loss

    optic atrophy

    papilledema

    other pituitary hormone abnormalities