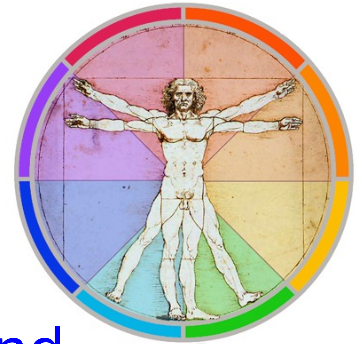
# HUBS191 Lecture Material

This pre-lecture material is to help you prepare for the lecture and to assist your note-taking within the lecture,
it is NOT a substitute for the lecture !

Please note that although every effort is made to ensure this pre-lecture material corresponds to the live-lecture there may be differences / additions.

# HUBS 191 2025
# Lecture 26



## Endocrine 2: The hypothalamus, pituitary and growth hormone

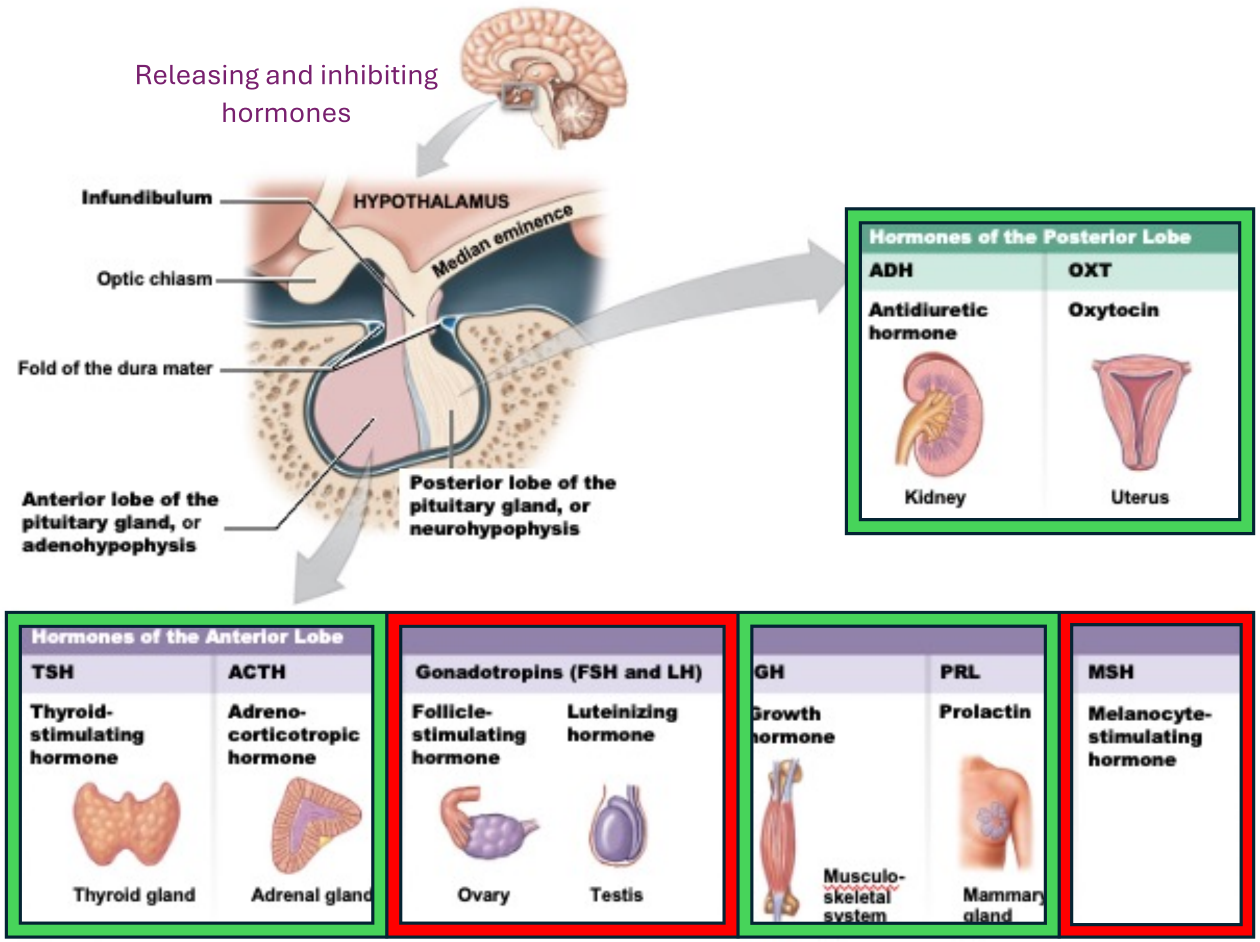
- Connections between hypothalamus and pituitary
- Hypothalamic-Hypophyseal portal circulation
- Posterior pituitary hormones
- Anterior pituitary hormones secretion and control
- Growth hormone

*Philip Kelly*
*HUBS Professional Practice Fellow*

## Lecture Objectives (updated)

- Understand how the hypothalamus connects to and controls the anterior and posterior pituitary gland.
- Name the hormones produced by the anterior pituitary and their respective hypothalamic releasing/inhibiting hormones
- Outline the secretion and effects of oxytocin and ADH
- Understand the effects of under or over-secretion of ADH
- Discuss the secretion and effects of human growth hormone (hGH)
- Outline the consequences of under or over-secretion of hGH

# Hypothalamus and Pituitary Gland




- Pituitary gland about 1cm in diameter located in the fossa of the sella turcica of the sphenoid bone at base of brain
- formerly referred to as the 'Master Gland' in that it secretes several hormones that control other endocrine glands....
- Now known that the hypothalamus secretes its own hormones that can control pituitary function
- Together the hypothalamus and pituitary play important roles in most aspects of growth, development, metabolism and homeostasis.

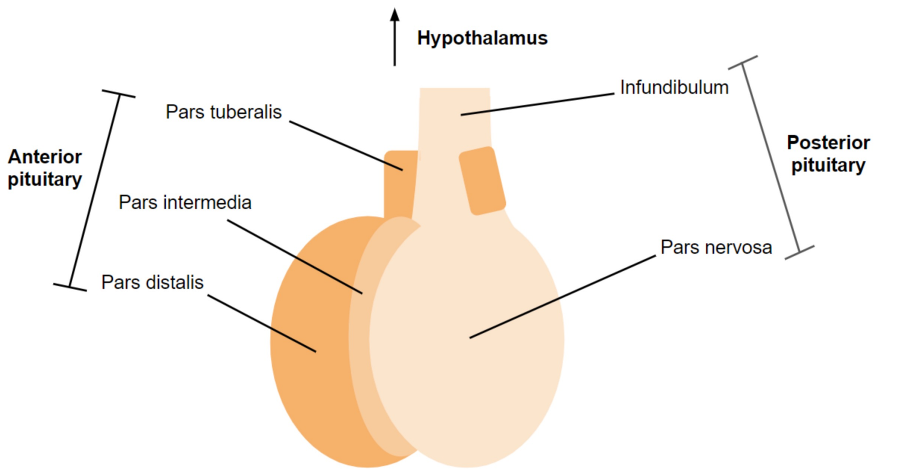
## Anterior pituitary (adenohypophysis)

- is derived from epithelial tissue and accounts for around 75% of the pituitary gland
    - Two parts:
        1. Pars distalis (the larger, inferior part)
        2. Pars tuberalis which wraps around infundibulum superiorly

## Posterior pituitary (neurohypophysis)

- is derived from neuroectoderm
- mostly composed of supportive glial-type cells called pituicytes
    - Two parts:
        1. Pars nervosa (larger bulbar portion)
        2. Infundibulum (connecting with the hypothalamus of brain)

- **Pars Intermedius (intermediate lobe)**
    - Lies between the anterior and posterior lobes
    - May produce melanocyte stimulating hormone (MSH) but mostly inactive in adult life
    - More developed in animals such as amphibians



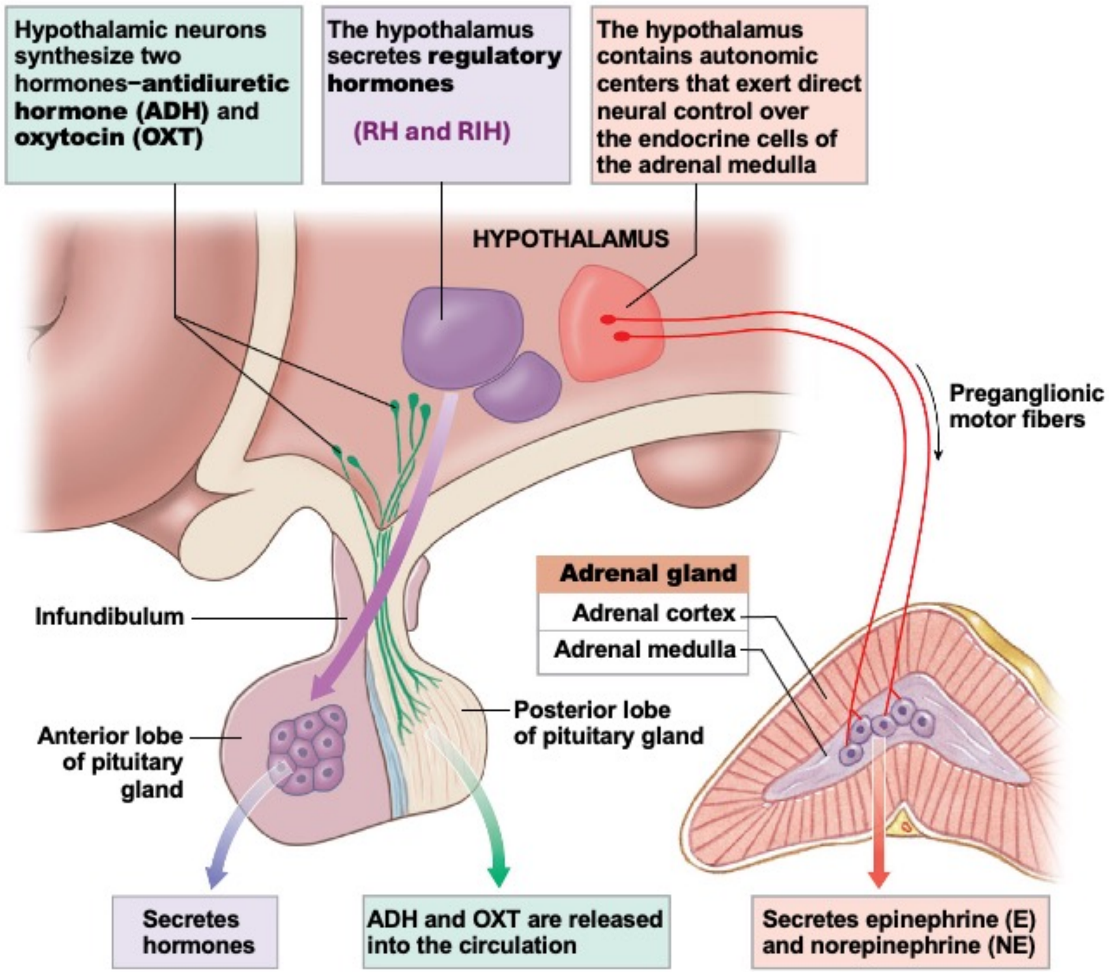

https://en.wikipedia.org/wiki/Anterior_pituitary#/media/File:Pituitary_Gland.png

## Different groups of neurons in the hypothalamus can:

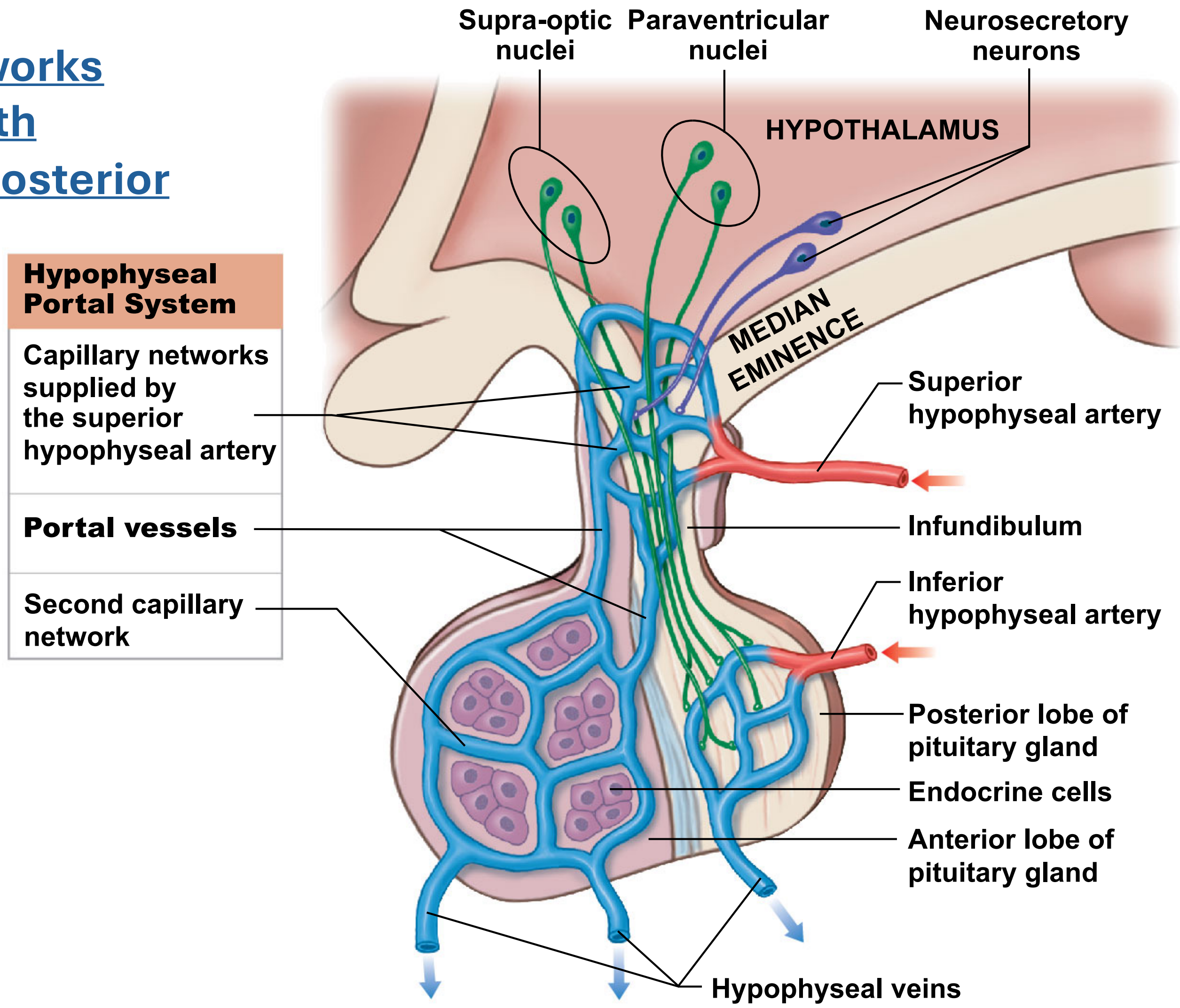
1. Control secretion of anterior pituitary via releasing hormones (RH) and release inhibiting hormones (RIH)

2. Synthesize hormones secreted by posterior pituitary

3. Directly control secretion of cells in the adrenal medulla

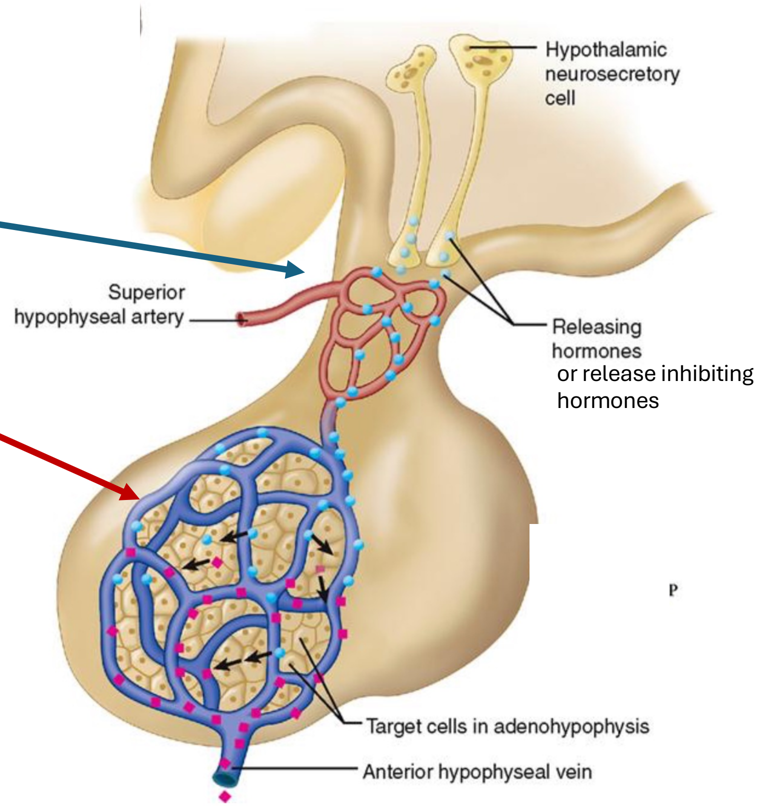


# Capillary networks associated with Anterior and posterior pituitary



# <u>Hypothalamic-hypophyseal Portal System</u> (hypothalmus to ant. Pit.)

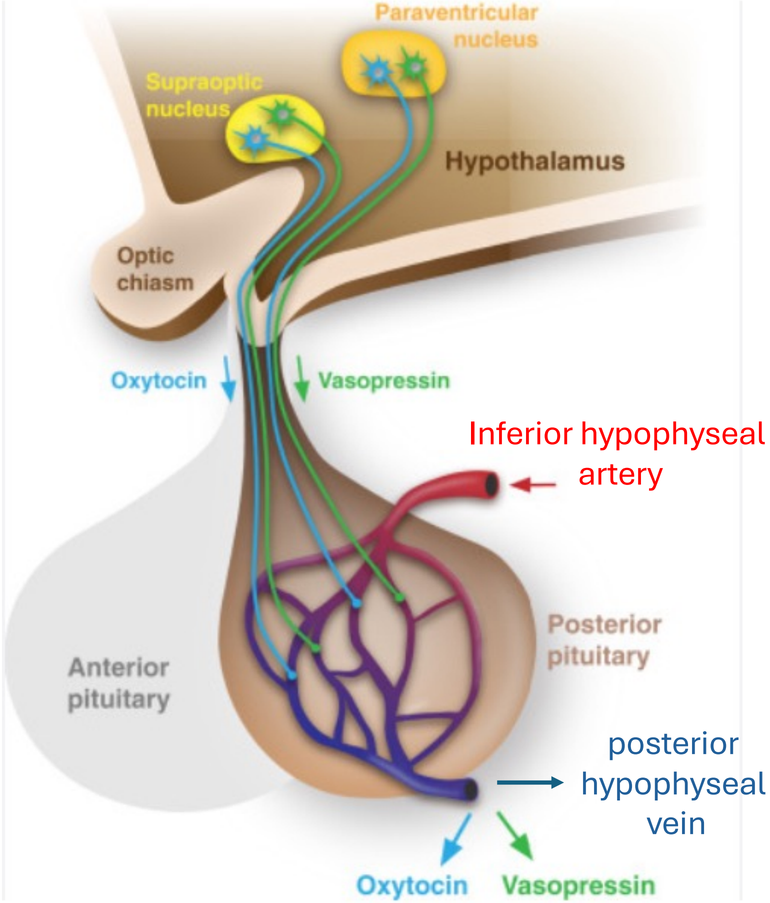
- ***Releasing hormones (RH) and/or release inhibiting hormones(RIH)*** secreted from hypothalamic neurons in region of median eminence at base of hypothalamus
- RH/RIH diffuse into ***1$^{o}$ capillary network*** (plexus) which is supplied by superior hypophyseal artery (branch of internal carotid)
- ***Portal veins*** then carry RH/RIH to ***2$^{o}$ capillary network*** in anterior pituitary
- RH/RIH diffuse out of 2$^{o}$ capillary plexus and stimulate or inhibit secretion of hormone from anterior pituitary cells
- Blood (containing anterior pituitary hormone) then drains into ***anterior hypophyseal veins*** to enter systemic circulation




https://basicmedicalkey.com/endocrine-glands/#cesec13

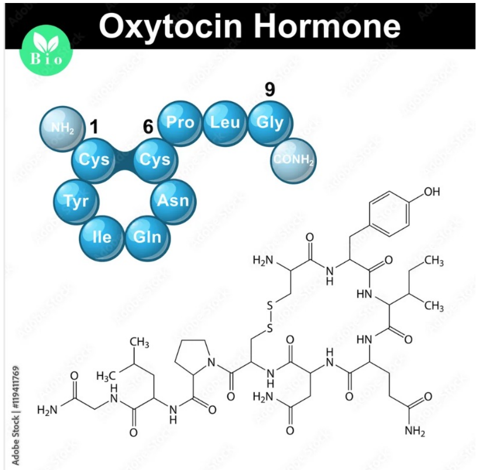
# Connection between Hypothalamus and Neurohypothesis

- Neurosecretory cells located in supraoptic (SON) and paraventricular nuclei (PVN) of the hypothalamus produce hormones ADH and oxytocin
- ADH and oxytocin packaged into secretory vesicles and transported along axons to terminals in posterior pituitary where they are stored.
- Hormones are released by exocytosis when action potentials arrive at terminals and diffuse into capillary plexus of posterior pituitary
    - ➢Supplied by inferior hypophyseal arteries
    - ➢Drained by posterior hypophyseal veins




Adapted from: https://www.sciencedirect.com/topics/medicine-and-dentistry/posterior-pituitary

# Posterior Pituitary Hormones – 1. Oxytocin




- **Peptide hormone** synthesized mostly in neurons of PVN
- Stored in nerve terminals in posterior pituitary

- Stimuli for release are:
  1. **Stretching of the cervix of the uterus during childbirth**
     - Afferent sensory impulses from cervix conducted to hypothalamus
     - APs initiated in neurons of PVN triggering release of oxytocin from terminals in posterior pituitary
     - Contraction of uterine smooth muscle (positive feedback during childbirth)

  2. **Infant suckling during breastfeeding**
     - Afferent sensory impulses from nipples conducted to hypothalamus
     - APs initiated in neurons of PVN triggering release of oxytocin from terminals
     - Myoepithelial cells in mammary glands >> milk letdown reflex

**FIGURE 1.4** **Positive feedback control of labour contractions during birth of a baby.** The broken return arrow with a positive sign surrounded by a circle symbolises positive feedback.
If the response enhances or intensifies the stimulus, a system is operating by positive feedback.

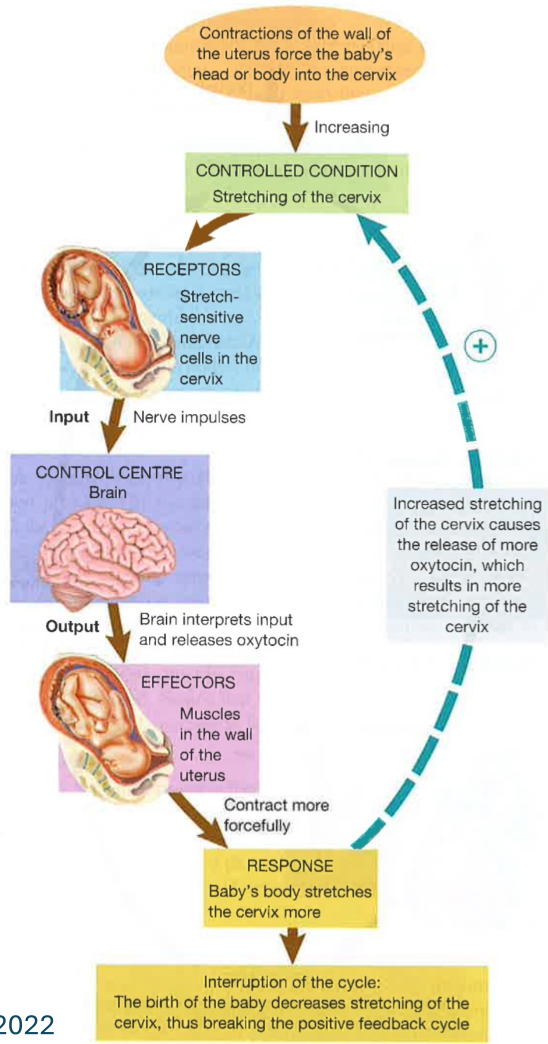
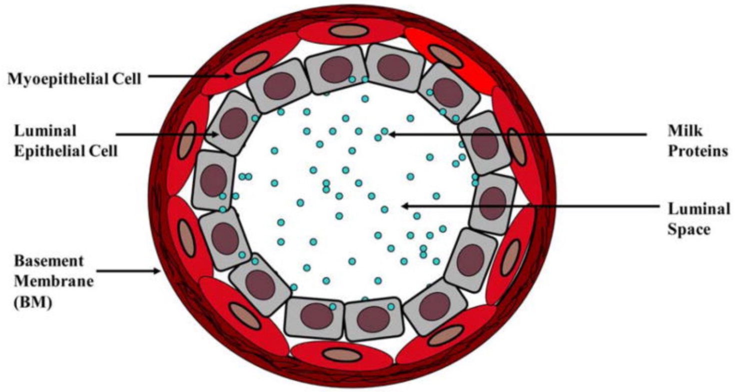
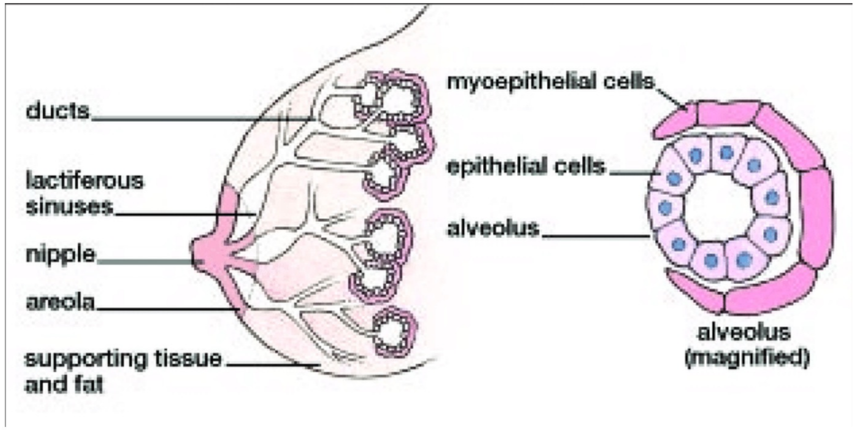



Diagram from Tortora & Derrickson, Principles of Anatomy and Physiology, 3rd Asia Pacific edition, Wiley 2022

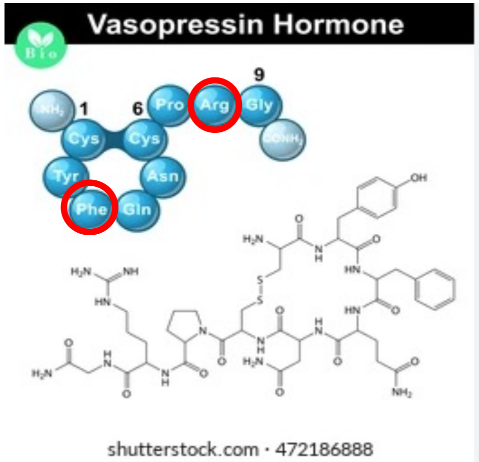



Clusters of epithelial cells form the alveolus. During lactation, these cells actively secrete milk into the lumen. When oxytocin, secreted by the posterior pituitary, reaches the mammary gland via the bloodstream, contraction of the myoepithelial cells pushes the milk down the ducts to pool in the lactiferous sinuses. Illustration by Marcia Smith.

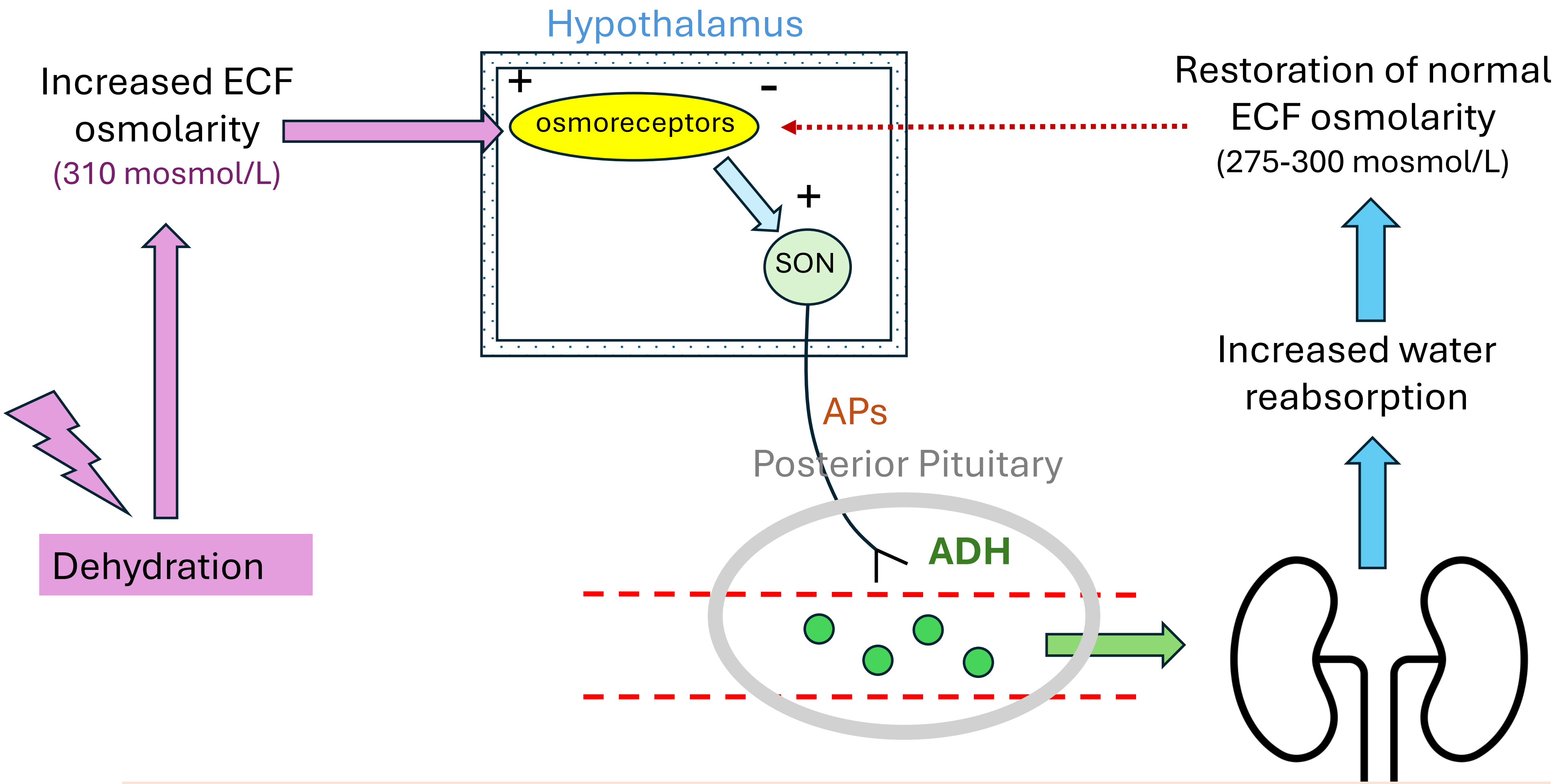
https://www.researchgate.net

# 2. Antidiuretic Hormone (ADH)



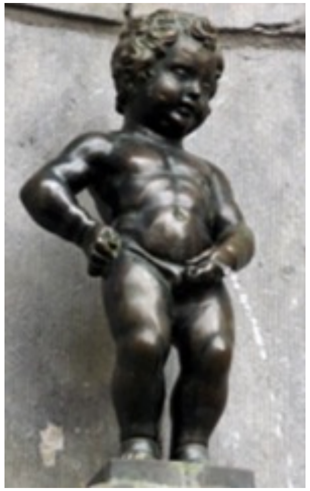

- **Peptide hormone** (2 aas different from oxytocin)
- Synthesized <u>mostly</u> in neurons of SON

- **Secreted in response to increased ECF osmolarity**
  - Detected by 'osmoreceptors' (neurons) in region of hypothalamus
  - Osmoreceptors signal neurosecretory cells triggering APs and release of ADH from terminals in posterior pituitary
  - ADH diffuses into capillary plexus and travels in blood to kidney
  - Binds to receptors on collecting duct cells in kidney and increases water reabsorption (more on this in renal lectures)
  - Restoration of ECF osmolarity (negative feedback)
  - Conversely, decreased ECF osmolarity reduces ADH secretion
  - At higher doses ADH constrict arterioles in the body and increase arterial pressure – hence the alternative name, vasopressin.




Response to overhydration will be the opposite i.e. less ADH release and less water reabsorption by the kidney

# Diabetes Insipidus



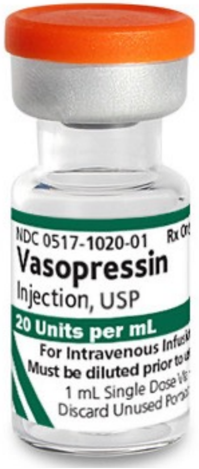
**1. Neurogenic** = Insufficient ADH secretion

- May occur following trauma, injury or infection in region of hypothalamus and posterior pituitary
- Large volumes of dilute urine due to reduced water reabsorption by collecting ducts of nephrons in kidney

→ **DEHYDRATION**

**2. Nephrogenic** = Kidneys don't respond to ADH

Genetic
Medication induced e.g. lithium
Secondary to renal disease



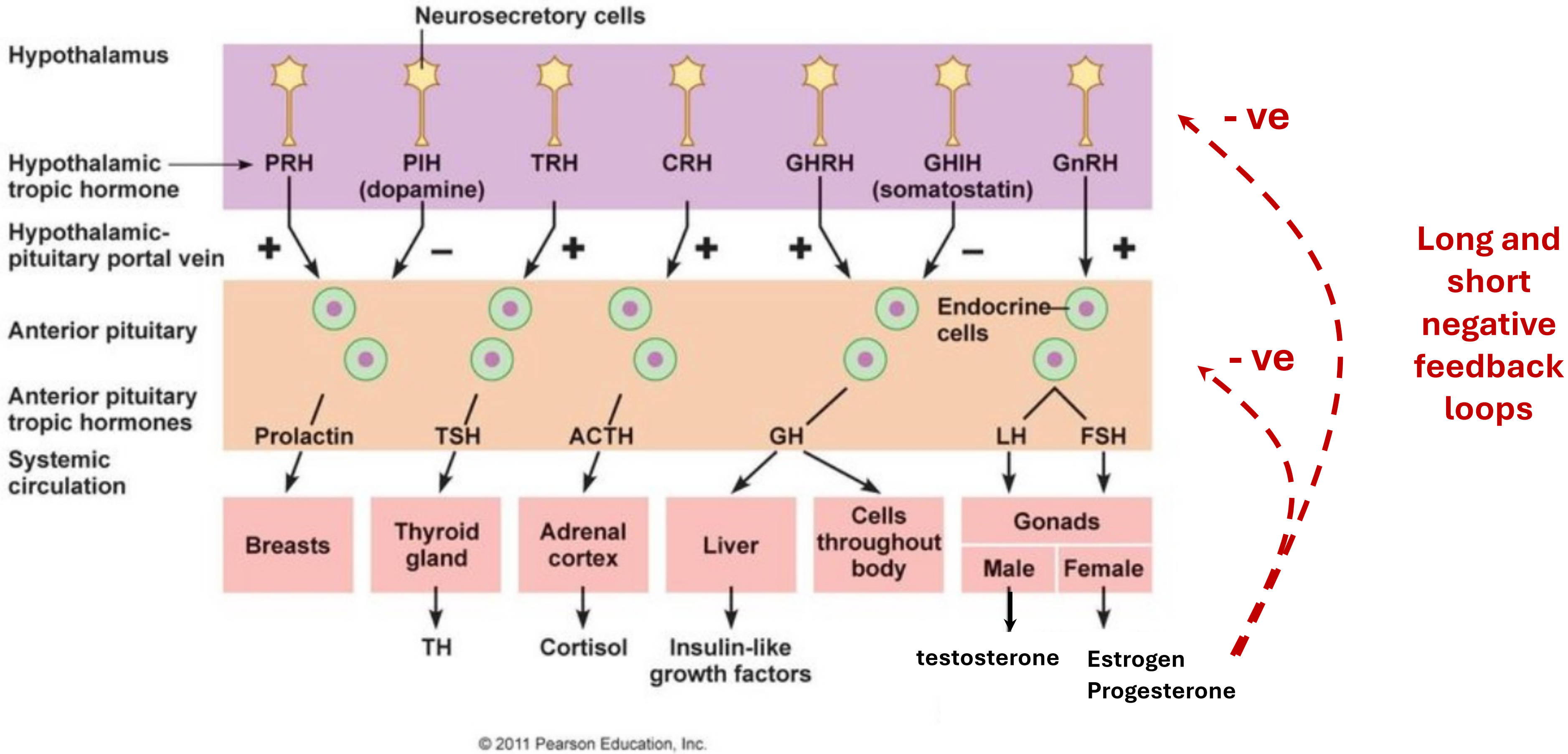
# Syndrome of Inappropriate ADH secretion (SIADH)

- Some medications and drugs such as MDMA (ecstacy) can cause trigger inappropriate release of ADH
- Coupled with hyperthermia and drinking lots of water this can lead to ⇒ **OVERHYDRATION**
- Hemodilution results in low ECF sodium (HYPOnatremia)
- Water moves along osmotic gradient into cells
- Brain swelling (cerebral oedema) can result in reduced level of consciousness, seizures, coma and death in some cases.

## Anterior Pituitary contains different types of secretory cells

| | |
|---|---|
| **Somatotrophs** → | growth hormone (GH) |
| **Thyrotrophs** → | thyroid stimulating hormone (TSH) |
| **Gonadotrophs** → | follicle stimulating hormone (FSH) |
| → | luteinizing hormone (LH) |
| **Lactotropes** → | prolactin |
| **Corticotropes** → | adrenocorticotropic hormone (ACTH) |

# Control of anterior pituitary hormone secretion



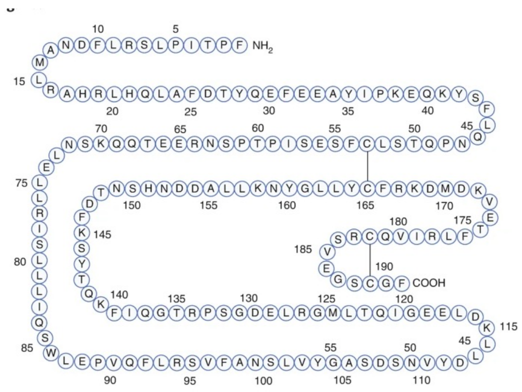
# Hypothalmic releasing and inhibiting hormones

- For most of the anterior pituitary hormones it is the releasing hormones that are more important but for prolactin a hypothalamic inhibitory hormone (dopamine) exerts more control

| Hypothalmic hormone | Effect on anterior pituitary |
|---|---|
| **Thyrotropin-releasing hormone (TRH)** | Release of thyroid stimulating hormone (TSH) |
| **Corticotropin-releasing hormone (CRH)** | Release of adrenocorticotropin (ACTH) |
| **Growth hormone- releasing hormone (GHRH)** | Release of growth hormone (GH) |
| **Growth hormone inhibitory hormone (GHIH) aka somatostatin** | Inhibition of growth hormone (GH) release |
| **Gonadotrophin releasing hormone (GnRH)** | Release of luteinizing hormone (LH) and Follicle stimulating hormone (FSH) |
| **Prolactin releasing hormone**<br>**Prolactin inhibitory hormone (PIH) = dopamine** | Release of prolactin<br>Inhibition of prolactin (PRL) release |

# Human Growth hormone (hGH)

- Protein hormone produced and secreted by somatotrophs of the anterior pituitary in response to GHRH
- **Promotes increased size of cells numbers of cells, particularly muscle, bone, and cartilage.**
- Increases growth rate of the skeleton and muscles during childhood and teenage years.
- In adulthood, helps to maintain mass of muscle and bones and promote healing of injuries and tissue repair.
- Can be produced recombinantly and used to treat GH deficiency (or in sports doping or as 'HRT')



https://link.springer.com


https://www.health.harvard.edu

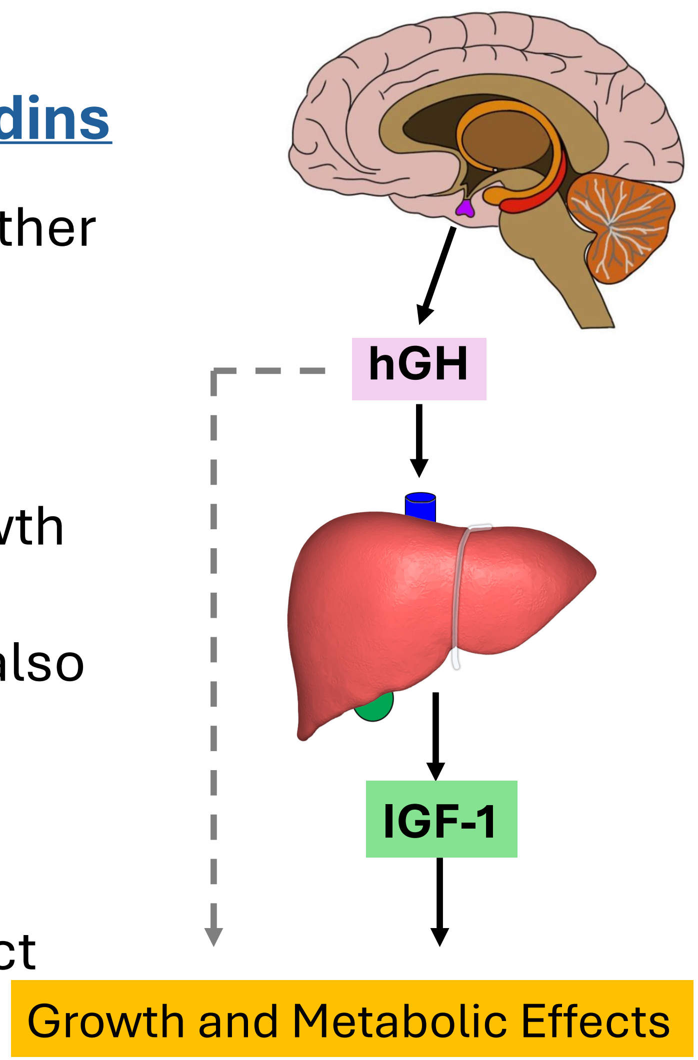
## hGH exerts most of its effect via somatomedins

- hGH causes liver (and to a lesser extent some other tissues) to form proteins called somatomedins which mediate growth hormone's effects

- **Somatomedins** also known as Insulin-like Growth Factors (IGFs)

  - Most important of these is **somatomedin C** also known as **insulin-like growth factor-1 (IGF-1)**

- **Most** (not all) of the growth effects of GH are thought to result from IGF-1 rather than the direct action of GH itself



# Metabolic Effects of GH

**Promotes growth and protein synthesis when nutrition state is favorable**
(synergistically with insulin)

- Increases amino acid transport into cells and promotes protein synthesis
- **Increases cartilage, muscle and bone growth**
- Increases cell size and number in many other tissues too

**Switches cell metabolism toward use of lipids as an energy source**

- Increases mobilization of fatty acids from adipose tissue (fasted state)
- increased use of fatty acids as energy source for cells
- glucose in blood available for cells that are more dependent on it as energy source e.g. neurons

**GH attenuates (weakens) some of insulins actions**

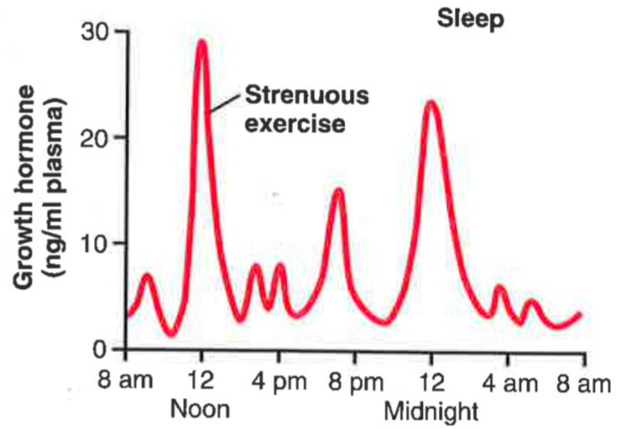
- less glucose taken up from blood by muscle and adipose tissue
- Increased glucose released into blood by liver

# Regulation of GH secretion

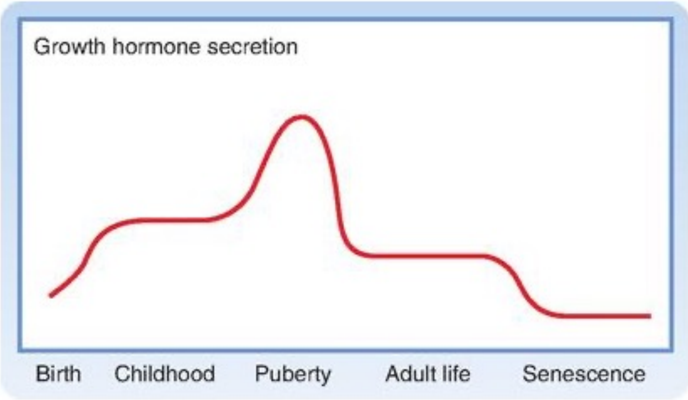
- Secreted in pulsatile manner with bursts every few hours.
- **Dual control** via releasing and inhibiting hormones.

- **GHRH** stimulates GH release in response to factors such as:
  - Deep sleep
  - Low blood glucose (hypoglycemia)
  - Strenuous exercise
  - Fasting or starvation
  - Trauma, stress
  - Testosterone, estrogen

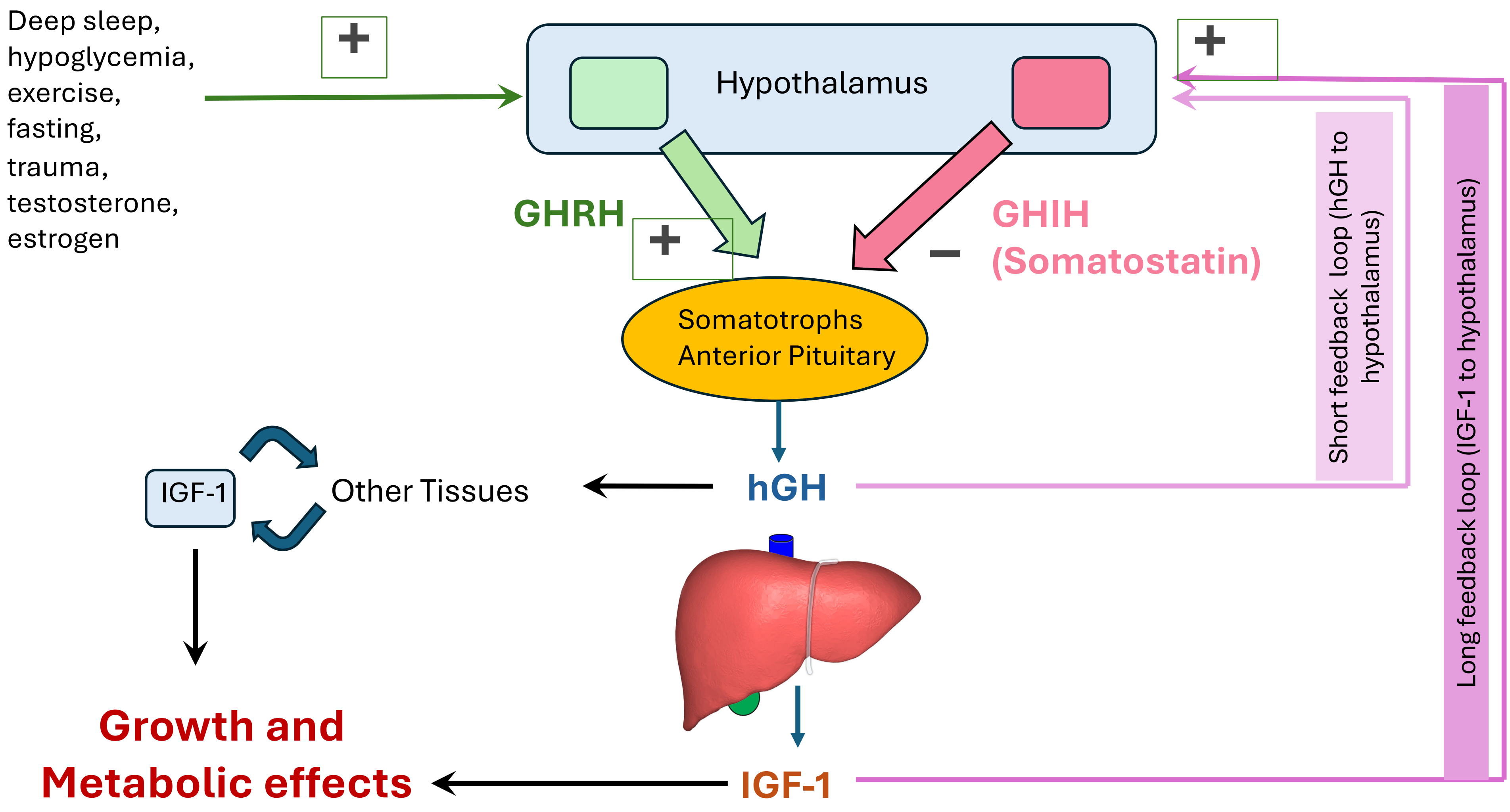
- **GHIH (somatostatin)** reduces GH secretion in response to factors such as:
  - Increased blood glucose
  - Increased fatty acids in blood
  - Increased somatomedins in blood
  - Aging




From Guyton, Figure 76-6, p945




After adolescence GH secretion decreases slowly with age, falling to around 25% adolescent level in very old age. Berne and Levy



Deep sleep, hypoglycemia, exercise, fasting, trauma, testosterone, estrogen
+
Hypothalamus
+
GHRH
+
GHIH (Somatostatin)
Somatotrophs Anterior Pituitary
Short feedback loop (hGH to hypothalamus)
Long feedback loop (IGF-1 to hypothalamus)
IGF-1
Other Tissues
hGH
Growth and Metabolic effects
IGF-1

# GH Disorders…

Lack of GH during childhood → **Dwarfism**

- (many other causes of dwarfism though)
- may be cured by administration of GH if pure GH deficiency and Tx commenced early enough

- Excess GH prior to closure of epiphyseal plates → **Gigantism**

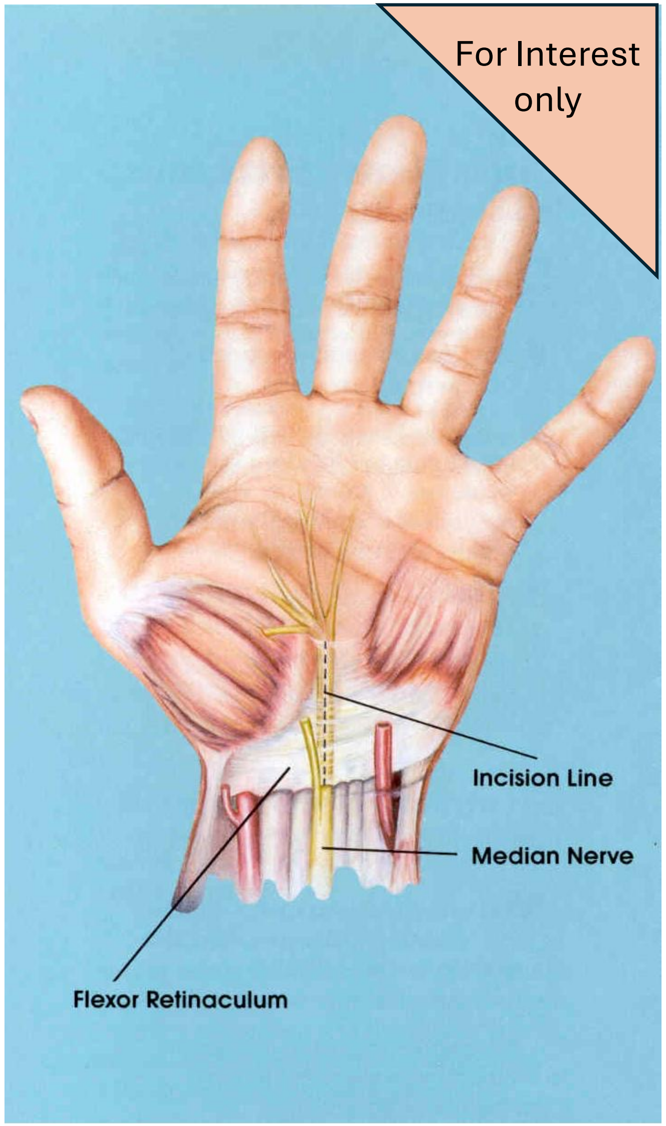
- Excess GH secretion after epiphyseal plates fuse → **Acromegaly**

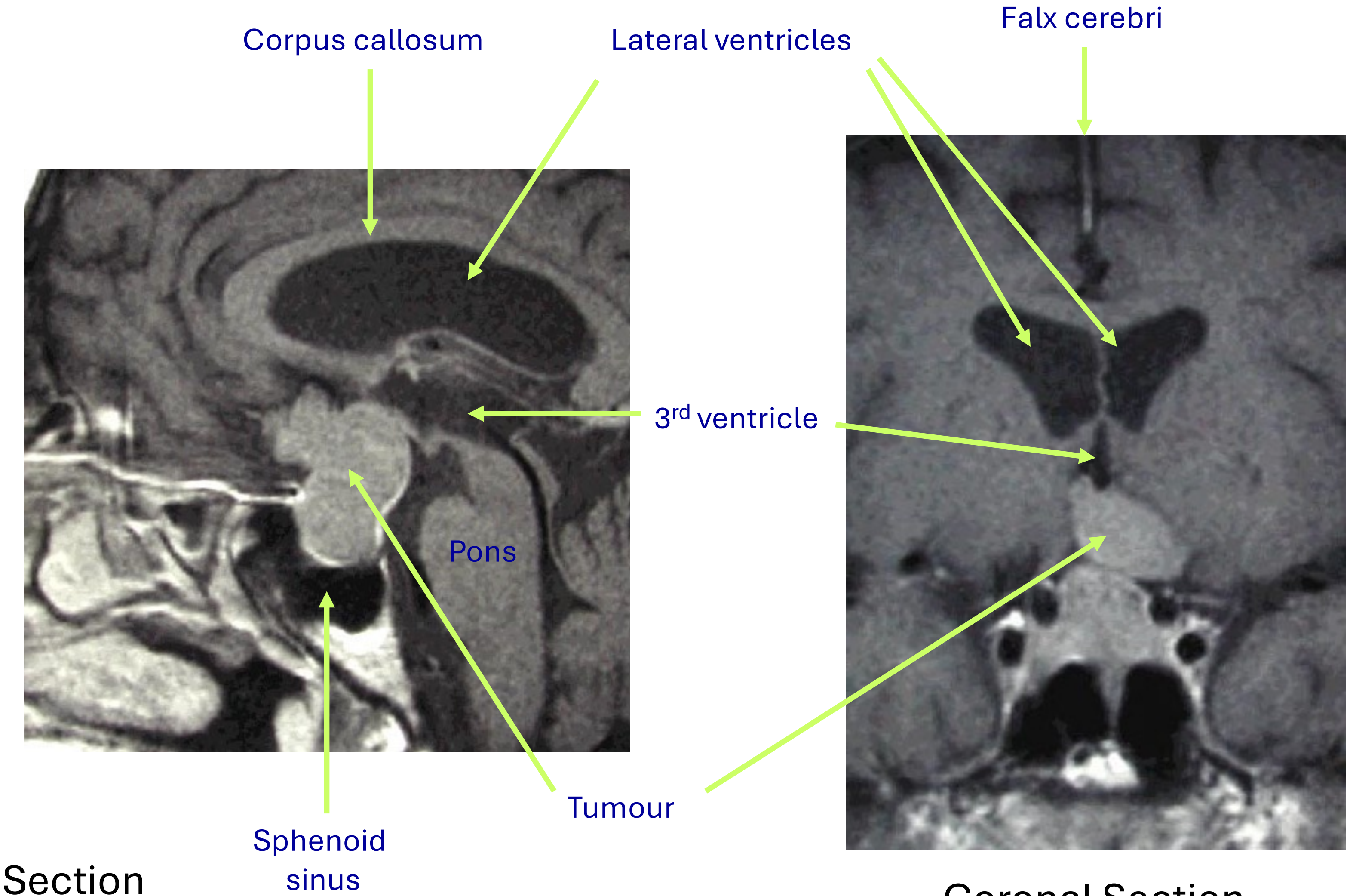
From Marieb's *Human Anatomy and Physiology*, 10th Ed., 2016, figure 16-6, p 629.

# Acromegaly Features

- Increased muscle, bone and internal organ mass
- Large ‘spade-like’ hands
- Thickened frontal bone
- Kyphosis (humpback)
- Large tongue
- Large mandible (lower jaw)
- Arthritis due to skeletal overgrowth
- Carpel tunnel syndrome
- Enlarged heart and high BP
- Hyperglycemia
- Visual disturbances (if due to tumour of pituitary)

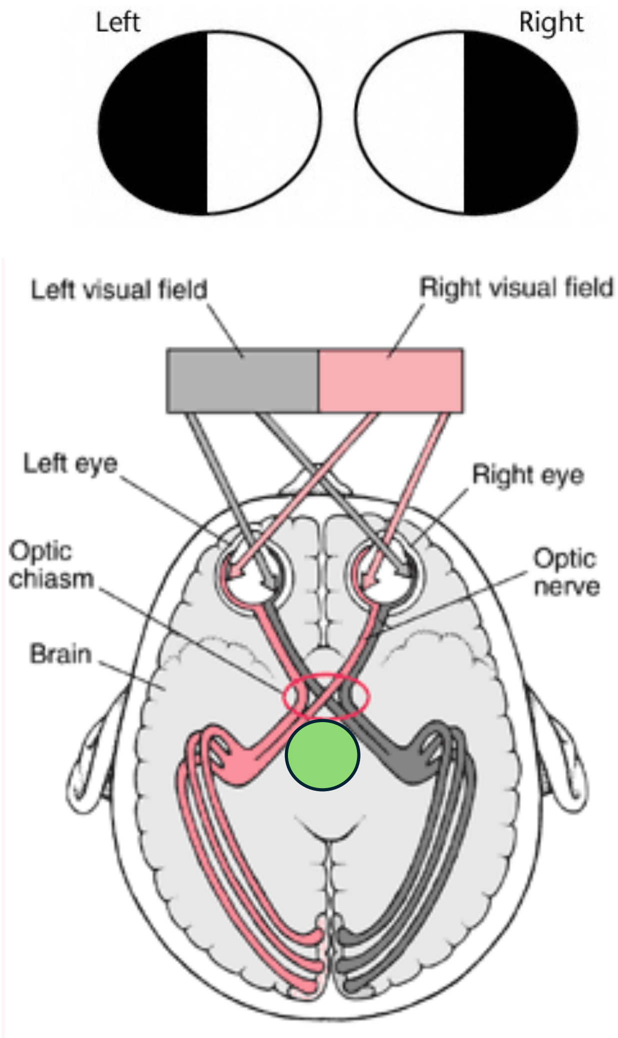
2.24m tall and 236kg


For Interest only
Incision Line
Median Nerve
Flexor Retinaculum




Saggital Section

Coronal Section




For interest only

Because the infundibulum (pituitary stalk) is immediately posterior to the optic chiasm, pituitary tumors tend to compress it causing visual field deficits such as bitemporal hemianopia

# Transphenoidal hypothesecomy

For interest only