Human endocrine system

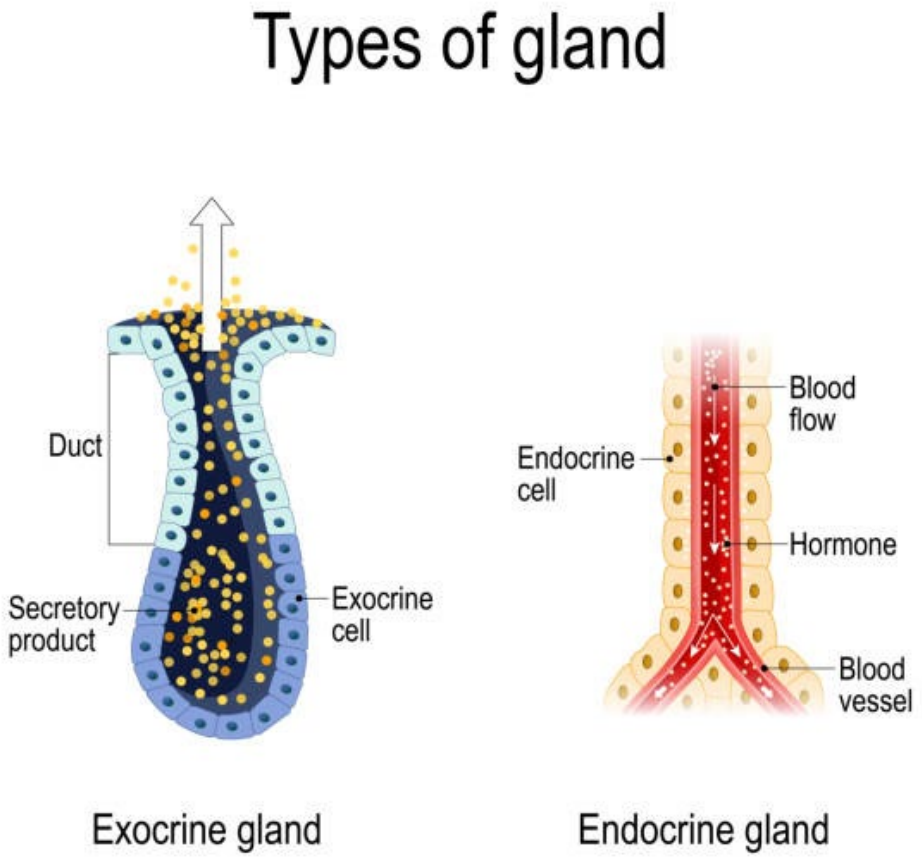
30.1.2024

Learning outcomes

- Understand the principles of hormonal activity and related anatomy
- Understand the following regulatory functions at general level:
  - Calcium homeostasis
  - Stress response
  - Glucose homeostasis
  - Fluid balance
  - Sodium homeostasis
  - Acid-base balance

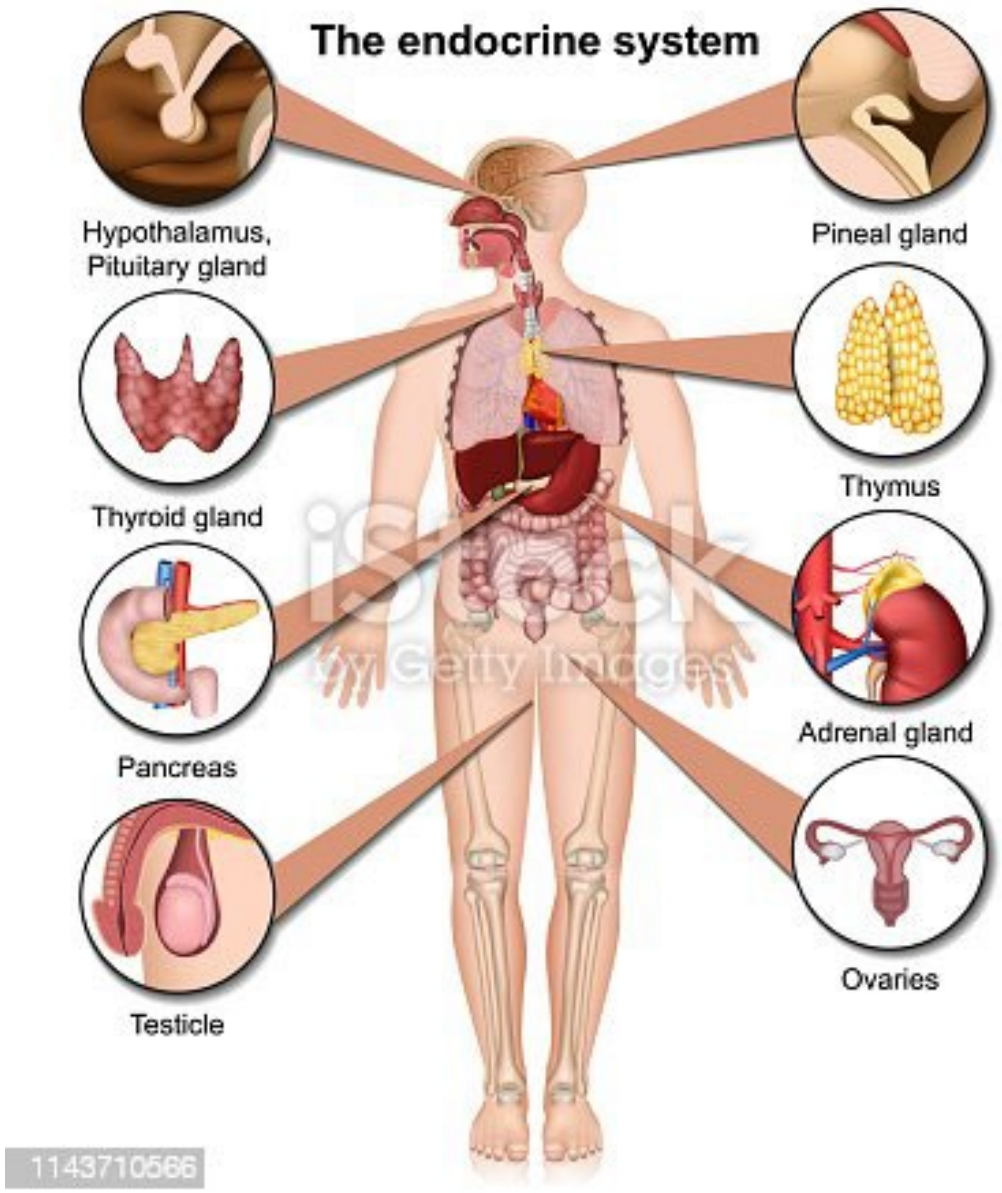
Hormonal activity

- Endocrine system includes all cells and tissues that produce hormones
- “additional” endocrine organs include the nervous system, stomach, kidney, heart
- Exocrine glands: sweat and oil glands
- Endocrine glands: secretion into the blood stream



https://www.istockphoto.com/fi/valokuvat/exocrine-gland

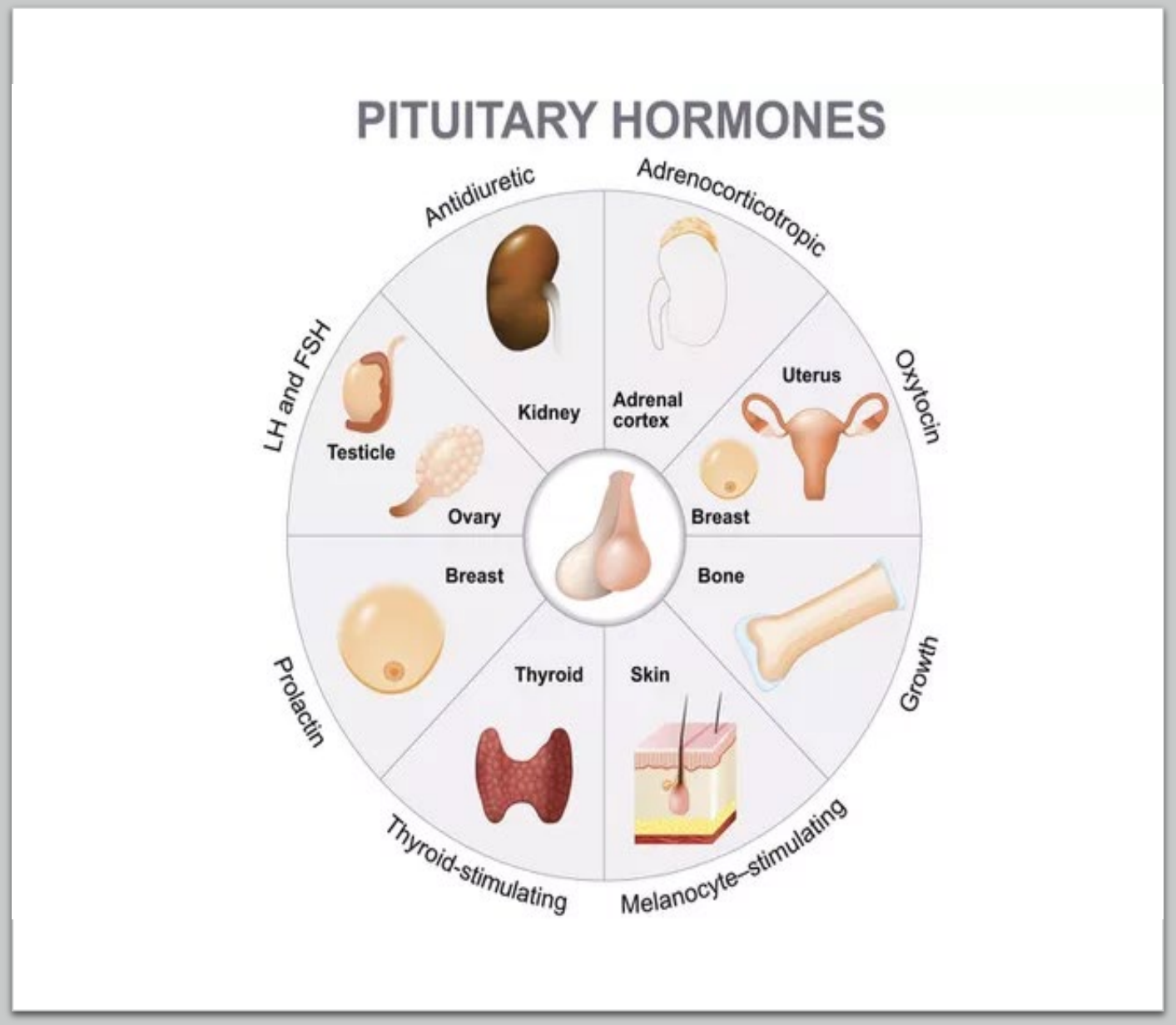
- Hormones are transported either as free molecules or bound to proteins (*e.g.*, albumin)
- Binding proteins help in stabilizing the hormone content
  - the hormones excreted by endocrine glands are active only when they are free
  - binding to proteins diminishes break-out of the hormone



iStock.com

Main functions of hormones

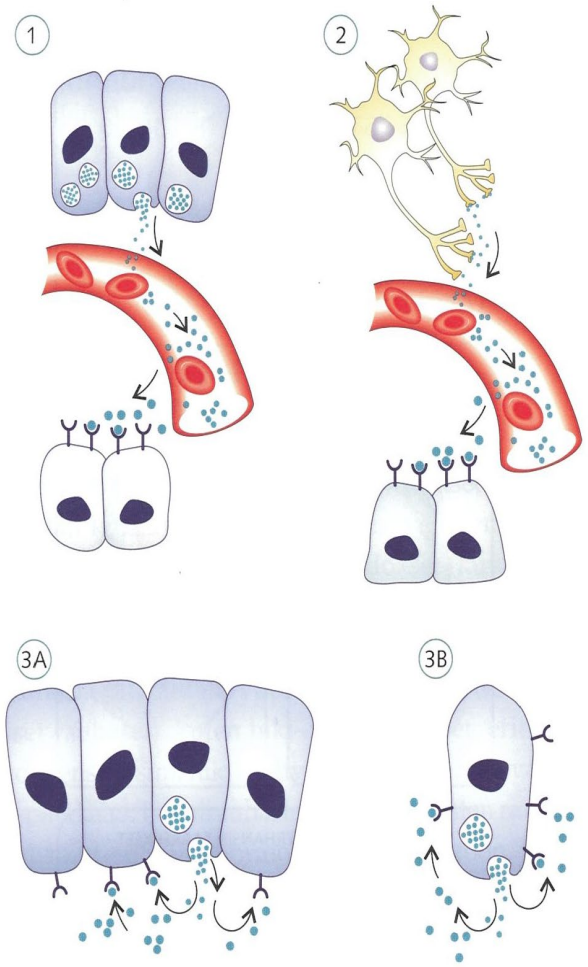
- Regulation of
  - Cellular metabolism
  - Energy balance
  - Sexual reproduction
  - Tissue growth and renewal
- Control growth and development
- Maintain homeostasis

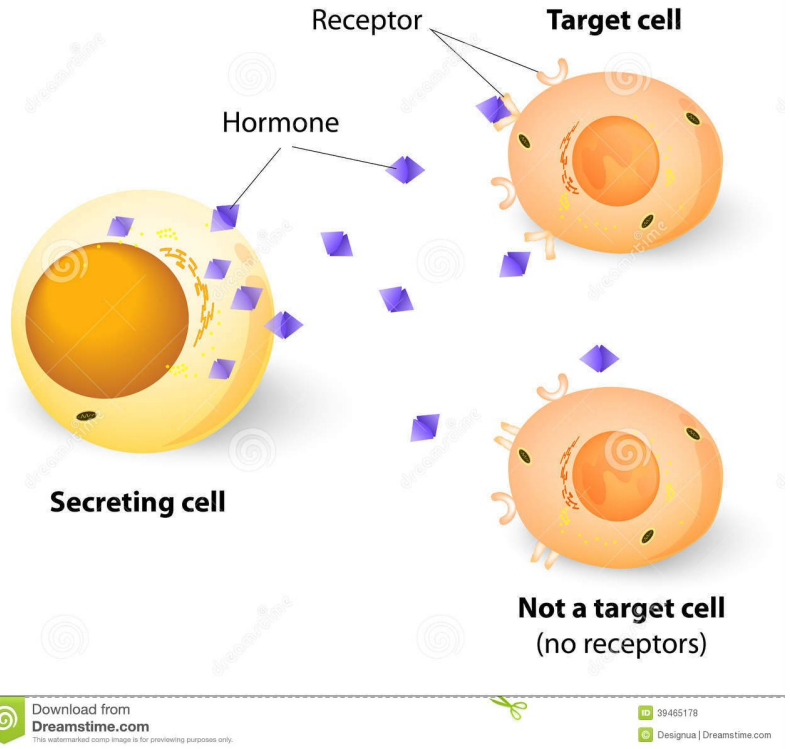


https://www.thoughtco.com/pituitary-gland-anatomy-373226

Hormones need a specific receptor in the target cell

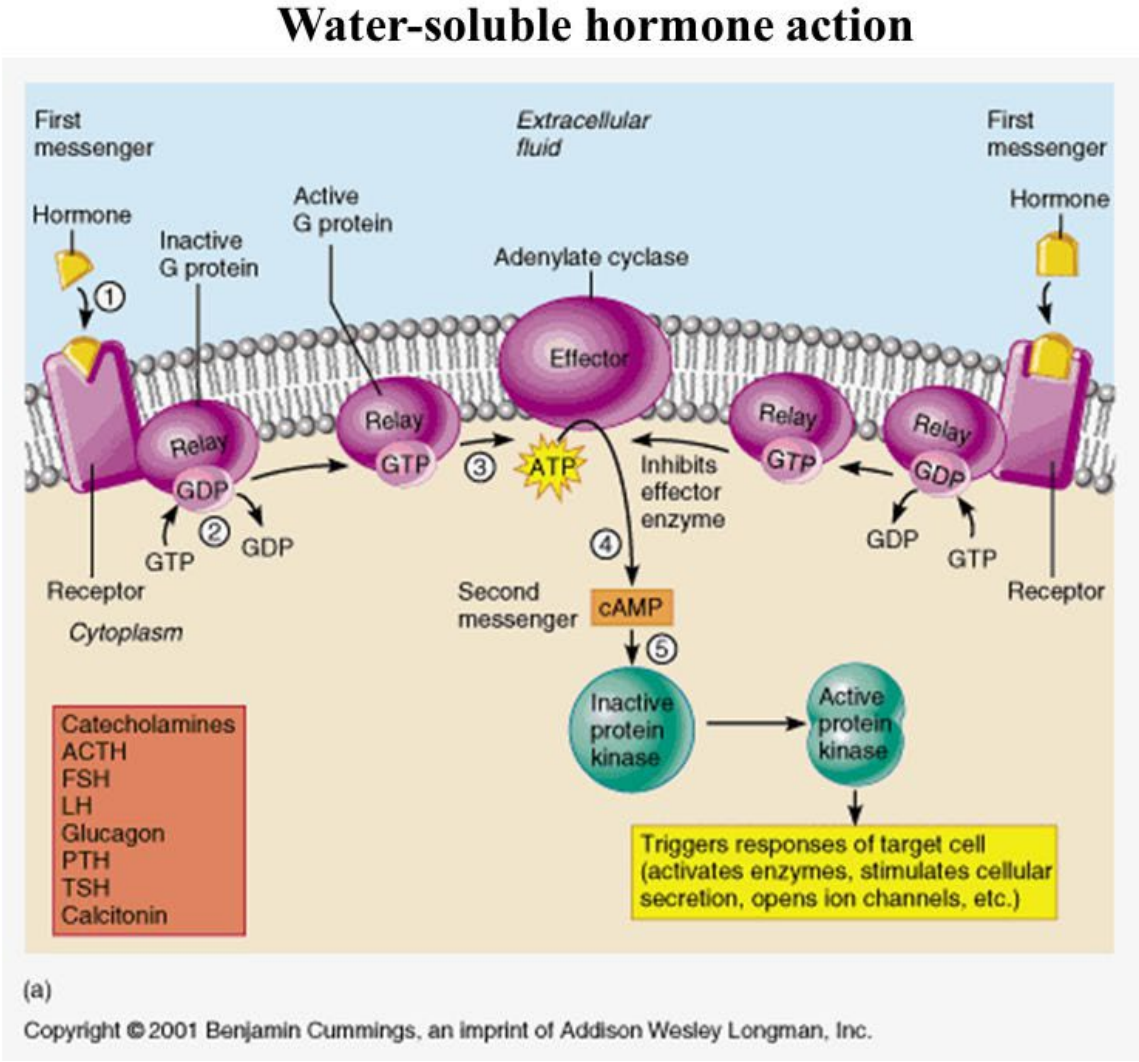
1) Hormones from an exocrine organ (thyroid gland, adrenal gland, pancreas) travel in the blood stream
2) Neuronal cells specialized in hormonal excretion (hypothalamus) release hormones into the blood stream (neuroendocrine effect)
3) Local effect: Paracrine or autocrine effect





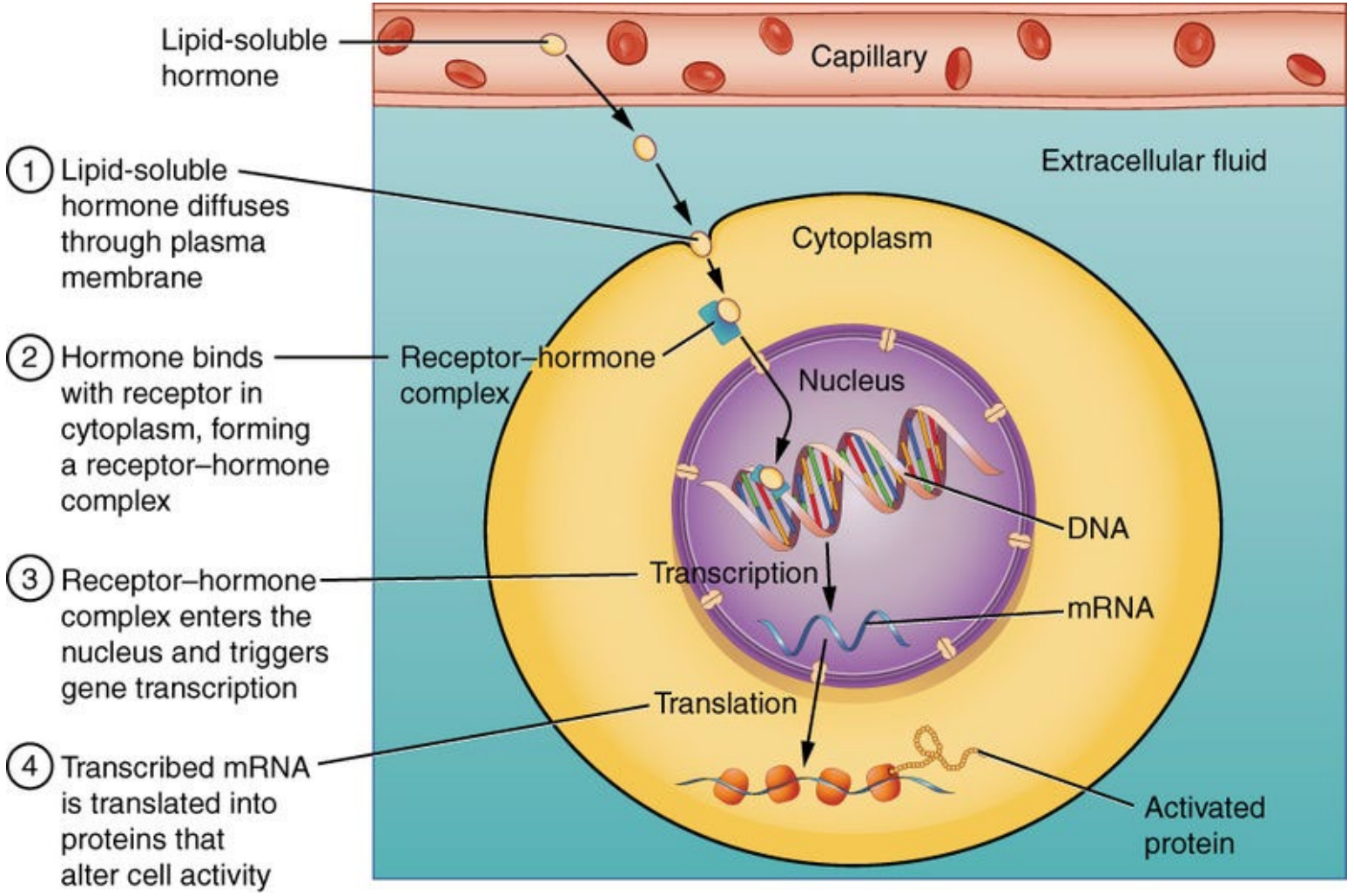
Karhumäki et al. 2017 Päästä varpaisiin

- **Water-soluble hormones** (amine hormones, peptides, proteins, eicosanoids) bind to membrane receptors
- Second messengers (e.g., cyclic adenosine monophosphate) inside the cell activate enzyme reaction cascades → *e.g.,* breaking down of glycogen and glucose
- Even small amount of hormone can result in significant changes



Karhumäki ym. 2017 Päästä varpaisiin

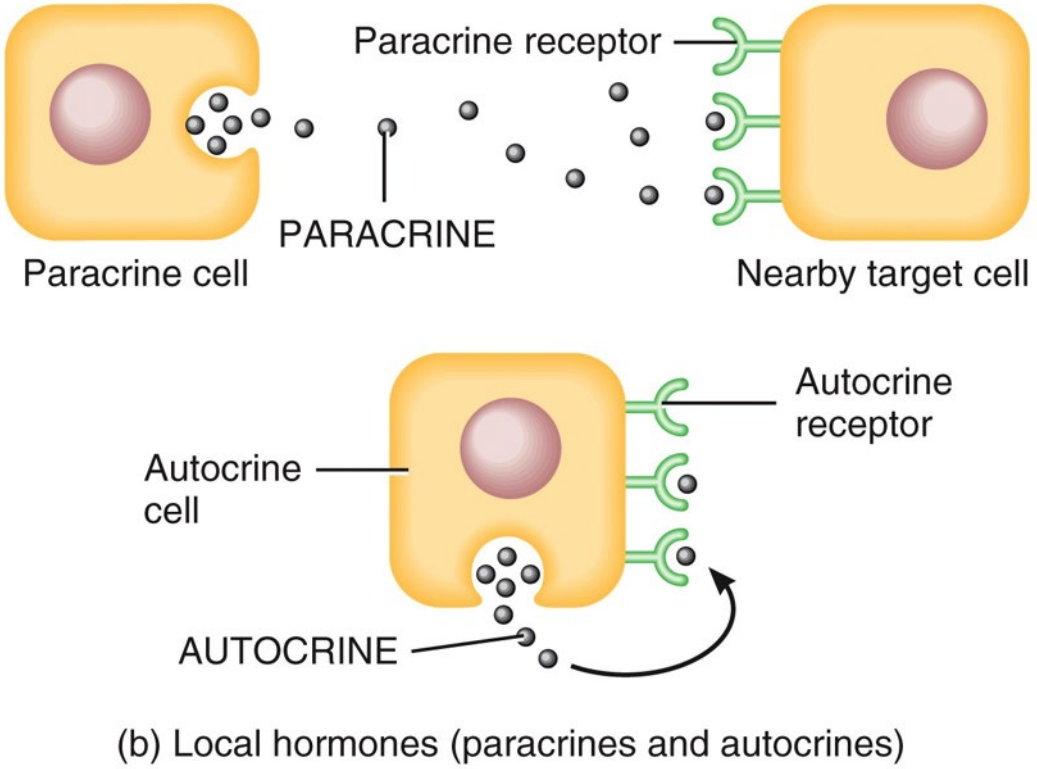
- **Lipid-soluble hormones** (steroids, vitamin D, thyroid hormones) diffuse into the cell
- The specific receptors reside within the cell, either in the nucleus or in the cytoplasm
- They increase or decrease protein synthesis in the cell



https://commons.wikimedia.org

Local hormones and growth factors

- Cell can interact with its neighbors via interstitial fluid
- Substances with paracrine effect are called *local hormones*
- *E.g.,* prostaglandins, thromboxane, leukotrienes
- Local hormones that regulate tissue growth and differentiation are called *growth factors*

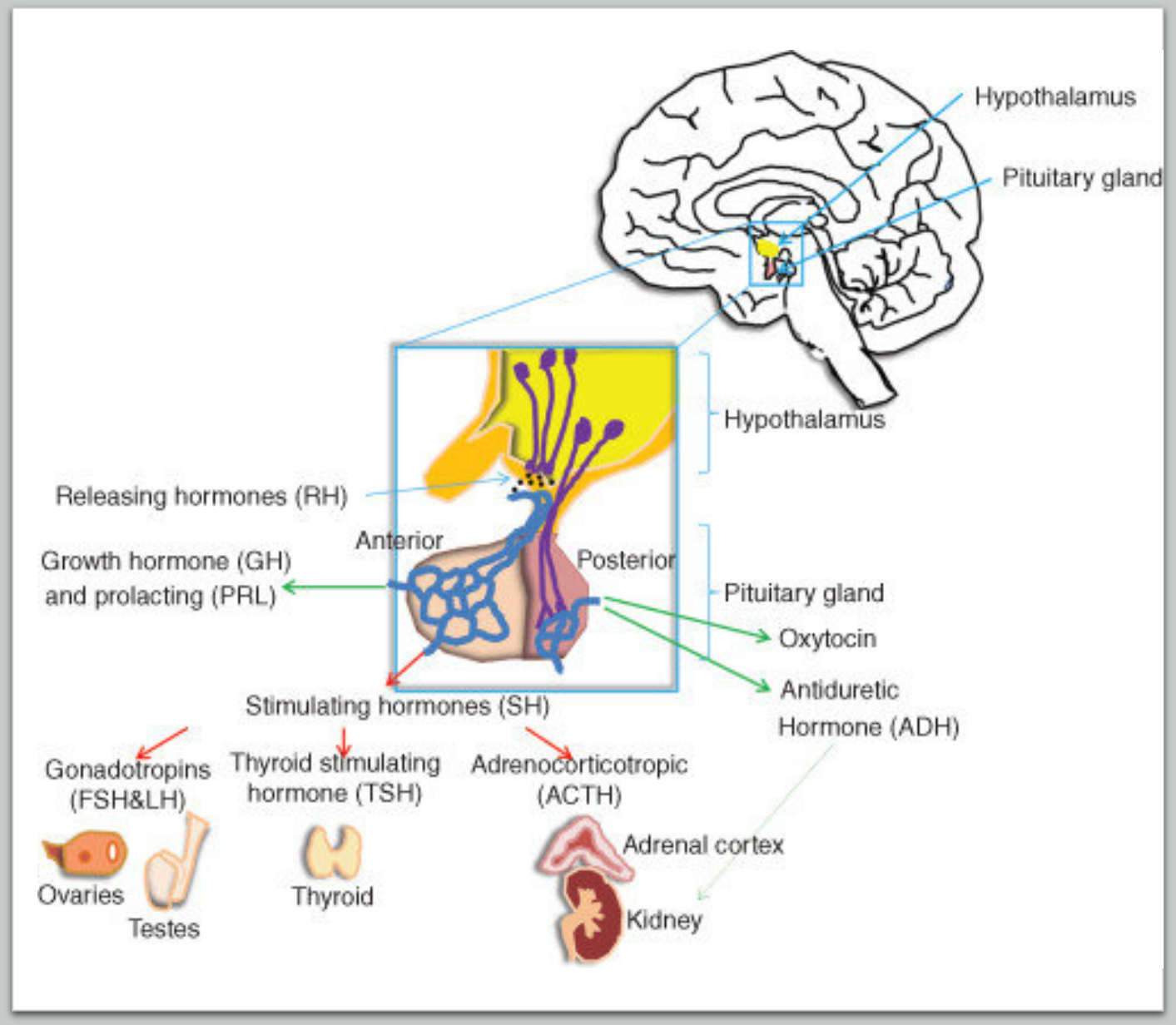


(b) Local hormones (paracrines and autocrines)

https://biology-forums.com/

Regulation of hormone excretion

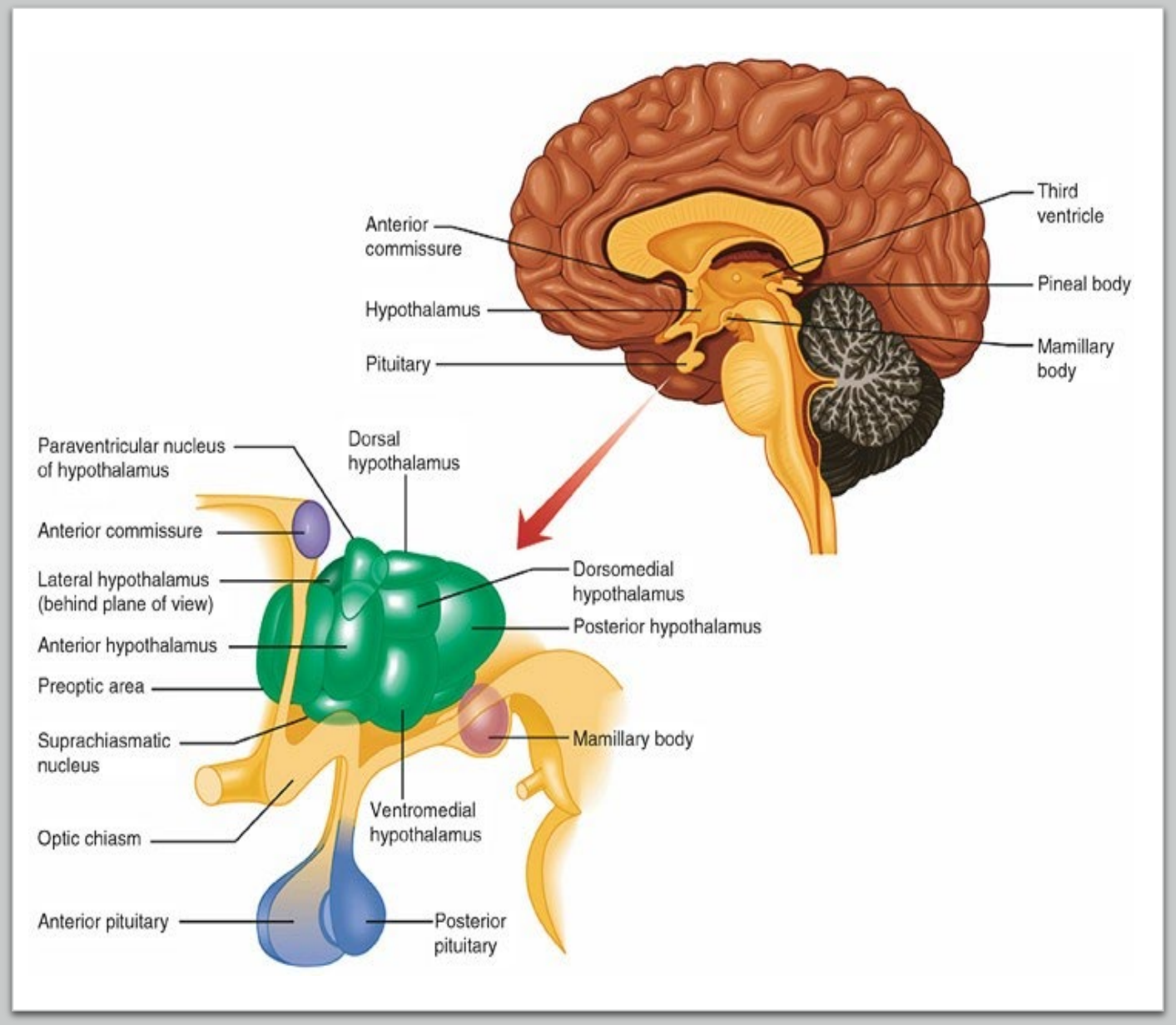
- The nervous system and the endocrine system have partially overlapping functions in maintaining homeostasis
- Hypothalamus produces hormones that regulate functions of pituitary gland, and it controls functions of many endocrine gland



Briscen and Ataca 2015

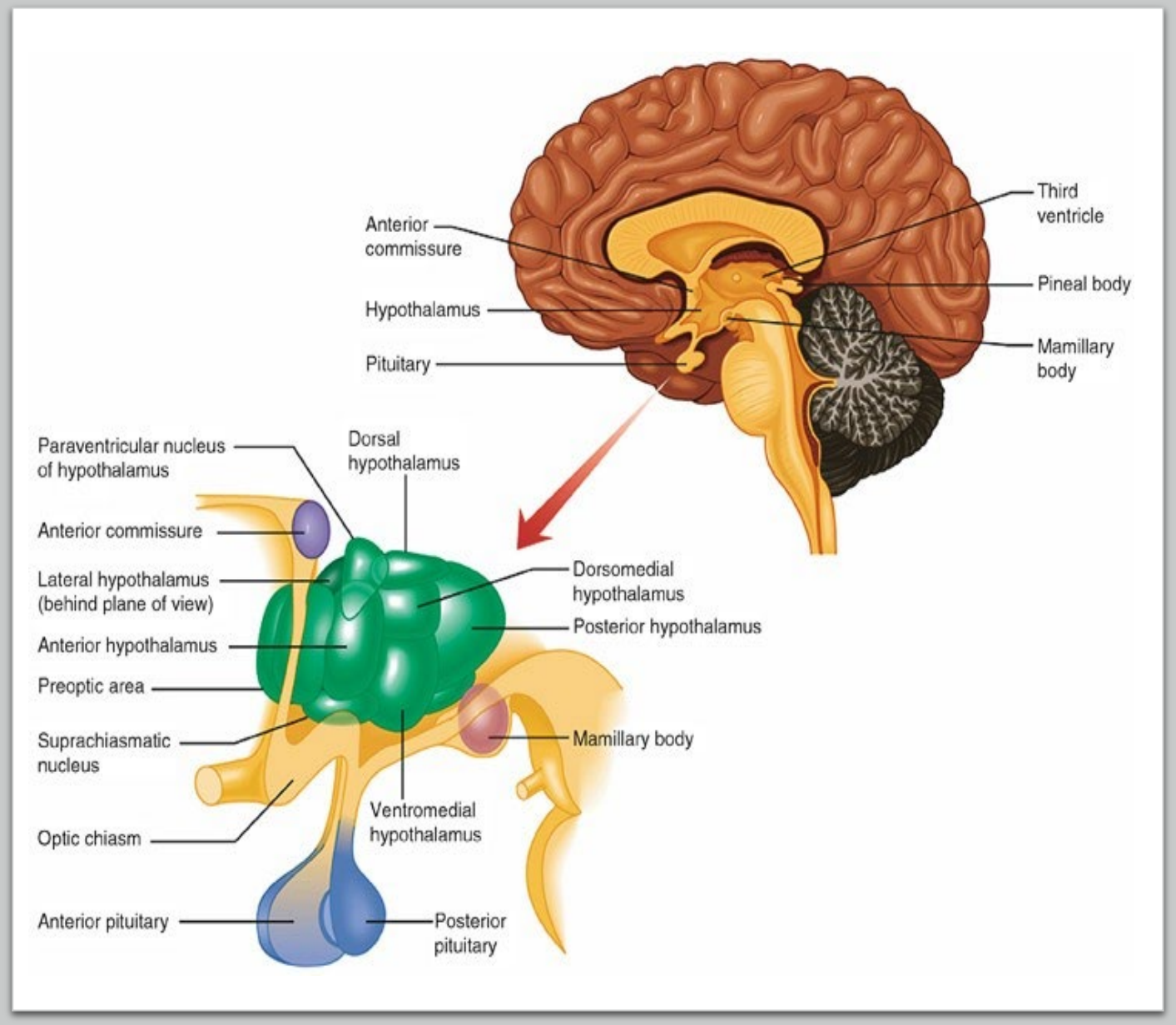
Hypothalamus

- Located below the thalamus in diencephalon
- Connected via blood stream to the pituitary gland
- Also neural connections to the posterior pituitary gland, brainstem, cortex
- Consists of specialized neurosecretory cells
- Regulates pituitary gland via releasing and inhibiting hormones



Gao and Horvath, 2009

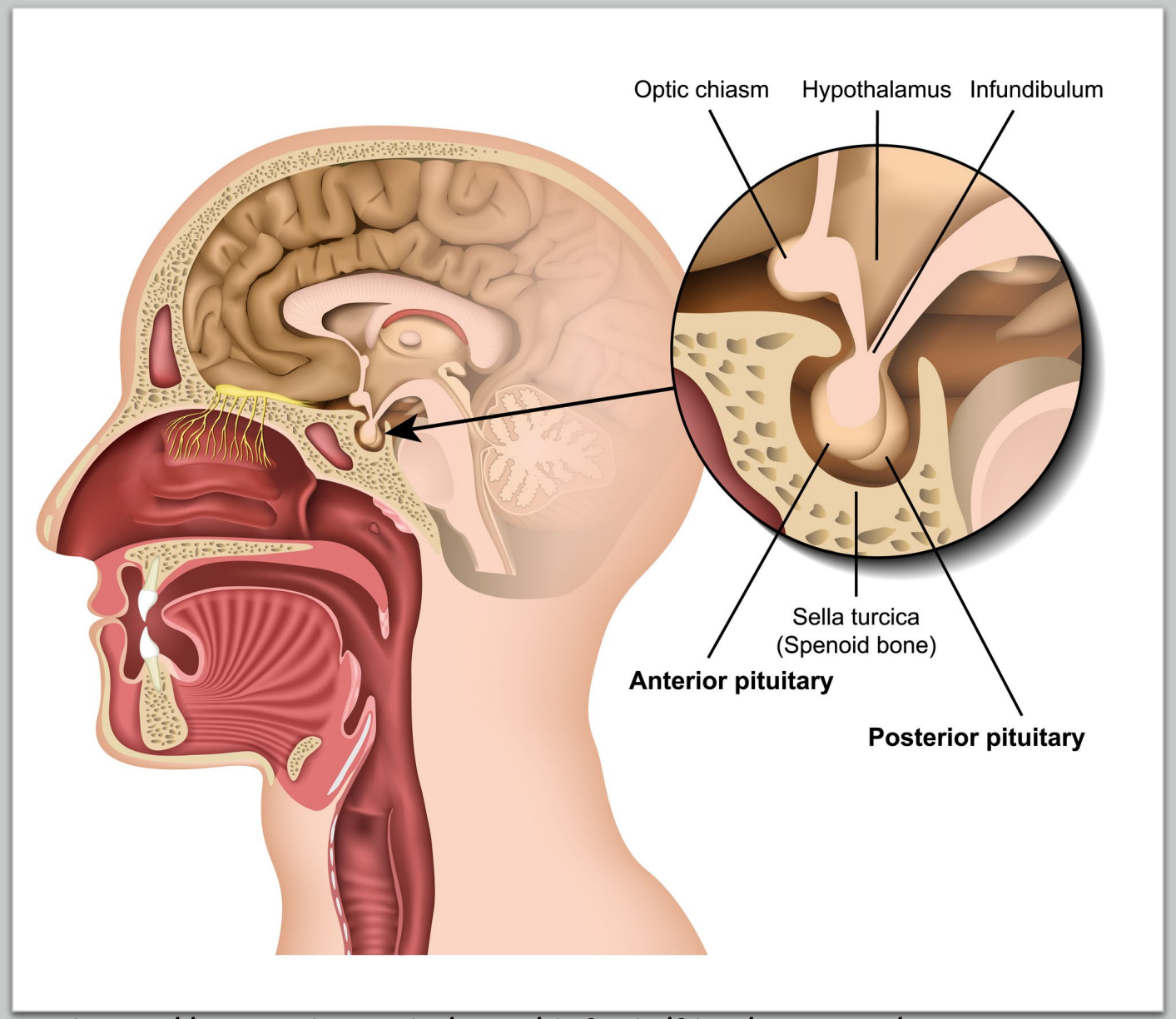
- Hypothalamus is regulated by negative and positive feedback, central and peripheral nervous system, stress
- Includes centers for controlling temperature, thirst, hunger
- Regulates feelings like hate, fear anger as a part of the limbic system
- Circadian rhythm
- Influences sexual behavior



Gao and Horvath, 2009

Pituitary gland

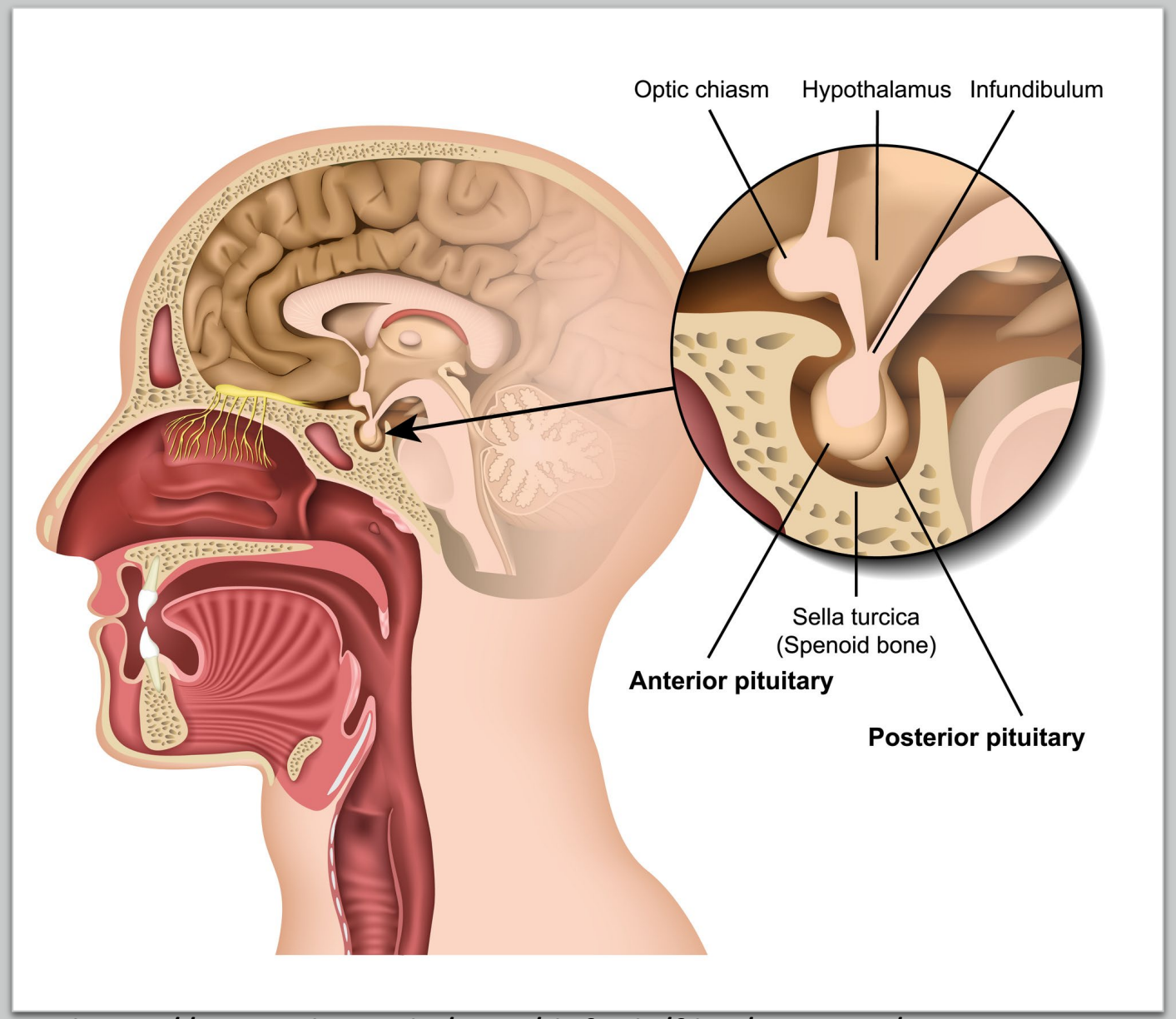
- Small, weight of 0.5-1 g
- Anterior and posterior parts (adenohypophysis and neurohypophysis)
- Anterior part releases 6 hormones of which growth hormone affects all the cells in a body
  - Increases blood glucose level
  - Protein synthesis and fat consumption increases
  - Affects mainly bone and muscle growth



https://www.ohsu.edu/sites/default/files/2020-01/pituitary-gland-anatomy.jpg

Pituitary gland

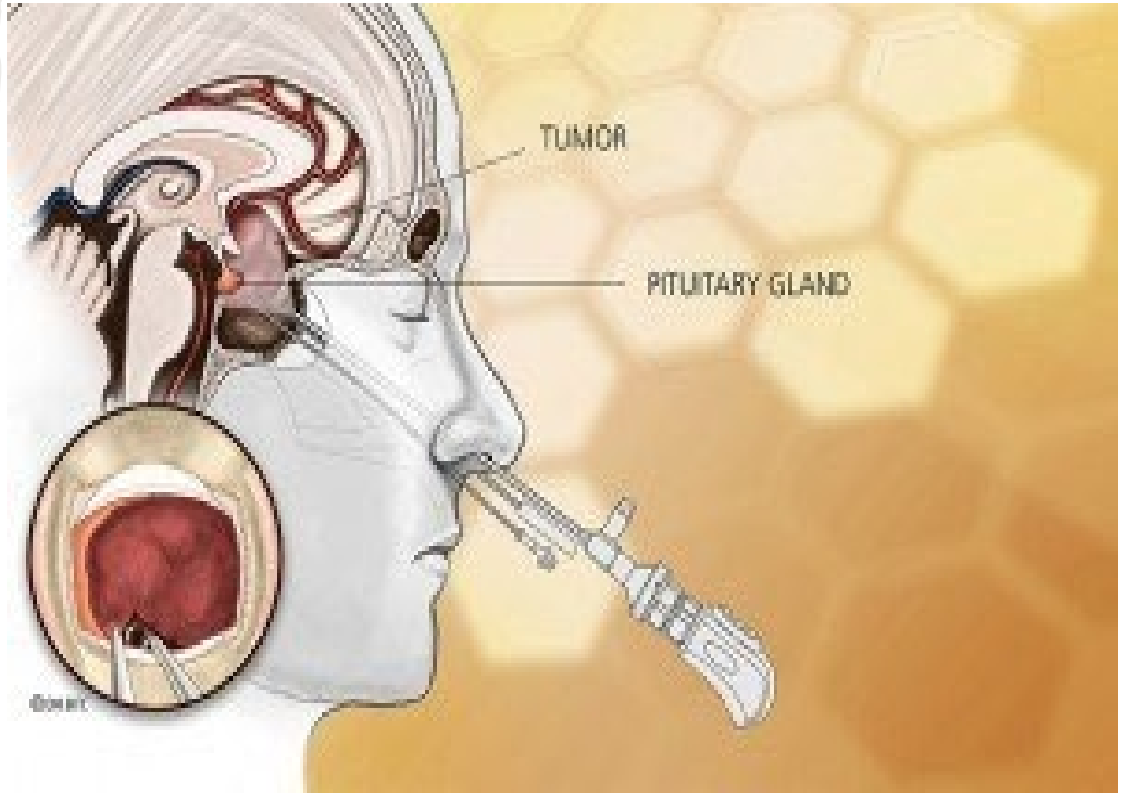
- Many hormones are rhythmically released (melatonin, growth hormone, etc.)
- Posterior pituitary stores and excretes two hormones produced by the hypo-thalamus (oxytocin and antidiuretic hormone)



https://www.ohsu.edu/sites/default/files/2020-01/pituitary-gland-anatomy.jpg

Hypopituitarism

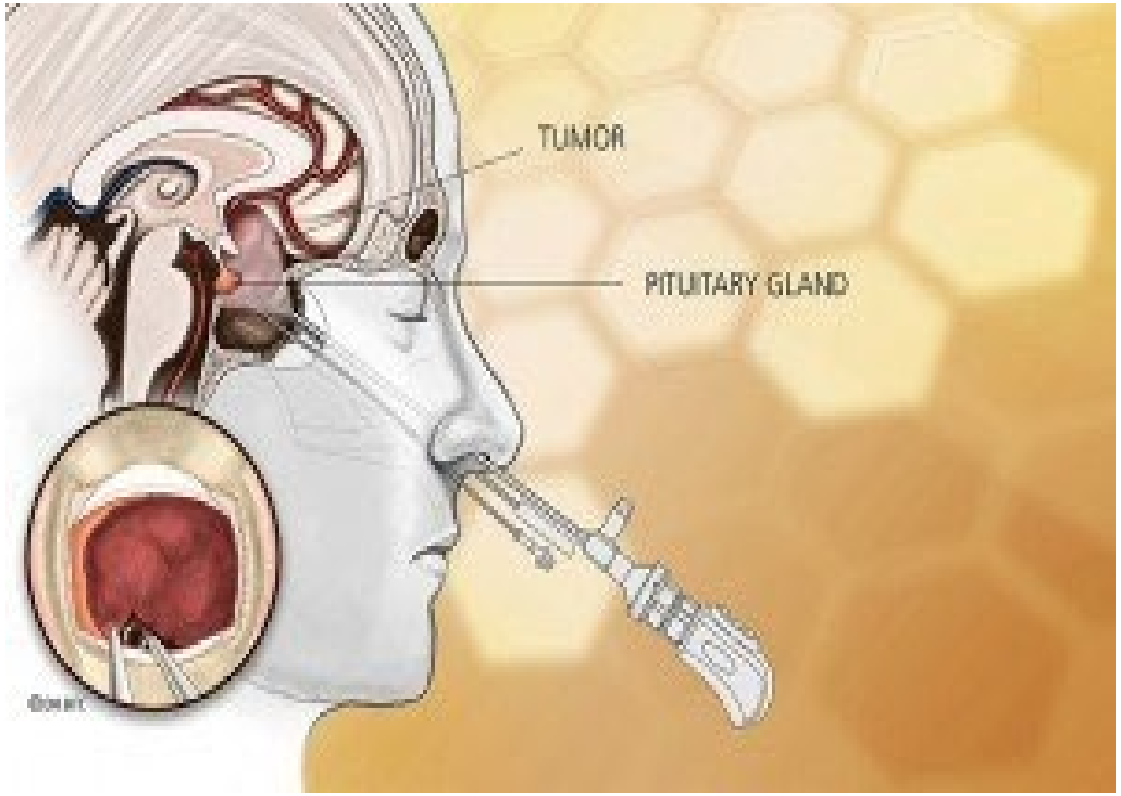
- Decreased release of growth hormone → Disturbed growth in a child, metabolic problems for adults
- Decreased release of thyreotropin which regulates thyroid gland → fatigue, weight gain, bradycardia
- Decrease release of corticotropin which regulates functions of adrenal gland → fatigue, weight loss, loss of appetite
- Decrease release of prolactin → lactation does not start after childbirth



https://www.pacificneuroscienceinstitute.org/pituitary-disorders/conditions/pituitary-adenomas/

Hypopituitarism

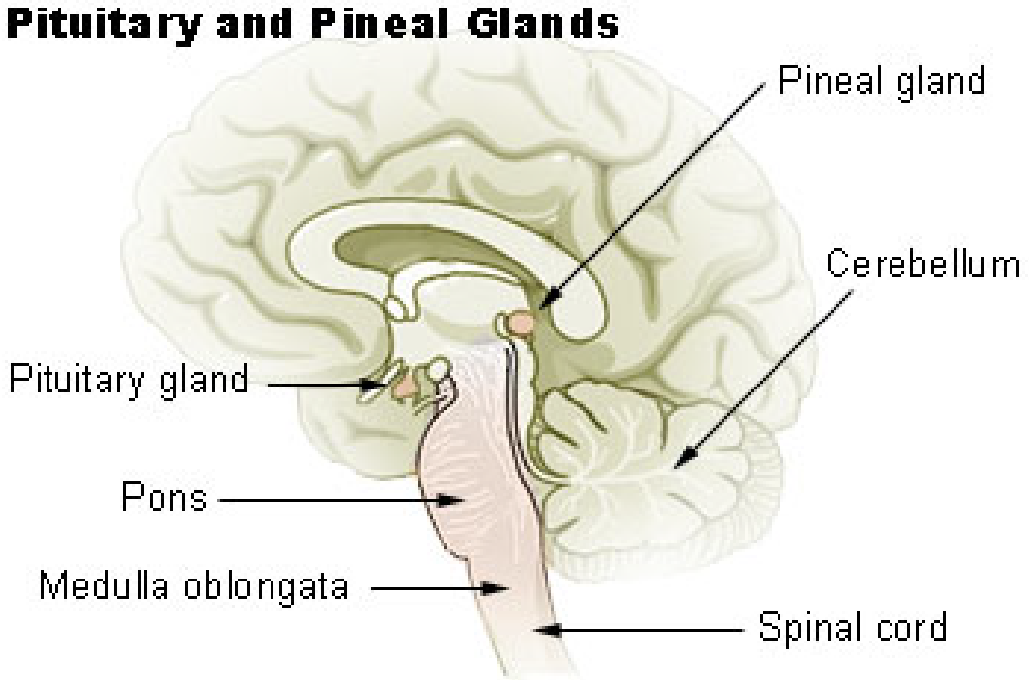
- Decreased release of LH (luteinizing hormone) ja FSH (follicle stimulating hormone) which regulate the production of sex hormones and gametes in testes and ovaries → infertility and sexual dysfunctions
- Decreased release of antidiuretic hormone (ADH) → Increased loss of water into urine
- Decreased release of oxytocin which participates in childbirth and lactation

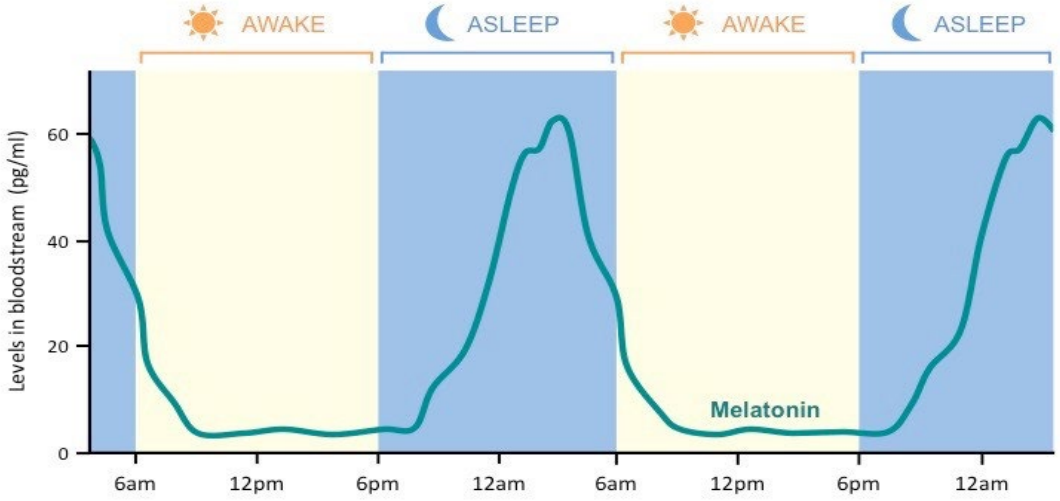


https://www.pacificneuroscienceinstitute.org/pituitary-disorders/conditions/pituitary-adenomas/

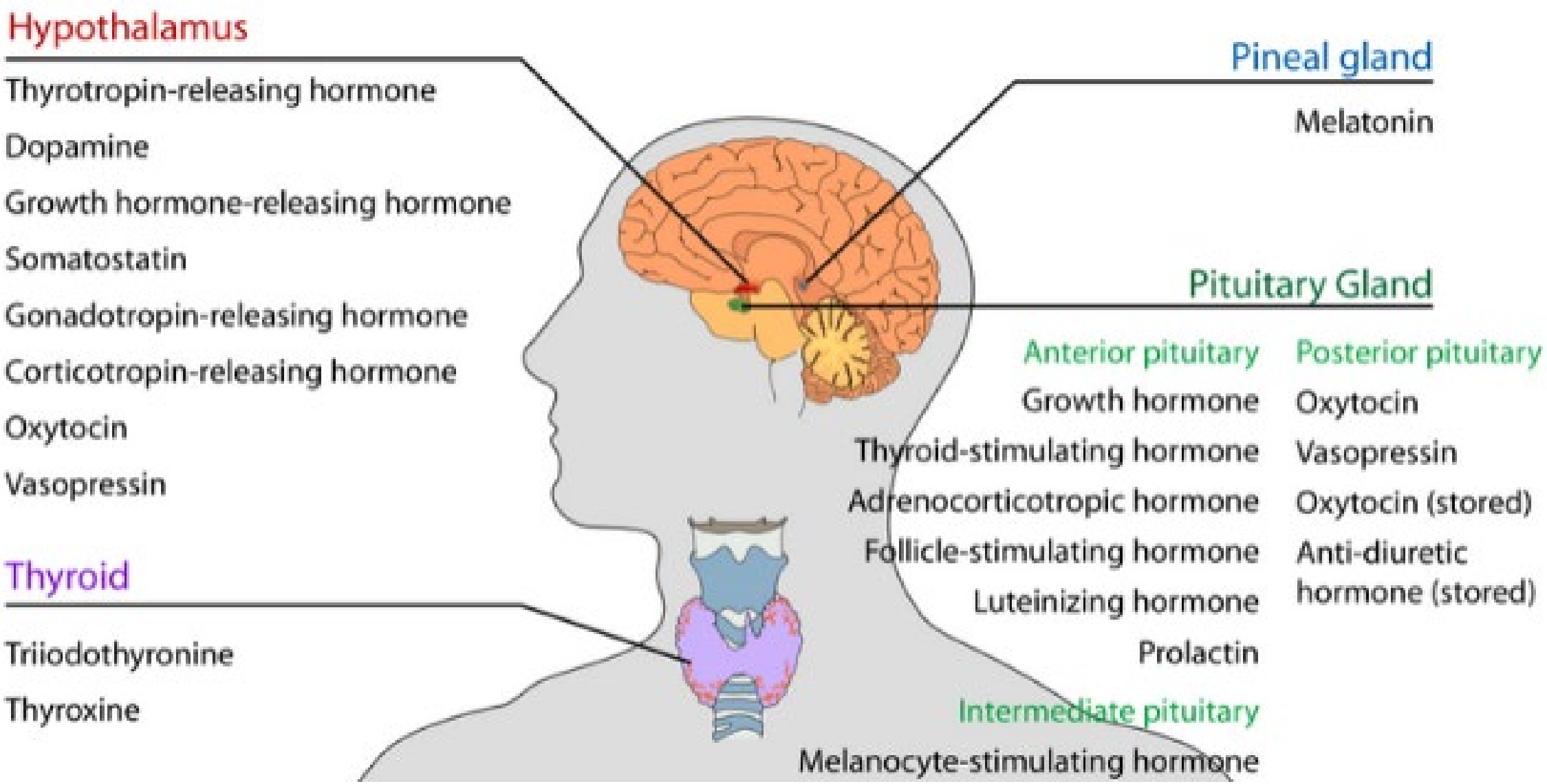
Pineal gland

- Corpus pineale (in latin)
- Produces melatonin
- Production greatest at night, while strong light inhibits the release
- Melatonin is sometimes used to relieve jet lag, but its effectiveness is unclear





Wikipedia, https://ib.bioninja.com.au/



https://revelinmotion.com/

Table 1. **Major hypothalamic releasing and inhibiting hormones**

Hypothalamic hormone secreted	Target anterior pituitary cells	Anterior pituitary gland secretion/release	Physiological result
Growth hormone-releasing hormone	Somatotrophs	Growth hormone	Stimulates growth
Growth hormone-inhibiting hormone	Somatotrophs	Inhibits growth hormone secretion	Inhibits growth
Prolactin-releasing hormone (hypothetical)	Lactotrophs	Prolactin	Thought to stimulate lactation
Prolactin-inhibiting hormone (hypothetical)	Lactotrophs	Inhibits prolactin secretion	Thought to inhibit lactation
Thyrotropin-releasing hormone	Thyrotrophs	Thyroid-stimulating hormone	Stimulates release of T3 and T4 (thyroxine), thereby increasing metabolism
Corticotropin-releasing hormone	Corticotrophs	Adrenocorticotropic hormone	Regulates glucocoticoids, mineralocorticoid and androgen secretion by the adrenal cortex
Gonadothropin-releasing hormone	Gonadotrophs	Luteinising hormone	Stimulates ovulation/progesterone secretion in females and testosterone secretion in males
Gonadothropin-releasing hormone	Gonadotrophs	Follicle-stimulating hormone	Stimulates maturation of ovarian follicles in females and spermatogenesis in males

https://www.nursingtimes.net/clinical-archive/

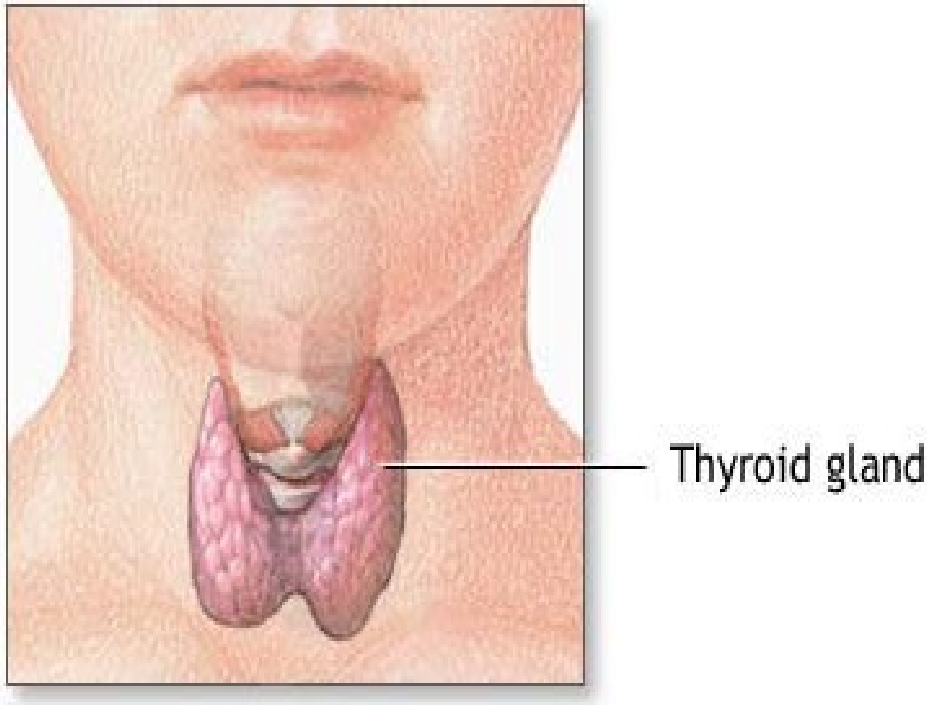
Pituitary Hormones

Hormone	Secretory Cell Type	Target	Effect
Growth hormone (GH)	Somatotrope	Liver and adipose tissue	Stimulation of growth and metabolism of carbohydrates and lipids
Prolactin (PRL)	Lactotrope	Mammary glands	Production of milk
Thyroid stimulating hormone (TSH)	Thyrotrope	Thyroid gland	Secretion of thyroid hormones
Follicle stimulating hormone (FSH)	Gonadotrope	Ovaries and testes	Regulates reproductive functioning
Luteinizing hormone (LH)	Gonadotrope	Ovaries and testes	Production of sex hormones
Adrenocorticotropic hormone (ACTH)	Corticotrope	Adrenal gland (cortex)	Secretion of glucocorticoids
ß-endorphin	Corticotrope	Opiod receptors	Inhibit pain perception

https://emedicine.medscape.com/article/1899167-overview

Thyroid gland

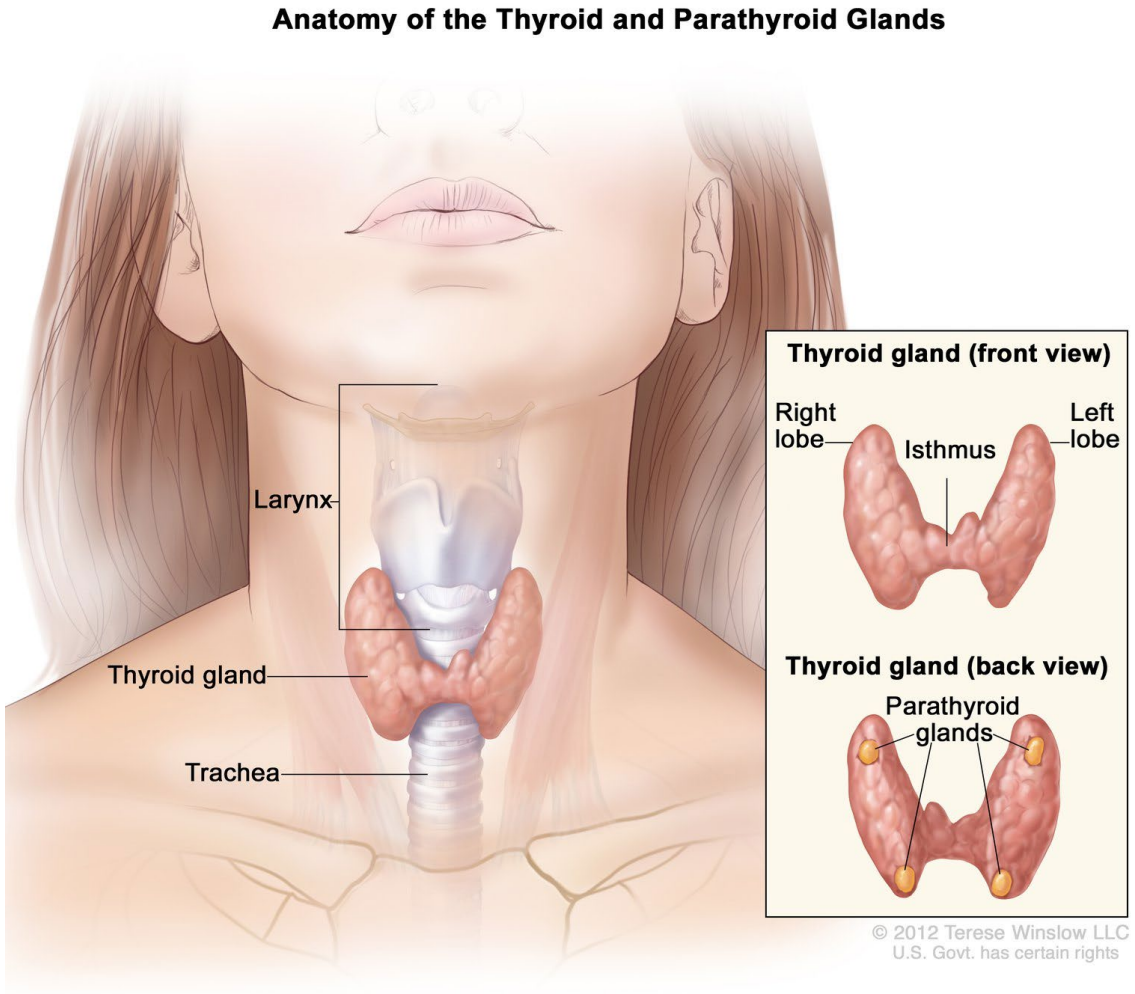
- Produces thyroid hormones and calcitonin
- Located below the larynx and in front of trachea (figure)
- Single layer of cuboidal epithelium that produces *thyroxin* (T4; 93%) and *triiodothyronine* (T3) hormones
- T4 → biologically active T3 in liver
- Hormone production requires iodine appr. 1 mg per week
- Important for the development of central nervous system
- *Calcitonin* promotes the storaging of calsium in the bones, and inhibits the release of Ca ad Pi from the bones



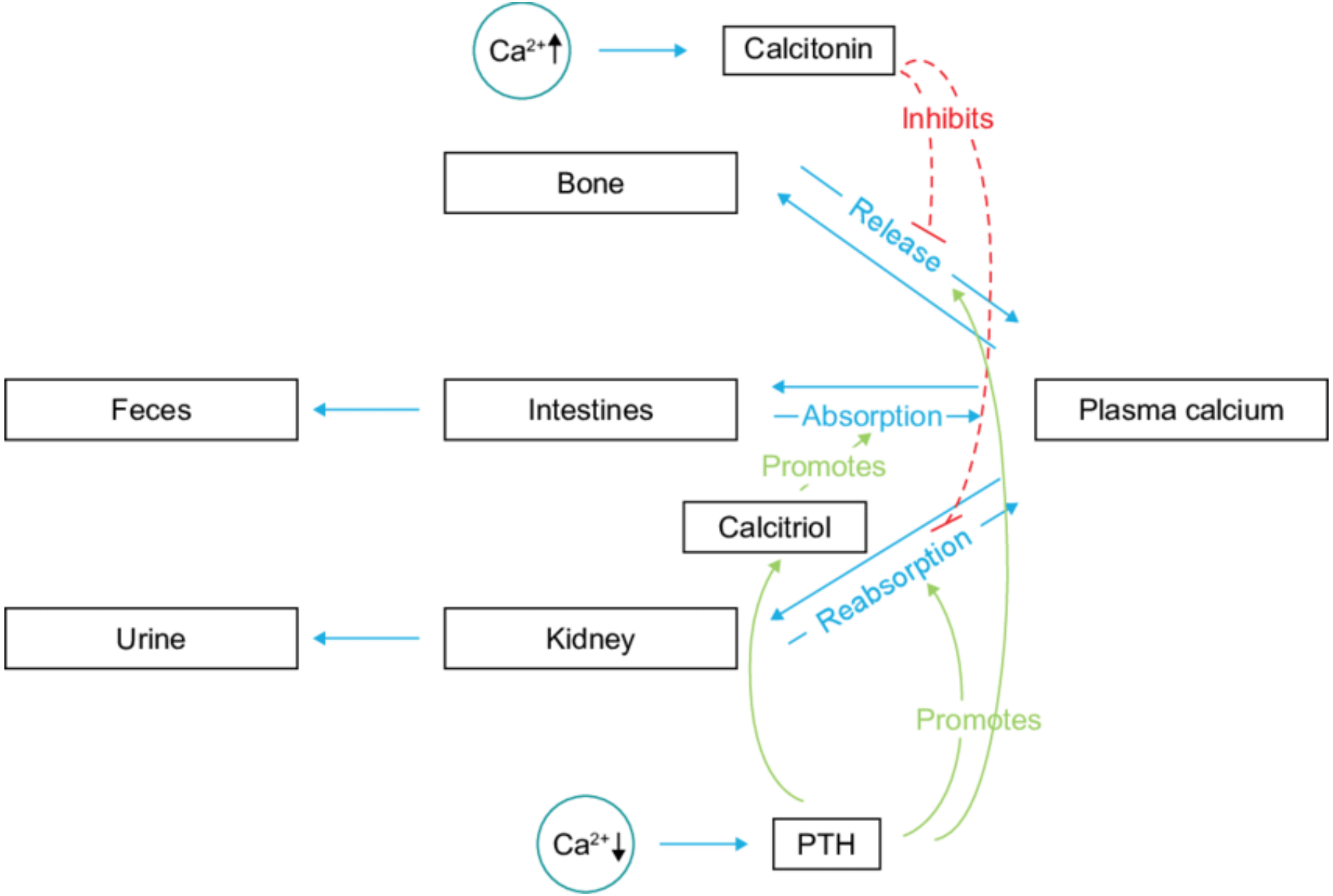
Wikipedia

Parathyroid glands and calcium metabolism

- Reside at the posterior part of the thyroid gland
- *Parathyroid hormone*: Regulates Ca, Pi, and Mg levels in plasma
  - Activates osteoclasts to release Ca from bones
  - Promotes the forming of active vitamin D in kidneys
  - Promotes reuptake of Ca from urine
- Ca is crucial for bone structure, nervous and muscular functions, for blood clotting and for enzyme functions



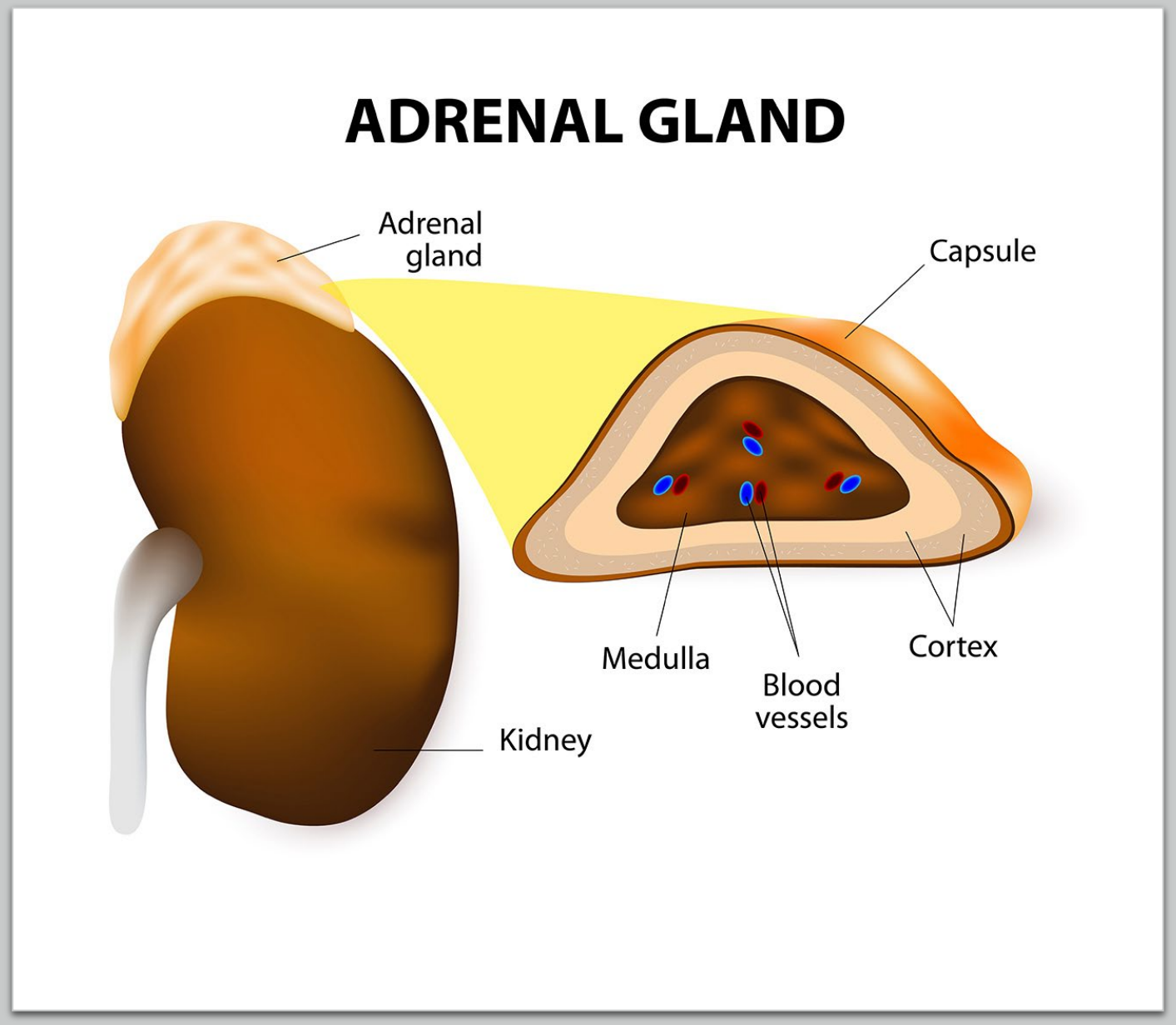
https://www.niddk.nih.gov/health-information/endocrine-diseases/primary-hyperparathyroidism


Ca2+↑
Calcitonin
Inhibits
Bone
Release
Feces
Intestines
Absorption
Plasma calcium
Promotes
Calcitriol
Reabsorption
Urine
Kidney
Promotes
Ca2+↓
PTH

Li et al. 2018

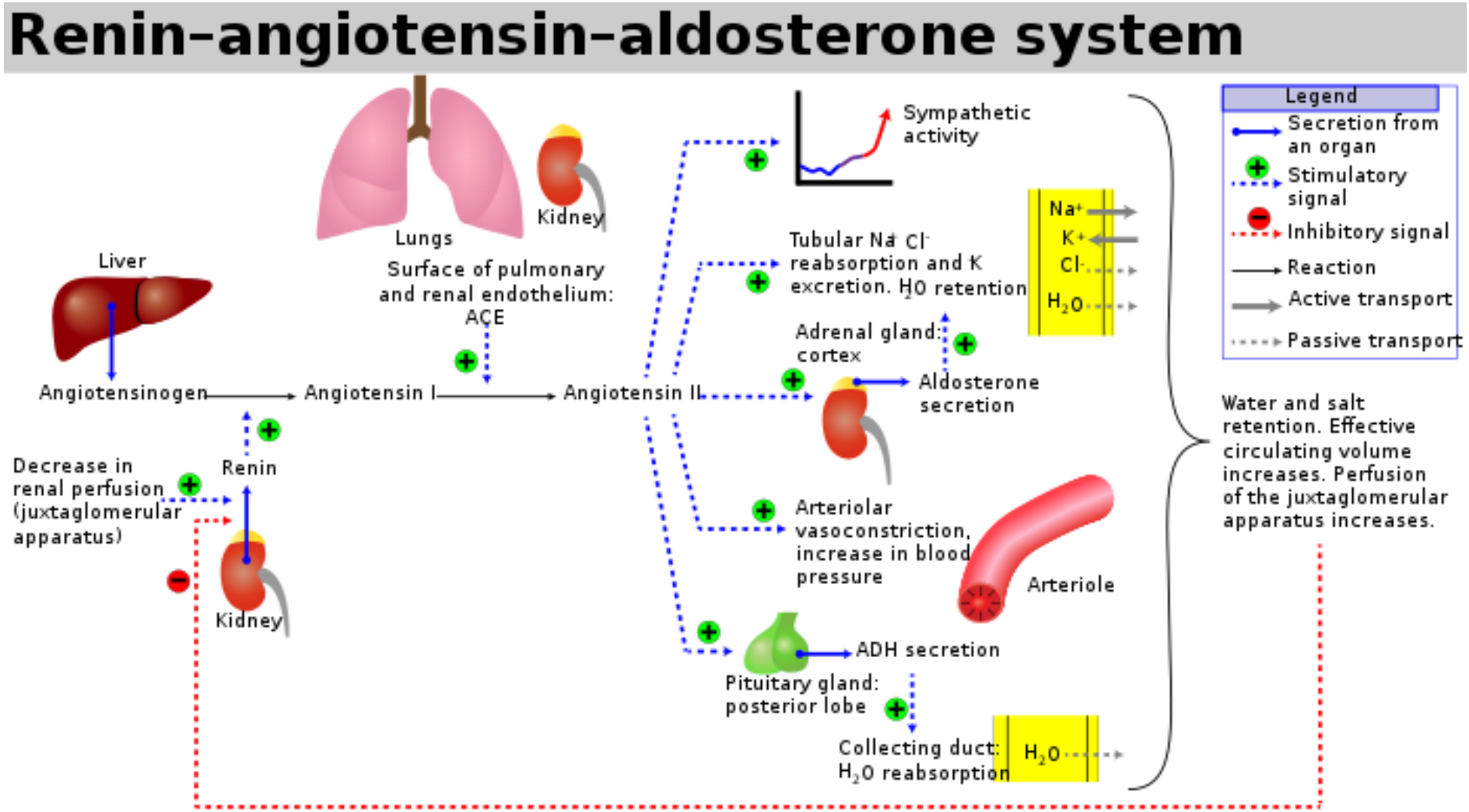
Adrenal glands

- Main functions in regulating salt balance and glucose metabolism
- Consist structurally and functionally of two parts: Cortex and medulla
- **Cortex**: aldosterone and cortisol



https://www.hopkinsmedicine.org/health/conditions-and-diseases/adrenal-glands

Aldosterone: Na^+-K^+ balance, blood pressure, blood volume, acid-base balance



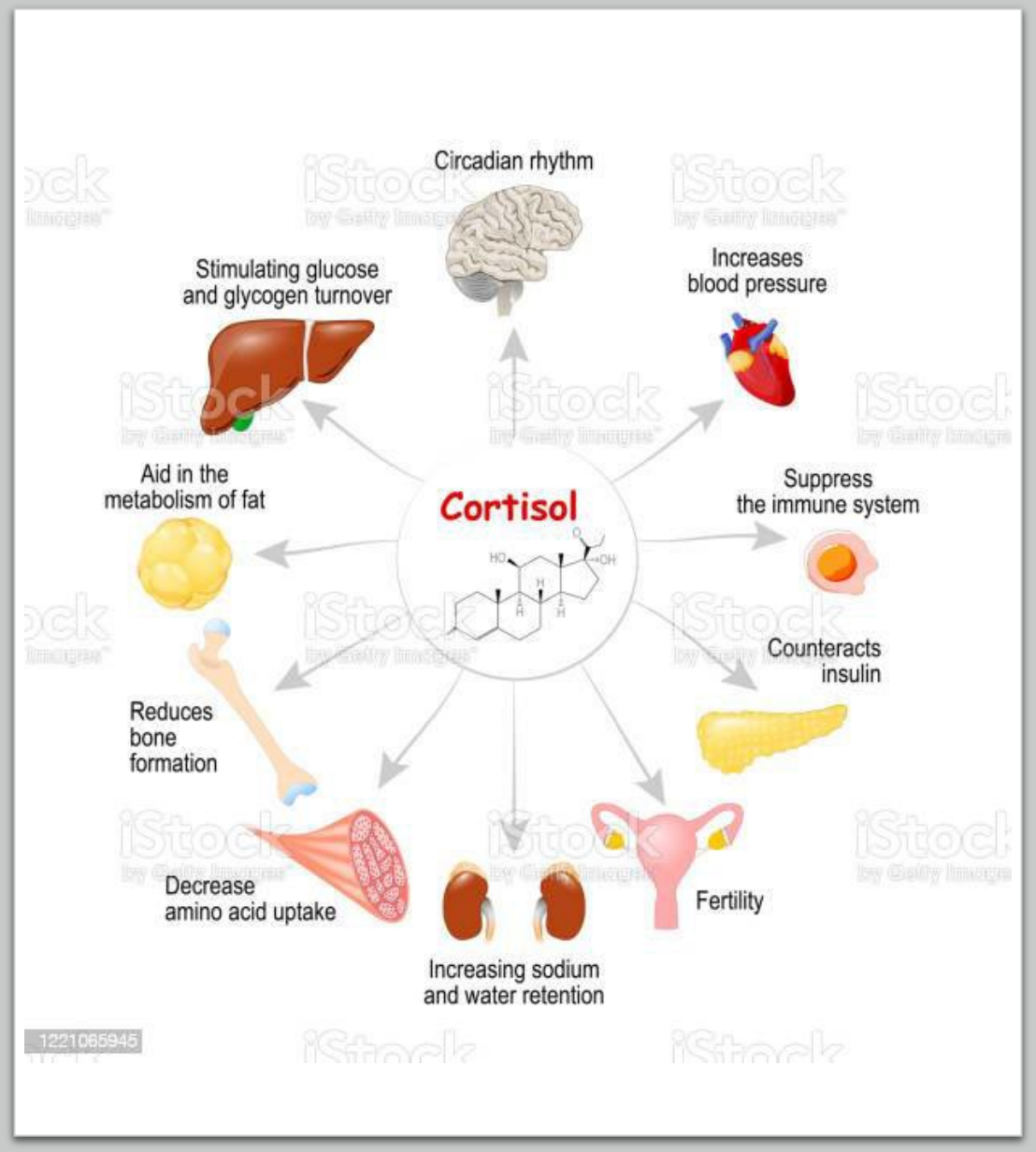
vVikipedia

Cortisol and other glucocorticoids

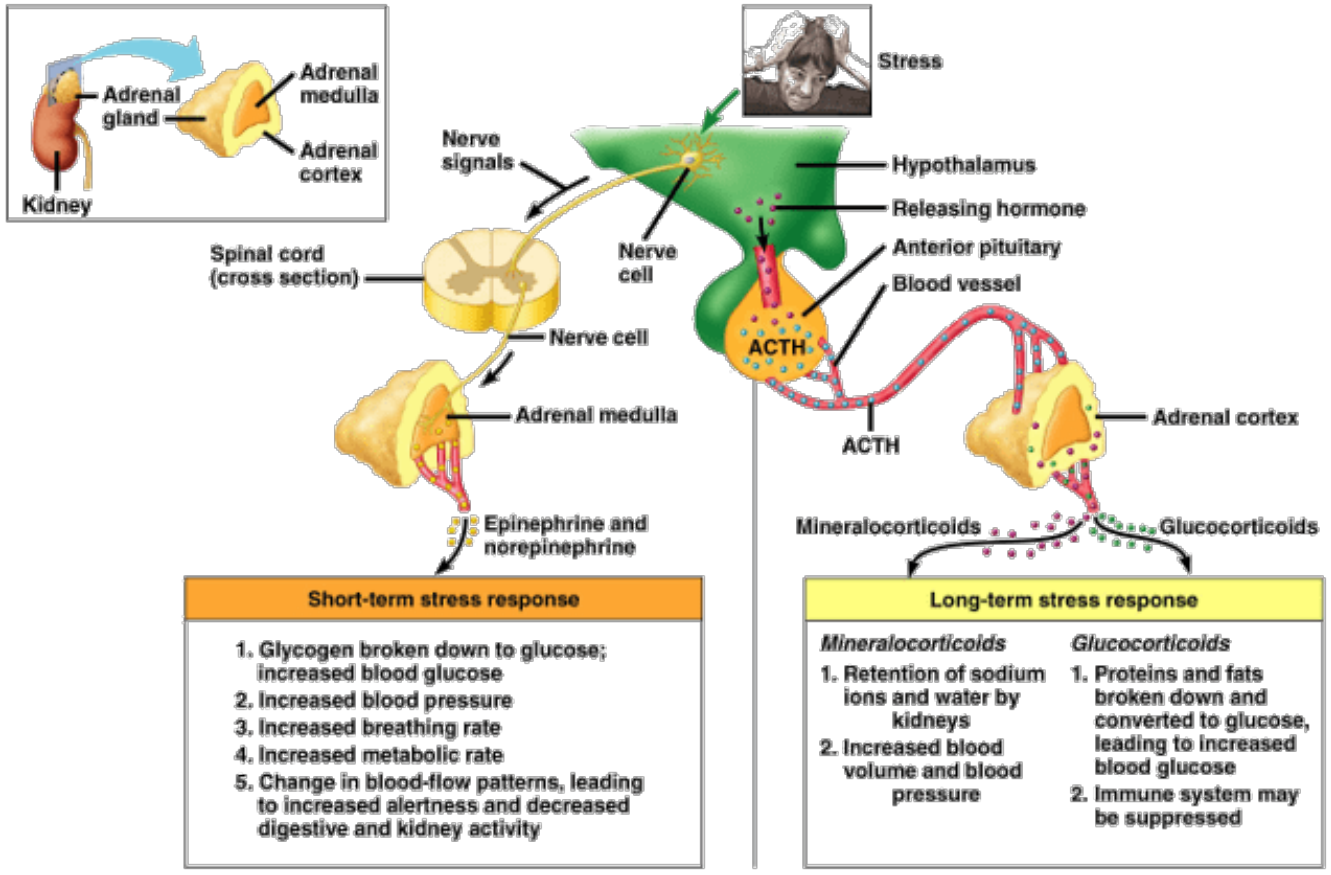
Prepare body for stress

1) Glucose metabolism: Reforming of glucose from fat acids and proteins in liver

2) Dampening of inflammatory reactions



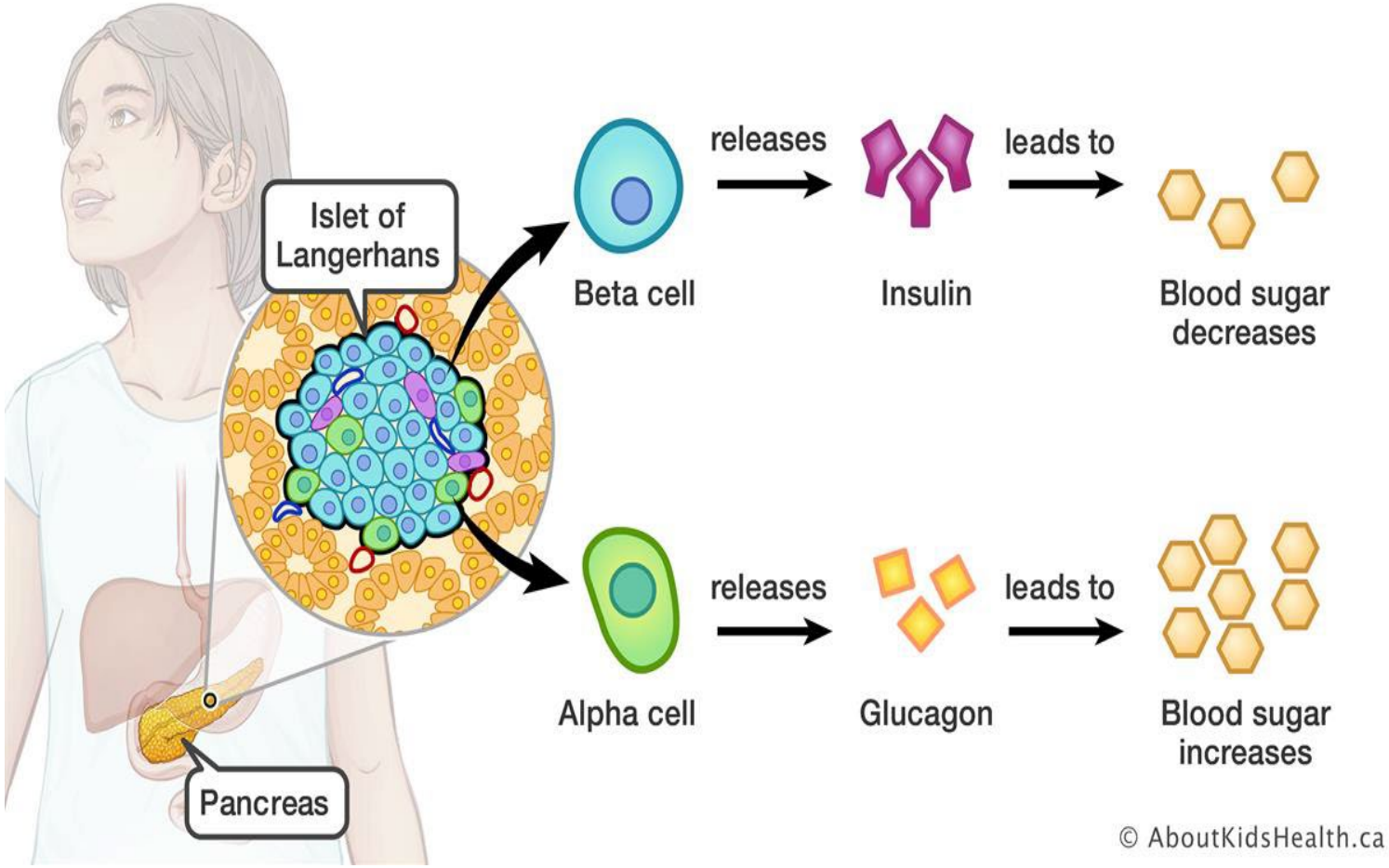
- **Adrenal medulla**: catecholamines such as adrenaline and noradrenaline
- Part of the autonomic nervous system
- *Adrenaline*: Glykogen broken down to glucose, heart rate increases, bronchial dilation (the “fight or flight” hormone)
- *Noradrenaline*: Constricts smooth muscles in the vascular walls

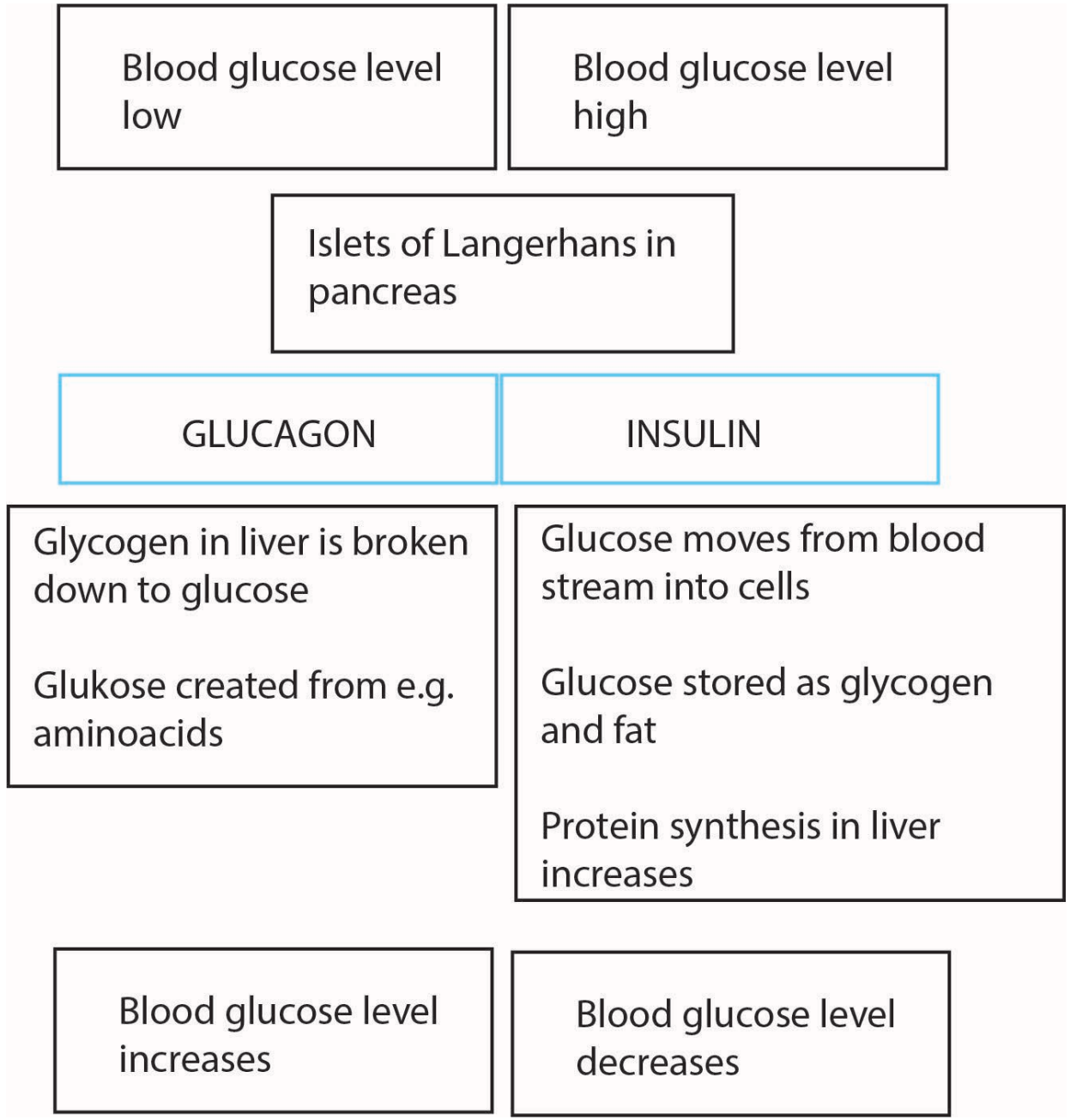


https://biology.reachingfordreams.com/

Pancreas & glucose regulation

- Pancreas is both an endocrine and exocrine organ
- Mainly exocrine → enzymes important to digestion
- Endocrine part = Langerhans islets (1-2%)
- Glucagon and insulin




Blood glucose level low
Blood glucose level high
Islets of Langerhans in pancreas
GLUCAGON
INSULIN
Glycogen in liver is broken down to glucose
Glukose created from e.g. aminoacids
Glucose moves from blood stream into cells
Glucose stored as glycogen and fat
Protein synthesis in liver increases
Blood glucose level increases
Blood glucose level decreases

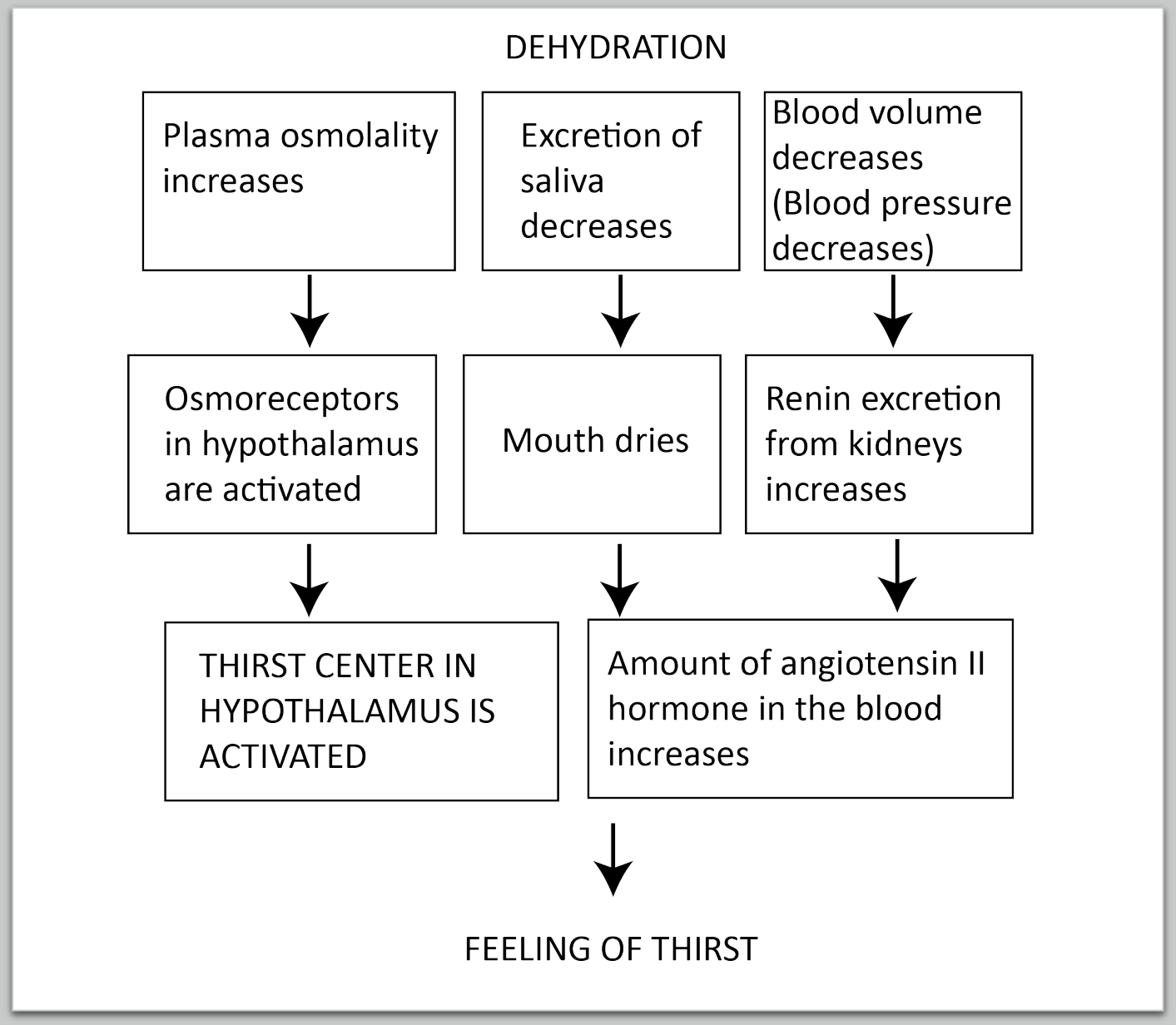
Endocrine Hormones

Gland	Hormones	Functions
Thyroid	Thyroxine	Regulates metabolism and temperature
	Calcitonin	Inhibits release of calcium from the bones
Parathyroid	Parathyroid hormone	Stimulates the release of calcium from the bones.
Islet cells (in the pancreas)	Insulin	Decreases blood sugar by promoting uptake of glucose by cells.
	Glucagon	Increases blood sugar by stimulating breakdown of glycogen in the liver.
Testes	Testosterone	Regulates sperm cell production and secondary sex characteristics.
Ovaries	Estrogen	Stimulates egg maturation, controls secondary sex characteristics.
	Progesterone	Prepares the uterus to receive a fertilized egg.
Adrenal medulla	Epinephrine - fight Norepinephrine - flight	Stimulates "fight or flight" response.
Adrenal cortex	Glucocorticoids	Part of stress response, increase blood glucose levels and decrease immune response. Example: Cortisol - helps regulate metabolism and helps your body respond to stress
	Aldosterone	Regulates sodium content in the blood.
Pineal gland	Melatonin	Sleep cycles, reproductive cycles in many mammals.

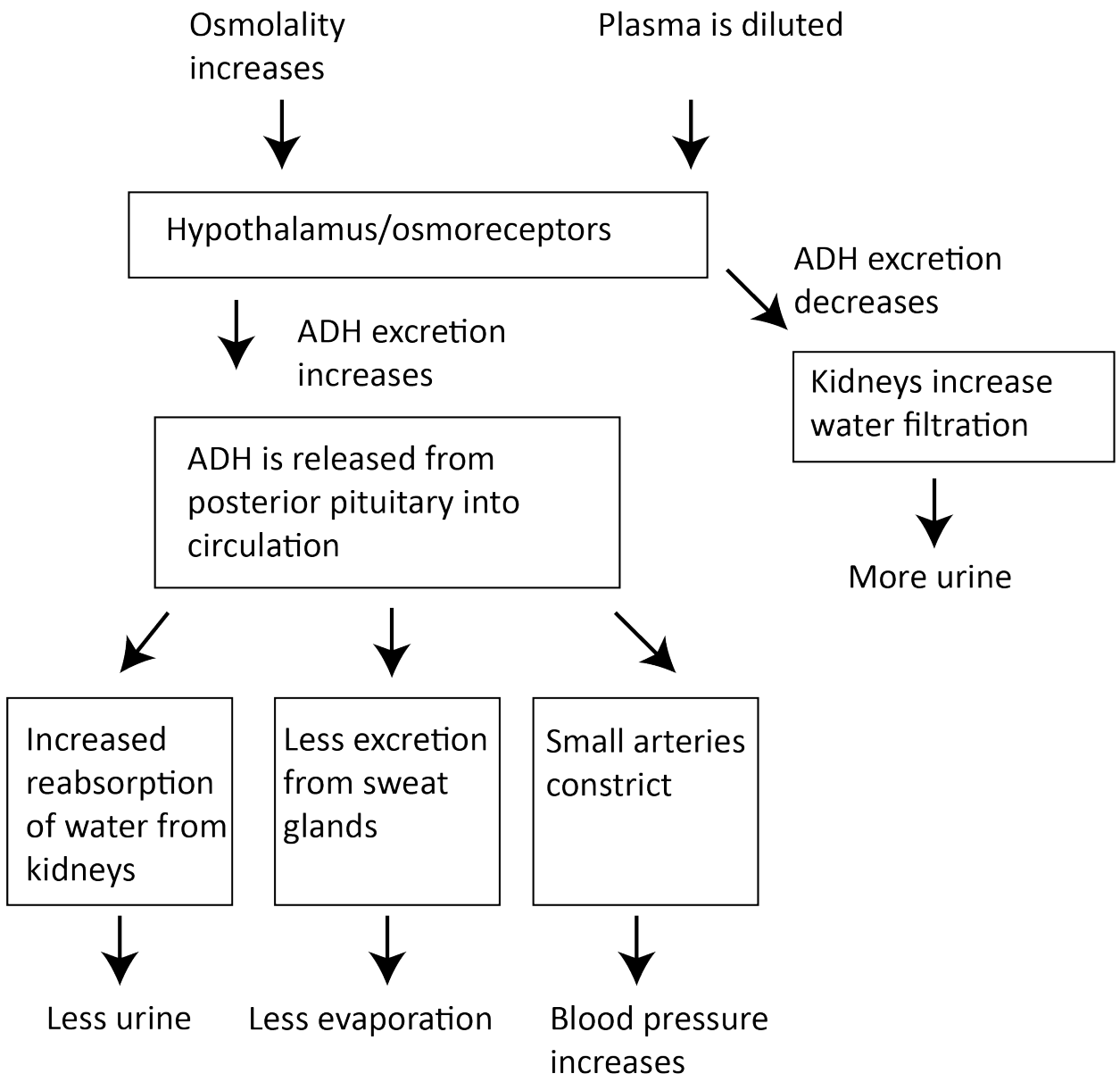
https://www.toppr.com/ask/question/whatare-endocrine-glands-identify-chief-endocrine-glands-the-hormones-produced-bythem-the-function-of-the/

Fluid balance

- The amount of extracellular fluids and their osmolality (= concentration of all chemical particles) are constantly regulated
- Kidneys have a significant role: Amount of urine varies 0.5-20 l/day
- Receptors in hypothalamus detect the changes in osmolality

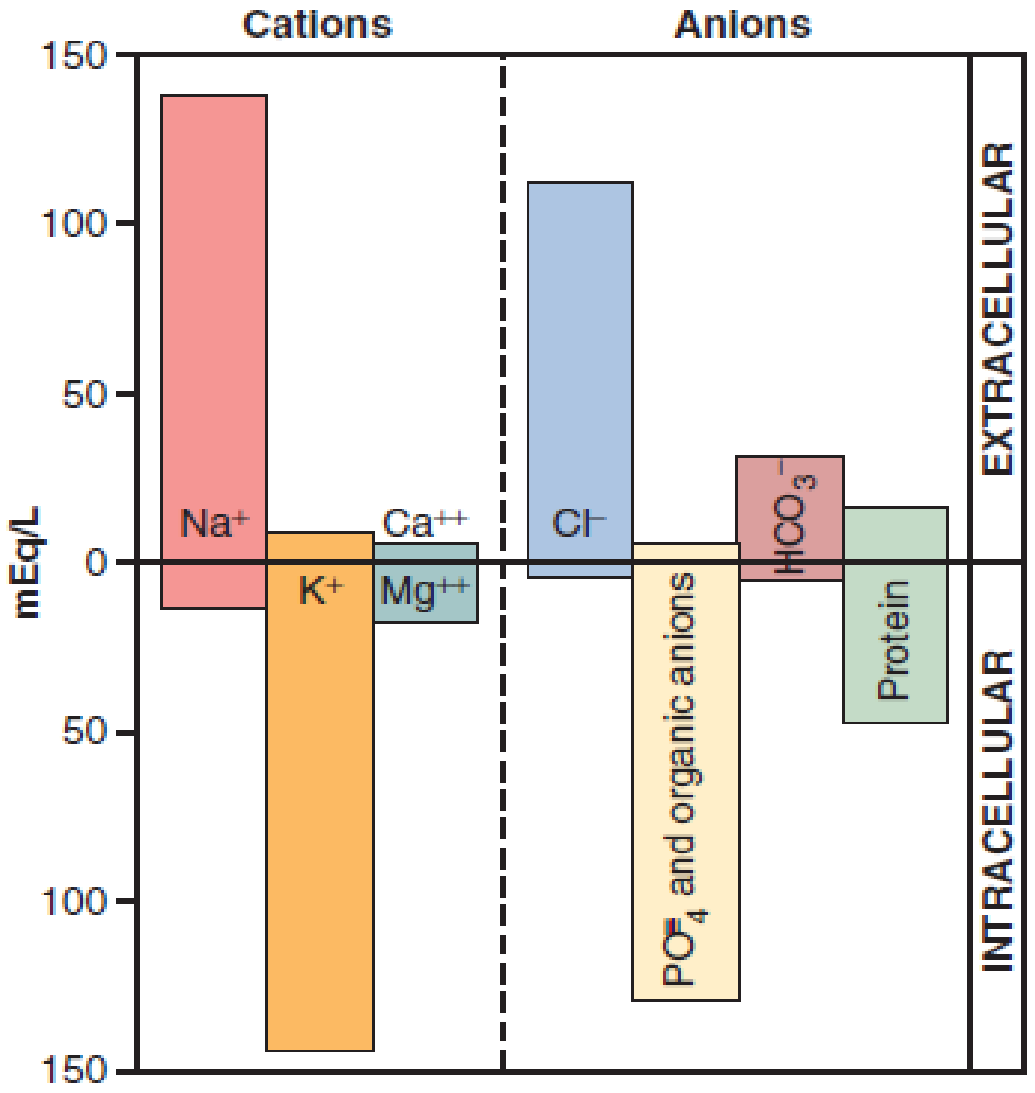


- If the osmolality increases too much, hypothalamus excretes antidiuretic hormone (ADH)
- ADH increases the amount of water reabsorbed back into the circulation from the kidneys



Electrolyte balance

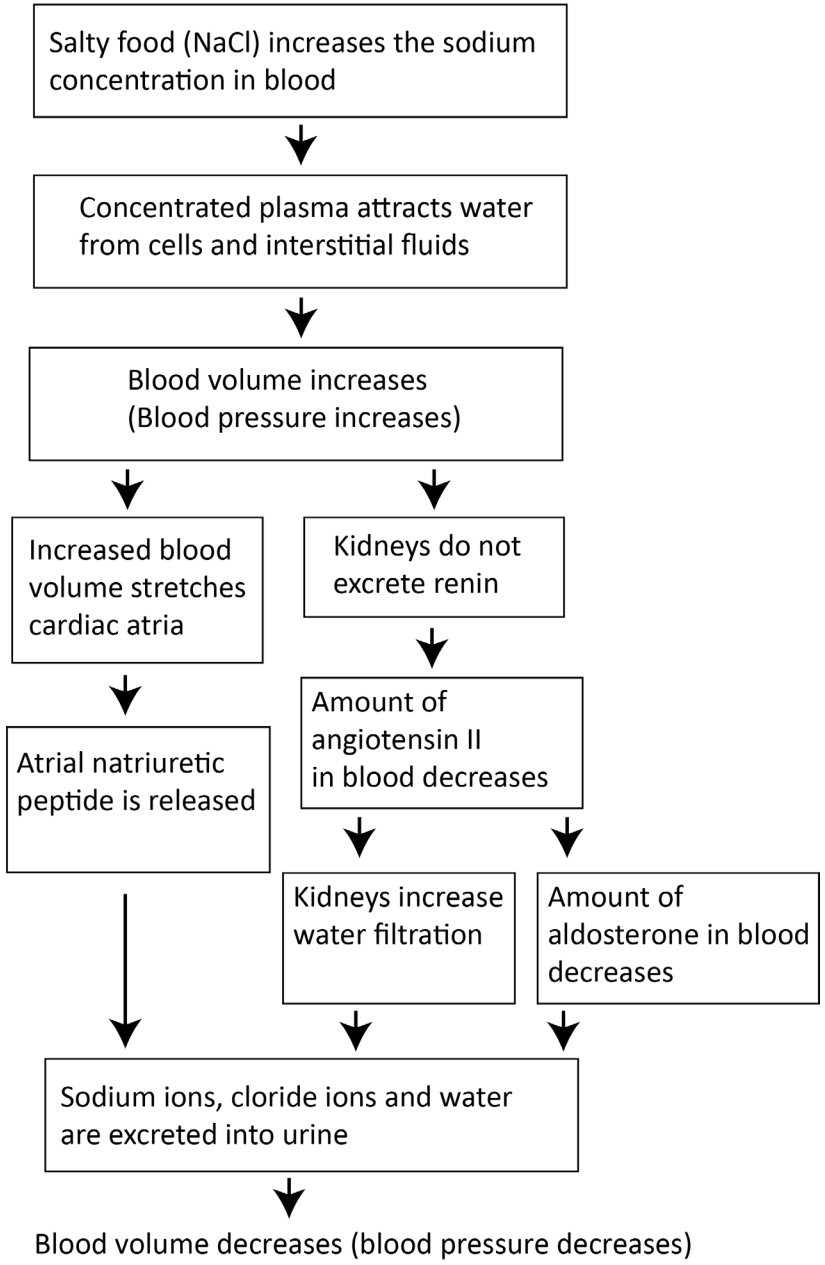
- Electrolyte concentration in intracellular and extracellular fluids almost constant
- Na^+ and K^+ ions are the most important
- Na^+ most important extracellular electrolyte that affects the fluid osmolality
- Electrolyte balance is closely connected to fluid balance: water follows Na^+ ions



Guyton & Hall, Medical Physiology

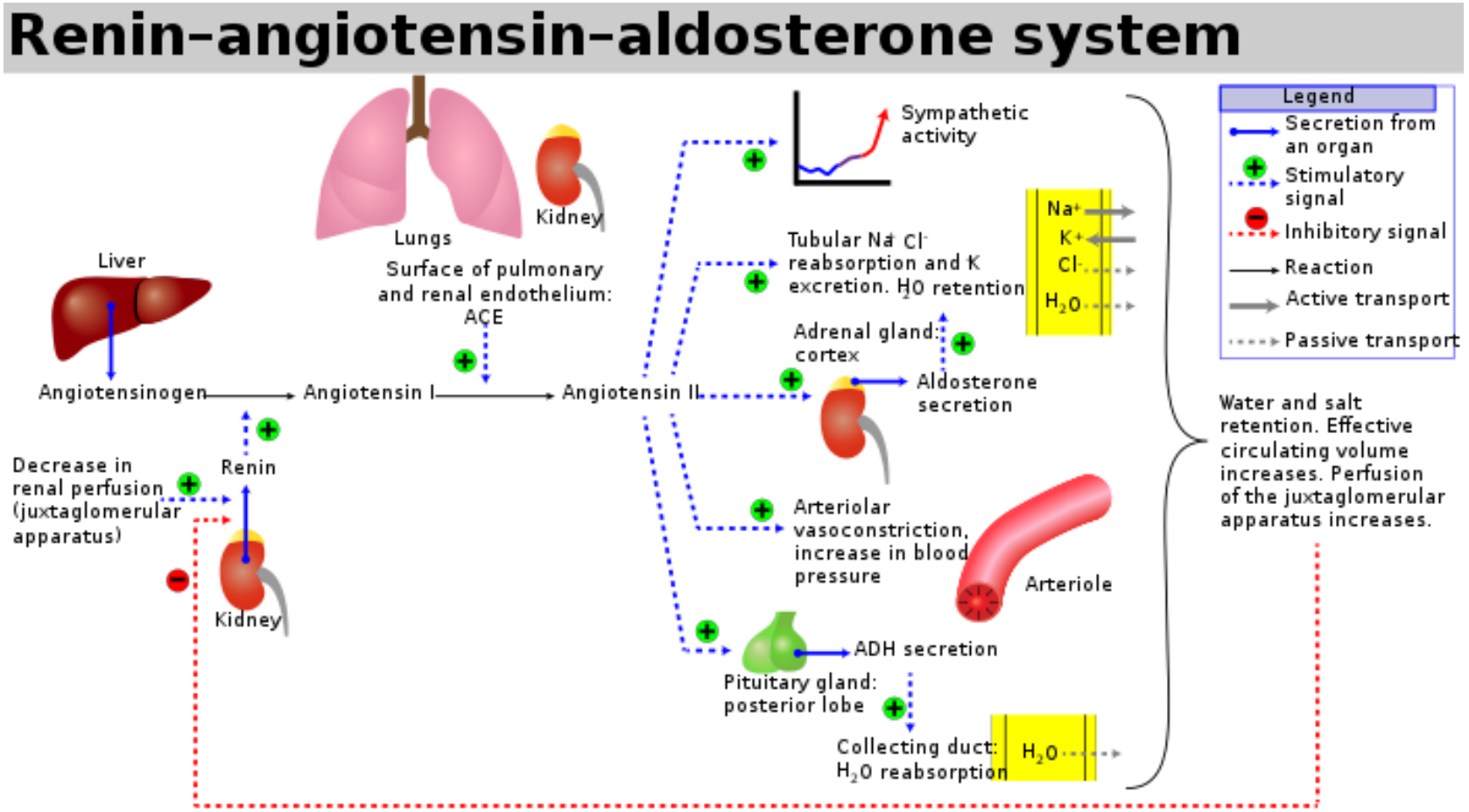
Excretion of sodium

- Atrial natriuretic peptide is excreted from the cardiac atria → dilates vessels and increases excretion of sodium and water into urine → plasma osmolality decreases
- Excessive accumulation of sodium in the body usually results from hypothalamic tumor or trauma, vomiting, excessive sweating (= loss of water)



Sodium reuptake

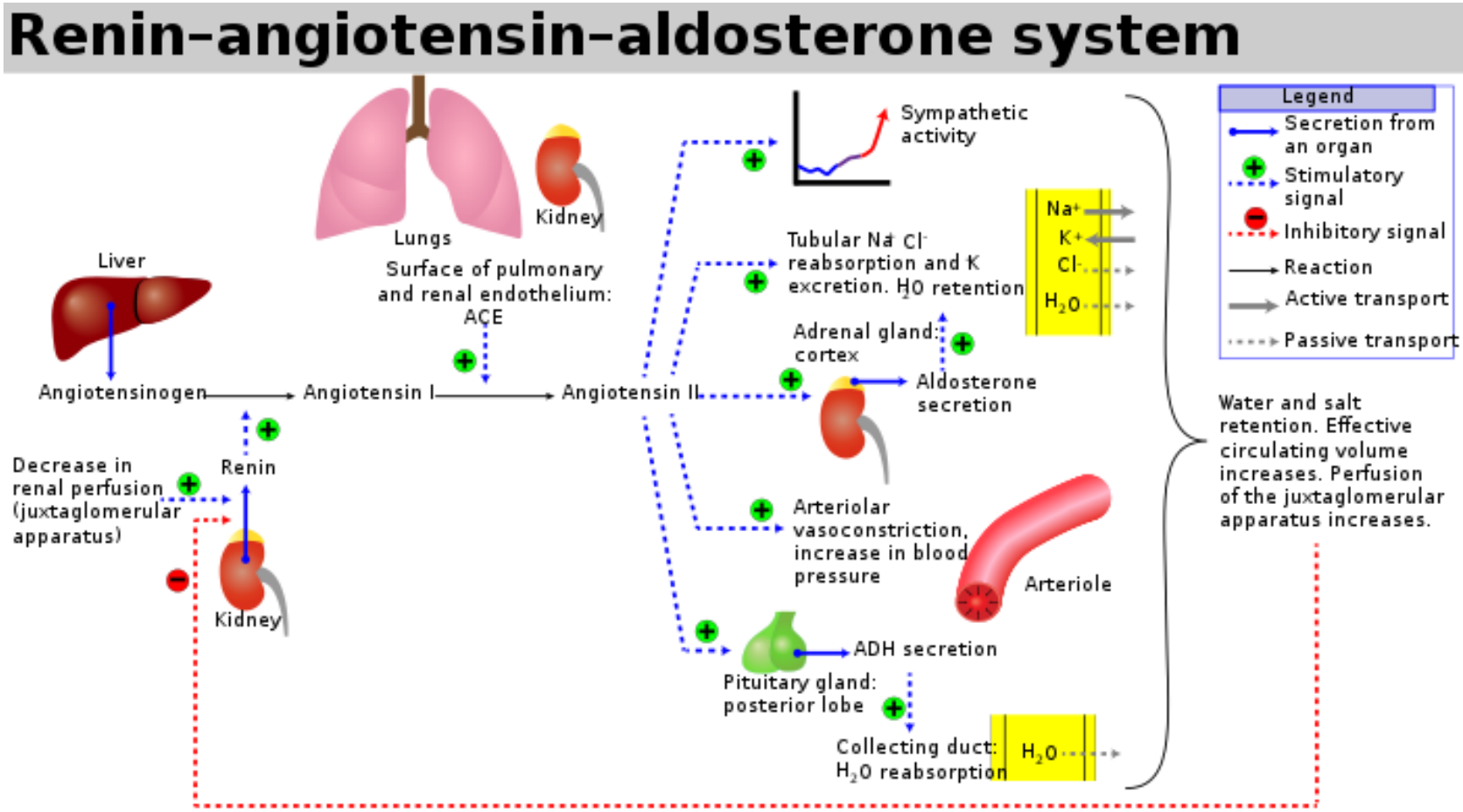
- Renin-angiotensin-aldosterone system (RAA)
- Renin is released from the kidneys → transforms angiotensinogen produced by liver into angiotensin I
- Angiotensin I is converted into angiotensin II in the lungs → activates aldosterone release from the adrenal gland cortex



Wikipedia

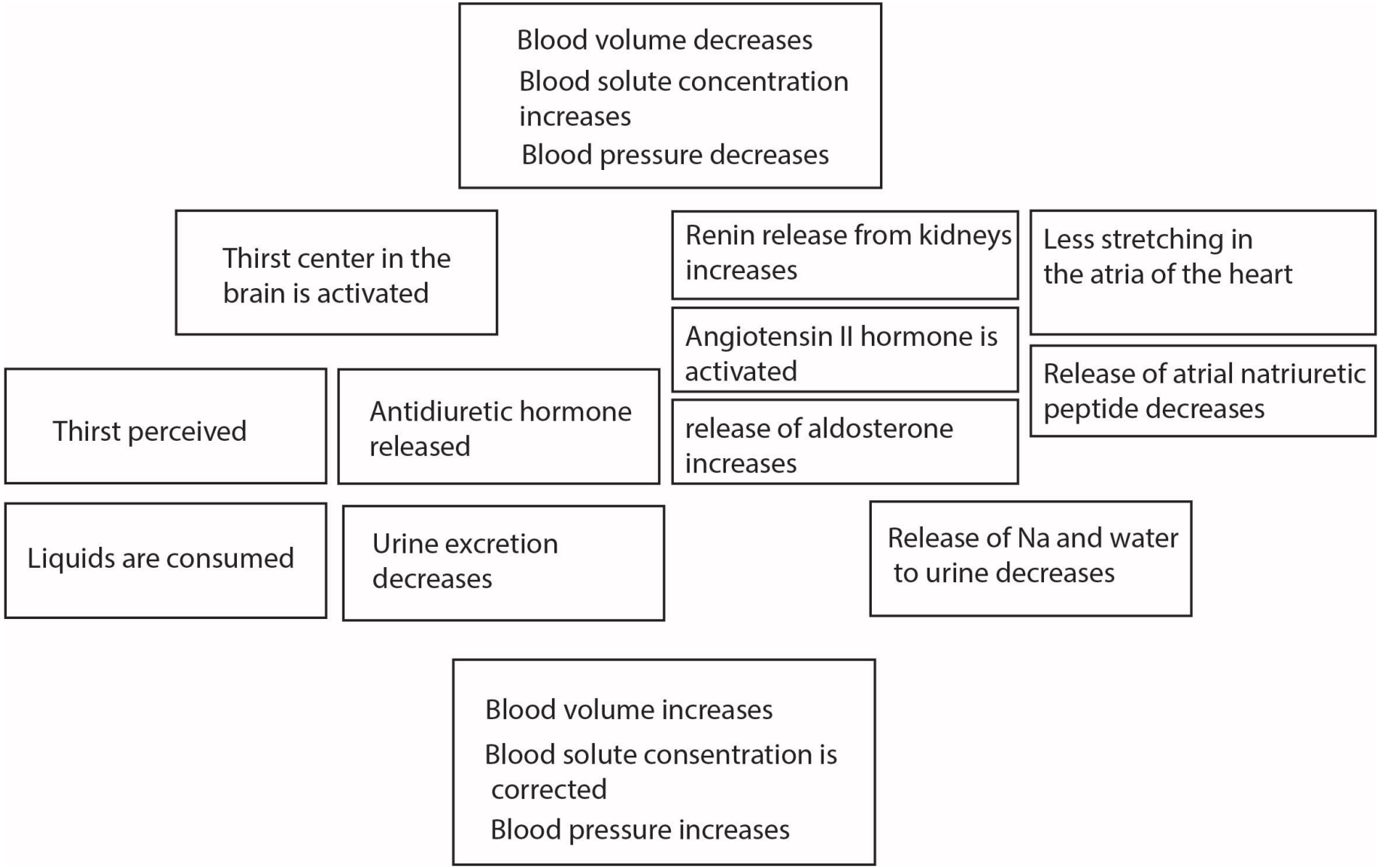
Sodium reuptake

- RAA regulates primarily the sodium balance
- Dehydration decreases sodium storages →
- RAA system activates



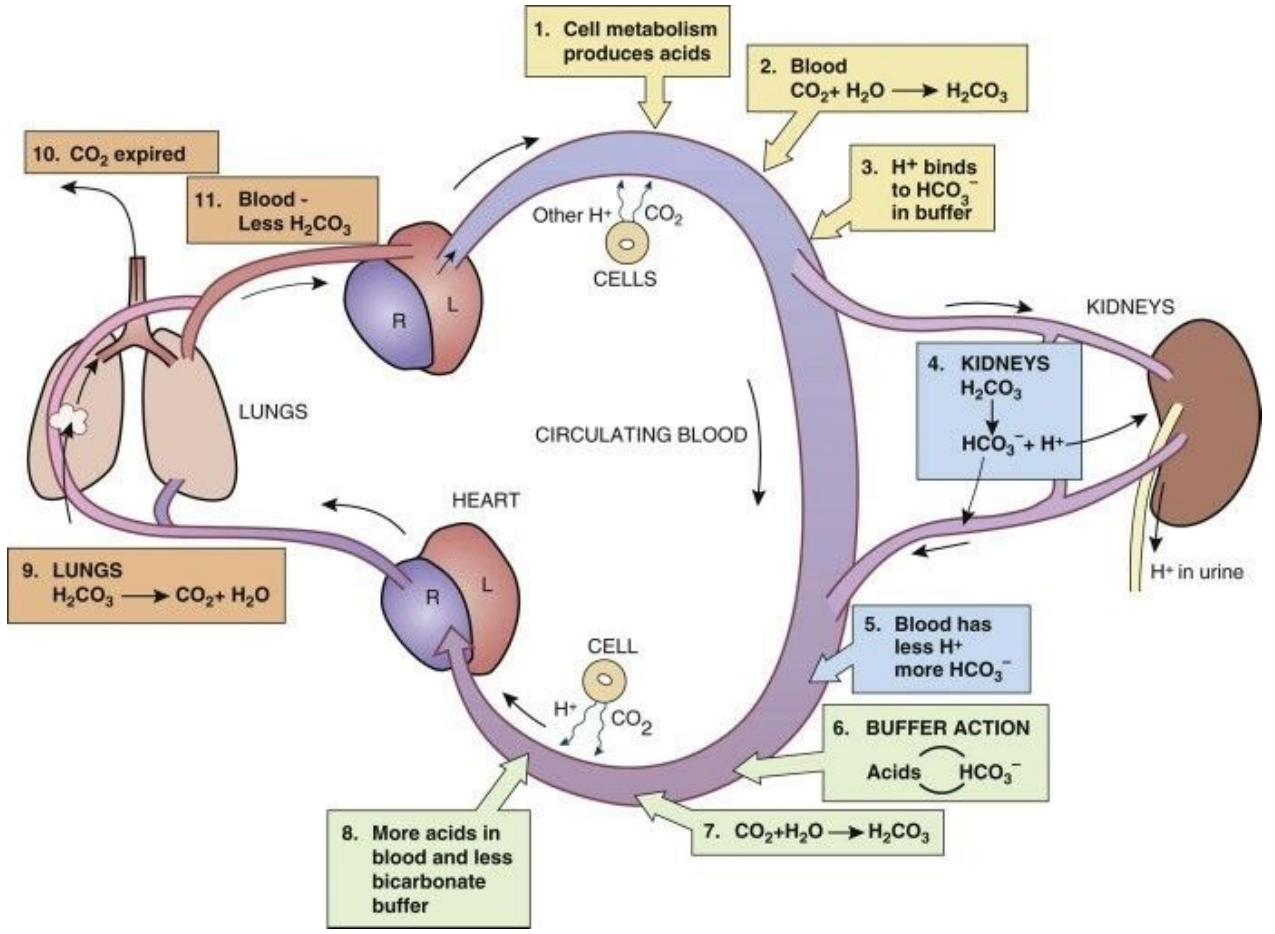
Wikipedia

Regulation of blood pressure



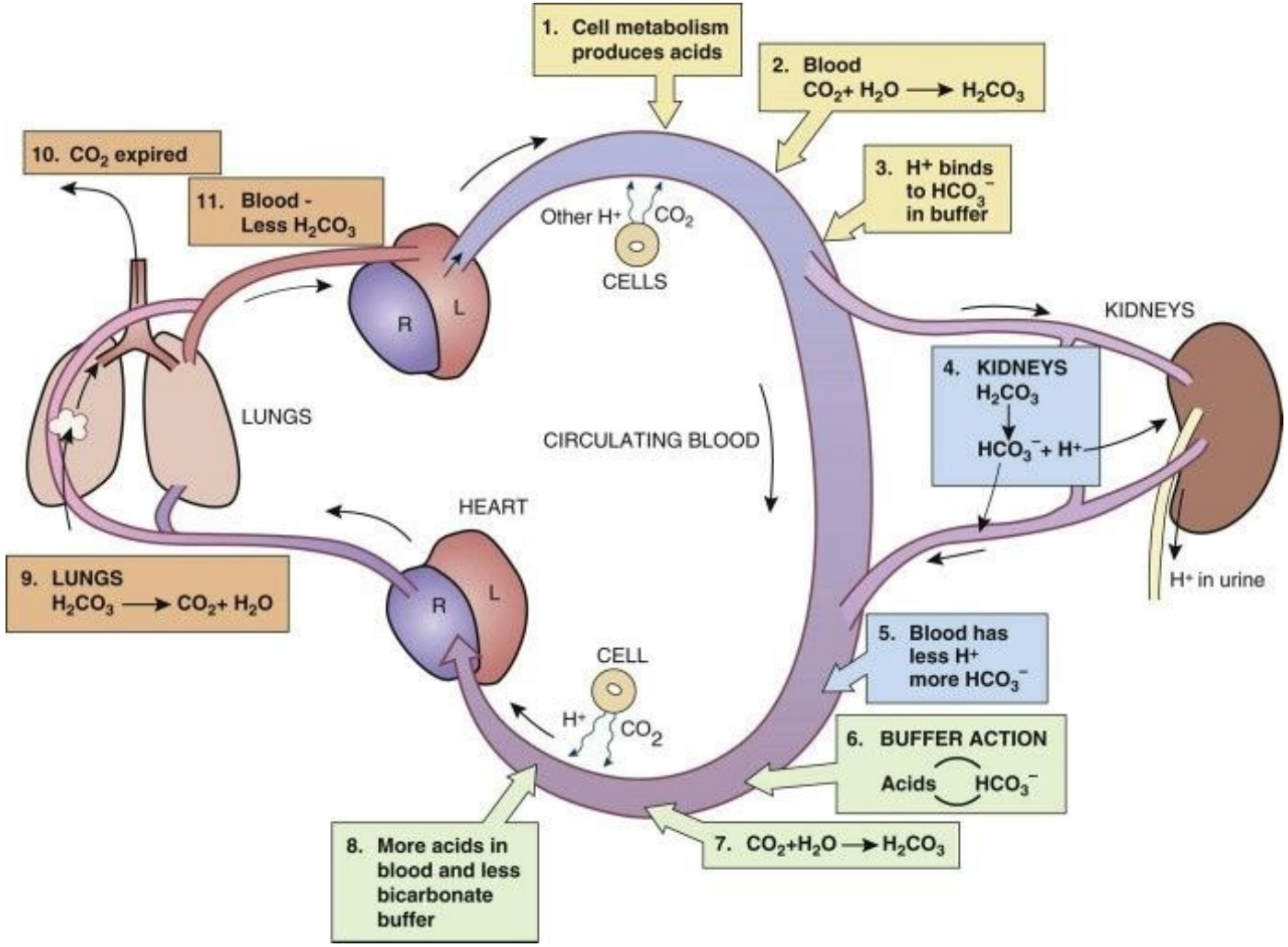
Acid - base balance

- Metabolism (=enzymatic reactions) requires specific acid base surroundings
- Most enzymes require specific pH
- *E.g.,* pH in stomach 1.0-2.0, in blood 7.35-7.45
- Body's acidity is largely based on CO_2 and nonorganic acids produced by the metabolism (phosphor, lactate, and fatty acids)



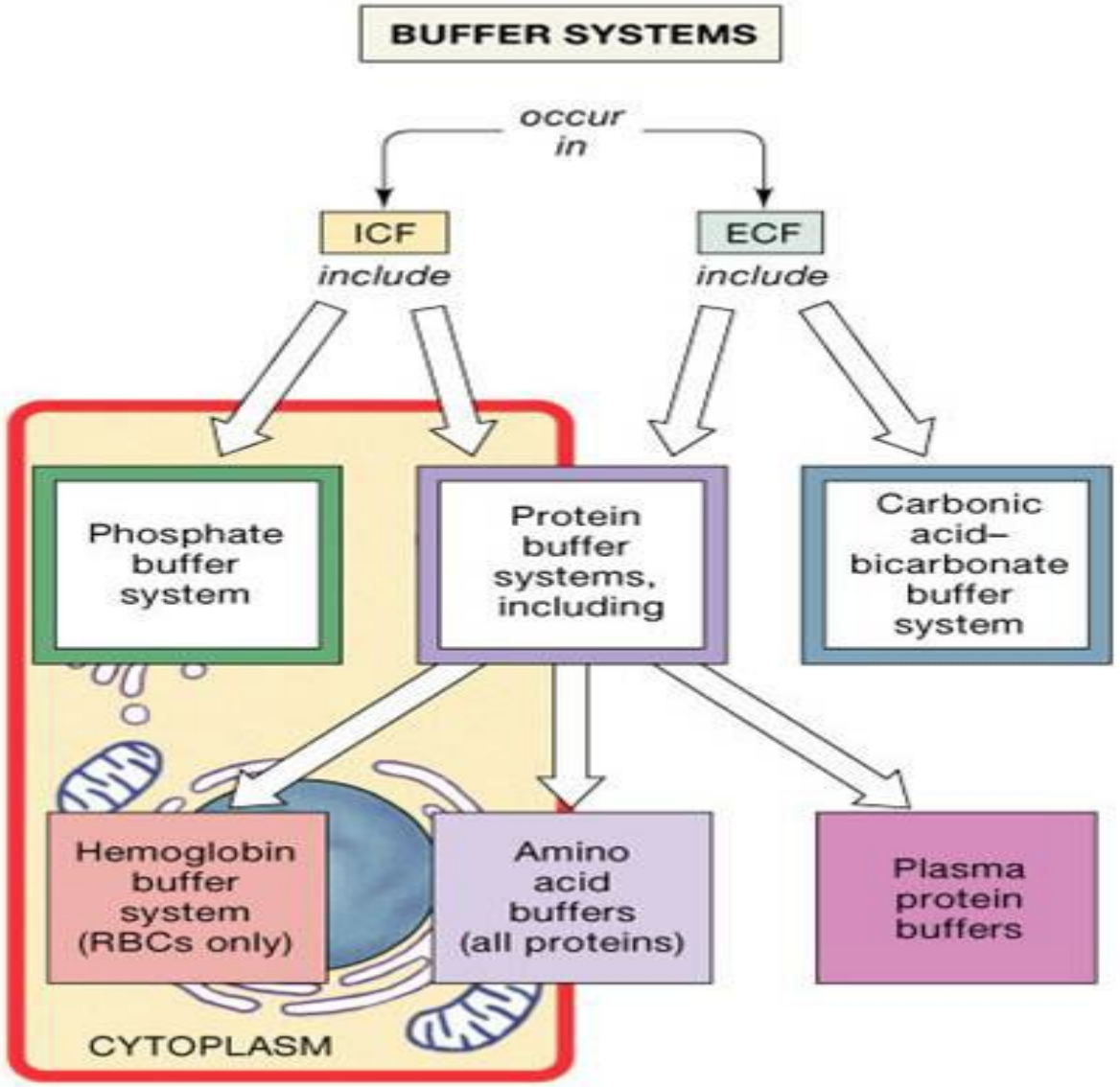
https://understandingnursingscience.wordpress.com/acid-base-balance/

- $CO_2 + H_2O \leftarrow\rightarrow H_2CO_3$
- pH is actively stabilized by three buffer systems: chemical buffers, breathing, kidney excretion
- **The chemical buffers** are fast but limited in their actions



https://understandingnursingscience.wordpress.com/acid-base-balance/

- The chemical buffer systems include carbonic acid bicarbonate system, phosphates, and proteins (e.g., hemoglobin and albumin)
- CO_2 produced by cells reacts with water → H_2CO_3 formed is rapidly broken into H^+ and bicarbonate ions that can balance the acidicity by binding to free H^+ ions
- CO_2 excreted by **breathing**
- **Kidneys** can excrete large amount of H^+ ions and reuptake bicarbonates



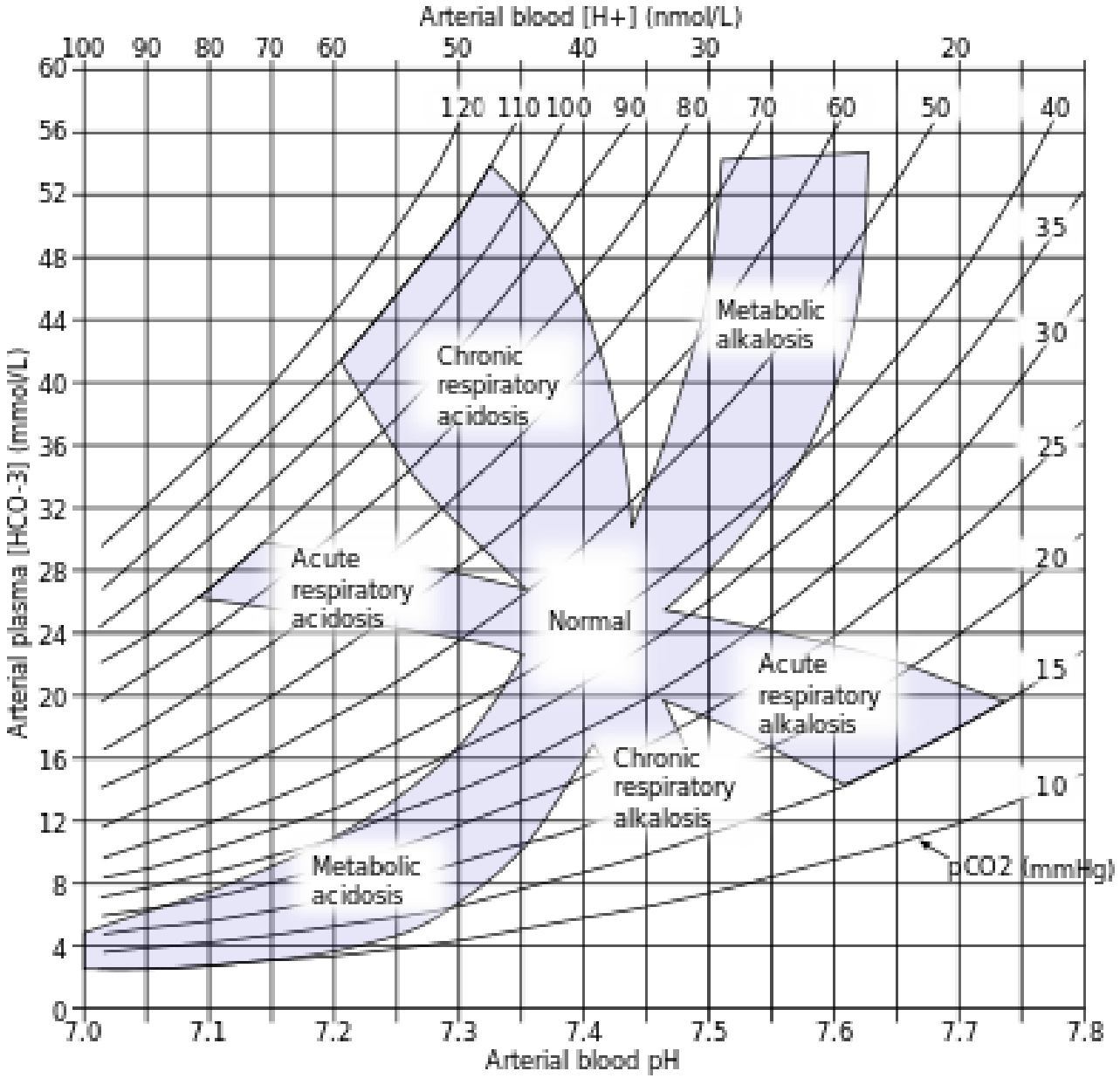
https://www.austincc.edu/apreview/EmphasisItems/Electrolytefluidbalance.html

- *Respiratory acidosis*
  Cause: CO_2 concentration increases due to pulmonary disease or ventilation problem

- *Respiratory alkalosis*
  Cause: Hyperventilation

- *Metabolic acidosis*
  Cause: Kidney failure, accumulation of ketone bodies in insulin-dependent diabetes

- *Metabolic alkalosis*
  Cause: Vomitting



Wikipedia