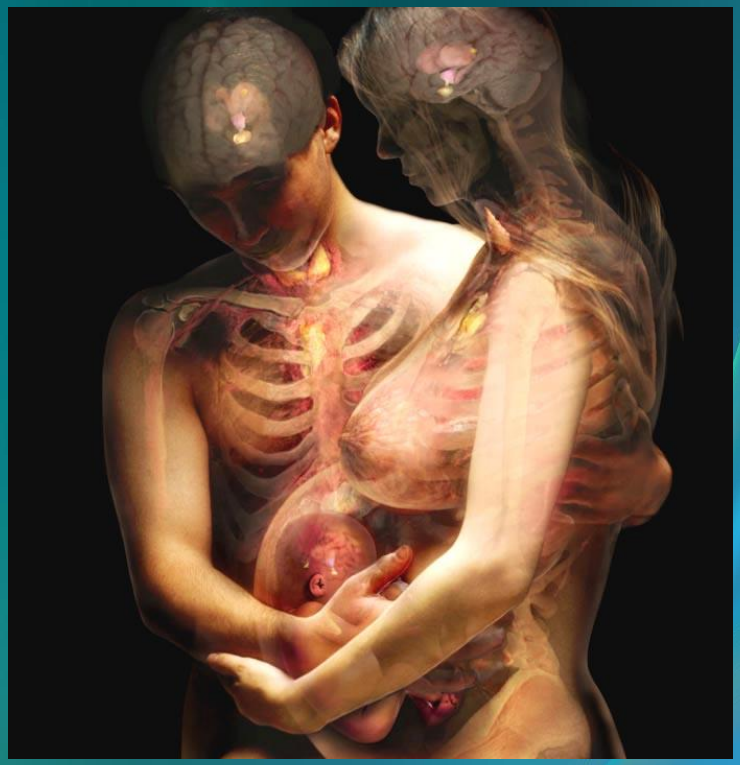
Saladin Chapter 17

The Endocrine System



Comparison of Nervous & Endocrine Systems

- **<u>Neuroendocrine System</u>**

  Nervous system controls through nerve impulses conducted by axons.

  Responses occur within milliseconds.

  Relatively local, specific effects.
  Stops when stimulus stops, adapts quickly.

Comparison of Nervous & Endocrine Systems

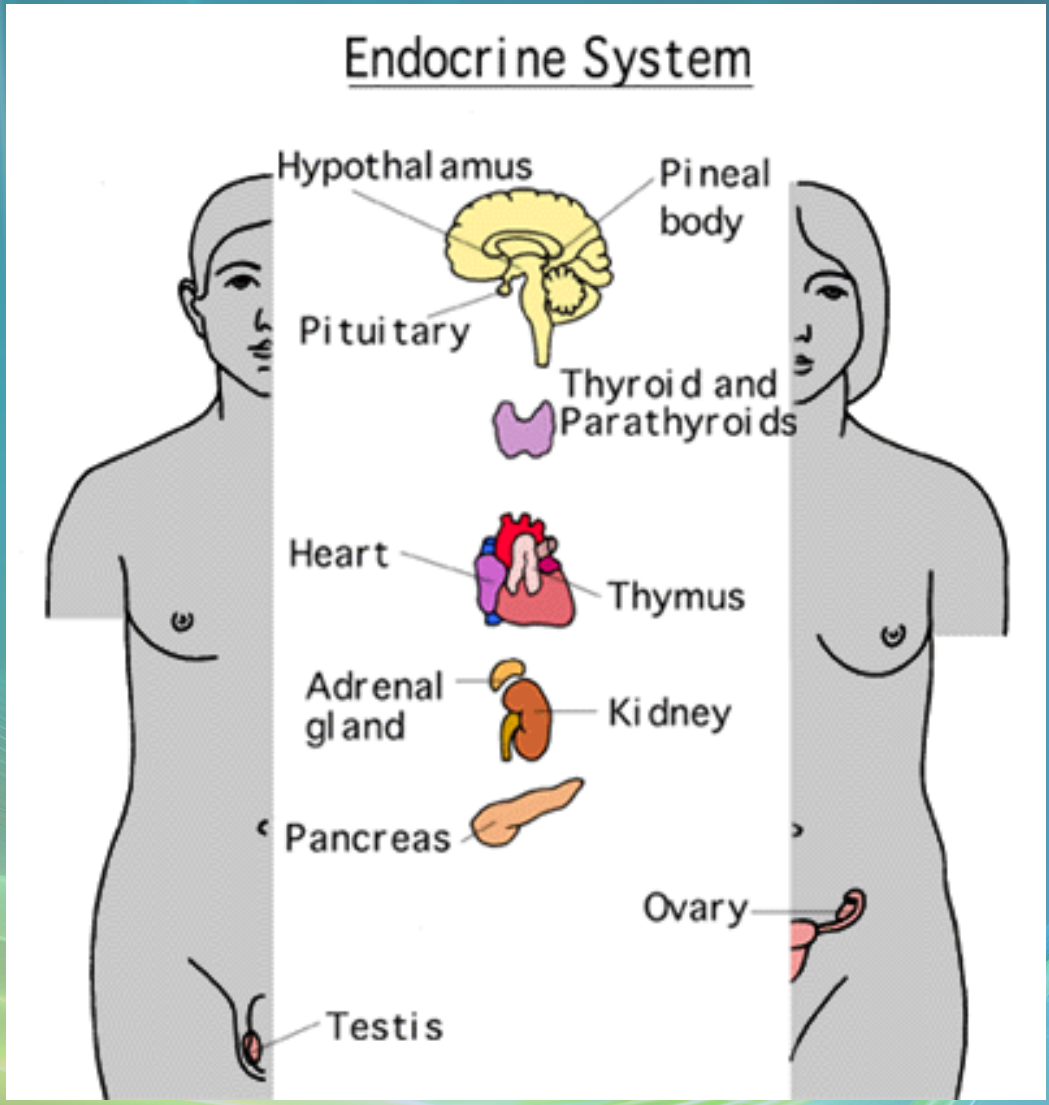
Endocrine system controls through hormones transported in the blood.

May have widespread general effects.

Responses occur after seconds to days & are more prolonged. Adapt slowly

Endocrine Glands - General

- No ducts – secretion into fluid around cells diffuses into capillaries.
- Pituitary, thyroid, parathyroid, adrenal and pineal are examples.
- Many organs have partial endocrine function – hypothalamus, thymus, pancreas, ovaries, testes, kidneys, stomach, small intestine, skin, heart.


Endocrine System
Hypothalamus
Pineal body
Pituitary
Thyroid and Parathyroids
Heart
Thymus
Adrenal gland
Kidney
Pancreas
Ovary
Testis

Endocrine Glands - General

– Hormones – long distance chemical messengers that travel in blood or lymph throughout body.

Hypothalamus & Pituitary Glands

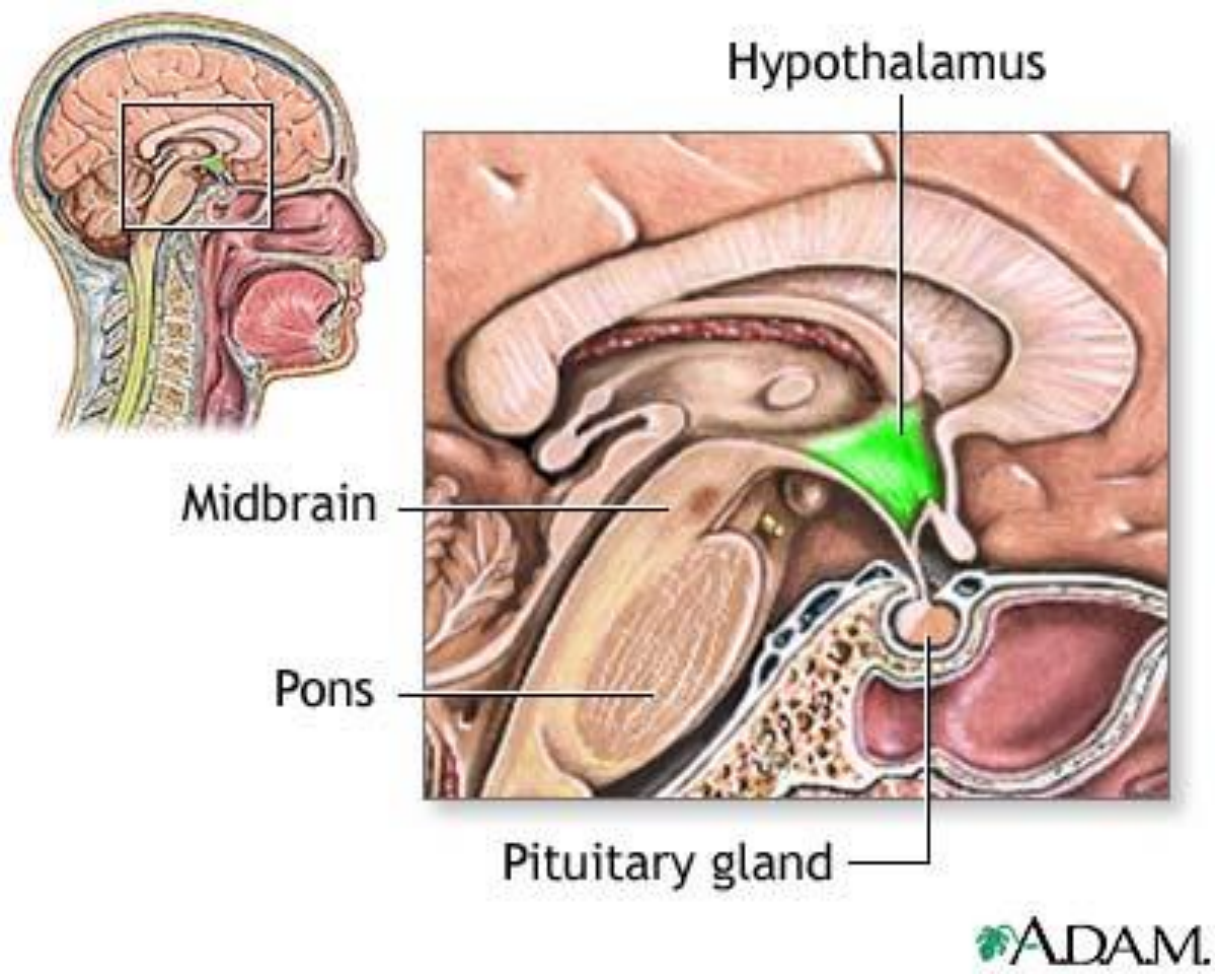
- <u>Anatomy</u>

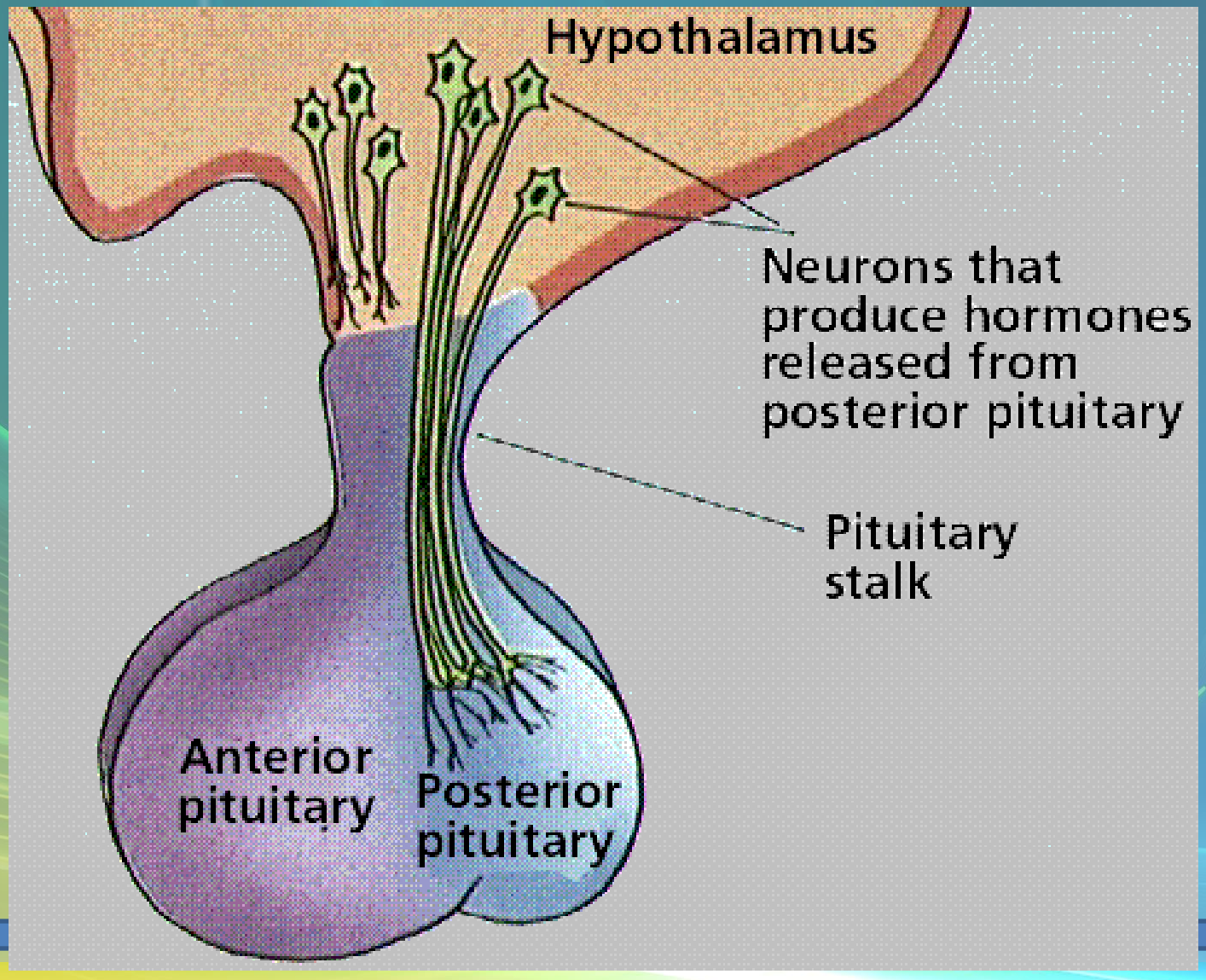
  Hypothalamus floor and walls of third ventricle. Interfaces with ANS

  Pituitary - Anterior [adenohypophysis]

  75% of gland – ectodermal origin

  Regulated by “releasing” hormones from hypothalamus – no neural connection – joined through hypophyseal portal system.


Hypothalamus
Midbrain
Pons
Pituitary gland
A.D.A.M.


Hypothalamus
Neurons that produce hormones released from posterior pituitary
Pituitary stalk
Anterior pituitary
Posterior pituitary

Hypothalamus & Pituitary Glands

5 kinds of gland cells produce trophic hormones (affect other endocrine tissues).

Somatotrophs (hGH)

Thyrotrophs (TSH)

Gonadotrophs (FSH, LH)

Lactotrophs (Prolactin)

Corticotrophs (ACTH, MSH)

Hypothalamus & Pituitary Glands

Posterior [neurohypophysis] – mass of neuroglia and nerve fibers.

25%, ectodermal origin; stores and releases hormones – doesn't make them

Ex. Oxytocin and ADH from hypothalamus

Hypothalamus

- In diencephalon – integrates nervous system & hormones & controls ANS.
- Synthesizes at least 9 hormones- 7 regulate the pituitary.
- Regulates growth and development, metabolism, homeostasis.

Hypothalamus

- Controls secretion of other hormones by other glands.

- Intimately in contact with pituitary by hypophyseal portal system [primary capillary plexus of infundibulum connected by hypophyseal portal veins with secondary capillary plexus in anterior pituitary.]

Hypothalamus Hormones

- A. **Growth Hormone Releasing Hormone (GHRH)**

  Target = anterior pituitary

  Effect = stimulates release of growth hormone (GH)

  Regulation = Plasma levels of glucose, fatty acids, and amino acids; sleep, ANS and other hormones.

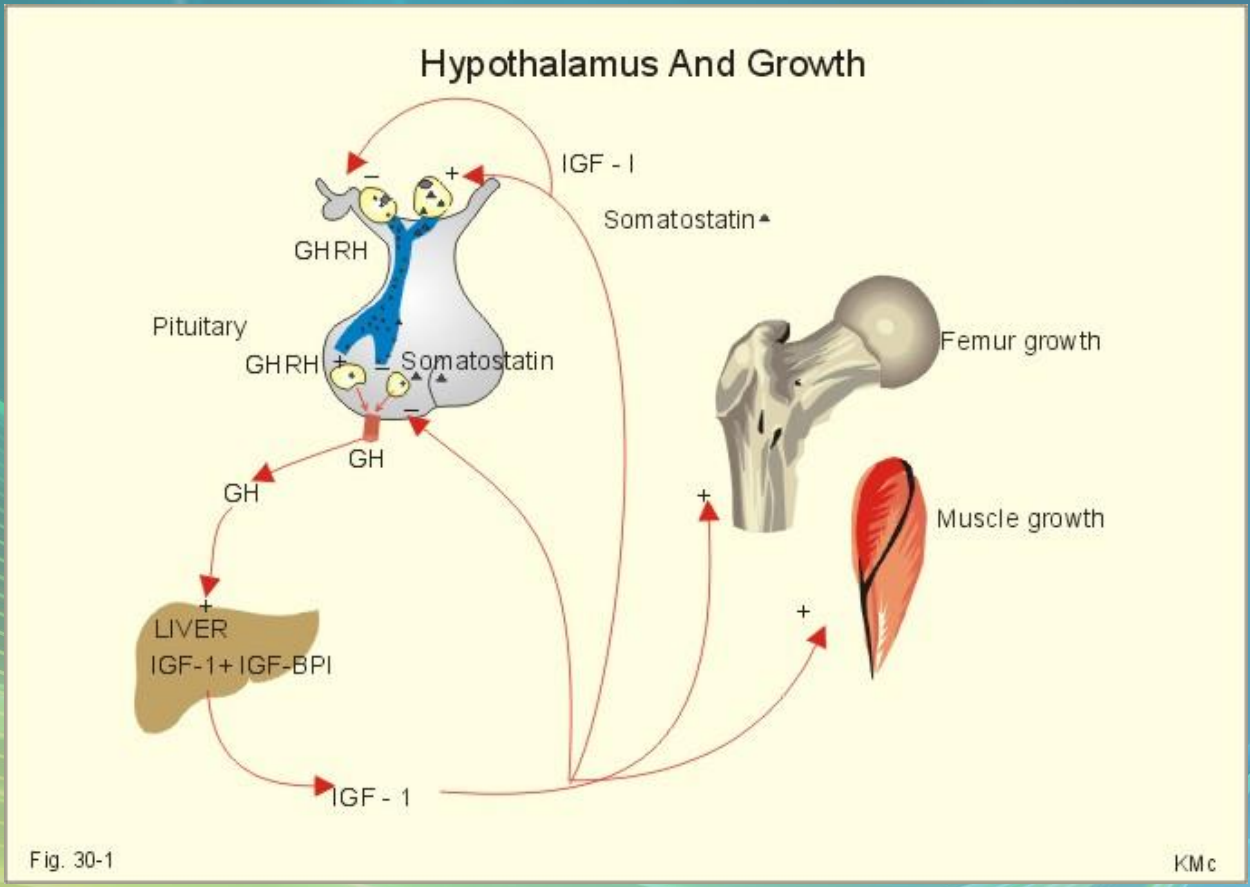
Hypothalamus Hormones

- B. **Growth Hormone Inhibiting Hormone (GHIH)**

  Target = anterior pituitary

  Effect = inhibit release of GH

  Regulation = Plasma levels of glucose, fatty acids and aa's


Hypothalamus And Growth
IGF - I
Somatostatin
GHRH
Pituitary
GHRH
Somatostatin
GH
GH
LIVER
IGF-1+IGF-BPI
IGF - 1
Femur growth
Muscle growth
Fig. 30-1
KMc

Hypothalamus Hormones

- C. **Thyrotropin Releasing Hormone (TRH)**

  Target = anterior pituitary gland

  Effect = stimulate release of Thyroid-stimulating hormone (TSH)

  Regulation = plasma levels of TSH and glucose; metabolic rate

Hypothalamus Hormones

- D. **Corticotropin Releasing Hormone (CRH)**

  Target = anterior pituitary gland

  Effect = stim. release of adrenocorticotropic hormone (ACTH)

  Regulation = blood glucose levels, stress, interleukin -1

Hypothalamus Hormones

- E. **Gonadotropin Releasing Hormone (GnRH)**

  Target = anterior pituitary gland

  Effect = stimulate release of Follicle Stimulating hormone (FSH) &Luteinizing hormone (LH)

Hypothalamus Hormones

Regulation:

Females - plasma estrogen & progesterone levels;

Males – plasma testosterone levels

Hypothalamus Hormones

- F. **Prolactin Releasing Hormone (PRH)**

  Target = anterior pituitary gland

  Effect = stim. release of prolactin (PRL)

  Regulation = suckling

Hypothalamus Hormones

- G. **Prolactin inhibiting Hormone (PIH)**

  Target = anterior pituitary

  Effect = inhibit PRL release

  Regulation = suckling, plasma estrogen & progesterone levels

Hypothalamus Hormones

** 2 hormones are produced in the hypothalamus, & stored in special cells in the posterior pituitary.

- H. **Oxytocin (OT) –** from paraventricular nucleus

  Target = smooth muscle in uterus and breast

  Effect = contraction of muscle (labor, milk ejection, sexual arousal – “cuddle” hormone.)

  Regulation = hormonal changes during pregnancy, suckling

Hypothalamus Hormones

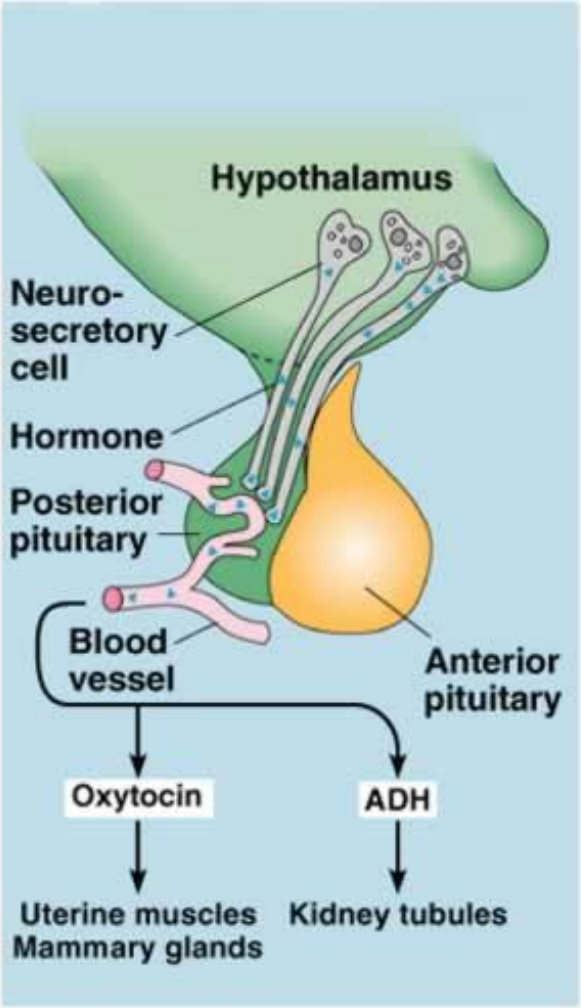
- I. **Antidiuretic Hormone (ADH)**[= vasopressin]

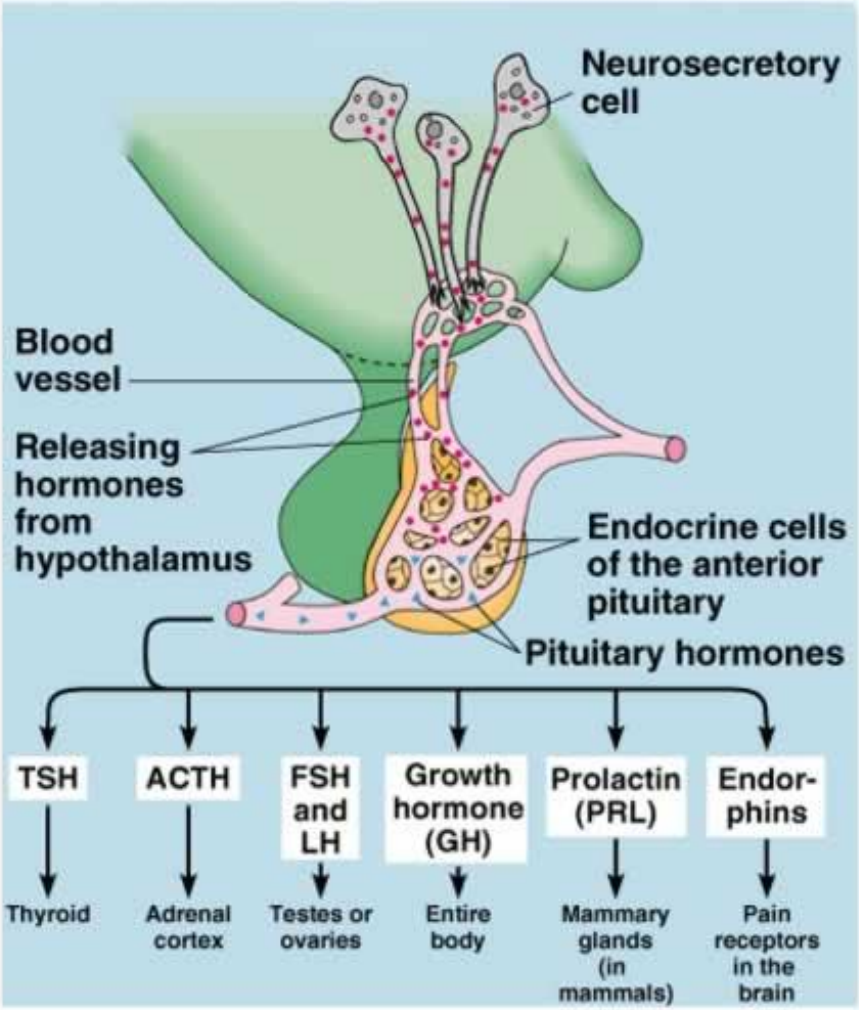
  Target = kidney

  Effect = decrease sweat and urine output; constrict arterioles & increase blood pressure

  Regulation = blood osmotic pressure, stress, drugs [alcohol inhibits ADH].

Hypothalamus &Pituitary Hormones





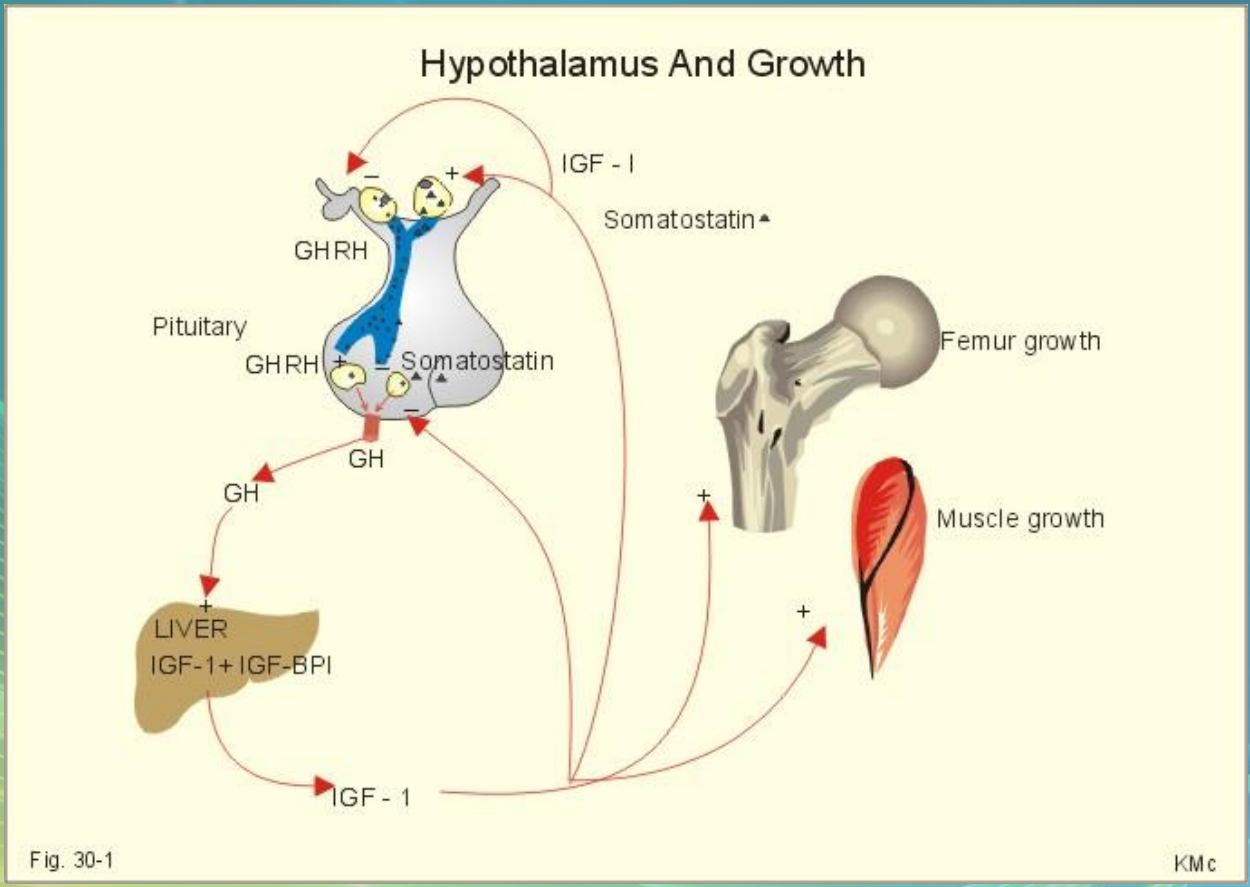
Pituitary Hormones

- **A. Human Growth Hormone (hGH) [Somatotropin]**

  Target = general [bones & skeletal muscles.]

  Effect = ↑ production of insulin-like growth factors. ↑ cell growth & division; ↑protein synthesis & fat catabolism, ↓glucose catabolism

  Regulation = GHRH, GHIH; also affected by stress, nutrition & sleep patterns.


Hypothalamus And Growth
IGF - I
Somatostatin
GHRH
Pituitary
GHRH
Somatostatin
GH
GH
LIVER
IGF-1+IGF-BPI
IGF - 1
Femur growth
Muscle growth
Fig. 30-1
KMc

Pituitary Hormones

- B. **Thyroid-stimulating Hormone (TSH)**

  Target = thyroid gland

  Effect = stim. secretion/release of T3 & T4

  Regulation = TRH

Pituitary Hormones

- C. **Adrenocorticotropic Hormone (ACTH)**

  Target = adrenal cortex

  Effect = stimulate glucocorticoids

  Regulation = CRH. Also affected by stress, hypoglycemia.

Pituitary Hormones

- D. **Follicle-Stimulating Hormone (FSH)**

  Target = gonads (ovary, testis)

  Effect:

  Stimulates production of gametes (male & female)

Pituitary Hormones

Stimulates production of estrogen (female)

Regulation = GnRH, inhibin, estrogen (F) & testosterone (M)

Pituitary Hormones

- E. **Luteinizing Hormone (LH)**

  Target = gonads

  Effect:

  (F) stimulates ovulation, formation of corpus luteum and prod. of Estrogen & Progesterone.

Pituitary Hormones

(M) stimulates prod. of testosterone, LH also called interstitial cell stimulating hormone (ICSH) in male

Regulation = GnRH

Pituitary Hormones

- F. **Prolactin (PRL)** or Lactogenic Hormone

  Target = breast

  Effect = milk production

  Regulation = PRH, PIH, estrogen.

Pituitary Hormones

- G. **Melanocyte-Stimulating Hormone (MSH)**

  Target = melanocytes

  Effect = increases production of melanin; CNS neurotransmitter

  Regulation = MRH, MIH

Pituitary Hormones

- <u>Control of Pituitary Secretion</u>

  Timing & amount of secretion are regulated by hypothalamus, brain centers & feedback from target organs.

  Hypothalamus & Cerebral Control – releasing & inhibiting hormones. Brain monitors conditions & stimulates their release.

Pituitary Hormones

Neuroendocrine reflexes affect posterior lobe of the pituitary - in response to neurosensation [e.g., suckling].

Feedback from targets – negative feedback inhibition for the most part [note oxytocin response is positive].

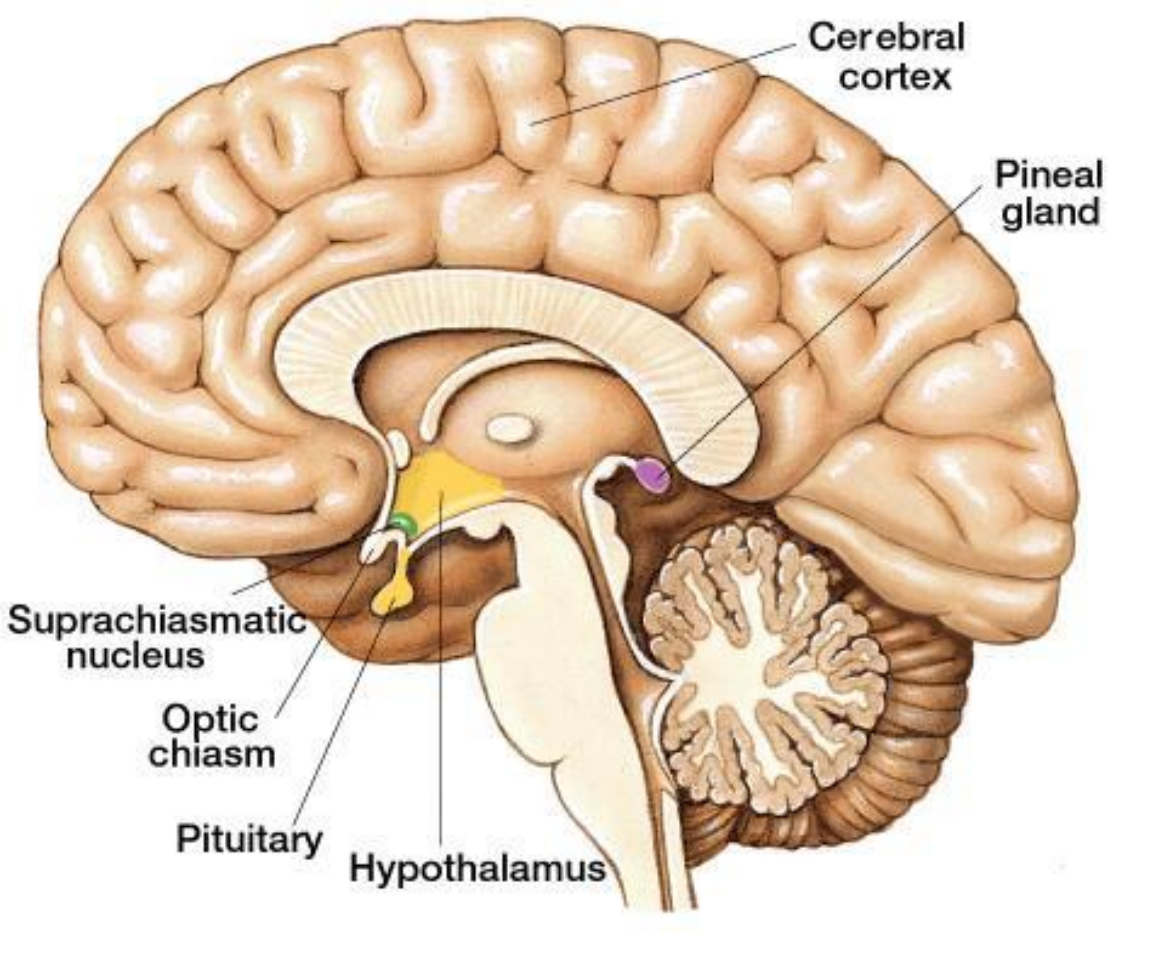
Pineal Gland

- Pineal Gland – roof of third ventricle – capsule of pia mater. Decreases in size with age.

  Cells = pinealocytes

  Function – not clear

  Produces melatonin [at night], & serotonin [by day] – may affect circadianrhythms, timing of puberty, & mood [SAD & PMS]

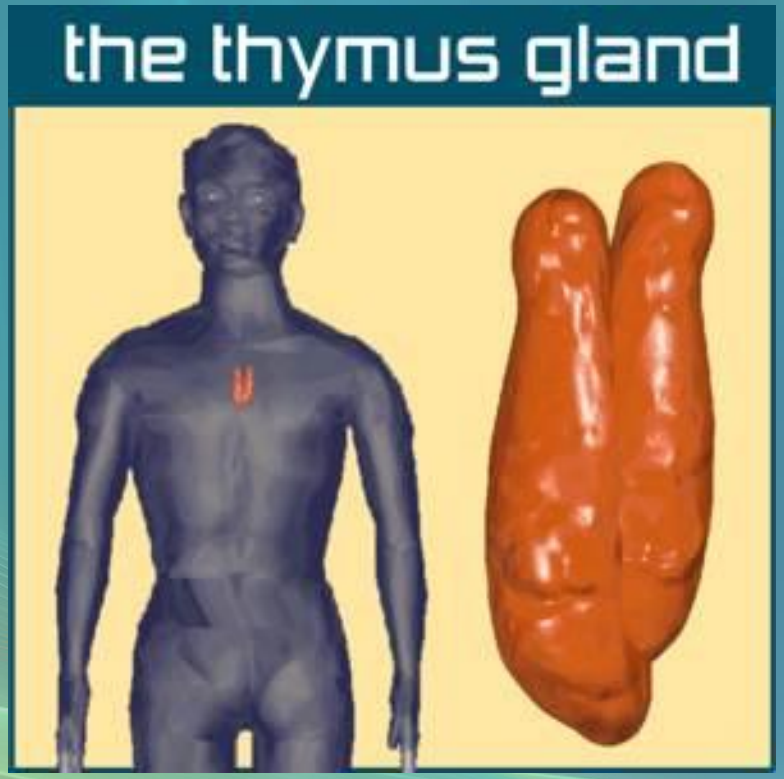

Cerebral cortex
Pineal gland
Suprachiasmatic nucleus
Optic chiasm
Pituitary
Hypothalamus

Thymus

- Thymus – over heart

  Functions in immunity, decreases in size with age.

  Produces thymopoietin & thymosin needed for T cell maturation.

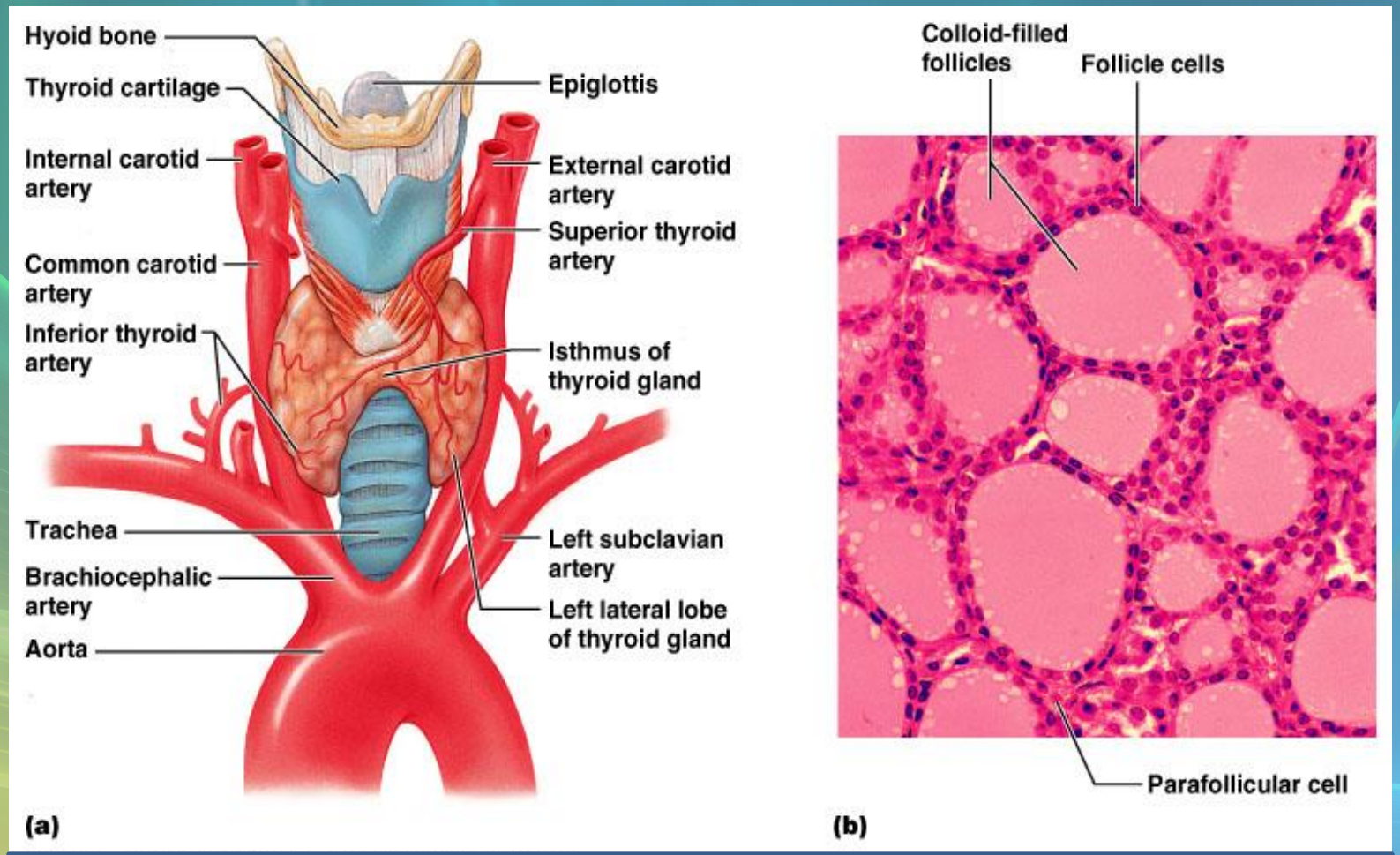

the thymus gland

Thyroid

- General

  Lateral lobes connected by isthmus anterior to trachea

  Follicles – made of follicular cells produce T3 & T4 upon TSH stimulation


Hyoid bone
Thyroid cartilage
Internal carotid artery
Common carotid artery
Inferior thyroid artery
Trachea
Brachiocephalic artery
Aorta
Epiglottis
External carotid artery
Superior thyroid artery
Isthmus of thyroid gland
Left subclavian artery
Left lateral lobe of thyroid gland
(a)
Colloid-filled follicles
Follicle cells
Parafollicular cell
(b)

Thyroid

Parafollicular cells – produce calcitonin

Hormones are stored in large quantities – only gland that does this - in colloid in follicle cavity.

Thyroid Hormones

- *T3, T4 [main]*

  Target – general

  Effect – regulate O_2 use, basal metabolic rate, growth & development - T3 more potent than T4

  Regulation – TSH from pituitary, TRH from hypothalamus

Thyroid Hormones

Calcitonin

Target – bone

Effect – inhibit osteoclasts, decrease Ca^{2+} release into blood, increase Ca^{2+} uptake into bone

Regulation – Ca^{2+} levels

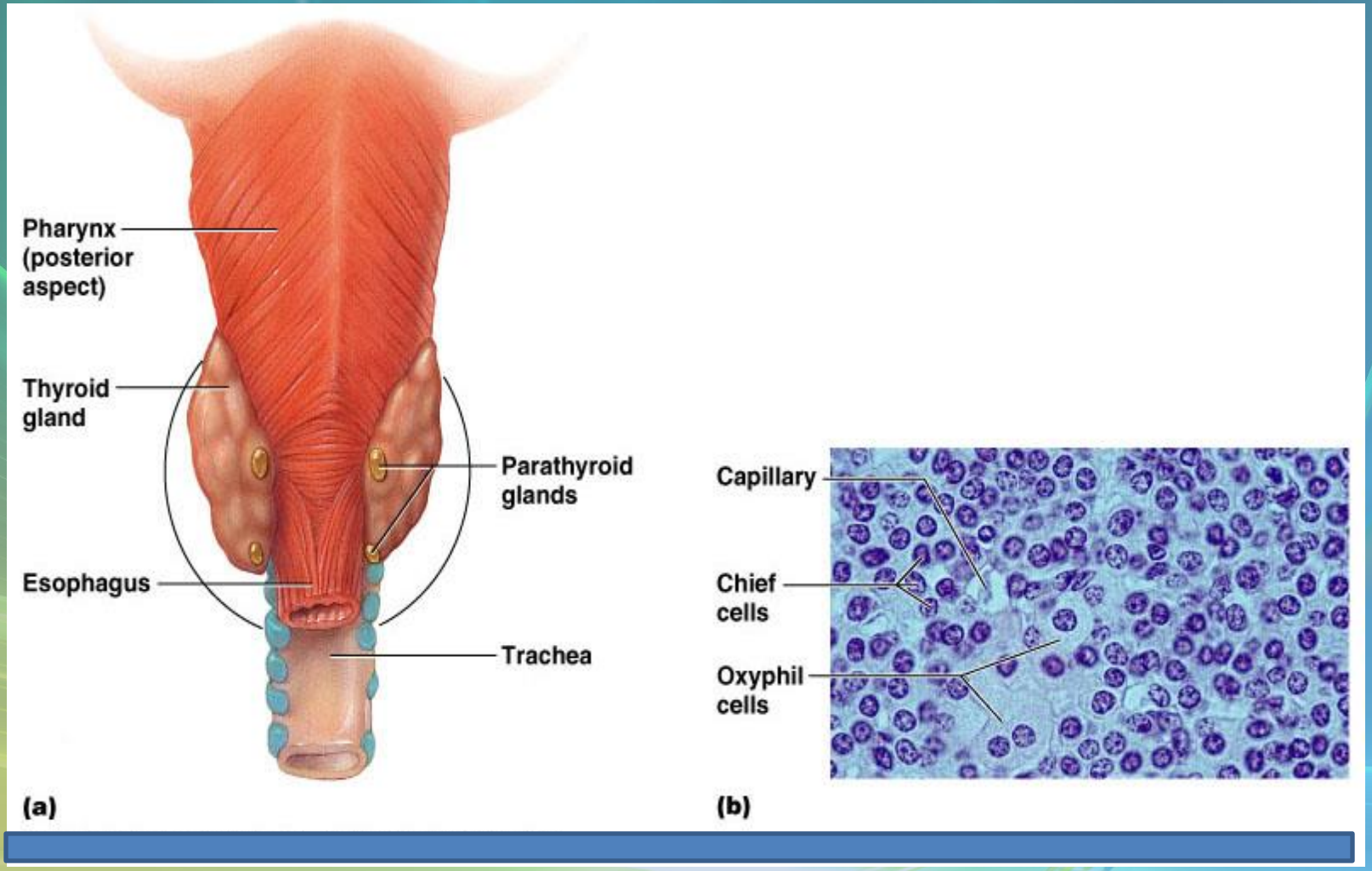
Parathyroids

- Posterior surface of lobes of thyroid – 2/ side

- Hormone –

  ↑ number & activity of osteoclasts.

  Most important hormone in regulation of Ca^{2+} balance.


Pharynx (posterior aspect)
Thyroid gland
Parathyroid glands
Esophagus
Trachea
(a)
Capillary
Chief cells
Oxyphil cells
(b)

Parathyroids

↑ bone resorption, which ↑blood Ca^{2+} & HPO_4^{2-}

Kidney changes: ↑ rate of removal of Ca^{2+} & Mg^{2+} from urine & return to blood

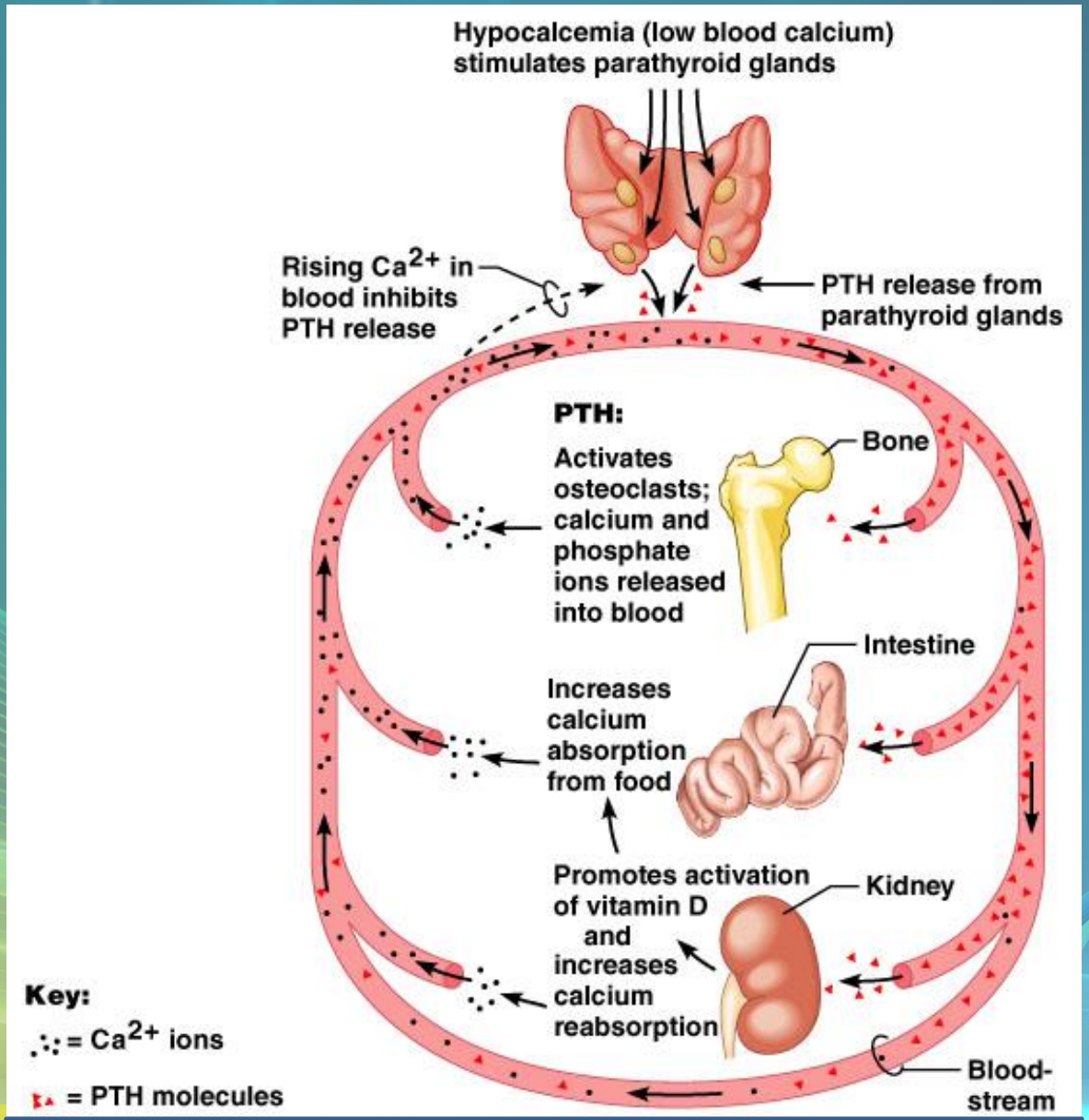
Net effect – ↑circulating Ca^{2+} & ↓ HPO_4^{2-}

Parathyroids

Calcitonin is PTH antagonist

Also promotes formation of calcitriol from vitamin D, which increases rate of Ca^{2+}, Mg^{2+}, & HPO_4^{2-} from GI

Control – Negative feedback via blood Ca^{2+} levels


Hypocalcemia (low blood calcium) stimulates parathyroid glands
Rising Ca^{2+} in blood inhibits PTH release
PTH release from parathyroid glands
PTH:
Activates osteoclasts; calcium and phosphate ions released into blood
Bone
Intestine
Increases calcium absorption from food
Promotes activation of vitamin D and increases calcium reabsorption
Kidney
Blood-stream
Key:
= Ca^{2+} ions
= PTH molecules

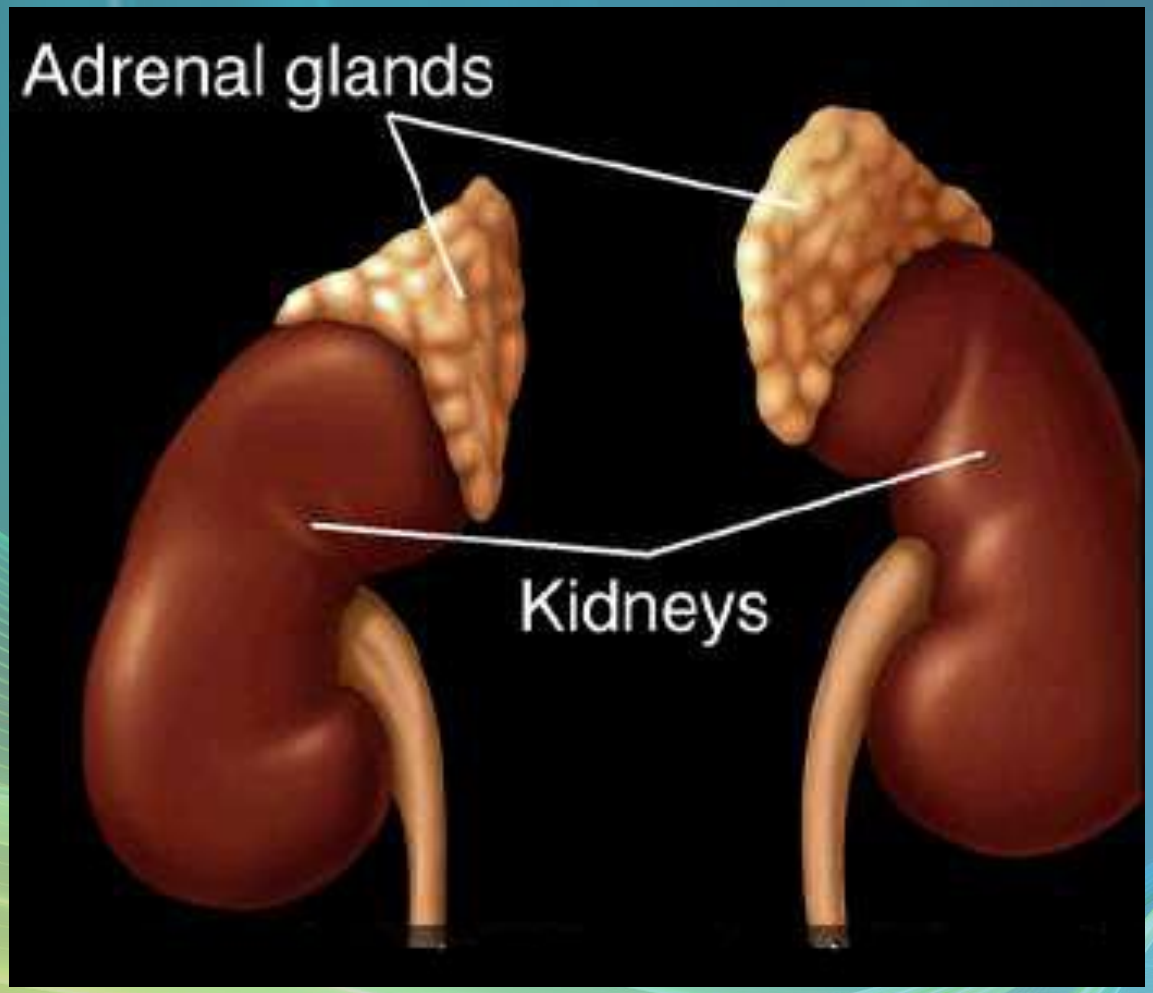
Adrenal Glands

- **Adrenal Glands** – 1 on top of each kidney – 2 regions – cortex & medulla

Adrenal Medulla

Inner part of adrenal – not essential to life.

Chromafin cells –sympathetic neurons specialized for hormone secretion.


Adrenal glands
Kidneys

Adrenal Glands

Produce catecholamines – epinephrine [80%] & norepinephrine – ANS sympathetic system [glycogenolysis, gluconeogenesis, glucose-sparing, etc.]

Link to cortex – under stress, catecholamine secretion stimulates corticosterone secretion.

Adrenal Glands

Cortex – 80-90%

Derived from mesoderm

Produce over 2 dozen steroid hormones essential to life from cholesterol.

Adrenal Cortex

3 zones:

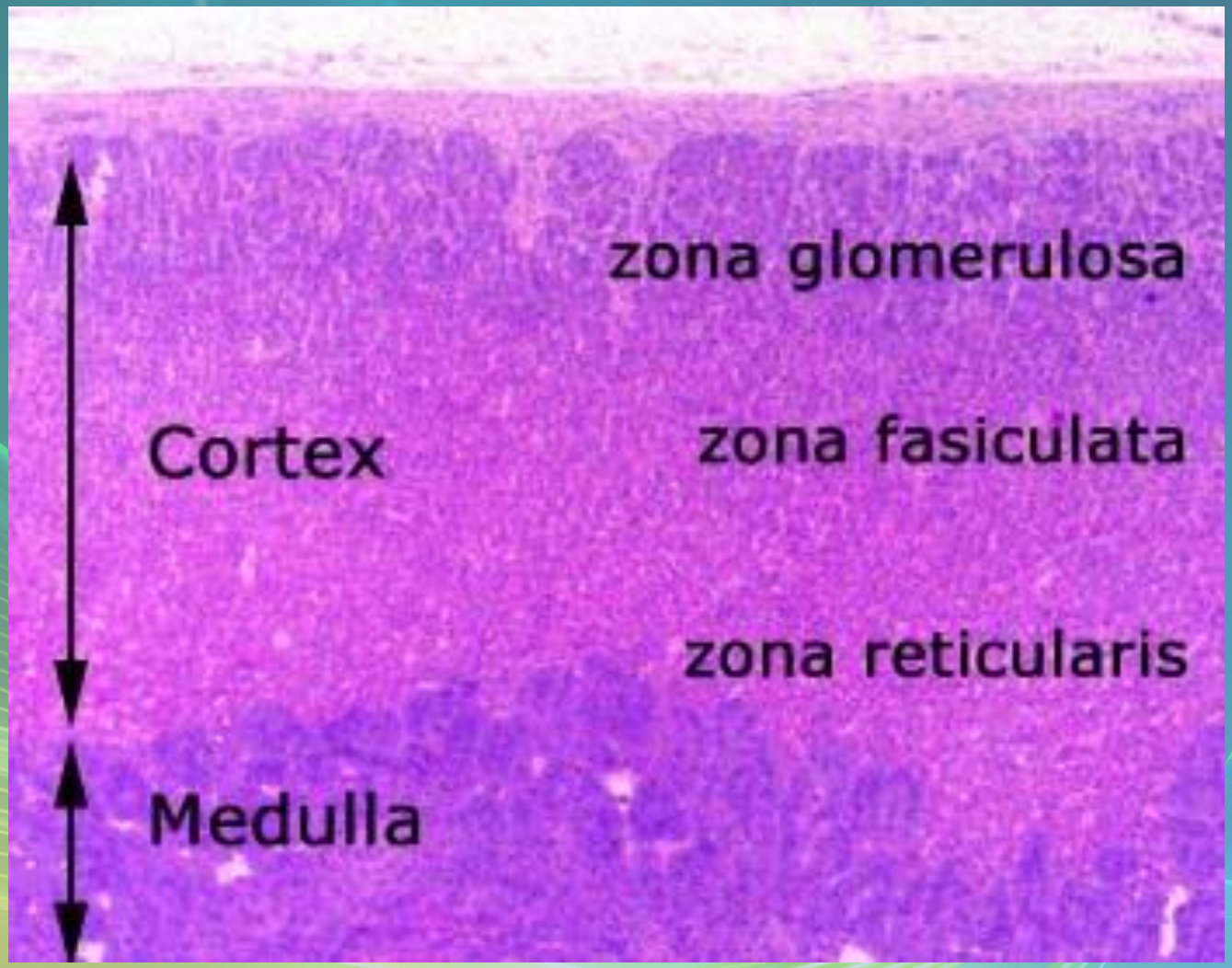
Zona glomerulosa – outer zone

Produces mineralcorticoids – affect Na^+ & K^+

Aldosterone – 95%

- Acts on kidney tubules

- Causes resorption of Na^+ which also increases resorption of Cl^-, HCO_3^- & H_2O


zona glomerulosa
Cortex
zona fasiculata
zona reticularis
Medulla

Adrenal Cortex

- Promotes secretion of K^+, which ↑ K^+ excretion

- Control – 4 mechanisms
  1. Renin-angiotensin pathway
  - » Decrease in blood volume causes decrease in blood pressure.
  - » This stimulates renin secretion by the kidney, which causes Angiotensinogen to be converted to angiotensin I in the liver.

Adrenal Cortex

- This promotes conversion to angiotensin II in the lung, which causes aldosterone secretion which ↑blood volume & ↑in blood pressure.

- A second target for angiotensin II is arteriole walls – they constrict which further increases blood pressure.

Adrenal Cortex

2. Plasma Na^+ & K^+ concentrations – ↑ inhibits, ↓ stimulates.

3. ACTH – in stress, causes ↑aldosterone.

4. ANP – inhibits renin-angiotensin system.

Adrenal Cortex

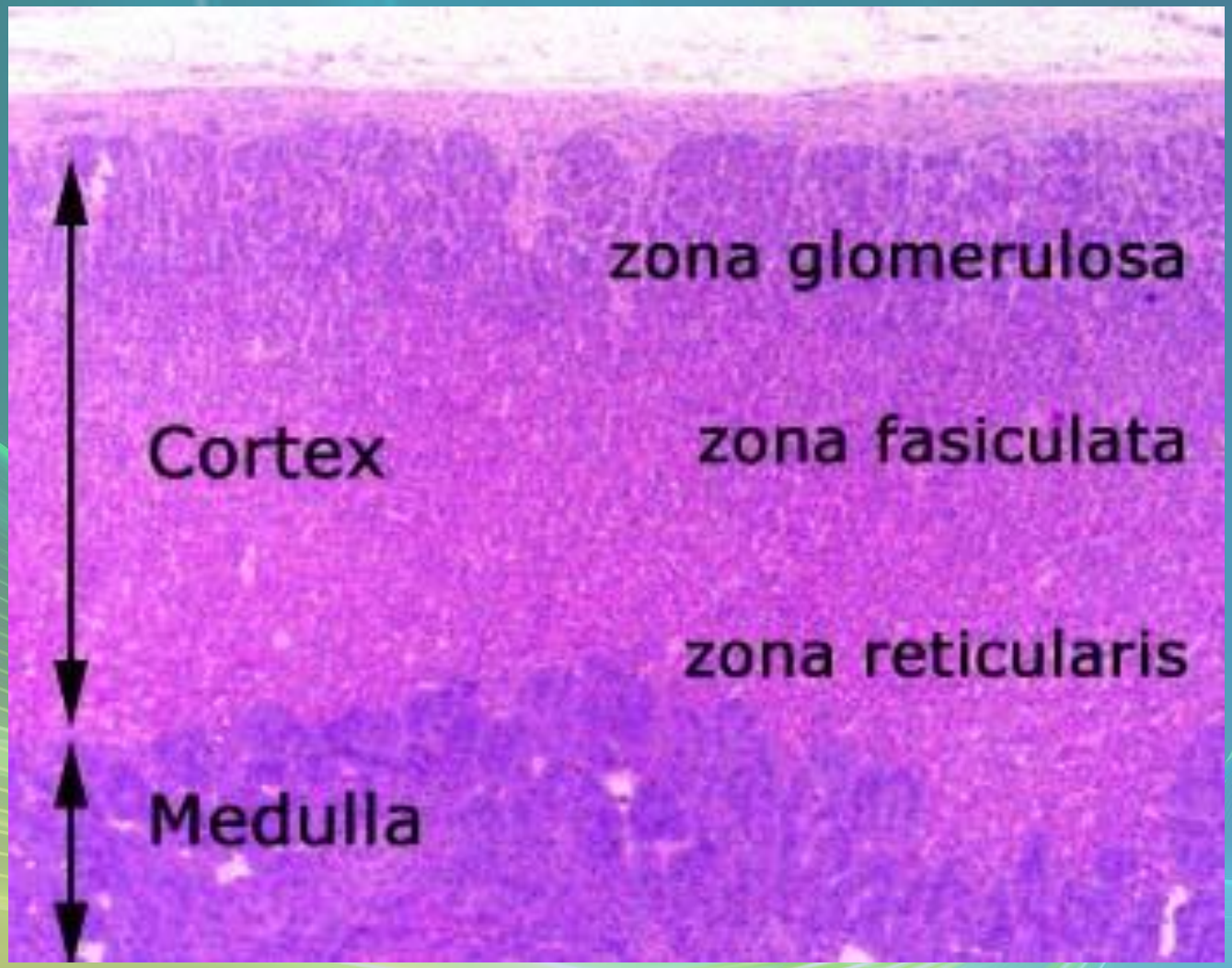
Zona fasciculata –> glucocorticoids regulate metabolism & resist stress

Cortisol [95%], corticosterone, cortisone,

Effects – stimulate:

Protein breakdown/construction

Gluconeogensis


zona glomerulosa
Cortex
zona fasiculata
zona reticularis
Medulla

Adrenal Cortex

Lipolysis – breakdown of lipids

Stress resistance – ↑ glucose & Bp

Anti-inflammatory – ↓mast cells which reduces release of histamine; also ↓vessel permeability which reduces swelling, but ***<u>also slows healing</u>***

Adrenal Cortex

Depression of immunity – helps with organ transplants

Control – negative feedback – blood levels of glucocorticoids ↓ → ↑ in CRH, which ↑release of ACTH, which goes to cortex & ↑glucocorticoid secretion.

Adrenal Cortex

Zona reticularis – produces androgens & some estrogens

- This is not significant in males since the testes make more

- In females – affect libido, increase axial & pubic hair,

- Affect pre-pubertal growth spurt

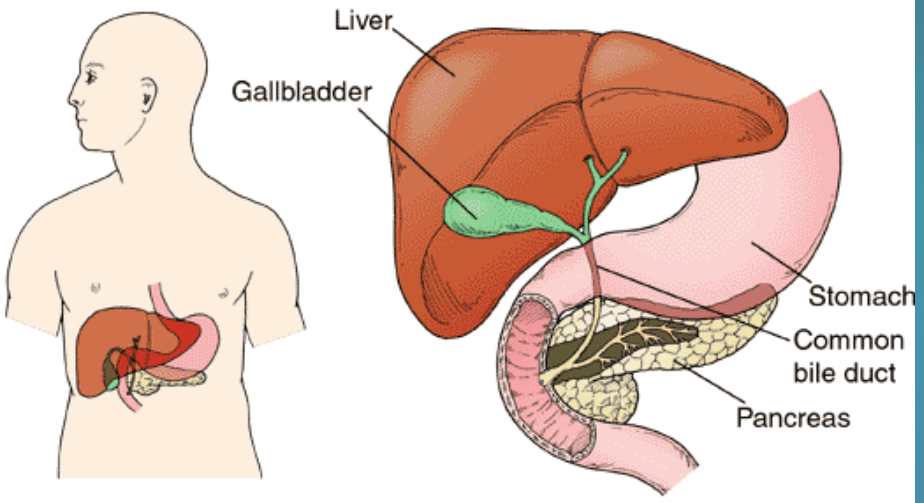
Pancreas

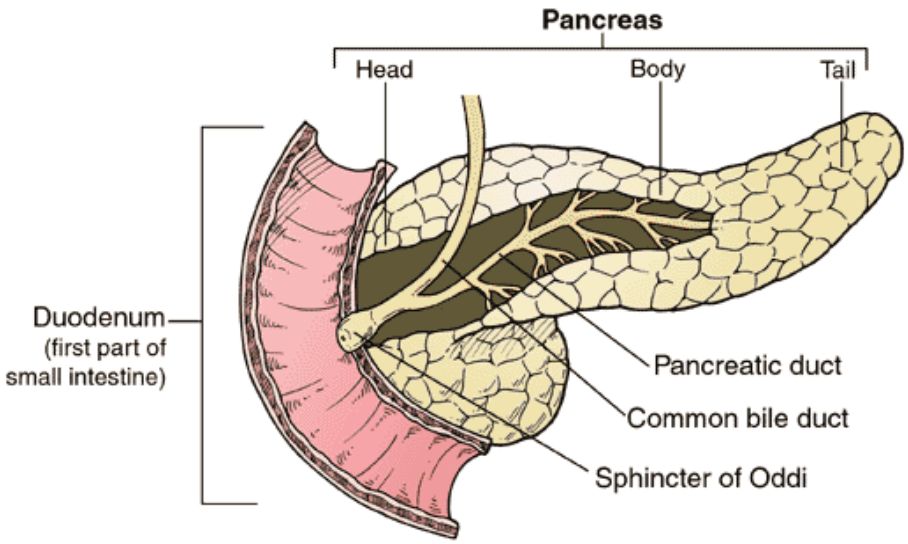
- Endocrine & exocrine – posterior & slightly inferior to stomach

  Exocrine function – 98% – production of digestive enzymes by acinar cells

  Endocrine function – Islets of Langerhans

Pancreas





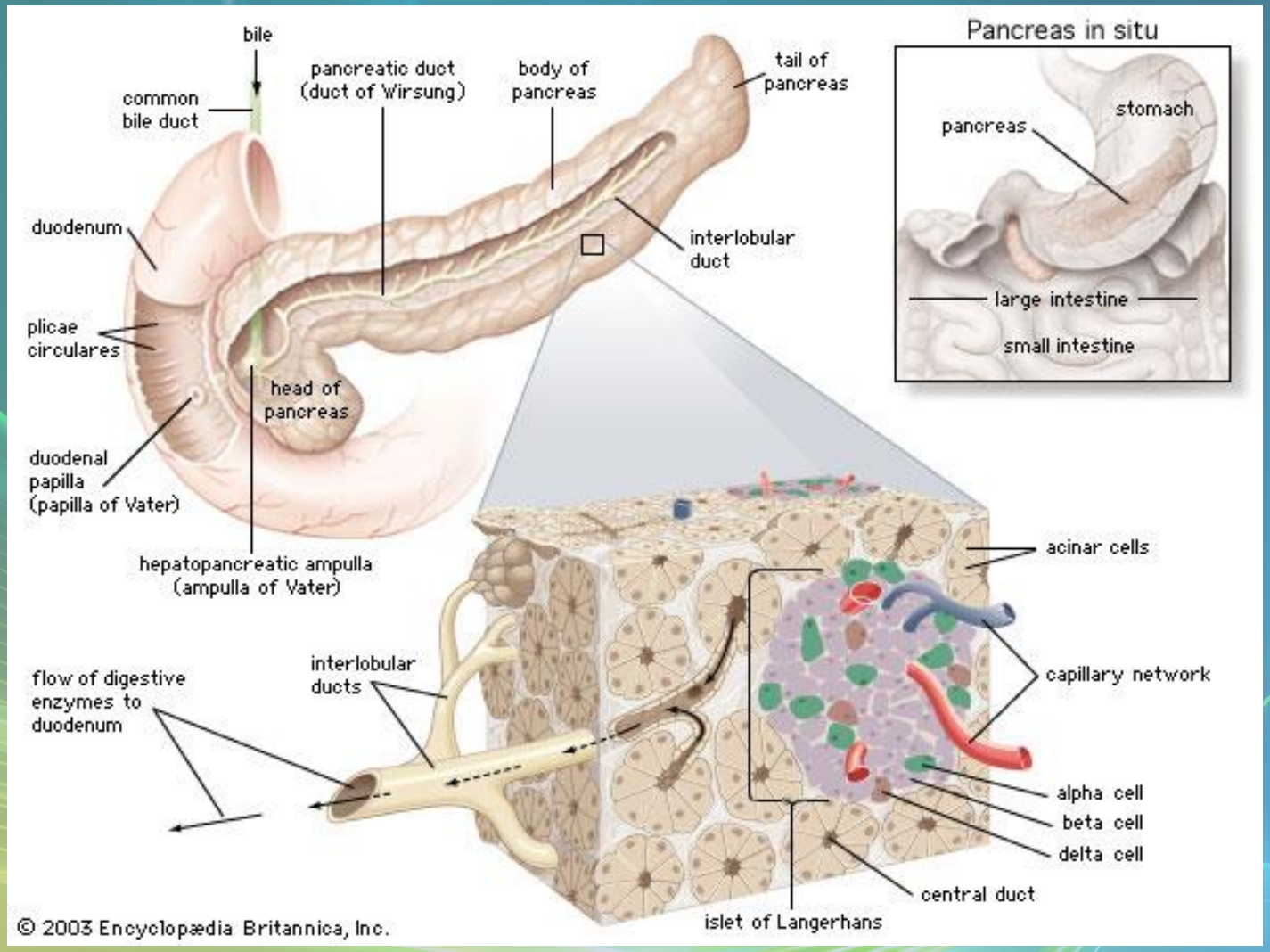
Pancreas

3 main types of cells

α–- produce glucagon

β – produce insulin

Δ – produce somatostatin


bile
common bile duct
pancreatic duct (duct of Wirsung)
body of pancreas
tail of pancreas
duodenum
interlobular duct
plicae circulares
head of pancreas
duodenal papilla (papilla of Vater)
hepatopancreatic ampulla (ampulla of Vater)
Pancreas in situ
pancreas
stomach
large intestine
small intestine
acinar cells
capillary network
flow of digestive enzymes to duodenum
interlobular ducts
alpha cell
beta cell
delta cell
central duct
islet of Langerhans
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Pancreatic Hormones

- Insulin

  Target – general

  Effect – ↓ blood glucose & ↑diffusion of glucose into cells [not kidney, liver & brain],↑glycogenesis, ↑ uptake of amino acids & peptide formation (↓ gluconeo-genesis), ↑ glucose change to fat & ↑ cellular respiration. ↓glycogenolysis.

Pancreatic Hormones

Regulation –blood levels of glucose, amino acids & fatty a's.

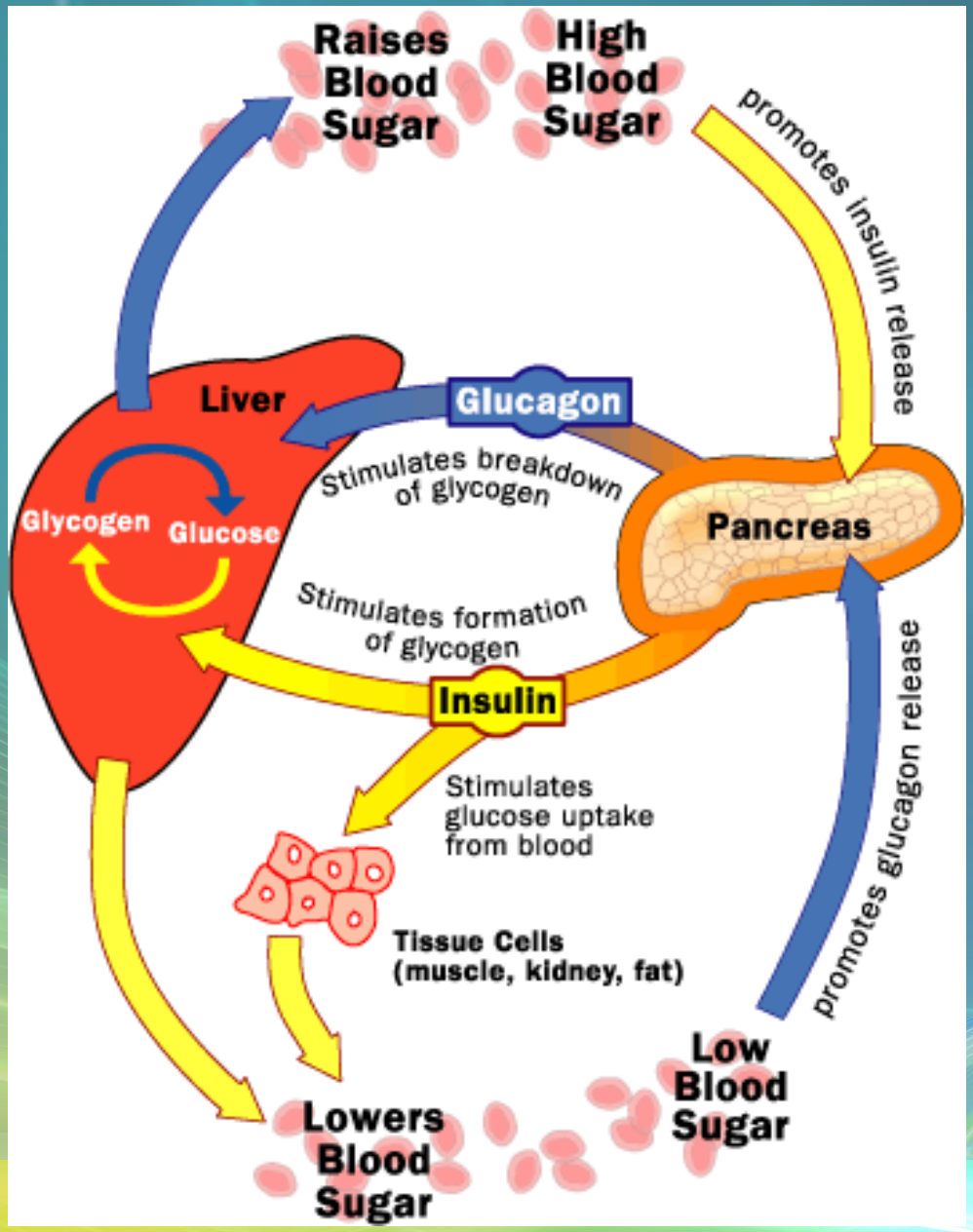
Pancreatic Hormones

- Glucagon

  Target – liver

  Effect: ↑blood glucose levels by stimulating gluconeogenesis & glycogenolysis.

  Regulation – blood glucose levels, ANS & Insulin


Raises Blood Sugar
High Blood Sugar
promotes insulin release
Liver
Glucagon
Stimulates breakdown of glycogen
Glycogen
Glucose
Pancreas
Stimulates formation of glycogen
Insulin
Stimulates glucose uptake from blood
Tissue Cells (muscle, kidney, fat)
promotes glucagon release
Low Blood Sugar
Lowers Blood Sugar

Pancreatic Hormones

- Somatostatin (GHIH)

  Target – digestive tract and pancreas

  Reduces acid secretion

  Inhibits secretion of glucagon

  Attenuates further insulin release

Ovaries

- <u>Ovaries</u>

  Estrogens [granulose cells of follicle & corpus luteum] & progesterone

  Regulate female reproductive cycle

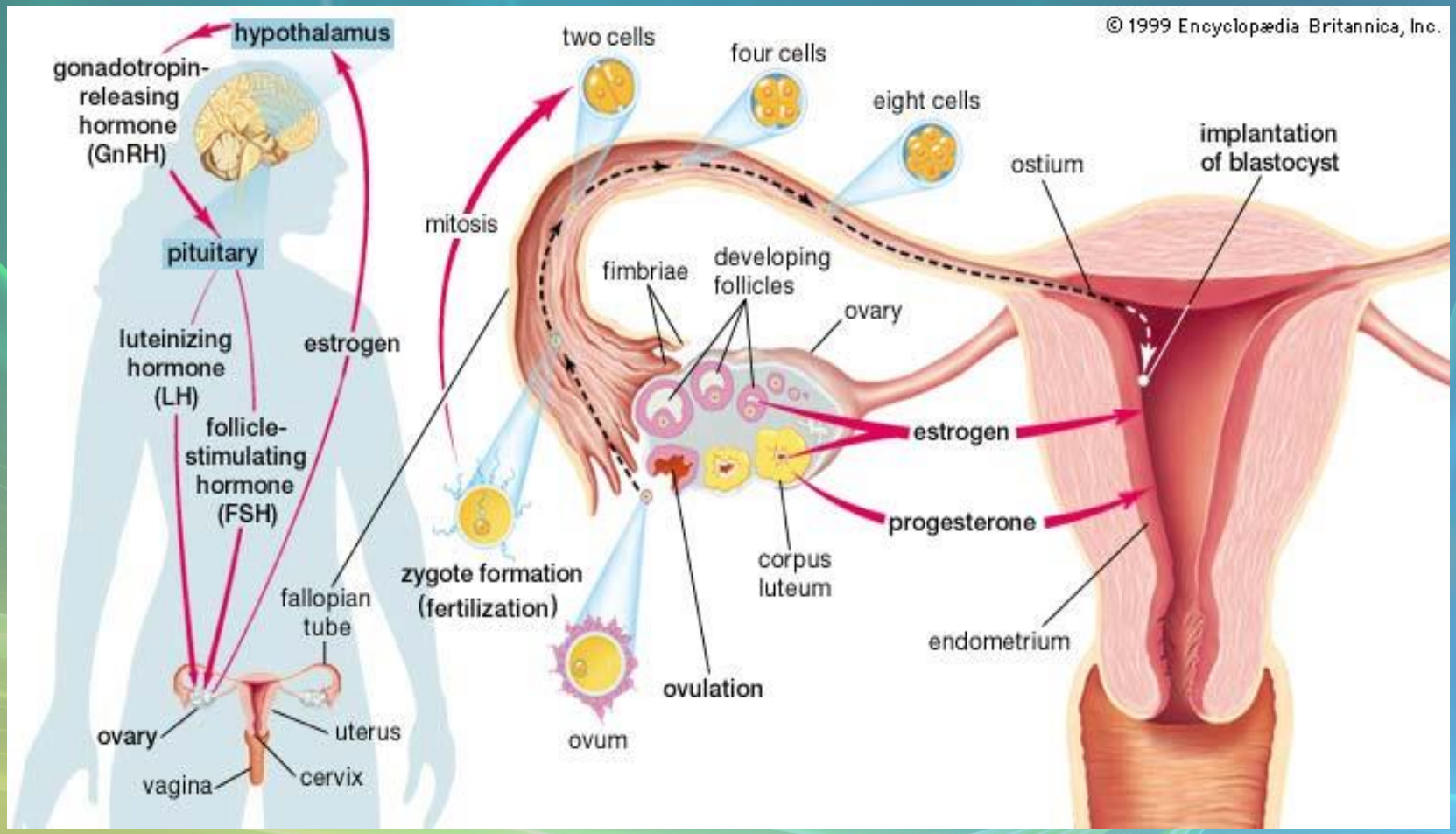
  Maintain pregnancy

  Prepare mammaries for lactation

Ovaries

Develop and maintain secondary sexual characteristics

Inhibin – suppresses FSH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hypothalamus
gonadotropin-releasing hormone (GnRH)
pituitary
luteinizing hormone (LH)
follicle-stimulating hormone (FSH)
estrogen
fallopian tube
ovary
uterus
vagina
cervix
mitosis
zygote formation (fertilization)
two cells
four cells
eight cells
fimbriae
developing follicles
ovary
ovulation
ovum
corpus luteum
estrogen
progesterone
ostium
implantation of blastocyst
endometrium

Testes

- <u>Testes</u>

  Testosterone – androgen [by interstitial cells]

  Regulates production of sperm, sex drive

Testes

Regulates development of male secondary characteristics

Inhibin [by Sertoli cells]

Heart

- Heart – ANP

  Reduces blood volume, pressure & sodium concentration.

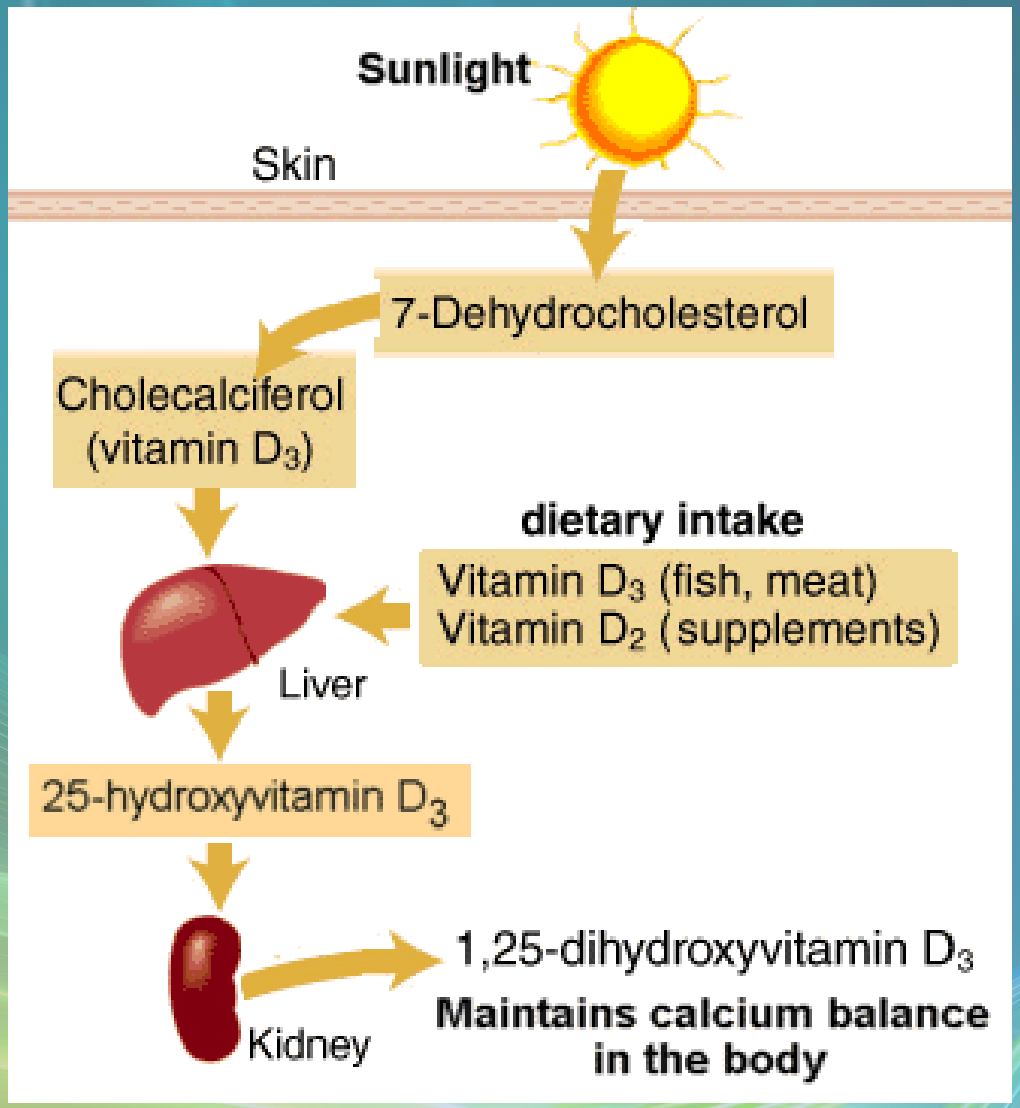
  Inhibits aldosterone

Skin

- Skin – Cholecalciferol

  Inactive vitamin D formed by UV radiation → liver → kidney for full activation [calcitriol].

  Essential for calcium absorption from intestines.


Sunlight
Skin
7-Dehydrocholesterol
Cholecalciferol
(vitamin D_3)
dietary intake
Vitamin D_3 (fish, meat)
Vitamin D_2 (supplements)
Liver
25-hydroxyvitamin D_3
Kidney
1,25-dihydroxyvitamin D_3
Maintains calcium balance
in the body

Others

- Liver – associated with production [often elsewhere] of 5 hormones – erythropoietin, angiotensin II, calcitriol, insulin-like growth factors I, Hepcidin [promotes uptake of iron]

- Kidney – Erythropoietin [Stimulates rbc production]. Calcitriol. Renin-angiotensin system

Others

- GI – Enteroendocrine cells

  Regulate digestive functions.

  Paracrines – local hormones.

- Placenta - Produces estrogen, progesterone, hCG.

Others

- Adipose –

  Leptin – secreted after glucose uptake – suppresses appetite.

  Resistin – an insulin antagonist.

Hormones & Their Actions

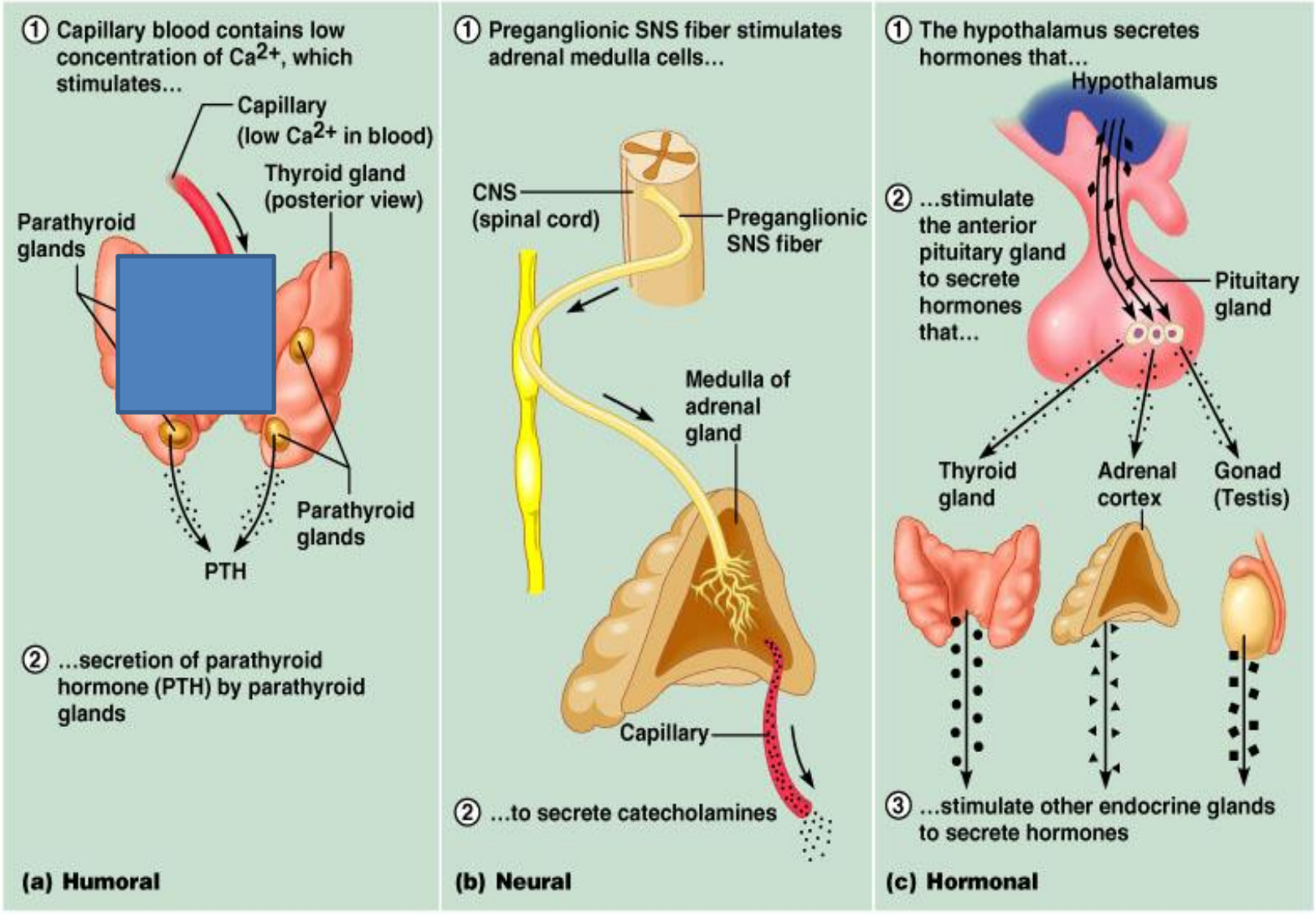
- **<u>Chemistry</u>**

  Steroids

  – Made from cholesterol nucleus with variable attachments.

  – Glands – gonads and adrenal

  – EX. Aldosterone, cortisol, vitamin D, androgens.


① Capillary blood contains low concentration of Ca^{2+}, which stimulates...
Capillary (low Ca^{2+} in blood)
Thyroid gland (posterior view)
Parathyroid glands
Parathyroid glands
PTH
② ...secretion of parathyroid hormone (PTH) by parathyroid glands
(a) Humoral
① Preganglionic SNS fiber stimulates adrenal medulla cells...
CNS (spinal cord)
Preganglionic SNS fiber
Medulla of adrenal gland
Capillary
② ...to secrete catecholamines
(b) Neural
① The hypothalamus secretes hormones that...
Hypothalamus
② ...stimulate the anterior pituitary gland to secrete hormones that...
Pituitary gland
Thyroid gland
Adrenal cortex
Gonad (Testis)
③ ...stimulate other endocrine glands to secrete hormones
(c) Hormonal

Hormones & Their Actions

Peptides and Proteins (3 – 200 amino acids)

- Synthesized in the rough endoplasmic reticulum. Some have CBH = glycoproteins - EX. – TSH, oxytocin, ADH, etc.

Hormones & Their Actions

Monamines - Amino acid – based

- Catecholamines – epinephrine, norepinephrine, dopamine from Tyrosine. Histamine from histidine. Serontonin, & melatonin from tryptophan.

- Thyroxine [thyroid hormones] - 2 iodinated tyrosine molecules coupled together. T3, T4

Hormones & Their Actions

- **<u>Hormone synthesis</u>**

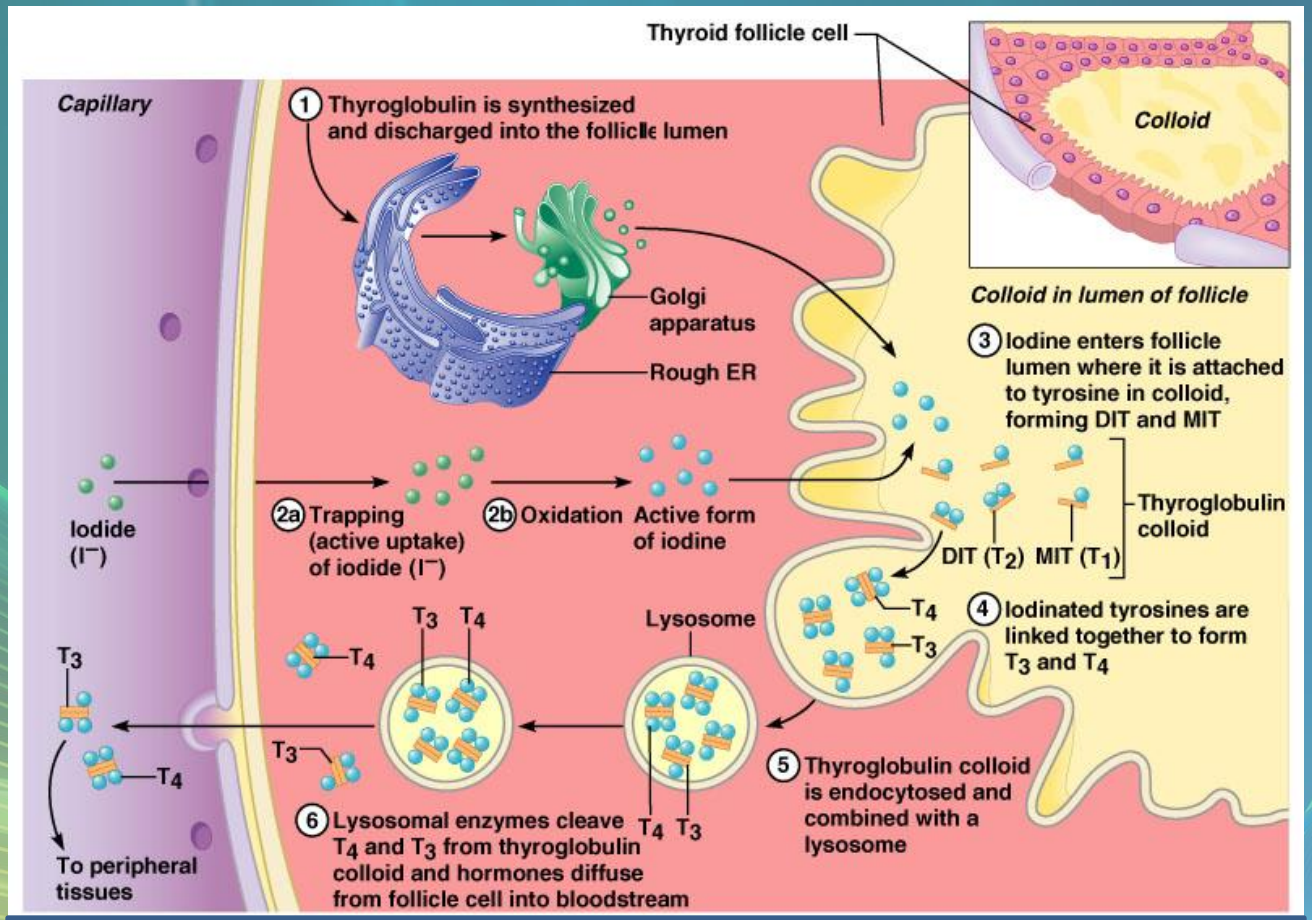
  Steroids – from cholesterol – vary in functional group attachments.

  Peptides – transcription, translation, etc. → inactive preprohormone → RER → prohormone → Golgi → secretion

Hormones & Their Actions

Monamines – thyroxine example

- Made from thyroglobulin – glycoprotein containing tyrosine – made by follicular cells.


Thyroid follicle cell
Colloid
Capillary
1 Thyroglobulin is synthesized and discharged into the follicle lumen
Golgi apparatus
Rough ER
Colloid in lumen of follicle
3 Iodine enters follicle lumen where it is attached to tyrosine in colloid, forming DIT and MIT
Thyroglobulin colloid
DIT (T2) MIT (T1)
Iodide (I⁻)
2a Trapping (active uptake) of iodide (I⁻)
2b Oxidation
Active form of iodine
T4
T3
4 Iodinated tyrosines are linked together to form T3 and T4
Lysosome
T3 T4
T4
T3
T3
T4
5 Thyroglobulin colloid is endocytosed and combined with a lysosome
6 Lysosomal enzymes cleave T4 and T3 from thyroglobulin colloid and hormones diffuse from follicle cell into bloodstream
T4 T3
To peripheral tissues

Hormones & Their Actions

- Add 3 or 4 I's
- Iodination process – $2I^- \rightarrow I_2$
- I_2 + Tyr → either 1 iodo or 2 iodo Tyr
- T1 +T2 → T3
- T2 + T2 → T4

Released from thyroglobulin by lysosomes

Transport – both carried in blood by thyroxin-binding globulin made in liver

Hormones & Their Actions

- **<u>Hormone Transport</u>**

  Monamines & peptides are mostly hydrophilic, easily transported in blood.

  Steroids & thyroid hormone are hydrophobic, moved by“transport” proteins – from liver.

  Transport proteins also protect from degradation & elimination.

Hormone Receptors & Modes of Action

- **<u>Hormone Target Cell Specificity</u>**

  Receptors – proteins or glycoproteins,

  on target cells – other cells not affected.

  Constantly replenished

Hormone Receptors & Modes of Action

Response to hormone concentration –

Saturation – all are occupied. ↑ hormone will have no effect.

Control – "if a hormone is prevented from interacting with its receptors, it cannot perform its normal functions."

Hormone Receptors & Modes of Action

Variable response – different cells may have receptors for the same hormone, but produce different responses to it.

EX. Insulin – In fat cells, it stimulates uptake of glucose & fat synthesis, in the liver it stimulates amino acid transport and glycogen synthesis, in the pancreas it inhibits glucagon-related reactions.

Hormone Receptors & Modes of Action

- **<u>Steroids and thyroid hormone</u>**

  Receptors are inside the target cell

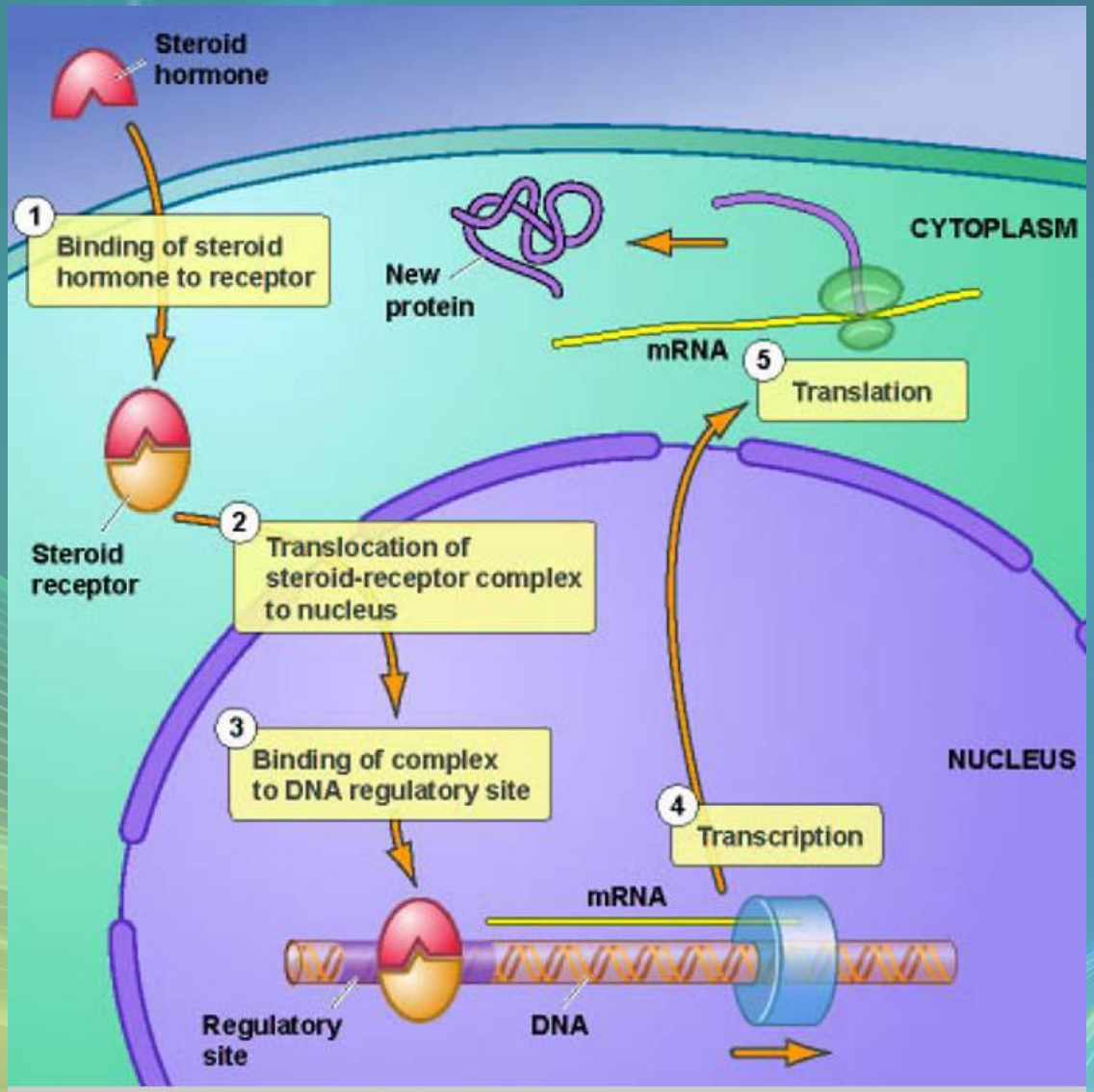
  Action: Diffuse from blood through plasma membrane into cell.

  Bind to & activate receptors.

Hormone Receptors & Modes of Action

Activated receptor binds to DNA.

DNA is transcribed, & new mRNA is produced that directs synthesis of proteins, usually enzymes.



Source: "Module 6," < http://www.thepepproject.net/ >

Hormone Receptors & Modes of Action

- Thyroid hormone:

  In cell all is converted to T3.

  T3 binds to mitochondria to ↑ cellular respiration; binds to ribosomes & ↑ rate of protein synthesis; binds to DNA receptors ↑ transcription.

Hormone Receptors & Modes of Action

- **<u>Peptides & catecholamines - Second Messenger Systems</u>**

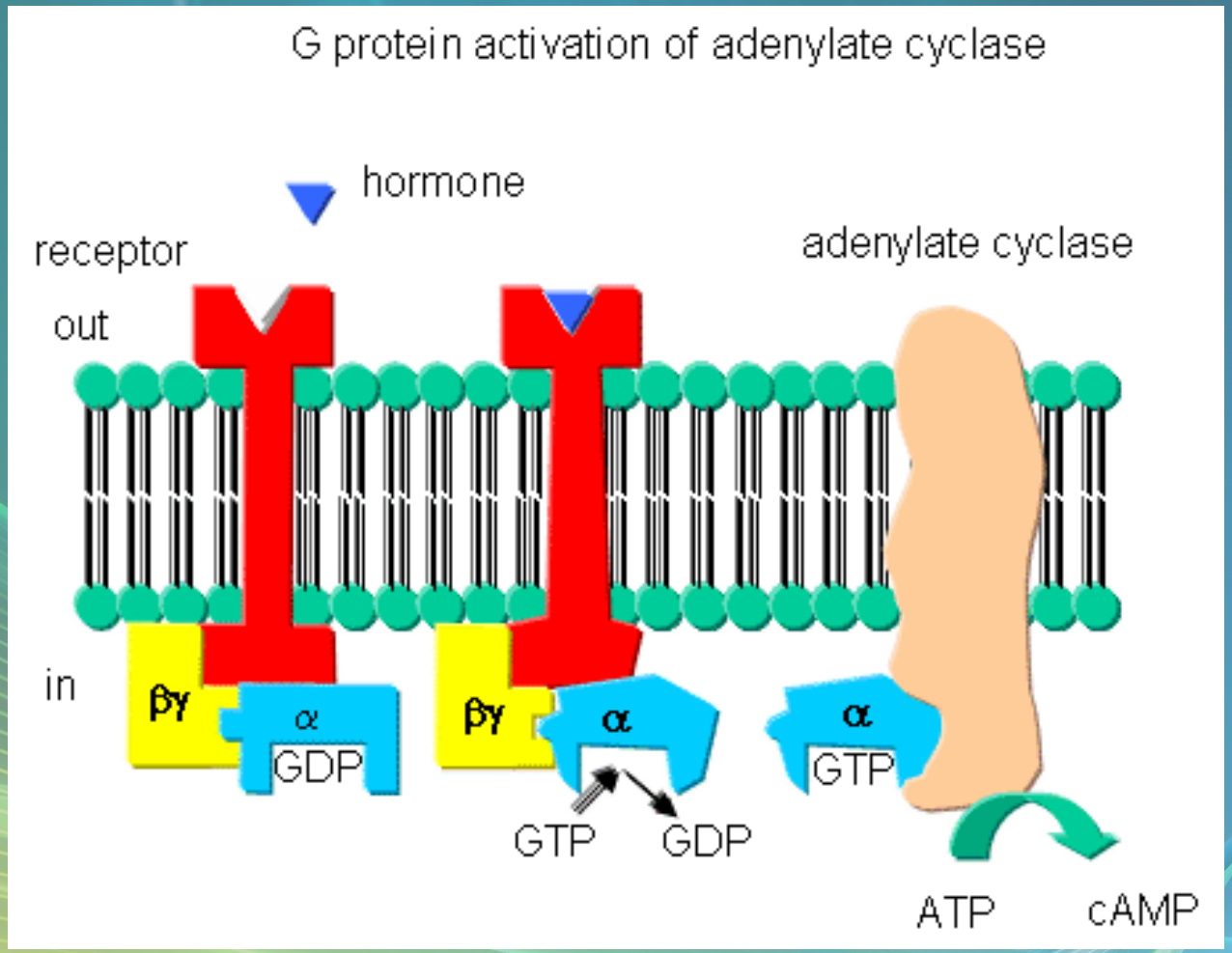
  Action [Ex. Glucagon]

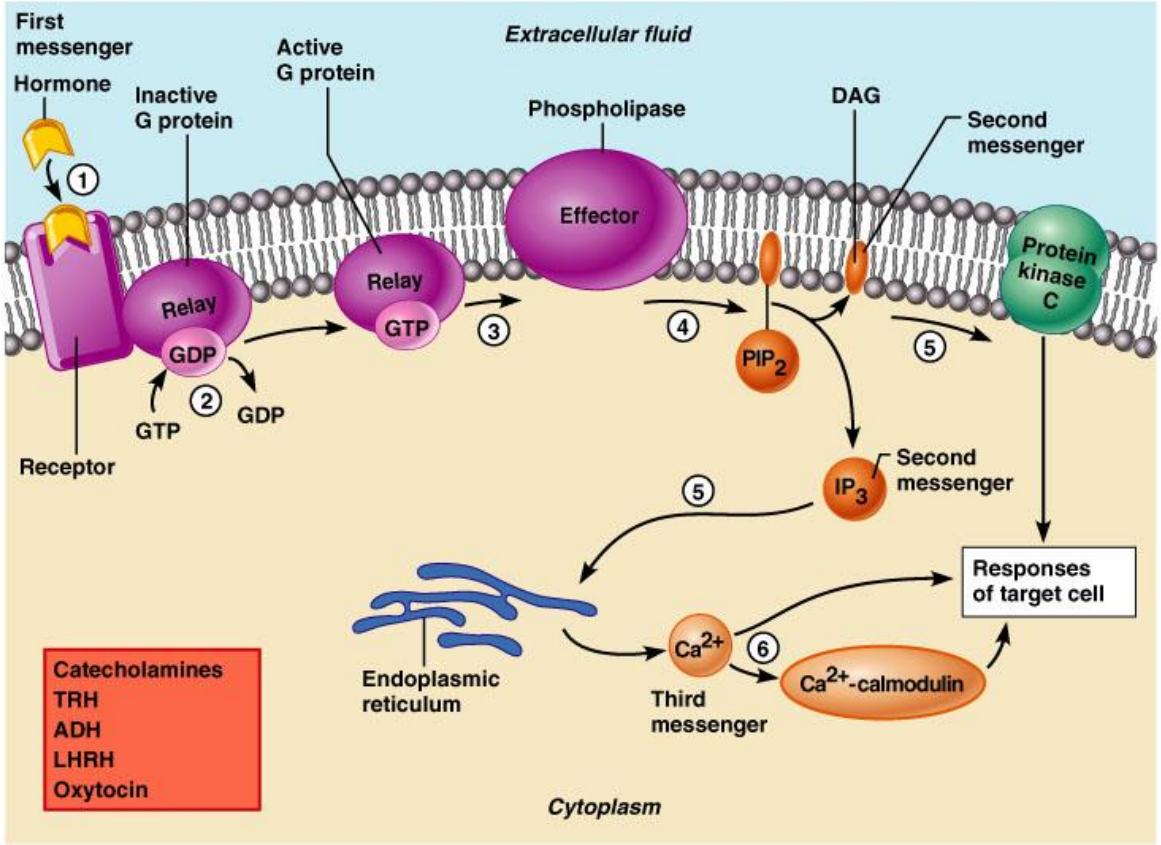
  Hormone diffuses from blood to target cell & binds to membrane receptor.

Hormone Receptors & Modes of Action

This activates “G” proteins attached to the inside of the membrane, which activates adenylate cyclase (AC) also on the inside AC converts ATP to cAMP in cytosol.

cAMP activates protein kinases (they add phosphates to proteins), either activating or inactivating the proteins.


G protein activation of adenylate cyclase
hormone
receptor
adenylate cyclase
out
in
βγ
α
GDP
βγ
α
α
GTP
GTP
GDP
ATP
cAMP


First messenger
Hormone
Inactive G protein
Active G protein
Extracellular fluid
Phospholipase
DAG
Second messenger
Effector
Protein kinase C
Relay
GDP
Relay
GTP
GTP
GDP
Receptor
PIP2
IP3
Second messenger
Responses of target cell
Endoplasmic reticulum
Ca2+
Third messenger
Ca2+-calmodulin
Catecholamines
TRH
ADH
LHRH
Oxytocin
Cytoplasm

Hormone Receptors & Modes of Action

Control:

Phosphodiesterase inactivates cAMP

Increasing or decreasing cAMP.

Increases with ADH, TSH, ACTH, glucagon, epinephrine etc.

Decreases occur with GHIH, ANP.

Hormone Receptors & Modes of Action

- Enzyme amplification – one hormone molecule may activate many G's, each of which may then activate many AC's, each of which may produce many cAMPs, etc.

Hormone Receptors & Modes of Action

- <u>Modulation of sensitivity</u>

  Down-regulation – number of receptors ↓when concentrations of hormone are high – tissues become less sensitive.

  Up-regulation – number of receptors ↑ when concentration of hormone ↓– tissue becomes more sensitive.

Hormone Receptors & Modes of Action

- **<u>Half-Life, Onset, and Duration of Activity</u>**

  Half-life – measures persistence of a hormone in circulation – usually a fraction of a minute to 30 minutes.

Hormone Receptors & Modes of Action

- <u>Hormone interactions:</u>

  Synergistic [works with another hormone for an effect] (ex:Testosterone needs FSH for normal sperm production)

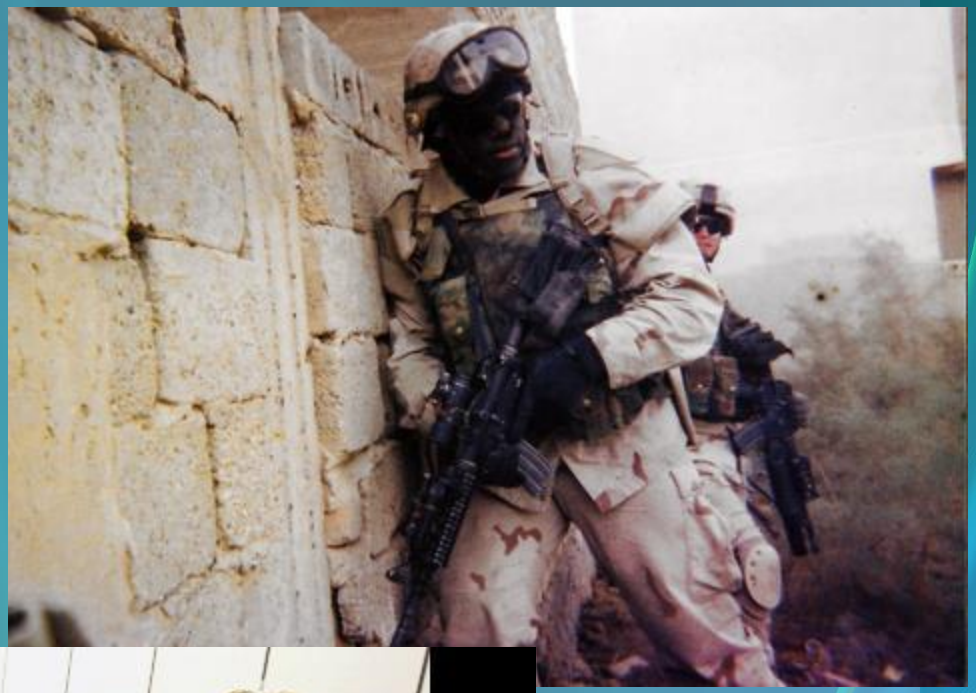
  Permissive [enhances response to another hormone secreted later] (Ex: Thyroid hormone increases the effect of epinephrine)

Hormone Receptors & Modes of Action

- <u>Hormone interactions:</u>
- **Antagonistic** [one hormone reduces the effectiveness of a second hormone] (Ex: During pregnancy, progesterone inhibits uterine response to estrogen)

General Adaptation Syndrome [GAS]

- Response to prolonged, extreme or unusual stress
- Stressor – and disturbance – temperature, toxins, poisons, heavy bleeding, emotional upheaval



General Adaptation Syndrome [GAS]

- GAS – 3 stages

  1 – Alarm Reaction = Fight or flight

  Hypothalamus stimulates ANS & adrenal medulla →epinephrine/ norepinephrine;

  Short lived

  Consumes glycogen stores

General Adaptation Syndrome [GAS]

2 – Resistance Stage [long-term]

Provide alternative fuels when glycogen has been depleted.

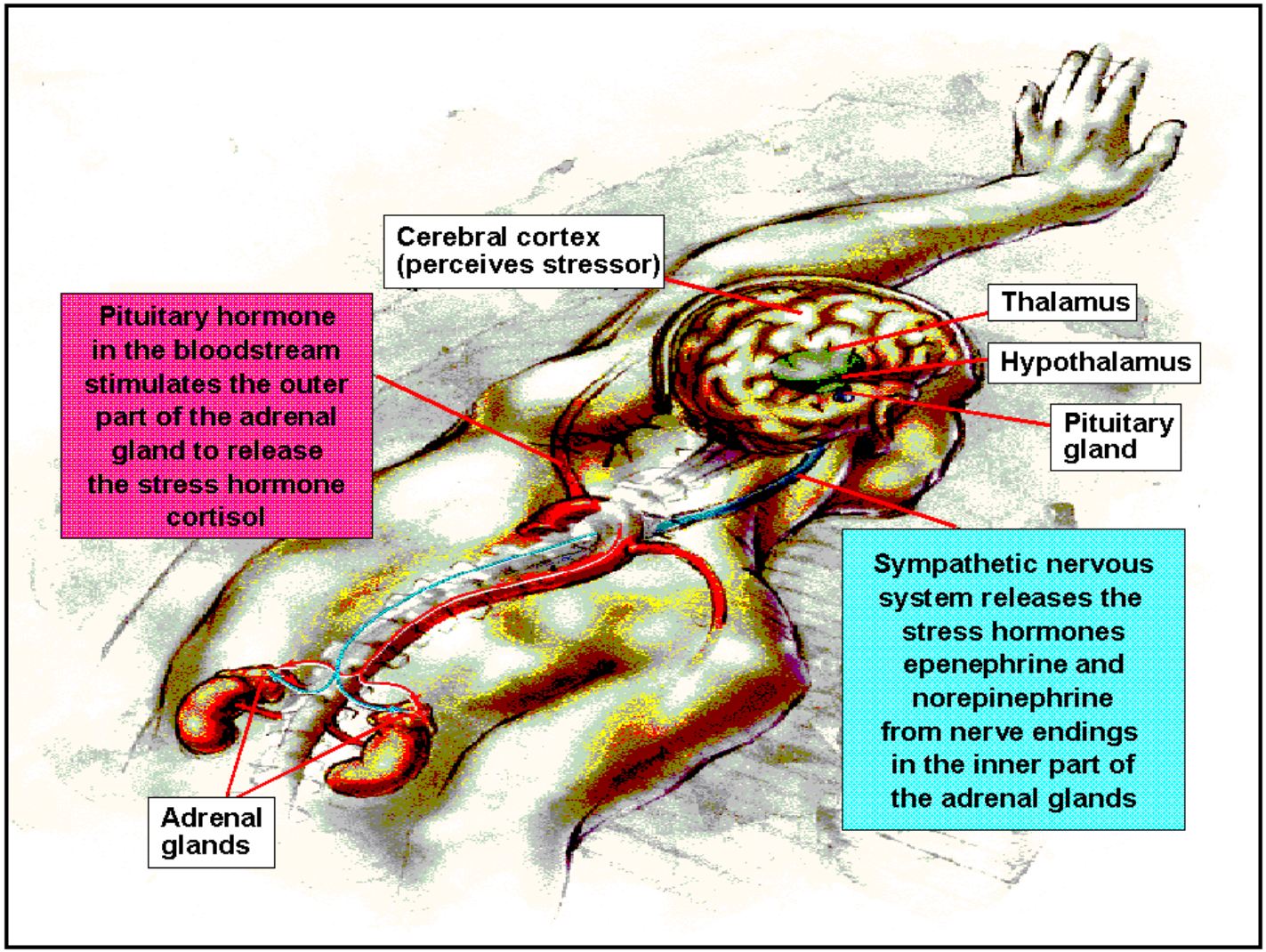
Dominated by cortisol. Cortisol counteracts insulin, contributes to causing gluconeogenesis. It also increases glycogen synthesis in the liver.

General Adaptation Syndrome [GAS]

Mediated by hypothalamus : CRH – stimulates ACTH production, which stimulates glucocorticoid [cortisol].

Fat breakdown, inhibits protein synthesis, immune response, etc.

If stress removed – body returns to normal.


Cerebral cortex (perceives stressor)
Thalamus
Hypothalamus
Pituitary gland
Pituitary hormone in the bloodstream stimulates the outer part of the adrenal gland to release the stress hormone cortisol
Sympathetic nervous system releases the stress hormones epenephrine and norepinephrine from nerve endings in the inner part of the adrenal glands
Adrenal glands

General Adaptation Syndrome [GAS]

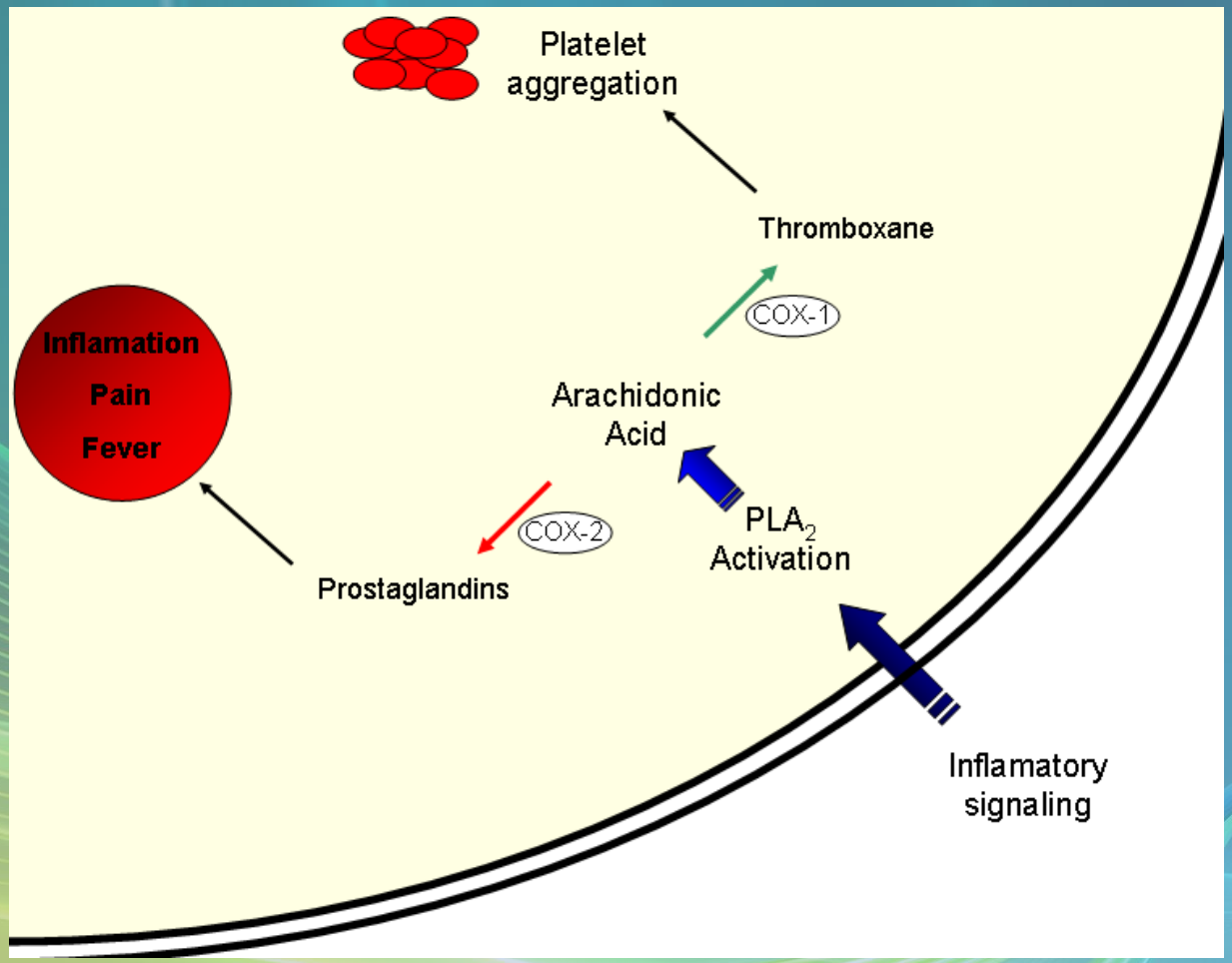
3 – Exhaustion – if stress continues past ability of Resistance Reaction to function → rapid decline & death [heart or kidney failure or overwhelming infection].

Stress

- Stress and Disease – stress can temporarily inhibit components of the immune system and produce gastritis, ulcerative colitis, irritable bowel syndrome, migraines, anxiety and depression.

Paracrines

- Eicosanoids – 20 C FA chains – derived from arachidonic acid in phospholipids in cell membranes. – Important considerations in pharmacology.


Platelet aggregation
Thromboxane
COX-1
Inflamation
Pain
Fever
Arachidonic Acid
COX-2
PLA2 Activation
Prostaglandins
Inflamatory signaling

Endocrine Disorders

- <u>Homeostatic Imbalances – hypothalamus/ pituitary</u>

  Hypersecretion of prolactin – may be due to adenohypophyseal tumors- inappropriate lactation, loss of menses, infertility.

Endocrine Disorders

Diabetes Insipidus – deficiency of secretion of ADH – Huge losses of urine, no sugar.

GH - Gigantism [hyper] & dwarfism [hypo]

Endocrine Disorders

- <u>Homeostatic Imbalances – Thyroid</u>

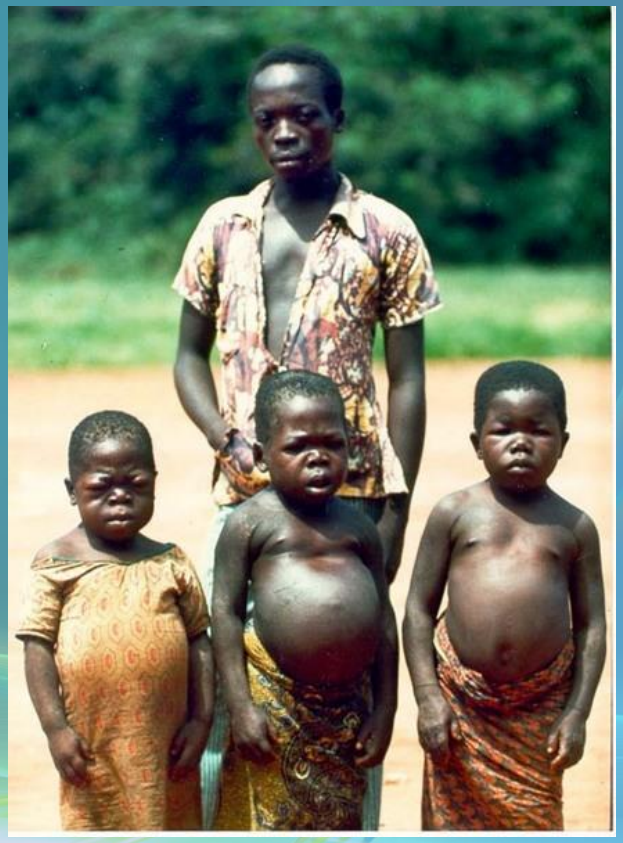
  Hypothyroidism – myxedema – may be from thyroid defect or failed TSH or TRH release.

  Low metabolic rate, chills, thick dry skin, puffy eyes, lethargy.

Endocrine Disorders

If due to lack of I – can develop goiter.

Infantile version = cretinism – can be prevented with thyroid hormone replacement therapy, can’t be reversed.



Endocrine Disorders

Hyperthyroidism – Grave's disease.

May be autoimmune disease.

Elevated metabolic rate, weight loss, rapid irregular heart beat, exophthalmos.

Endocrine Disorders

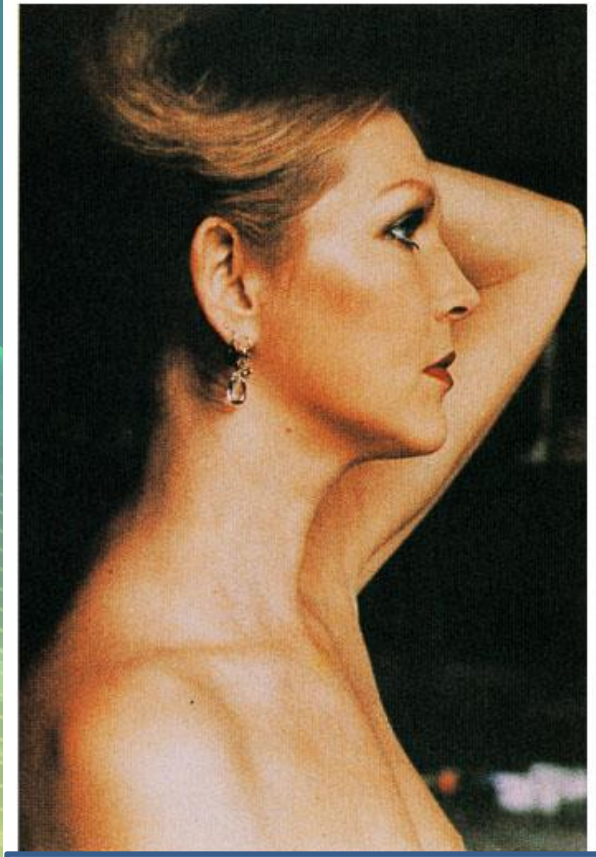
- <u>Homeostatic Imbalances – Adrenal Cortex</u>

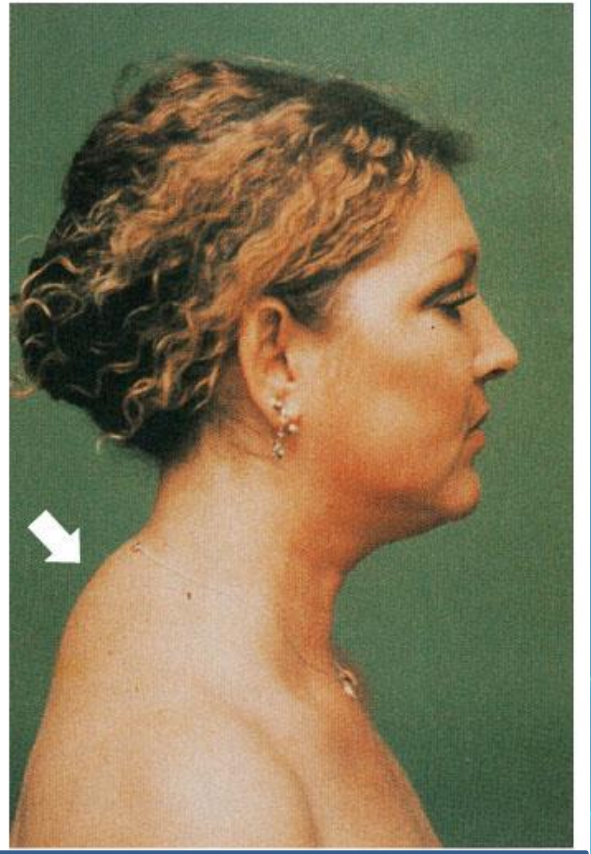
Cushing's Disease

Overproduction of glucocorticoids

Buffalo hump on back, edema, hypertension.

Due to steroid therapy or pituitary tumor.





Endocrine Disorders

Addison's Disease – hyposecretion.

Fluid loss and hypotension.

Endocrine Disorders

- <u>Homeostatic Imbalances – Pancreas</u>

  Diabetes Mellitus –hyposecretion or hypoactivity of insulin.

  Elevates blood sugar levels, glycosuria, weight loss.

  Ketoacidosis [from lipemia].

Endocrine Disorders

3 signs – polydipsia [excessive thirst], polyphagia [excessive hunger], polyuria [huge urine output].

Also hyperglycemia, glycosuria, ketonuria.

Endocrine Disorders

- Type I – insulin-dependent [juvenile].

  Involves depletion of beta cells.

  Requires insulin supplementation.

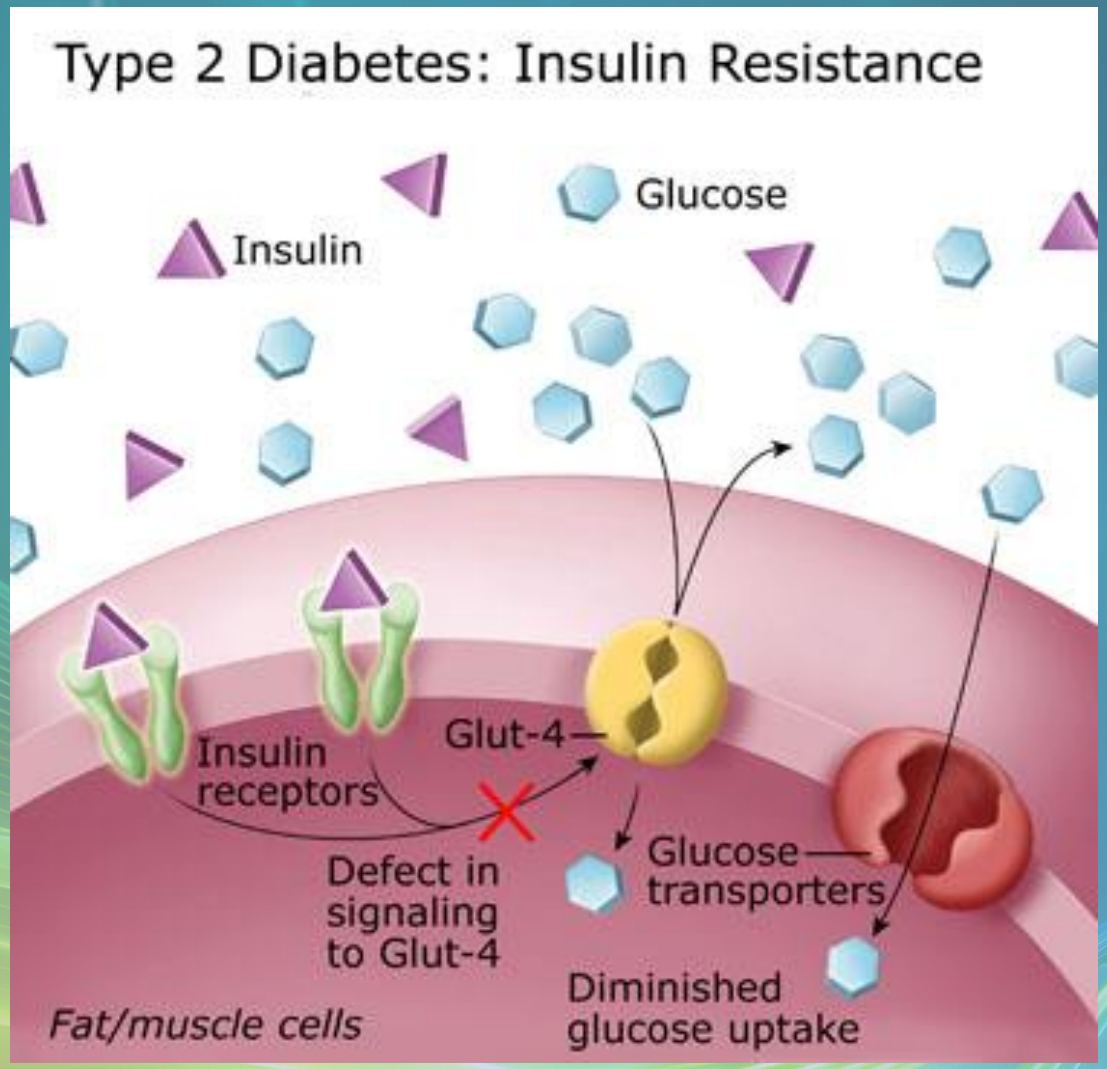
Endocrine Disorders

- Type II – non-insulin dependent [insulin levels are normal or elevated].

  Problem is insulin resistance.

  Adult-onset [40+].

  Associated with obesity.


Type 2 Diabetes: Insulin Resistance
Insulin
Glucose
Insulin receptors
Glut-4
Defect in signaling to Glut-4
Glucose transporters
Diminished glucose uptake
Fat/muscle cells

Endocrine Disorders

Fat catabolism →↑ free FA's → ↑ ketone bodies → osmotic dieresis, flushing of Na & K, acidosis → diabetic coma.

Endocrine Disorders

- Long-term degenerative effects on vascular and nervous system – compromised circulation → gangrene.
- Nerve damage → impotence, loss of sensation, etc.

Diabetic retinopathy

Diabetic gangrene

Endocrine Disorders

- Hypoglycemia – excess insulin, low blood sugar, anxiety, tremors, weakness.