Endocrinology
(How to take history)

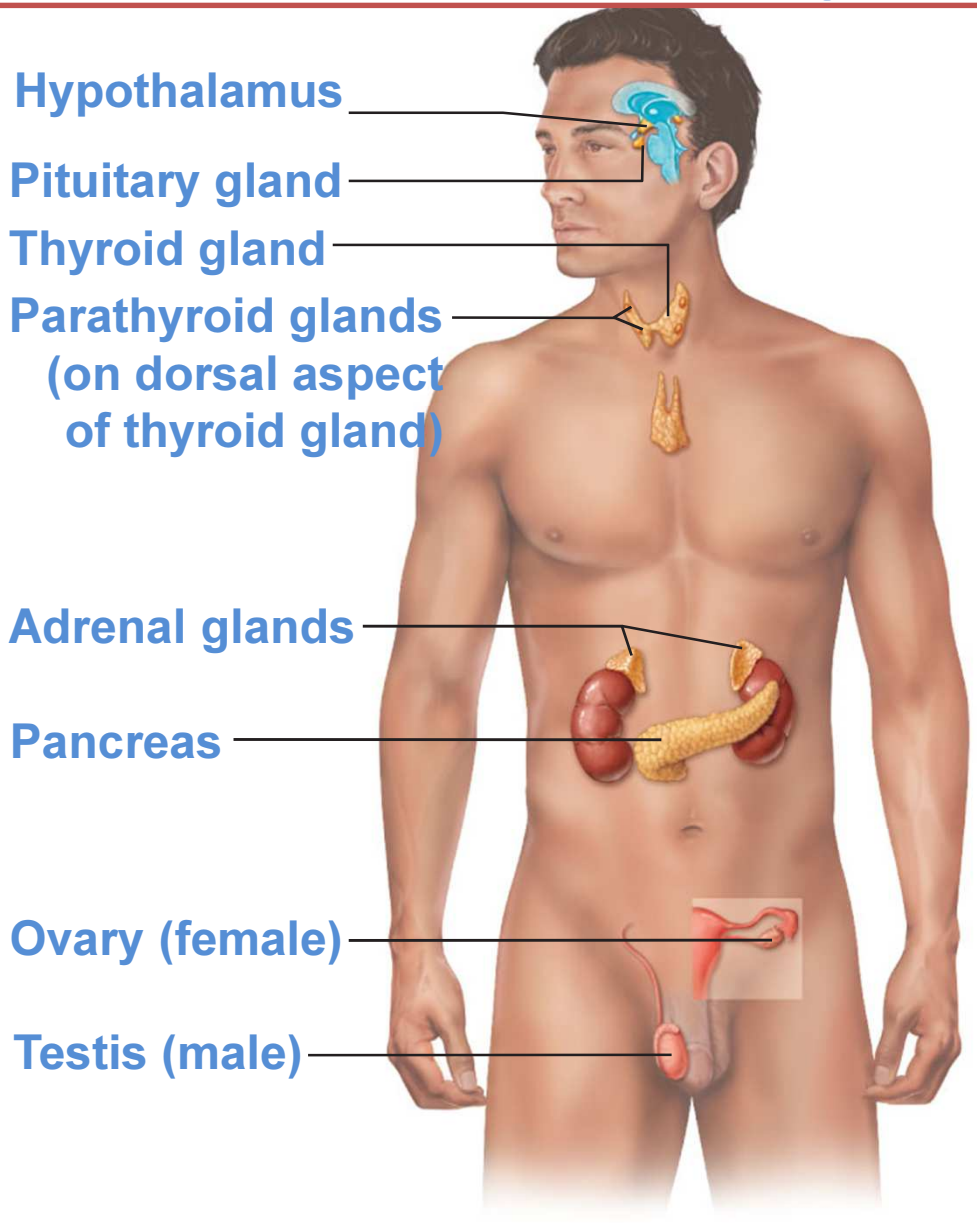
Dr Mousa Tuwati Alfakhri

28/11/2020

Endocrinology

- Endocrinology concerns synthesis, secretion and action of hormones.
- Hormones are chemical messengers released from endocrine glands coordinate activities of many different cells.
- Endocrine diseases affect multiple organs and systems.

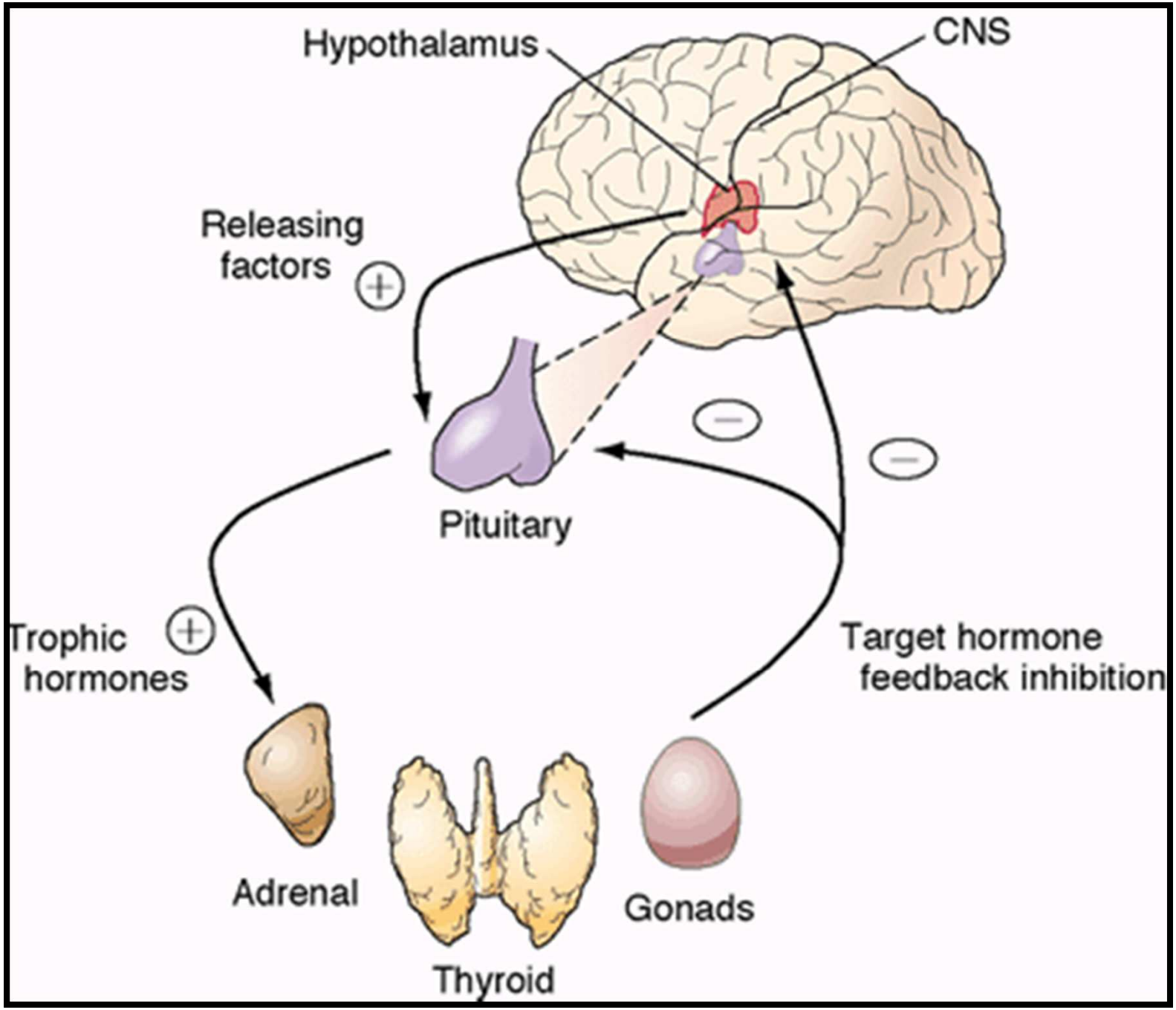
Glands of the Endocrine System



- Some endocrine glands, such as parathyroids and pancrease, respond directly to metabolic signals, but most are controlled by hormones released from pituitary gland.

- Pituitary hormone secretion is controlled by substances produced in hypothalamus.

- Hormone release in hypothalamus and pituitary is regulated by numerous stimuli and through feedback control by hormones produced by target glands (thyroid, adrenal cortex and gonads). These integrated endocrine systems are called ‘axes’.


Hypothalamus
CNS
Releasing factors
+
Pituitary
−
−
Trophic hormones
+
Target hormone feedback inhibition
Adrenal
Thyroid
Gonads

Classification of endocrine disease

Hormone excess

- Primary gland over-production
- Secondary to excess trophic hormone

Hormone deficiency

- Primary gland failure
- Secondary to deficient trophic hormone

Non-functioning tumours

Hypothalamus

- “Master" gland, lies below thalamus in walls and floor of third ventricle ,consists of group of nuclei (supraoptic and paraventricular) .
- Produce and release hormones that stimulate anerior pituitary gland,namely:

➢ Growth hormone releasing hormone (GRH)

➢ Thyrotropic-releasing hormone (TRH)

➢ Corticotropin releasing hormone (CRH)

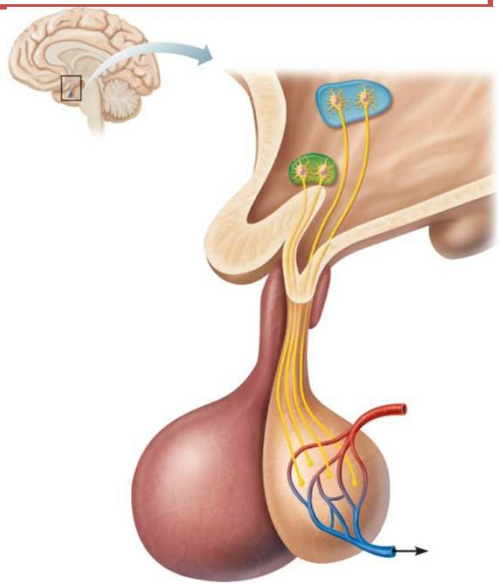
➢ Gonadotropin-releasing hormone (GnRH)

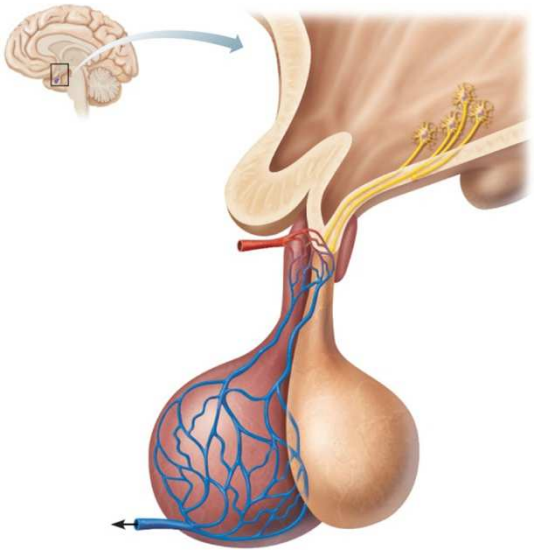
➢ Prolactin inhibiting hormone(PIH)

- Also hypothalamus synthesize **oxytocin and antidiuretic hormone (ADH)** which released from posterior pituitary

The Pituitary Gland

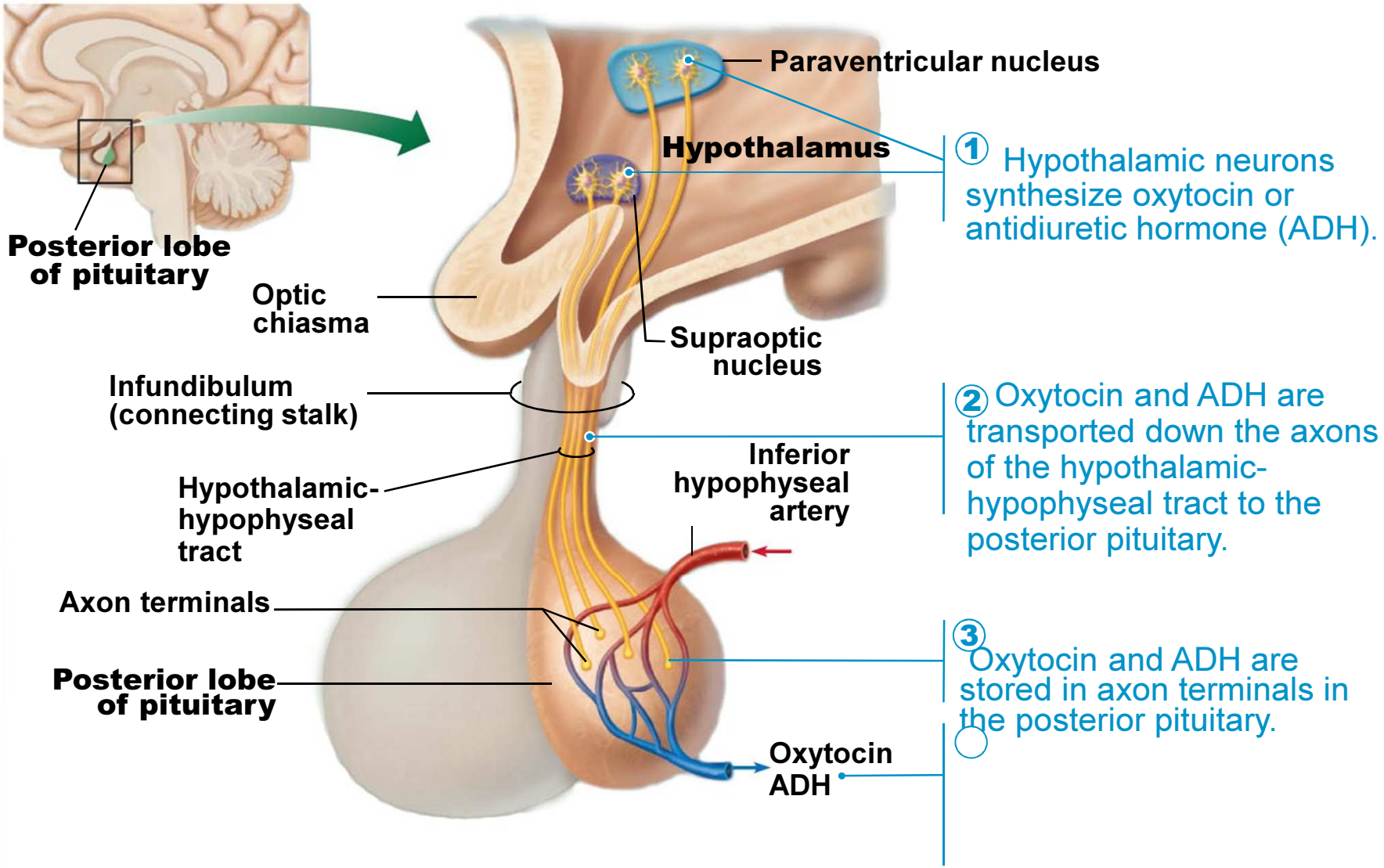
- known as hypophysis, pea-sized gland located at base of brain. It is enclosed in sella turcica and bridged over by fold of dura mater called diaphragma sellae, with sphenoidal air sinuses below and optic chiasm above,it Connected to hypothalamus by pituitary stalk.
- Comprised of two very different glands; anterior pituitary and posterior pituitary
- Anterior pituitary (adenohypophysis)
- Posterior pituitary (neurohypophysis)





Posterior lobe (neurohypophysis)

- Posterior pituitary hormones are **oxytocin and antidiuretic hormone (ADH)**
- They are synthesised in the hypothalamus and transported down nerve axons(hypothalamic-hypophyseal tract) , to be released from the posterior pituitary


Posterior lobe of pituitary
Optic chiasma
Infundibulum (connecting stalk)
Hypothalamic-hypophyseal tract
Axon terminals
Posterior lobe of pituitary
Paraventricular nucleus
Hypothalamus
Supraoptic nucleus
Inferior hypophyseal artery
Oxytocin
ADH
1 Hypothalamic neurons synthesize oxytocin or antidiuretic hormone (ADH).
2 Oxytocin and ADH are transported down the axons of the hypothalamic-hypophyseal tract to the posterior pituitary.
3 Oxytocin and ADH are stored in axon terminals in the posterior pituitary.

Oxytocin

- Stimulates uterine contractions during childbirth
- Also triggers milk ejection in women producing milk

Antidiuretic Hormone(ADH, vasopressin)

- Enhances water retention
- Hypothalamic osmoreceptors respond to changes in the solute concentration of the blood
- When plasma osmolality is high:

➢ Osmoreceptors transmit impulses to hypothalamic neurons

➢ Hypothalamic neurons make & release more ADH

➢ ADH acts on kidneys to cause water retention

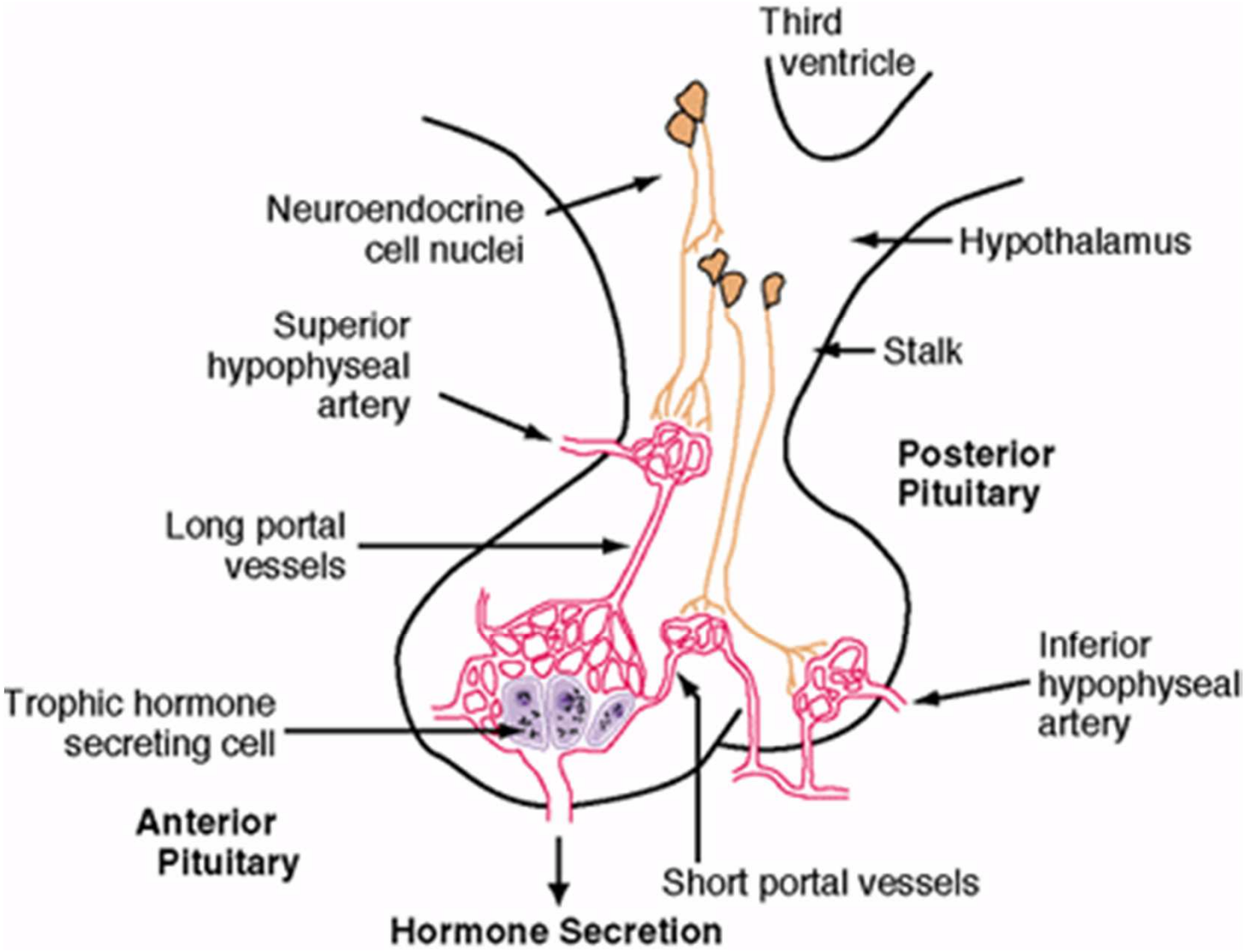
Homeostatic Imbalances of ADH

- ADH deficiency: Diabetes Insipidus
- ADH hypersecretion :syndrome of inappropriate ADH secretion (SIADH)

Anterior Pituitary(adenohypophysis)

Trophic hormones	Target tissues	Hormone effects
Anterior pituitary gland		
Growth hormone, GH	All cells, especially growing cells	Stimulates body growth in childhood; causes switch to fats as energy source
Adrenocorticotropic hormone, ACTH	Adrenal cortexes	Stimulates release of corticosteroidal hormones cortisol and aldosterone
Thyroid-stimulating hormone, TSH	Thyroid	Stimulates release of thyroid hormones thyroxine and triiodothyronine
Follicle-stimulating hormone, FSH	Ovaries or Testes	FSH stimulates development of sex cells (ovum or sperm)
Luteinizing hormone, LH	Ovaries or Testes	LH stimulates release of hormones (estrogen, progesterone or testosterone)
Prolactin, PRL	Mammary glands	Stimulates production and release of milk

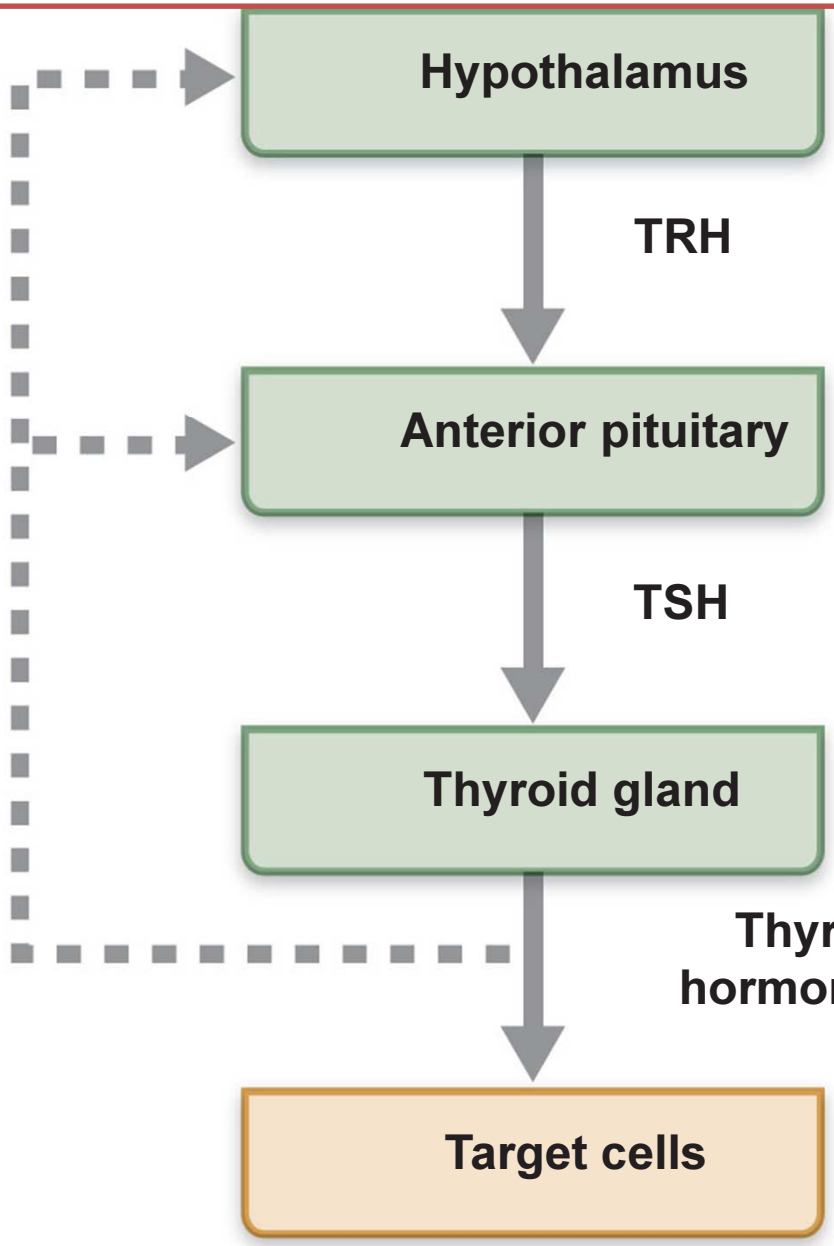
Hypothalamic–Pituitary Axis



Growth hormone

- GH excess in childhood leads to gigantism
- GH excess in adulthood leads to acromegaly
- GH deficiency in childhood leads to dwarfism
- GH deficiency in adulthood leads to loss of muscle & bone strength and sometimes cognitive changes

Thyroid-Stimulating HormoneTSH (Thyrotropin)



Regulation:

- Stimulated by thyrotropin-releasing hormone (TRH)
- Inhibited by rising blood levels of thyroid hormones that act on the pituitary and hypothalamus

Adrenocorticotropic Hormone ACTH (Corticotropin)

- Secreted by corticotrophs of the anterior pituitary
  Stimulates adrenal cortex to release corticosteroids

- Regulation of ACTH release
  - Triggered by hypothalamic corticotropin-releasing hormone (CRH) in daily rhythm
  - Internal and external factors such as fever, hypoglycemia, and stressors can alter release of CRH

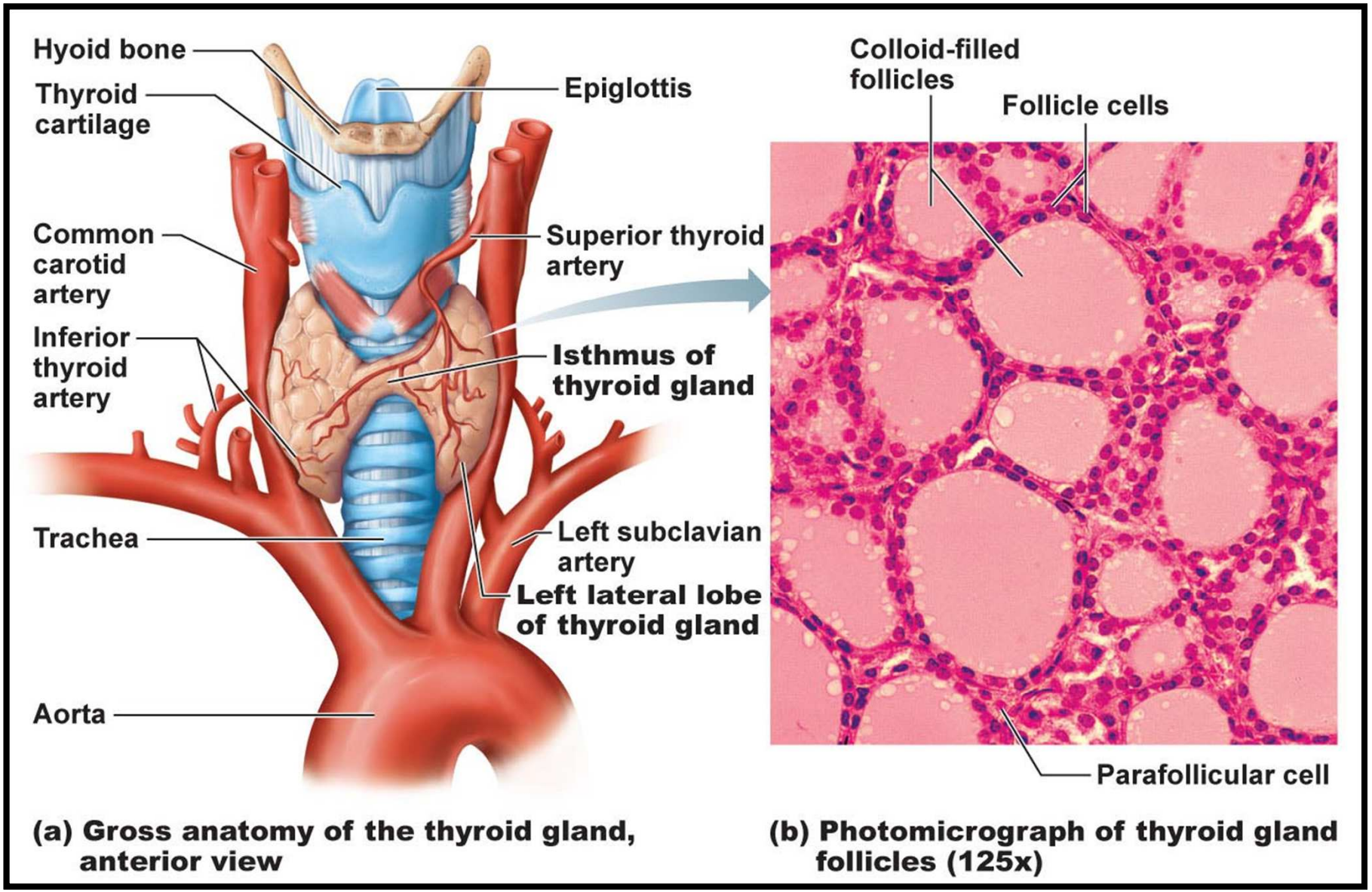
Gonadotropins

- Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) Secreted by gonadotrophs of the anterior pituitary
- FSH stimulates gamete (ovum or sperm) production
- LH promotes production of gonadal hormones
- Regulation of gonadotropin release
  - Triggered by the gonadotropin-releasing hormone (GnRH) during and after puberty
  - Suppressed by gonadal hormones (feedback)

Prolactin (PRL)

- Secreted by lactotrophs of the anterior pituitary
- Stimulates milk production
- Regulation of PRL release
  - Primarily controlled by prolactin-inhibiting hormone (PIH) (Dopamine)
- Blood levels rise toward the end of pregnancy
- Suckling stimulates PRL release and promotes continued milk production

Thyroid Gland



Thyroid Hormone

- Actually two related compounds
  - T_4 (thyroxine); has 2 tyrosine molecules + 4 bound iodine atoms
  - T_3 (triiodothyronine); has 2 tyrosines + 3 bound iodine atoms

Affects virtually every cell in body

- Major metabolic hormone
- Increases metabolic rate and heat production (calorigenic effect)
- Plays a role in
  - Regulation of tissue growth
  - Development of skeletal and nervous systems
  - Reproductive capabilities

Hypothalamic-Pituitary-Thyroid Axis

HYPOTHALAMUS - TRH

ANT. PITUITARY - TSH

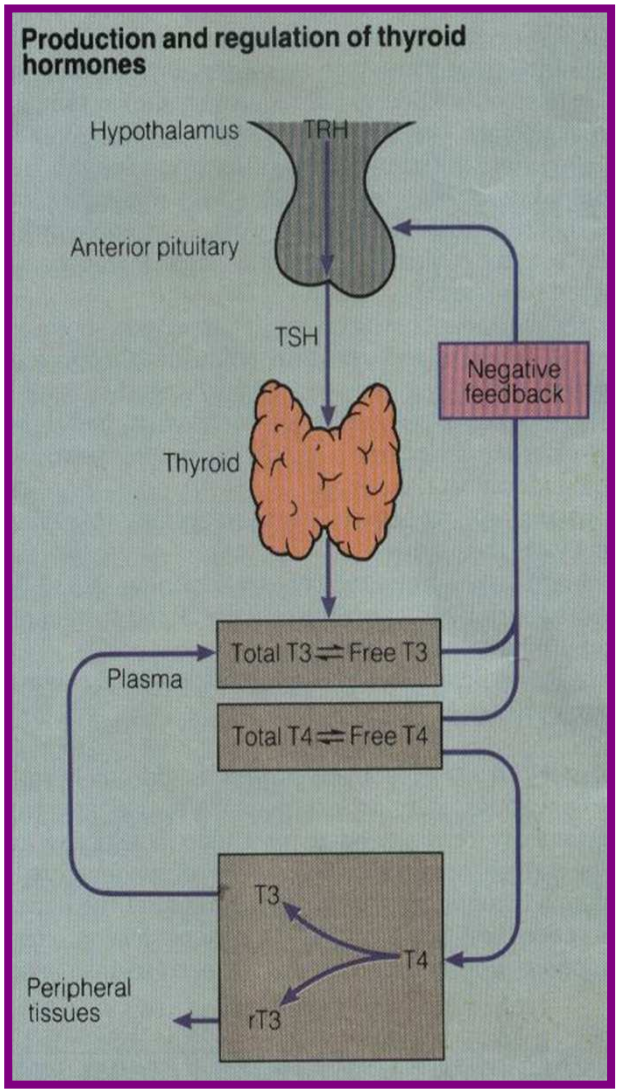
TSH -R

THYROID T4 and T3

PLASMA T4 + FT4

PLASMA T3 + FT3

TISSUES FT4 to FT3



Hyperthyroidism

- Increased thyroid hormones synthesis and secretion.
- in most cases it is primary hyperthyroidism caused by thyroid diseases (e g Graves disease, Multinodular goiter, Toxic thyroid adenoma).
- very rare it is secondary hyperthyroidism due to increase TSH production by pituitary gland (TSH secreting pituitary adenoma)

Symptoms of thyrotoxicosis

Common symptoms

- Weight loss despite normal or increased appetite
- Heat intolerance
- Diaphoresis
- Palpitation
- Hands tremor
- Dyspnoea
- Fatigue
- Ansomnia
- Nervousness / Anxiety

Less common symptoms

- Diarrhoea
- psychosis
- Muscle weakness
- Pruritus, alopecia
- Amenorrhoea/oligomenorrhoea
- Infertility, spontaneous abortion
- Loss of libido, impotence

Thyrotoxic crisis or Thyroid Storm

- Acute increase in T4 and T3 can cause thyrotoxic crisis or acute thyroid storm.
- The possible cause is decompensation of pre-existing hyperthyroid state after stressor (Surgery, anesthesia, infection, trauma).

Hypothyroidism

- Hypothyroidism is chronic deficiency of T4 & T3.
- Usually primary, from disease of the thyroid(Surgical removal or radioiodine ablation of thyroid , Hashimoto's thyroiditis (chronic inflammation of the thyroid)
- May be secondary to hypothalamic pituitary disease (reduced TSH drive) (e g hypophysectomy or pituitary radiation)

Symptoms of hypothyroidism

- Tiredness/malaise
- Weight gain
- Constipation
- Cold intolerance
- Poor memory
- Depression
- Arthralgia
- Muscle weakness/Stiffness
- Menorrhagia

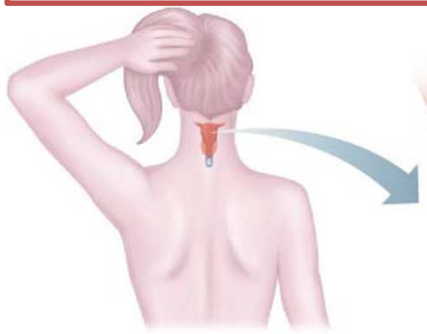
Myxedema Coma

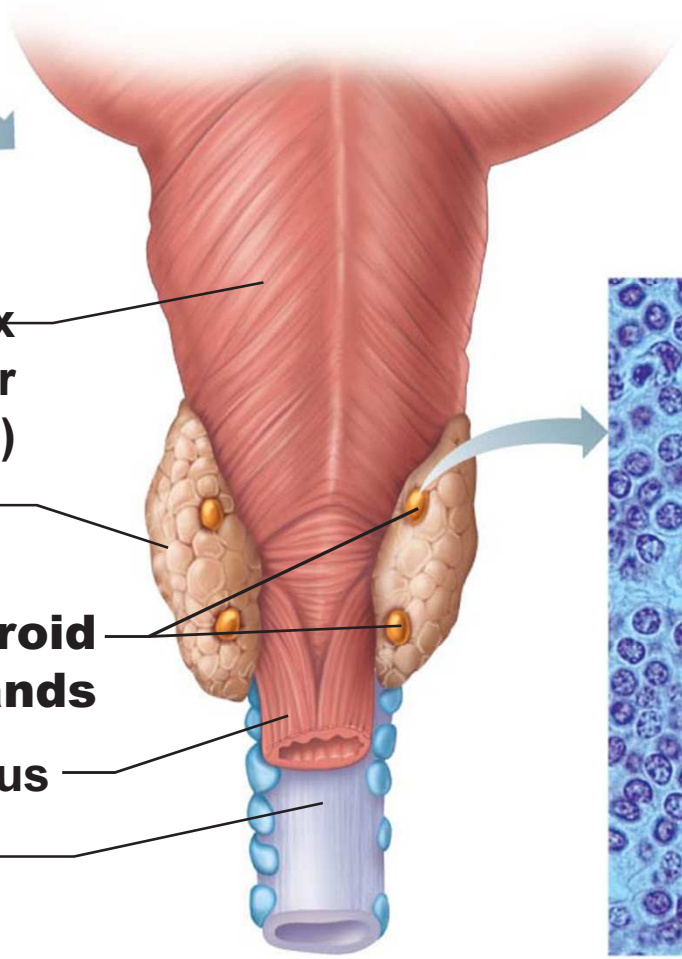
- Acute deficiency or T4 and T3.
- Possible causes include:

➢ Insufficient thyroid supplementation

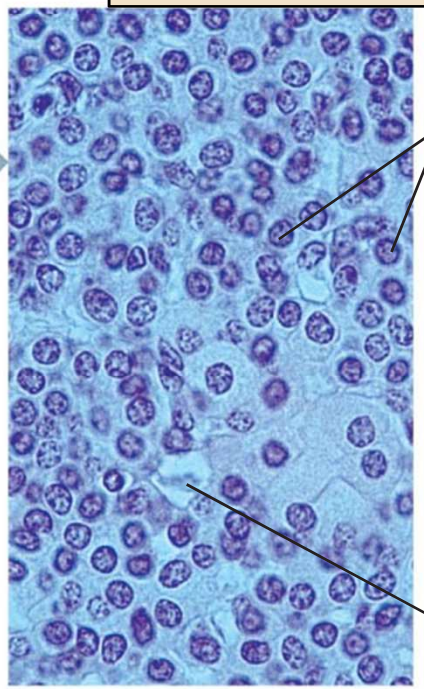
➢ Increased stressors in patients with hypothyroidism (e.g. trauma, cold, anesthesia, infection)

Parathyroid Glands



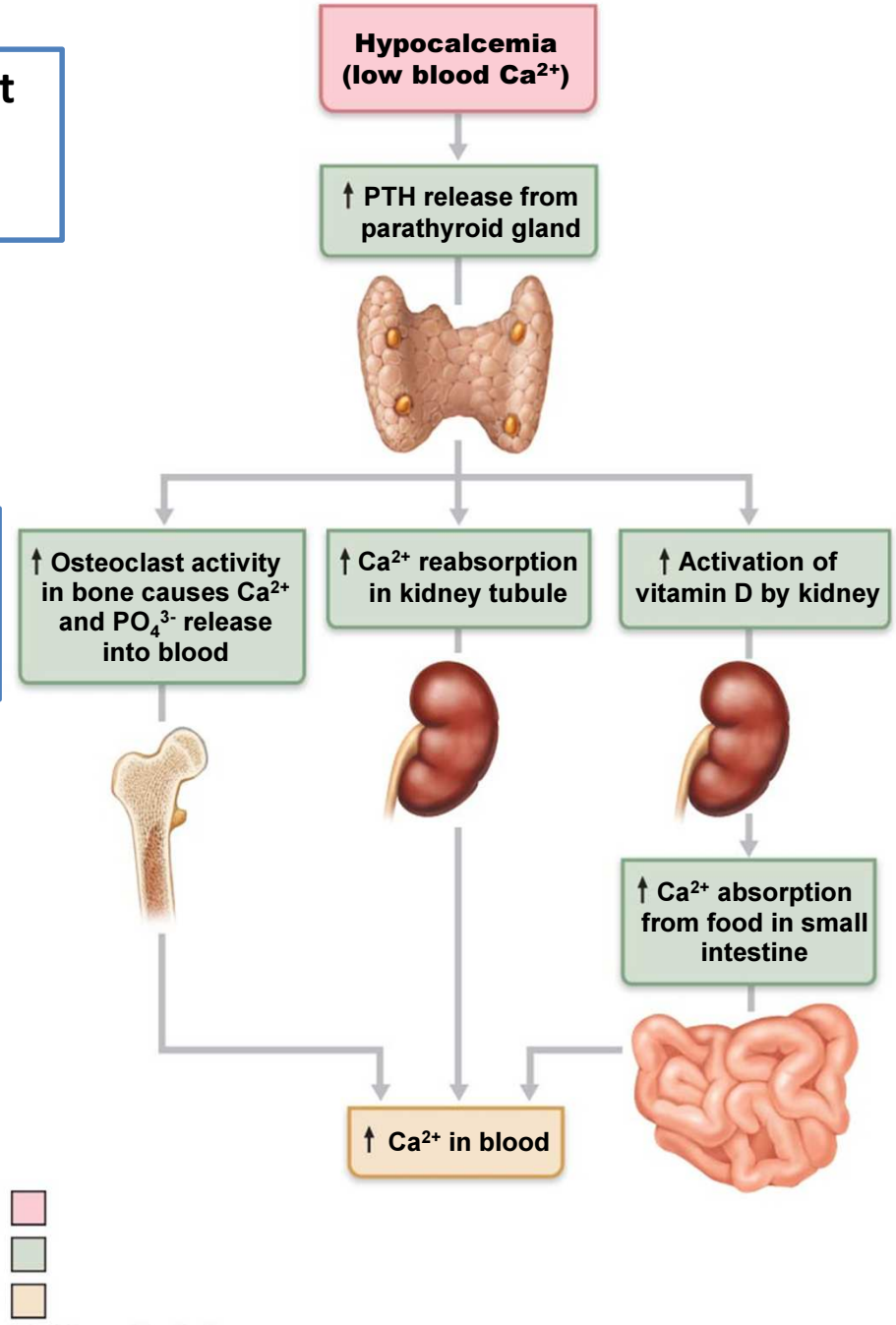


Usually four (up to eight) tiny glands embedded in the posterior aspect of the thyroid



PTH is most important hormone for calcium homeostasis

Increases blood calcium levels 3 ways



Homeostatic Imbalances of PTH

- **Hyperparathyroidism**

Due to parathyroid adenoma or hyperplasia

- Symptoms of elevated serum Calcium :Polyuria ,polydapsia ,Abdominal pain ,constipation, fatigue,muscle weakness renal colic ,Imaired concentration and memory and Depression
- Reduction of bone mass density causing bone pain arthralgia,and osteoprosis

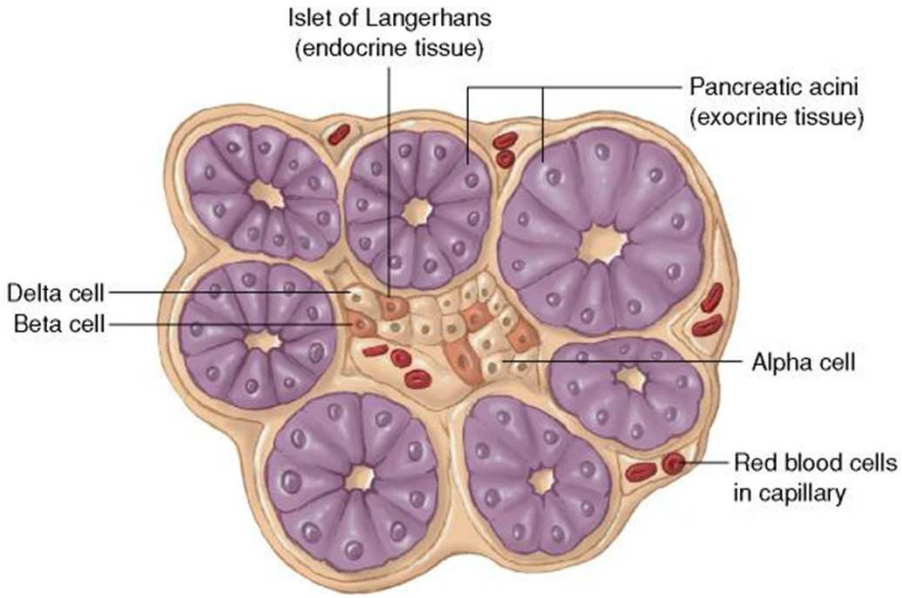
- **Hypoparathyroidism**

Due to gland trauma or removal

- ➢ Symptoms of hypocalcemia:
- ✓ Peri-oral and digital paraesthesiae
- ✓ Tetany and carpopedal spasm
- ✓ Seizure
- ✓ respiratory paralysis, and death if untreated

Pancreas

- Has both exocrine and endocrine cells
  - Acinar cells (exocrine) produce an enzyme-rich juice for digestion
  - Pancreatic islets (islets of Langerhans) contain endocrine cells
    - Alpha (α) cells produce **glucagon**
    - Beta (β) cells produce **insulin**



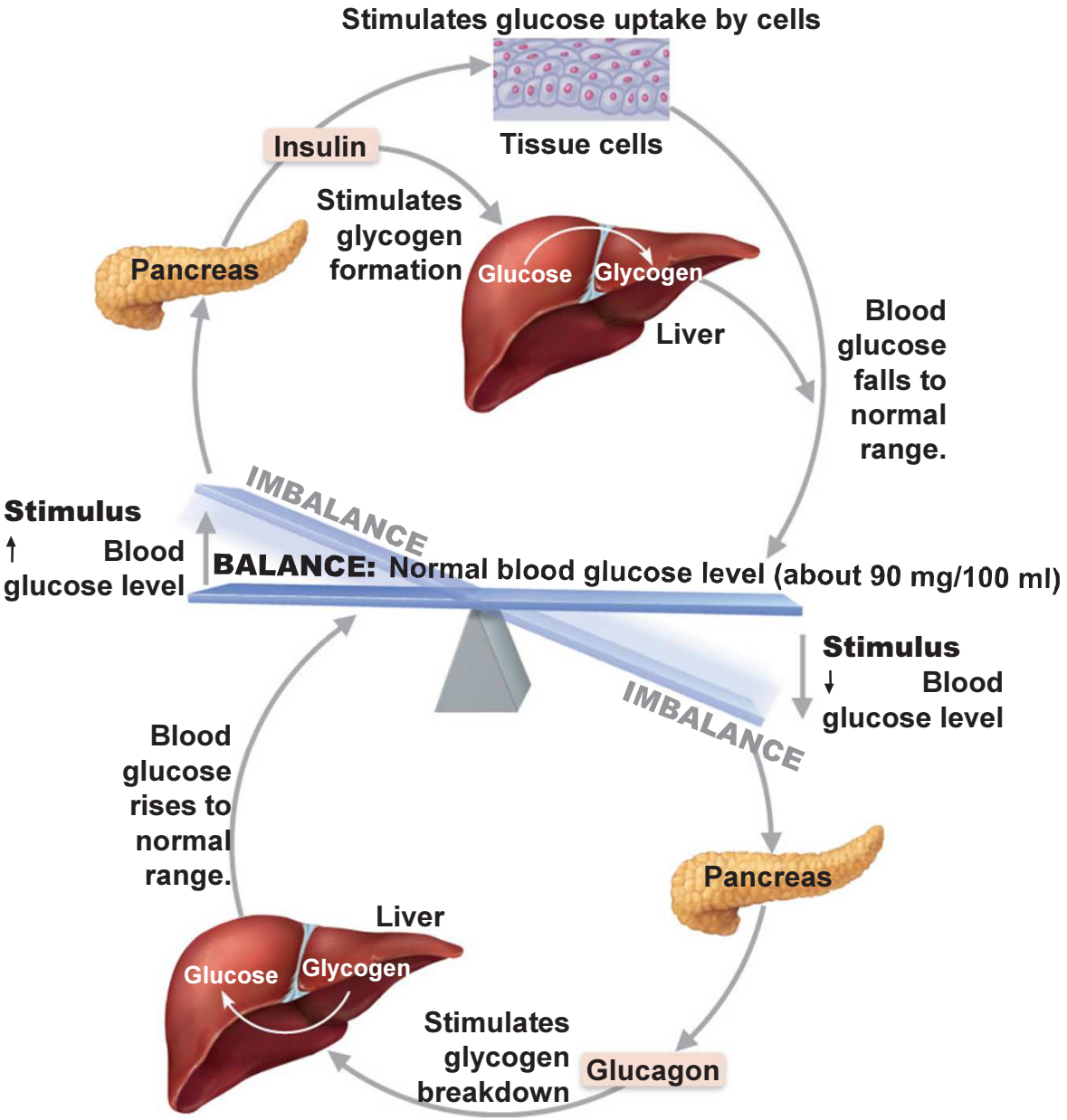
Glucagon and Insulin

Glucagon

- Major target is the liver, where it promotes
  - Glycogenolysis—breakdown of glycogen to glucose
  - Gluconeogenesis—synthesis of glucose from amino cide
  - Release of glucose to the blood

insulin

- Lowers blood glucose levels
- Enhances transport of glucose into fat and muscle cells
- Inhibits glycogenolysis and gluconeogenesis
- The primary stimulus for insulin release is the elevated blood glucose


Stimulates glucose uptake by cells
Tissue cells
Insulin
Stimulates glycogen formation
Pancreas
Glucose
Glycogen
Liver
Blood glucose falls to normal range.
IMBALANCE
Stimulus
↑ Blood glucose level
BALANCE: Normal blood glucose level (about 90 mg/100 ml)
Stimulus
↓ Blood glucose level
IMBALANCE
Blood glucose rises to normal range.
Pancreas
Liver
Glucose
Glycogen
Stimulates glycogen breakdown
Glucagon

Homeostatic Imbalances of Insulin

Diabetes Mellitus:

Characterised by increase in plasma blood glucose (hyperglycaemia). result of absolute decreased production of insulin (Type 1) or resistance of cells to circulating insulin (Type 2).

Hyperinsulinism:

Excessive insulin secretion; results in hypoglycemia, disorientation, unconsciousness

Diabetic Ketoacidosis (DKA)

- Acute, major, life-threatening complication of diabetes, charecterised by high blood glucose ,high serum concetration of ketones ,low blood PH.
- Mainly occure in type 1 diabetes
- Symptoms of hyperglycemia (Polyuria, Polydipsia, Polyphagia) and symptoms of acidosis(abdominal pain , vomiting ,headach ,fatigability,decrease level of consciousness ,coma)

Hyperosmolar hyperglycemic state(HHS)

- (HHS) is a serious condition with high mortality most frequently seen in older persons.
- The possible cause is lack of circulating insulin in Type 2 diabetics, leading to a hyperosmolar and hyperglycemic state without ketone production.
- Common precipitating factors include infection, myocardial infarction, cerebrovascular events or drug therapy (e.g. corticosteroids).

Insulinoma

- Insulinoma are the most common cause of hypoglycemia resulting from endogenous hyperinsulinism.
- It is neuroendocrine tumour of islets cell of pancreas

Hypoglycemia

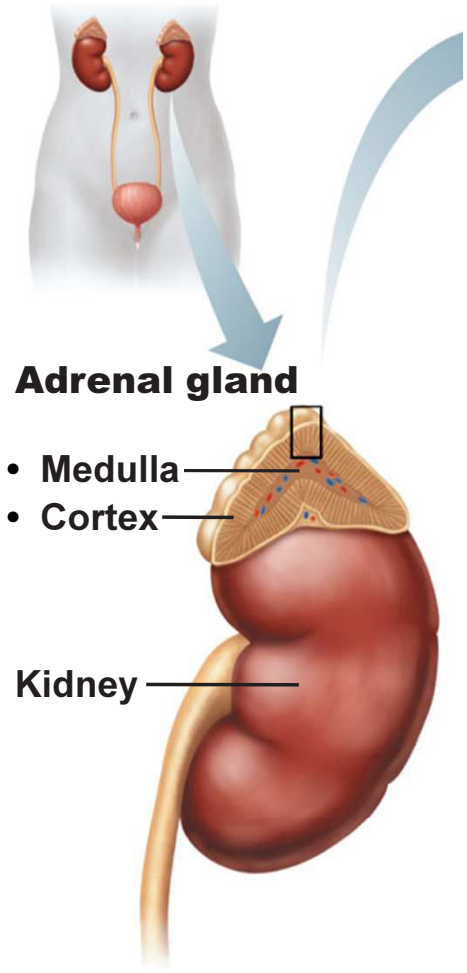
Decreased blood glucose level (<70 mg/dL) may be caused by increased insulin production, secretion, and/or administration

Symptoms of hypoglycemia:

- palpitation
- Diaphoresis
- Polyphagia
- Dizziness
- Weakness

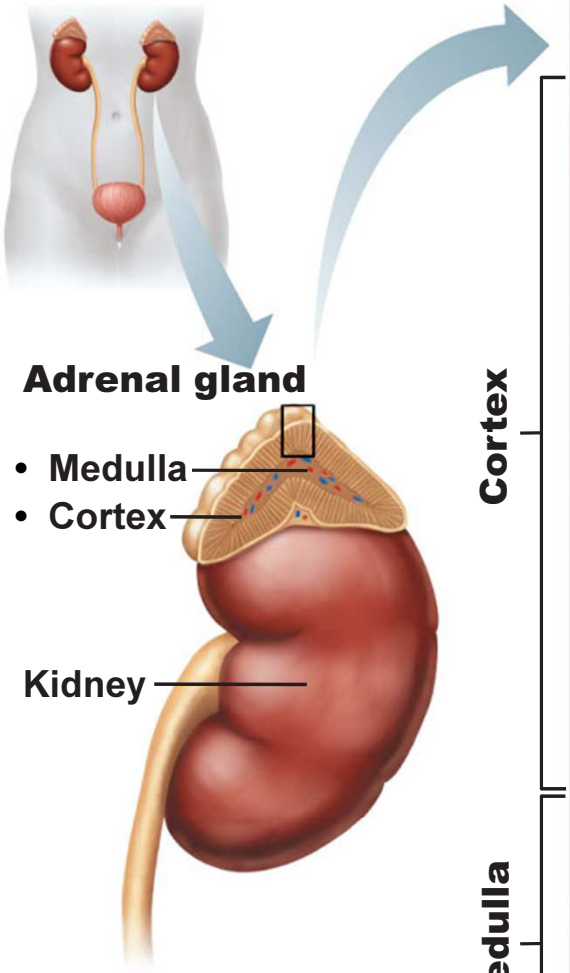
- Nervousness
- Agitation
- confusion
- Seizures
- Coma

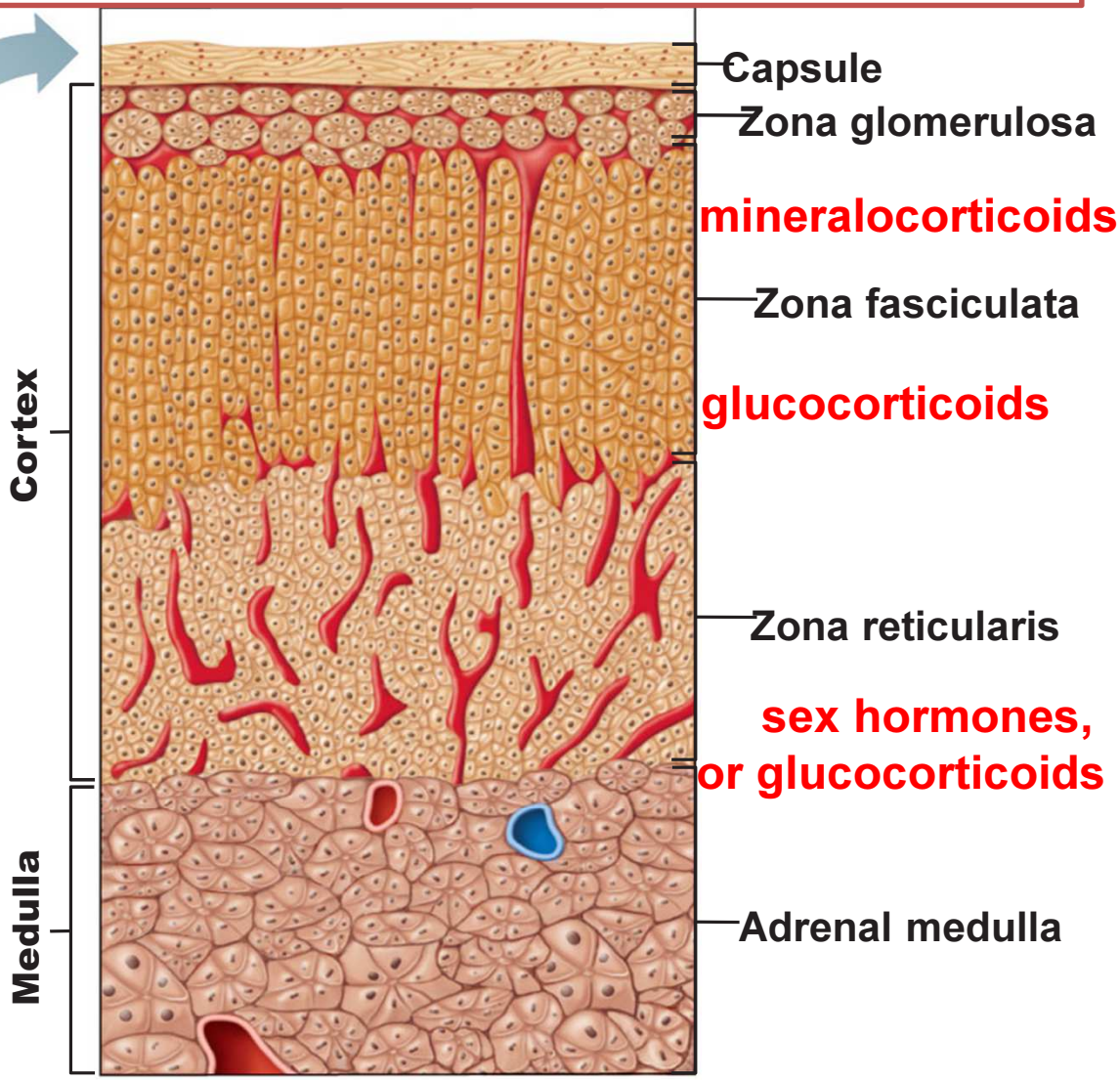
Adrenal (Suprarenal) Glands



- Paired, pyramid-shaped organs atop the kidneys
- Structurally and functionally, they are two glands in one
  - **Adrenal medulla**—nervous tissue; part of the sympathetic nervous system
  - **Adrenal cortex**—three layers of glandular tissue that synthesize and secrete corticosteroids

Adrenal Cortex





Mineralocorticoids

- Regulate electrolytes (primarily Na^+ and K^+) in ECF
- **Aldosterone** is the most potent mineralocorticoid
  - Stimulates Na^+ reabsorption and water retention by the kidneys; elimination of K^+
  - Mechanisms of Aldosterone Secretion

1. Renin-angiotensin mechanism: decreased blood pressure stimulates kidneys to release renin, triggers formation of angiotensin II, a potent stimulator of aldosterone release
2. Plasma concentration of K^+: Increased K^+ directly influences the zona glomerulosa cells to release aldosterone

Homeostatic Imbalances of Aldosterone

Hyperaldosteronism may be primary, or it may

be secondary to an extra-adrenal cause.

- **Primary hyperaldosteronism**

autonomous overproduction of aldosterone,either due to Bilateral idiopathic hyperaldosteronism (IHA) or Adrenocortical neoplasm(**Conn's syndrome)**.

Charecterised by Hypertension and Hypokalemia

- **Secondary hyperaldosteronism**

aldosterone release occurs in response to activation of the renin-angiotensin system(due to renal artery stenosis ,congestive heart failure ,nephrotic syndrome,..)

Glucocorticoids (Cortisol)

- **Cortisol (hydrocortisone)** is the only significant glucocorticoid in humans
  - Released in response to ACTH, patterns of eating and activity, and stress
  - Prime metabolic effect is gluconeogenesis—formation of glucose from fats and proteins
  - Promotes rises in blood glucose, fatty acids, and amino acids – saves glucose for brain

- Keep blood sugar levels relatively constant
- Maintain blood pressure by increasing the action of vasoconstrictors

Homeostatic Imbalances of Glucocorticoids

Endogenous Cushing's syndrome caused by chronic over-production of cortisol by adrenal glands, either as result of adrenal tumour or because of excessive production of ACTH by pituitary tumour **(Cushing's disease) or** ectopic ACTH production by other tumours.

Clinical features of overproduction of cortisol

- Central obesity
- Proximal muscle weakness
- Hypertension
- Headaches
- Psychiatric disorders
- purple striae
- Spontaneous echymoses
- Facial plethora
- Hyperpigmentation
- Acne
- Hirsutism
- Fungal skin infections
- Osteopenia

Cortisol hyposecretion

Primary Adrenal Insufficiency or Addison's Disease

Addison's disease is chronic deficiency or secretion of cortisol from adrenal cortex.

Secondary Adrenal Insufficiency

Secondary adrenal insufficiency is chronic deficiency of ACTH from anterior pituitary, resulting in reduction of cortisol release from adrenal cortex

Clinical features :

- Nausea
- Abdominal pain
- Fatigue
- Malaise
- Weakness
- Orthostatic hypotension
- Hyperpigmentation (only in primary adrenal insufficiency)

Adrenal Crisis

- Adrenal crisis is acute decrease cortisol secretion from the adrenal cortex or an acute deficiency of ACTH from the anterior pituitary.
- Cherecterised by : hypovolemia,hypotension, and hypoglycemia

Possible causes include:

- Decompensation in a patient with chronic adrenal insufficiency
- Abrupt cessation of chronic steroid administration

Adrenal Medulla

- Chromaffin cells secrete epinephrine (80%) and norepinephrine (20%)
- These hormones cause
  - Blood vessels to constrict
  - Increased HR
  - Blood glucose levels to rise
  - Blood to be diverted to the brain, heart, and skeletal muscle

- Epinephrine stimulates metabolic activities, bronchial dilation, and blood flow to skeletal muscles and the heart
- Nor-epinephrine influences peripheral vasoconstriction and blood pressure

Adrenal Medulla

- **Hypersecretion**

Pheochromocytoma is adrenal medulla neoplasm resulted in increase epinephrine and norepinephrine from the adrenal medulla

Cherecterised by
Hyperglycemia, increased metabolic rate, rapid heart beat and palpitations, hypertension, intense nervousness, sweating

- **Hyposecretion**

Not problematic

Adrenal catecholamines are not essential to life

Gonads

Ovaries in female and testes in males

	Target tissues	Hormone effects
Ovaries		
Estrogen	Most cells particularly those of female reproductive tract	Stimulates development of secondary sexual characteristics, plays role in maturation of egg prior to ovulation
Progesterone	Uterus	Stimulates uterine changes necessary for successful pregnancy
Testes		
Testosterone	Most cells, particularly those of male reproductive tract	Stimulates development of secondary sexual characteristics, plays role in development of sperm cells

Male hypogonadism

- Hypogonadism in male refers to decrease in one or both of two major functions of testes: sperm production or testosterone production.
- These abnormalities can result from disease of the testes (primary hypogonadism) or disease of pituitary or hypothalamus (secondary hypogonadism)

Clinical features :

- Decrease in energy, mood
- Decrease libido and erectile dysfunction
- Gynaecomastia
- Decrease in sexual hair, muscle mass and strength, and bone mineral density
- Infertility

Female hypogonadism

it is due to lose of ovarian function either as result of ovearian disease or because of hypothamic or pituitary diseases

Clinical features:

- Decrease in energy, mood ,and libido
- Decrease bone mineral density
- Hot flushing
- Vaginal dryness
- Amenorrhea
- Infertlity

Focused Endocrine history

When conducting a focused endocrine assessment on your patient, both subjective and objective data are needed.

Components may include:

- Chief compliant
- Present health status
- Past health history
- Current lifestyle
- Psychological status
- Family history

Presenting problems in endocrine disease

- Endocrine diseases present in many different ways and to clinicians in many different specialities .
- commonly it presented with classical symptoms related to specific hormone deficiency , however, the presentation is with **non-specific symptoms** or with **asymptomatic** biochemical abnormalities is frequent
- Endocrine diseases are encountered in differential diagnosis of common complaints including electrolyte abnormalities , hypertension, obesity and osteoporosis .

Presenting complaints

- It is important to begin by obtaining a thorough history of complaints related to the endocrine system. You will need to elicit information about any complaints of endocrine disease or disorders.Endocrine disease usually manifests as the presence of one or more of the following:

- Fatigue or lethargy
- Weight gain or loss
- Dizziness
- depression, irritability, or anxiety
- Decreased libido

- Nausea and vomiting
- Changes in urinary or bowel habits
- Changes in vision
- heat or cold Intolerance
- Change in appetite

Examples of non-specific presentations of endocrine disease

Symptom	Most likely endocrine disorder(s)
Lethargy	Hypothyroidism, diabetes mellitus, hyperparathyroidism, hypogonadism, adrenal insufficiency, Cushing's syndrome
Weight gain	Hypothyroidism, Cushing's syndrome
Weight loss	Thyrotoxicosis, adrenal insufficiency, diabetes mellitus
Polyuria and polydipsia	Diabetes mellitus, diabetes insipidus, hyperparathyroidism, hypokalaemia (Conn's syndrome)
Heat intolerance	Thyrotoxicosis, menopause

Examples of non-specific presentations of endocrine disease....cont

Symptom	Most likely endocrine disorder(s)
Palpitations	Thyrotoxicosis, phaeochromocytoma
Headache	Acromegaly, pituitary tumour, phaeochromocytoma
Muscle weakness (usually proximal)	Thyrotoxicosis, Cushing's syndrome, hypokalaemia (e.g. Conn's syndrome), hyperparathyroidism, hypogonadism
Coarsening of features	Acromegaly, hypothyroidism

Examples of non-specific presentations of endocrine disease

Symptom	Most likely endocrine disorder(s)
Bone fragility and fractures	Hypogonadism, hyperthyroidism, Cushing's syndrome,and hyperparathyroidism
Erectile dysfunction	hypogonadism, diabetes mellitus,prolactinoma,acromegaly
Resistant hypertension	Conn's syndrome, Cushing's syndrome, phaeochromocytoma, acromegaly
Sweating	Hyperthyroidism, hypogonadism, acromegaly, phaeochromocytoma
Flushing	Hypogonadism (especially menopause)
neck swelling	Simple goitre, Graves' disease, Hashimoto's thyroiditis

Examples of non-specific presentations of endocrine disease....cont

Symptom	Most likely endocrine disorder(s)
Depressed mood or Nervousness	Hypothyroidism can cause depression Hyperthyroidism, pheochromocytoma can cause nervous behavior
twitching or muscle spasms numbness, tingling, or pain in feet, or hands	hypoparathyroidism can cause twitching and muscle spasms from calcium depletion Numbness and tingling can be neuropathy from diabetes, or low calcium from hypoparathyroidism

Menstrual history

- Oligomenorrhea and amenorrhea: hyperthyroidism,cushing syndrome, hypogonadism , prolactinoma

- Menorrhagia- hypothyroidism

Past health history

- Any history of chronic illness : diabetes mellitus, hypertension,....
- History tuberculosis : adrenal insufficiency
- Any surgical operation eg thyroidectomy ,any neck surgery, or brain surgery (hypothalamus, puituitary)
- Exposure to radiation (hypothalamus, puituitary, thyroid , and parathyroid)

Drug history

Any chronic drug use

- Corticosteroid (iatrogenic cushing)
- Lithium –hypothyroidism
- Amidaron –hypo and hyperthyroidism
- Antifungal druges(fluconazole ,itraconazole)- suppress cotrisol synthesis and secretion

Social history and life style

- Smoking
- Alcohol intake(hypogonadism,gynaecomastia)

Pseudocushing syndrome

- Sexual history (married , libido ,erectile dysfunction,infertility)

Family history

family history of any endocrine disease, Some disorders are hereditary

- Diabetes mellitus
- Thyroid
- Parathyroid
- Adrenal diseases

Conclusion

- Not like other systems ,endocrine system disorders in most situation presented with non-specific complaints,and seek medical advise to aclinician with different specialties such as a cardiologist,gastroenterologist ,or even neurologist
- Objective Complaints are not the only way of presentation of endocrine disease as many of them are asymptomatic and could presented with electrolytes disturbance or high blood pressure


Thank You
For Your Atten