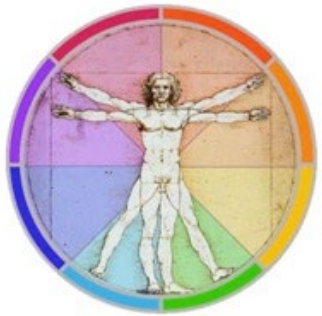
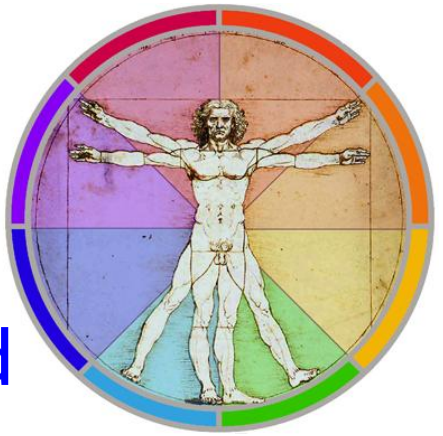
HUBS 191 Lecture Material

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 28



Endocrine IV: The adrenal glands and stress response

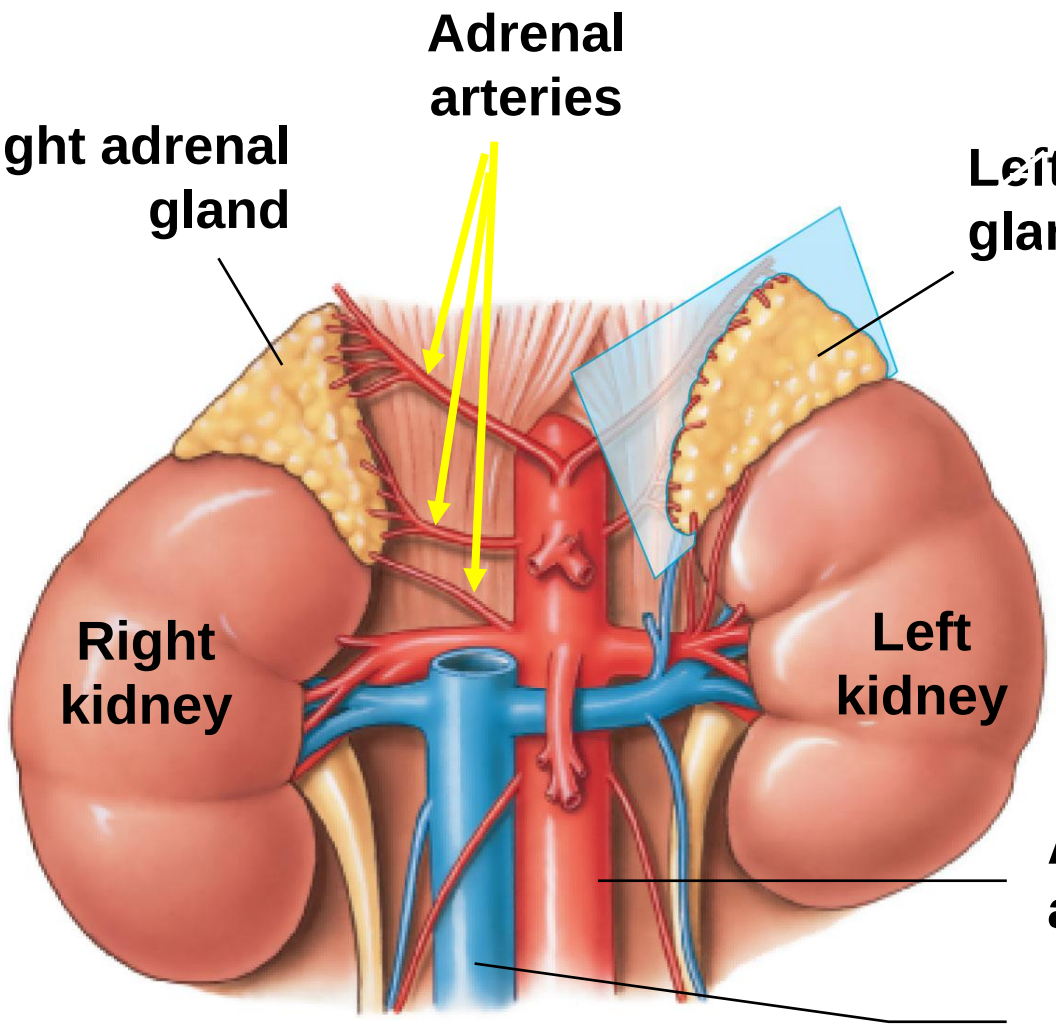
- The adrenal glands
- ACTH
- glucocorticoids
- Aldosterone
- Adrenal Disorders
- The Stress response

Philip Kelly
HUBS Professional Practice Fellow

Learning Objectives (Updated)

- Describe the location and structure of the adrenal glands.
- Outline the relationship between the hypothalamus and the adrenal medulla
- Explain how the adrenal medulla functions as part of the sympathetic nervous system.
- Discuss the control of glucocorticoid secretion
- Describe the metabolic and physiological effects of cortisol
- Outline the stimuli for aldosterone release and outline its physiological effects
- Have a basic understanding of selected adrenal gland disorders.
- Understand the phases of the stress response.

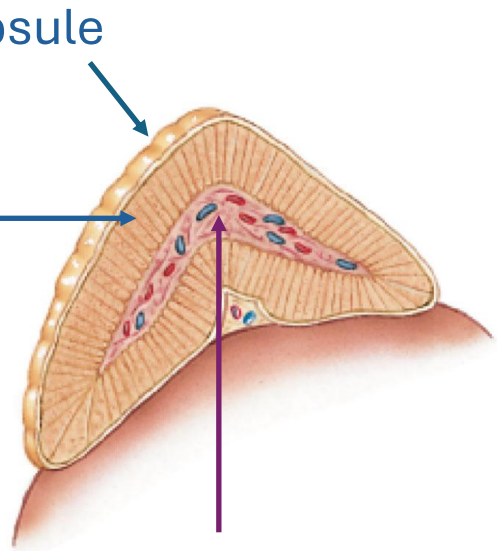
Note typo L27: **Infantile Hypo~~para~~thyroidism** can be due to:



Cortex

Corticosteroids

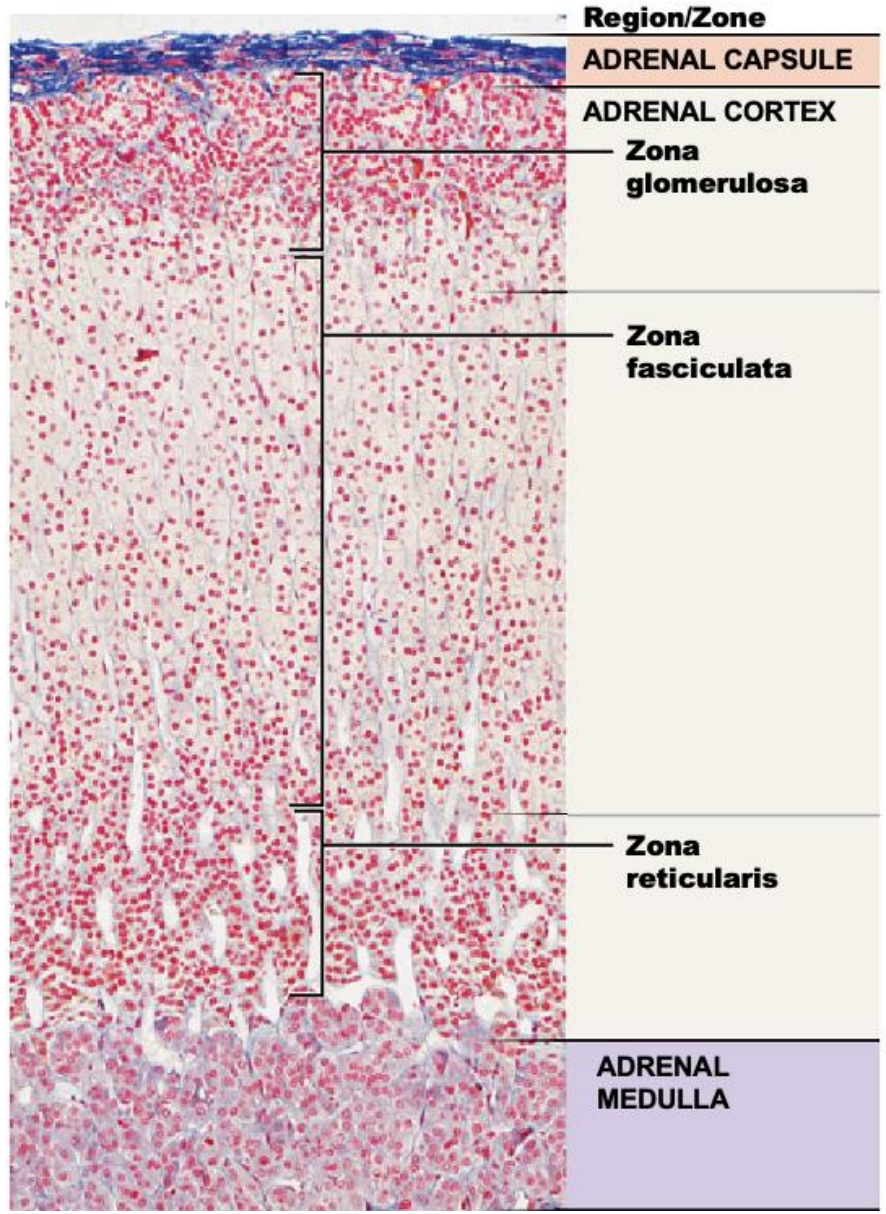
- Glucocorticoids
- Mineralocorticoids
- Sex hormones



Medulla

Adrenaline + noradrenaline (catecholamines)

Adrenal gland histology



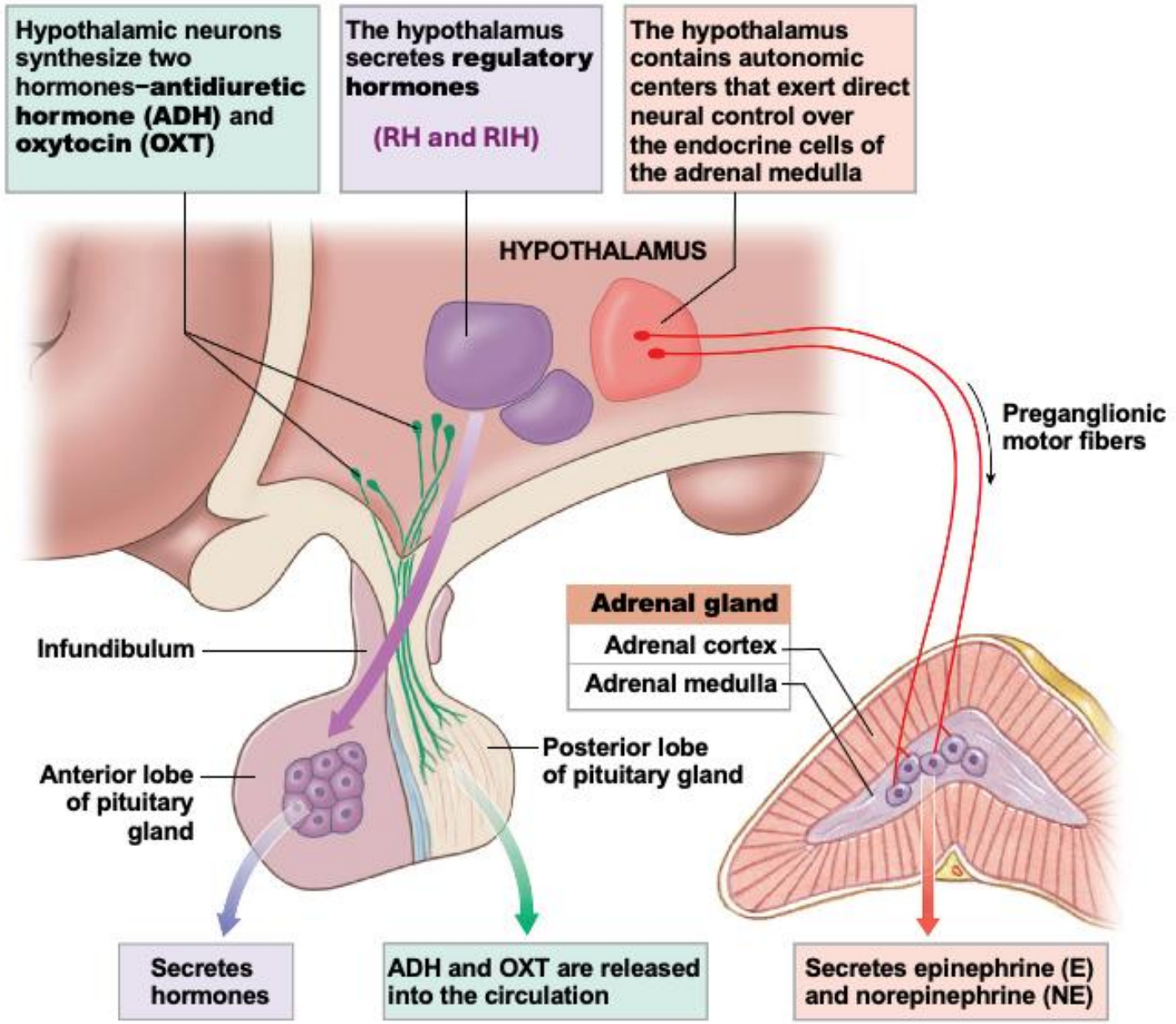
- **Zona glomerulosa**
  - Produces Aldosterone (mineralocorticoid)
  - Increases sodium reabsorption in kidney and potassium excretion
  - Aldosterone secretion stimulated by angiotensin II and high potassium
- **Zona fasciculata**
  - Middle zone
  - Secretes glucocorticoids (e.g. cortisol)
- **Zona reticularis**
  - Inner zone of adrenal cortex
  - Secretes adrenal androgens
  - Role in fetal and pre-pubertal development + mild effects in females after puberty
- **Adrenal Medulla**
  - secretes adrenaline (80%) and noradrenaline

Different groups of neurons in the hypothalamus can:

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

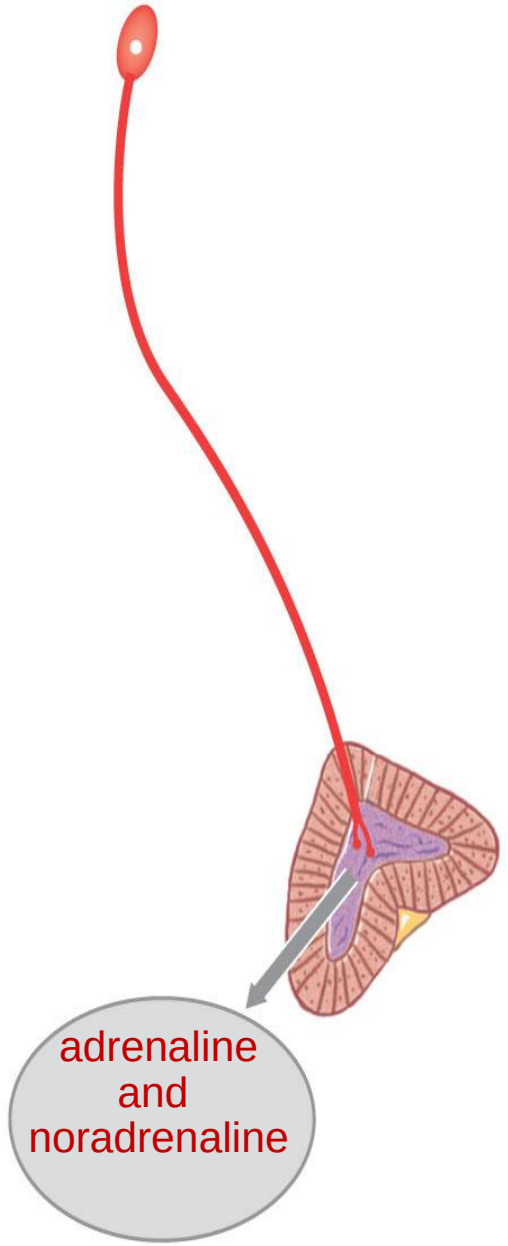
2. Synthesize hormones secreted by posterior pituitary

3. Directly control secretion of cells in the adrenal medulla



Adrenal Medulla

- Functionally related to the SNS
- Neurons in hypothalamus analogous to **preganglionic sympathetic neurons**
  - axon terminals release ACh onto nicotinic acetylcholine receptors (nAChRs) on chromaffin cells in adrenal medulla' >> depolarization
- **Chromaffin cells** in medulla are analogous to postganglionic sympathetic neurons (but without axons)
  - Secrete adrenaline and noradrenaline into blood
  - Will therefore affect all cells in the body with the right receptors i.e. alpha and beta adrenergic receptors.
  - G-protein coupled receptors
  - Exact effect though will also depend on the type of cell



Physiological Effects of adrenaline/noradrenaline

- **Activate 'fight or flight' responses.**
- Exact response with depend on:
  - Which hormone (noradrenaline or adrenaline)
  - Which receptors are present on the cell
  - Type of cell (cardiac muscle, smooth muscle, adipose, liver

- **Generally, will produce effects associated with promoting immediate survival in threatening situations.**
  - Increased heart rate, cardiac output and blood pressure
  - Increased blood flow to heart and skeletal muscle
  - Relaxation of smooth muscle in airways
  - Reduced blood flow to GI tract and kidneys
  - Pupil dilation, sweating
  - Glycogen breakdown in muscle and liver
  - Fat breakdown in adipose tissue

Phaeochromocytoma

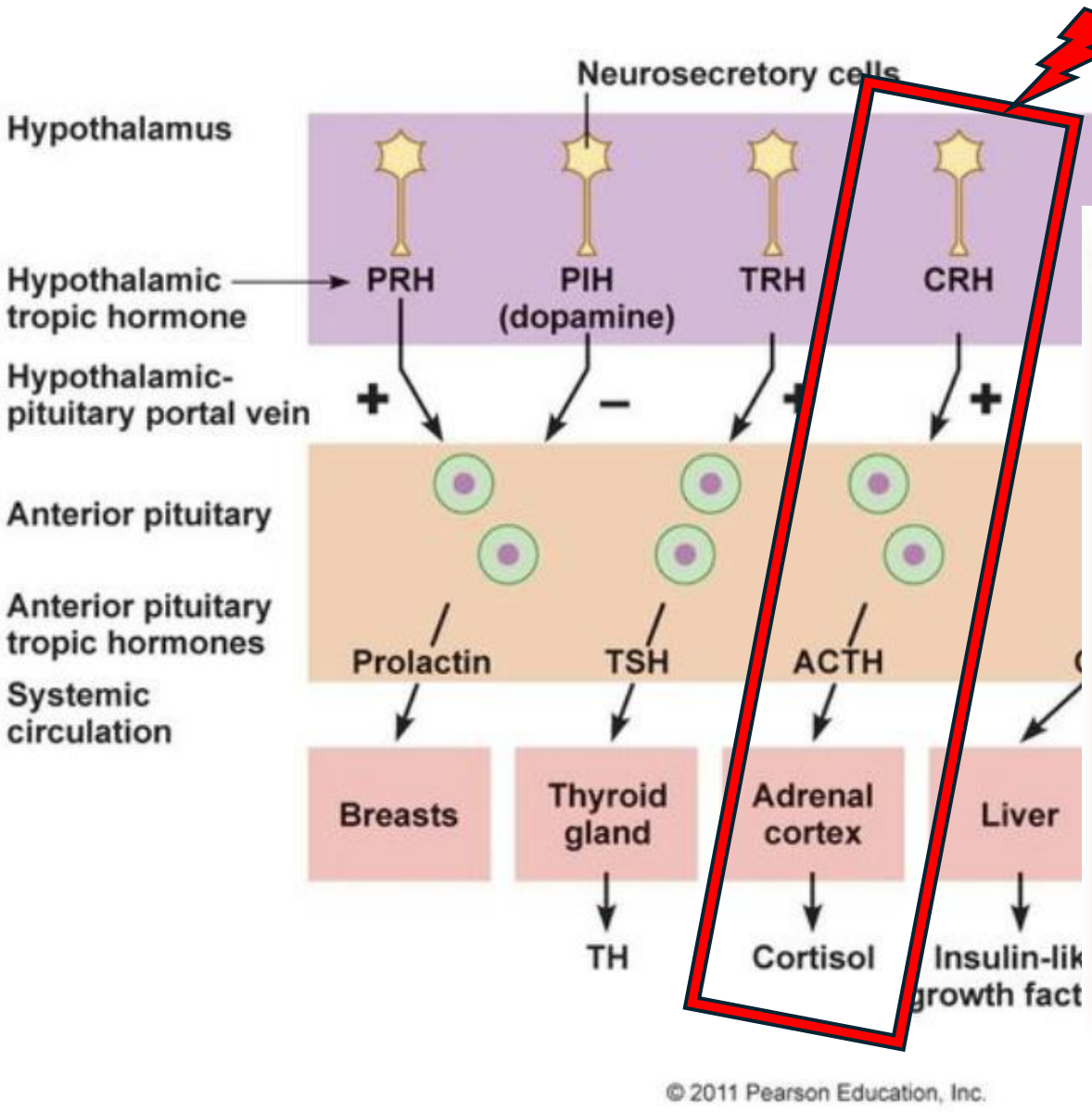
- A rare benign tumour of the adrenal medulla derived from chromaffin cells

- Results in increased secretion of:
  - Adrenaline (Epinephrine)
  - Noradrenaline (Norepinephrine)

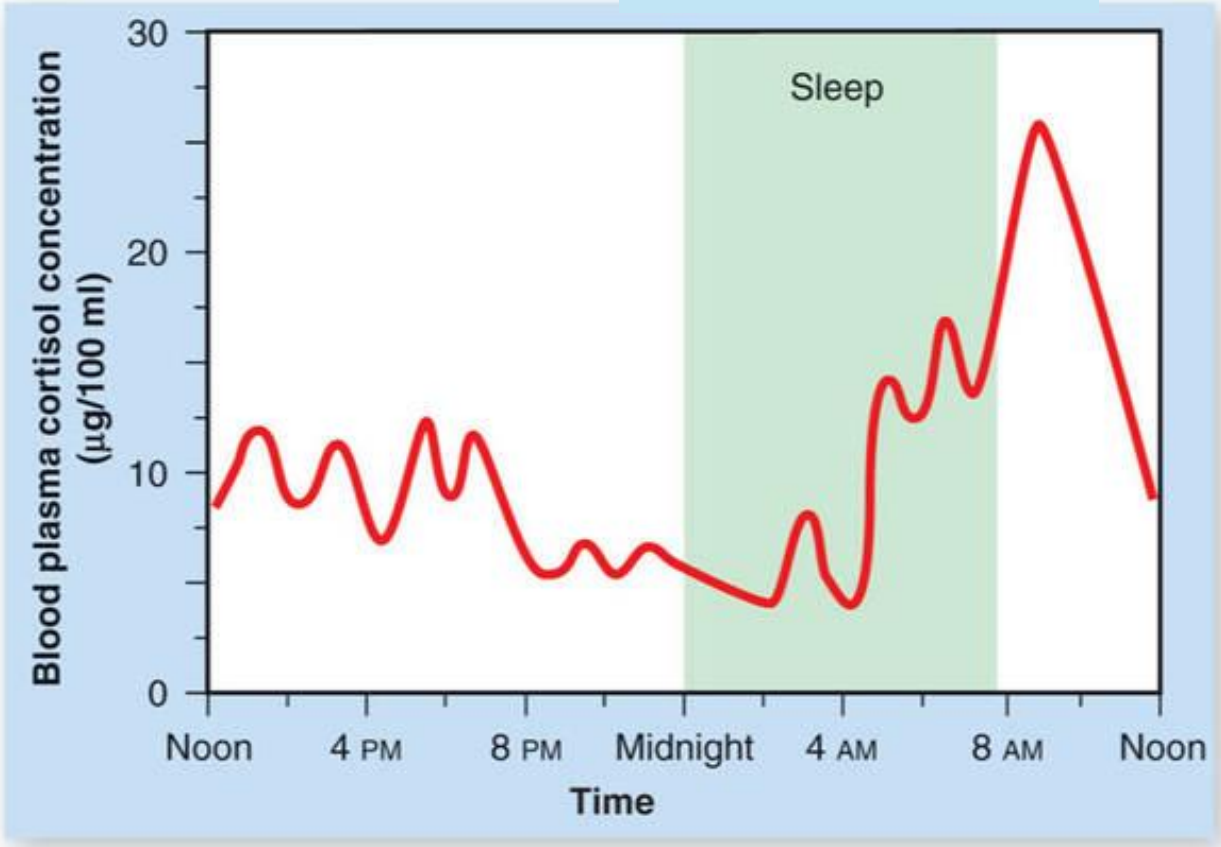
Symptoms may include:

Tachycardia (↑ heart rate), hypertension (↑ BP)
Anxiety / apprehension
Hyperglycemia
Nausea/vomiting
Headache
Sweating

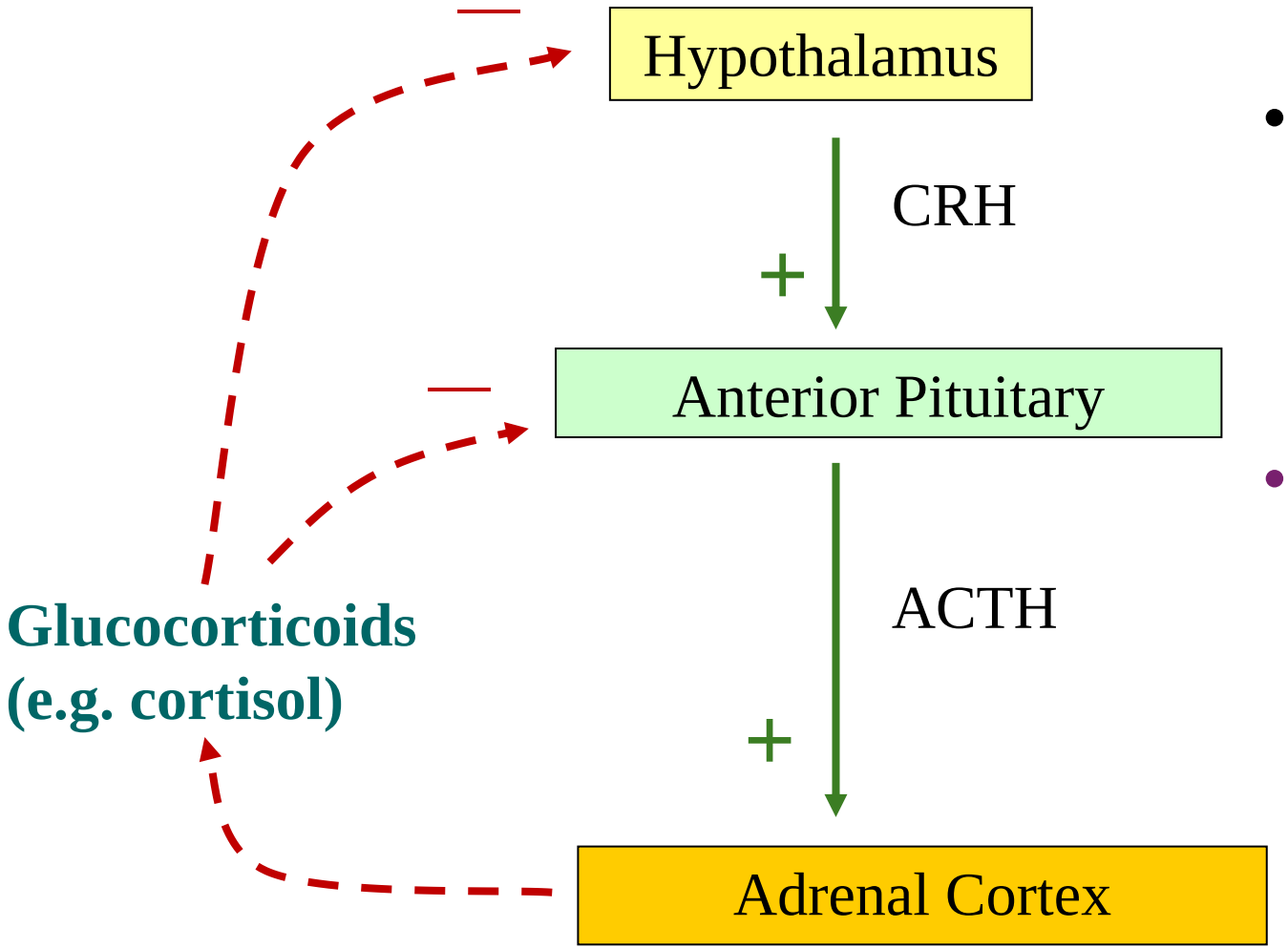
Secretion of corticosteroids



Diurnal rhythm



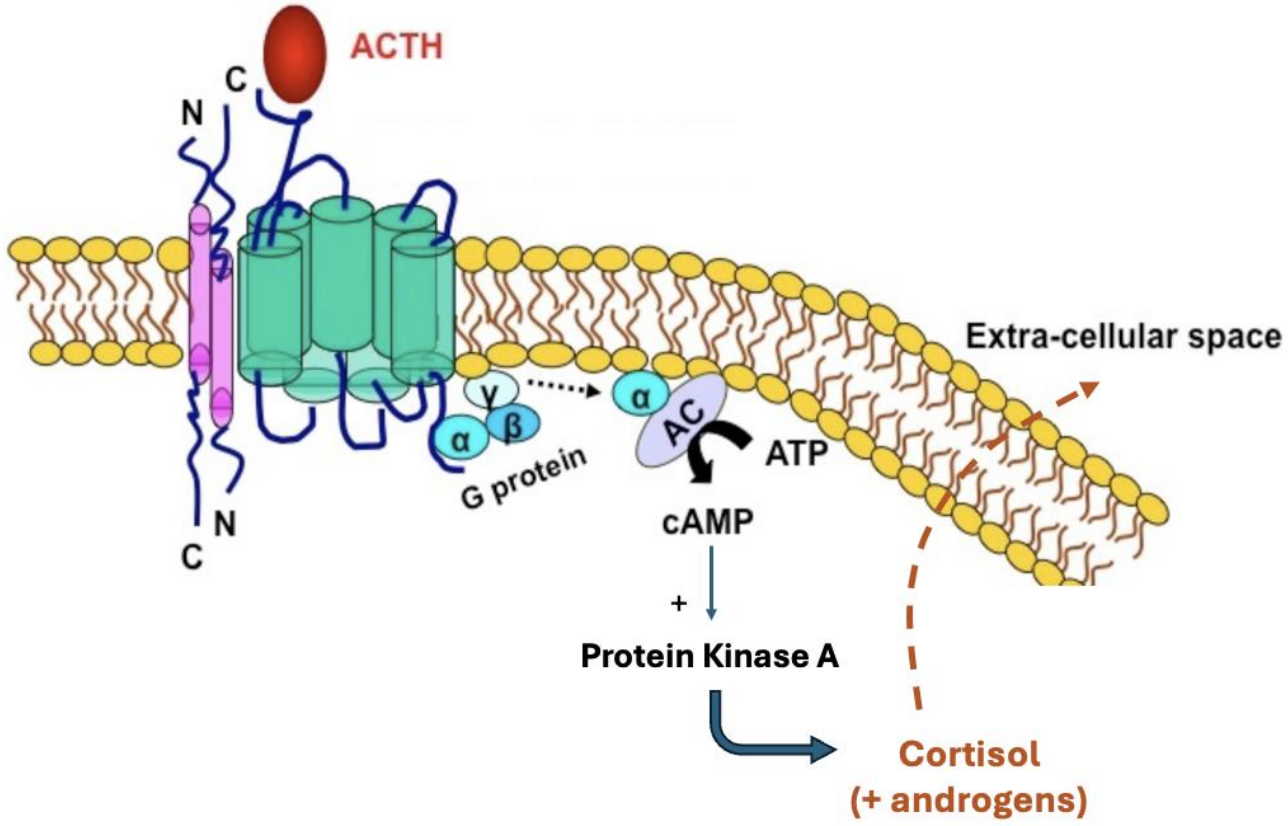
Control of glucocorticoid secretion



- Hypothalamic neurons secrete **corticotrophin releasing hormone** (CRH) – peptide hormone
- CRH acts on anterior pituitary causing it to secrete ACTH in **diurnal** pattern
  - Peak early morning, trough late afternoon
- **Other factors increasing CRH secretion include:**
  - **Physical stress or trauma**
  - **hypoglycemia**
  - **Emotional stress e.g. fear**
  - **Infection**

Adrenocorticotropic hormone (ACTH)

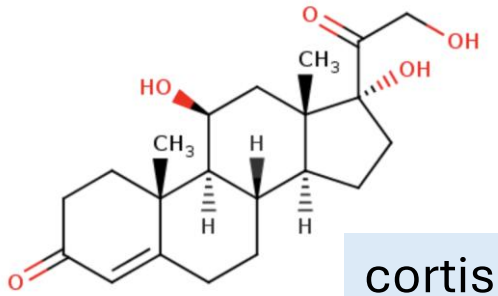
- **ACTH** is a peptide hormone produced by corticotropes cells of the anterior pituitary
- **ACTH** acts on the inner 2 layers of the adrenal cortex (zona fasiculata and zona reticularis)
  - **Glucocorticoids**
  - **Sex hormones** (mostly androgens)
- **ACTH** binds with G-protein coupled receptors in adrenal cortex
- **ACTH** Increases **cortisol** and adrenal androgen synthesis by increasing expression/activity of steroidogenic enzymes.



Adrenocortical hormones are bound to plasma proteins in blood e.g cortisol-binding globulin or albumin

Glucocorticoids help resist physiological stress

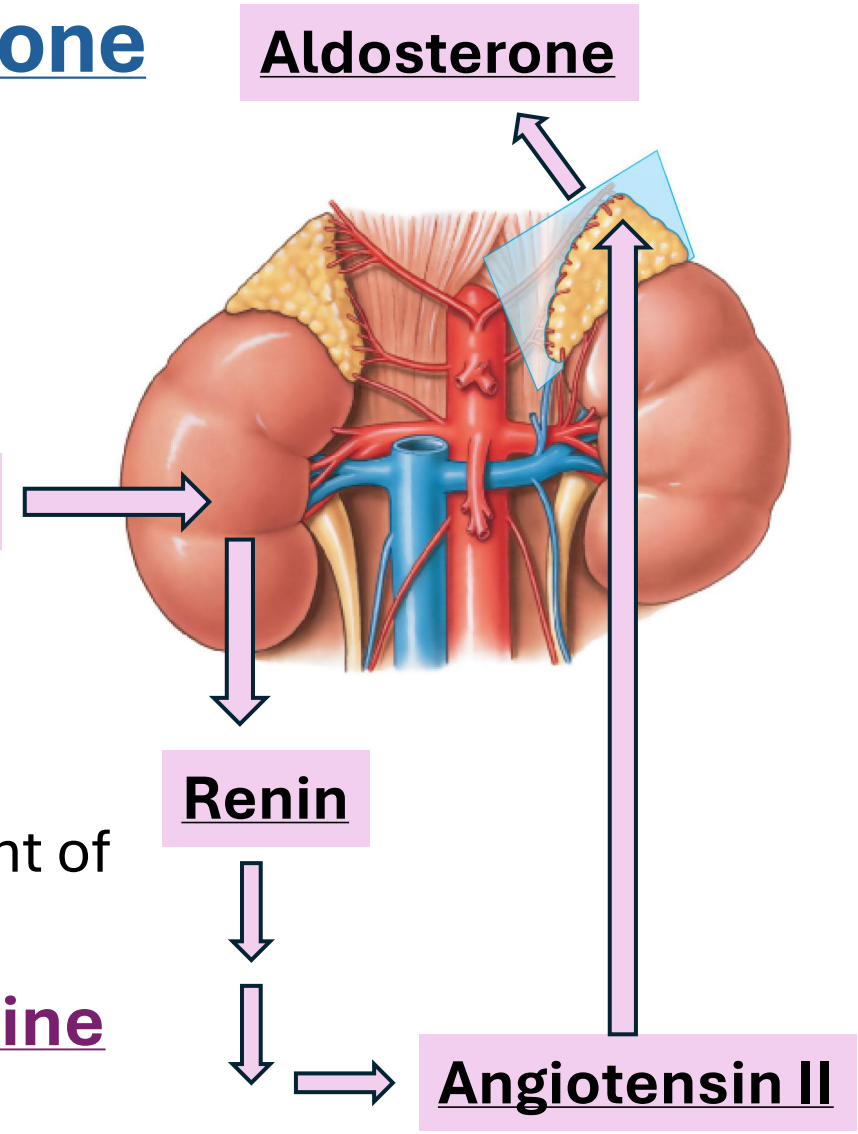
- **Increase responsiveness to catecholamines** (so help maintain BP)
- **Increase gluconeogenesis in the liver**
  - synthesis of new glucose from amino acids, glycerol, lactate, etc
- **Mobilizes amino acids from extrahepatic tissues especially muscle**
- **Promotes mobilization of lipids from fat**
  - Increased free fatty acids and glycerol in plasma
  - Decreases glucose utilization particularly in muscle cells
  - More glucose available in blood for brain cells
  - Increased BGL then stimulates secretion of insulin, but tissues less sensitive to insulin's effect due to action of glucocorticoids >> insulin resistance.
- **Reducing/limiting inflammatory and/or immune reactions.**



cortisol

Function and Regulation of Aldosterone

- **Secreted by cells of Zona glomerulosa in response to:**
  - Activation of the renin-angiotensin system (i.e angiotensin II)
  - High ECF potassium
  - Low ECF sodium
- **Aldosterone acts on nephrons in kidney to increase reabsorption of sodium**
  - Sodium is main ECF cation and a major determinant of ECF volume (and therefore blood pressure)
- **Increases renal excretion of potassium in urine**

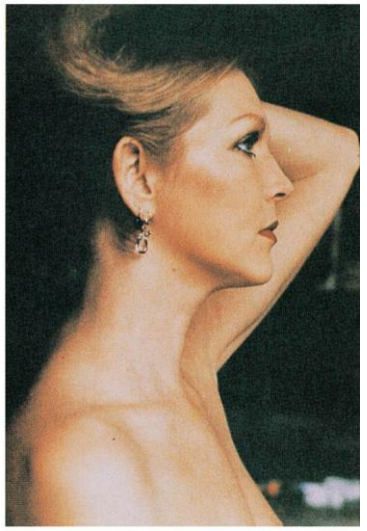


- Aldosterone can also promote reabsorption of sodium by epithelial cells of sweat, salivary glands, and in the intestines

Cushing's Syndrome

- **This is due to an excess of glucocorticoids and may result from:**
  - administration of exogenous corticosteriods such as hydrocortisone, prednisone, dexamethasone, etc

- **2^{o} to overproduction of ACTH** (Cushing's disease)
  - some hypothalamic or ant. pituitary tumours
  - Other tumours that may oversecrete ACTH

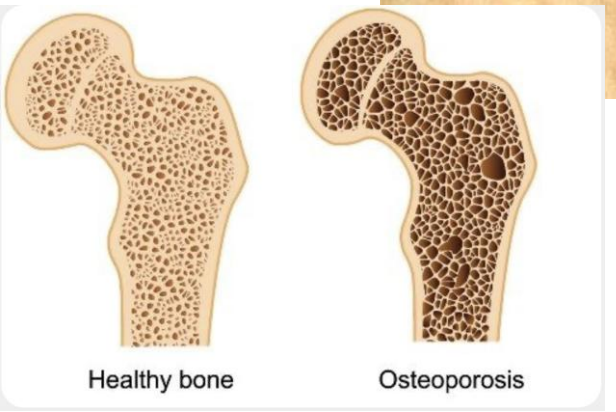


- **Adrenal neoplasia**
  - Adenoma (benign)
  - Carcinoma (malignant)

Marieb's Human Anatomy and Physiology, 10th Ed., 2016, figure 16-15, p 639.

Manifestations of Cushing's

- Increased protein catabolism with loss of muscle
- Increased gluconeogenesis and impaired insulin response
- Hypertension
- Osteoporosis (inhibits osteoblasts)
- Hirsuitism
- Immunosuppression
- Thin skin that tears and bruises easily
- Striae (stretchmarks)
- Psychological changes



Addison's Disease (1°adrenal insufficiency)

John F Kennedy
Notice the far thinner face of his brother Robert, behind him.

Jane Austen
describes "sufferings [of] feverish nights, weakness and languor" and also concern for her "looks," which turned "black and white and every wrong colour." Jane died of Addison's in 1817

http://ist-socrates.berkeley.edu/~jmp/JeremyLO2.html

Atrophied adrenals

Hyperpigmentation due to ↑↑ ACTH

Addison's Disease Causes include:

- Autoimmune adrenalitis
- Infections e.g. TB
- metastatic cancer

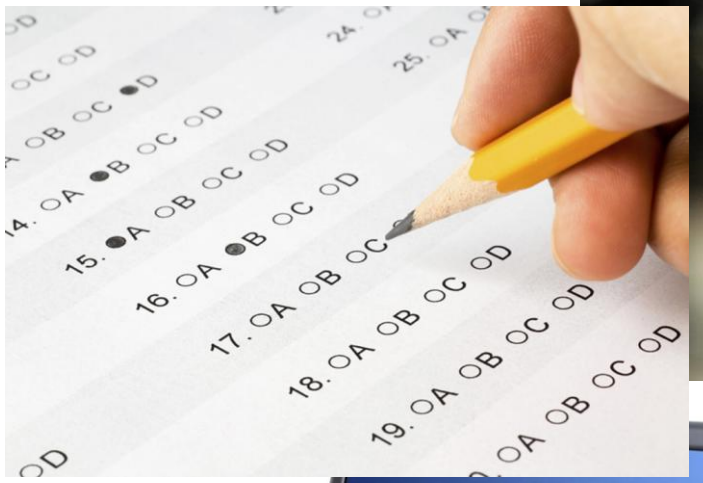
Loss of BOTH glucocorticoids (cortisol) AND mineralocorticoids (aldosterone)

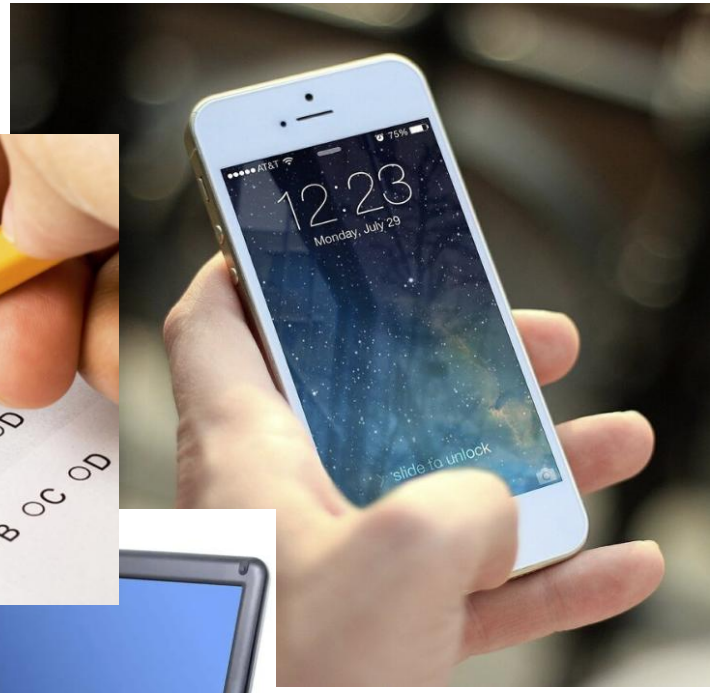
- Altered metabolism and difficulty maintaining BGL
- Low sodium, BP and ECF volume
- Hyperkalaemia (high potassium)
- Weakness, weight loss

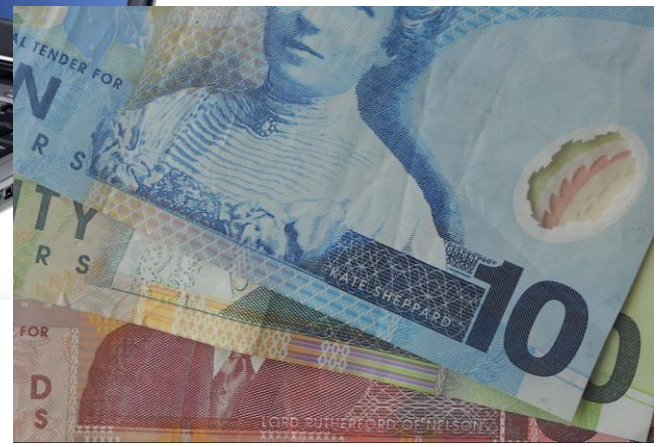
'Addisonian Crisis' may lead to shock and death.

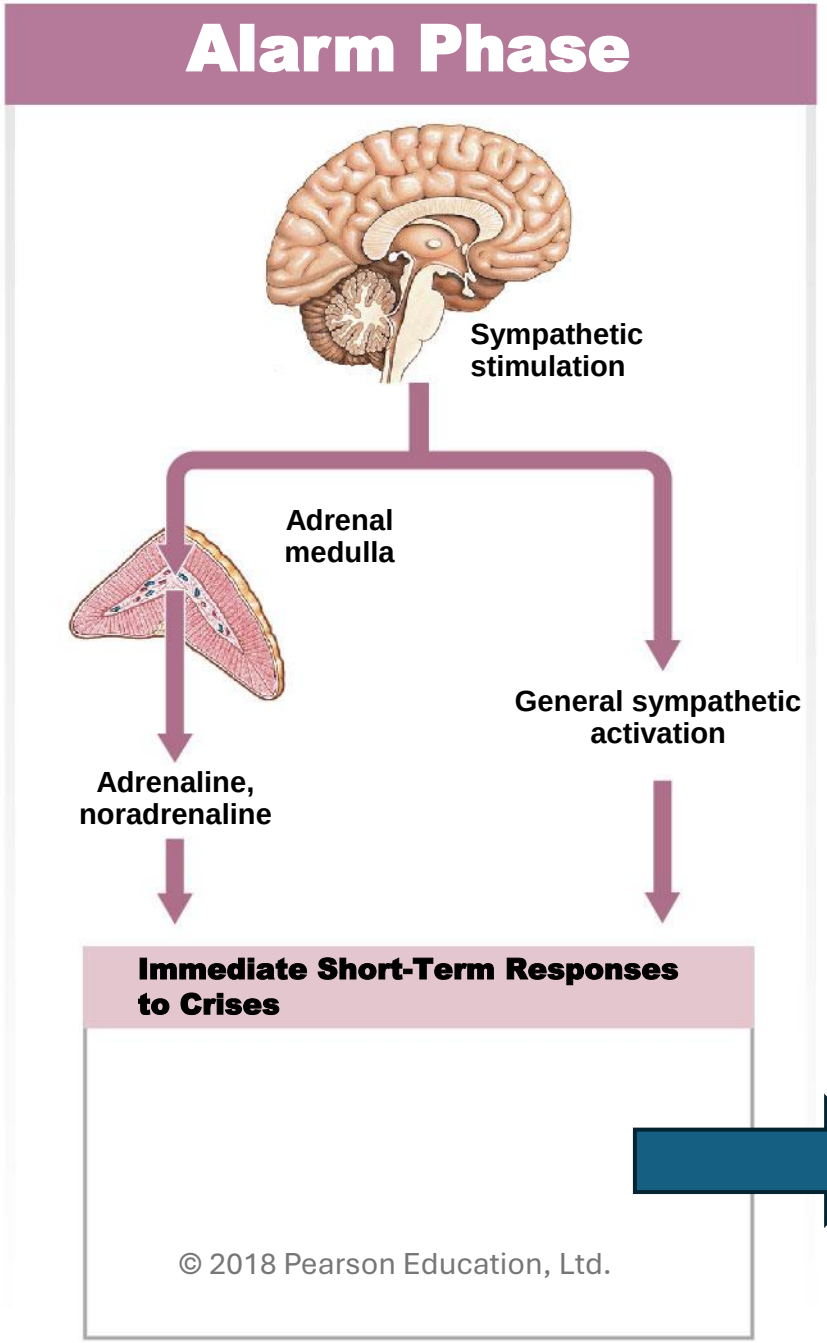
Treatment = replacement of glucocorticoid and mineralocorticoid

The Stress Response – some things have changed….







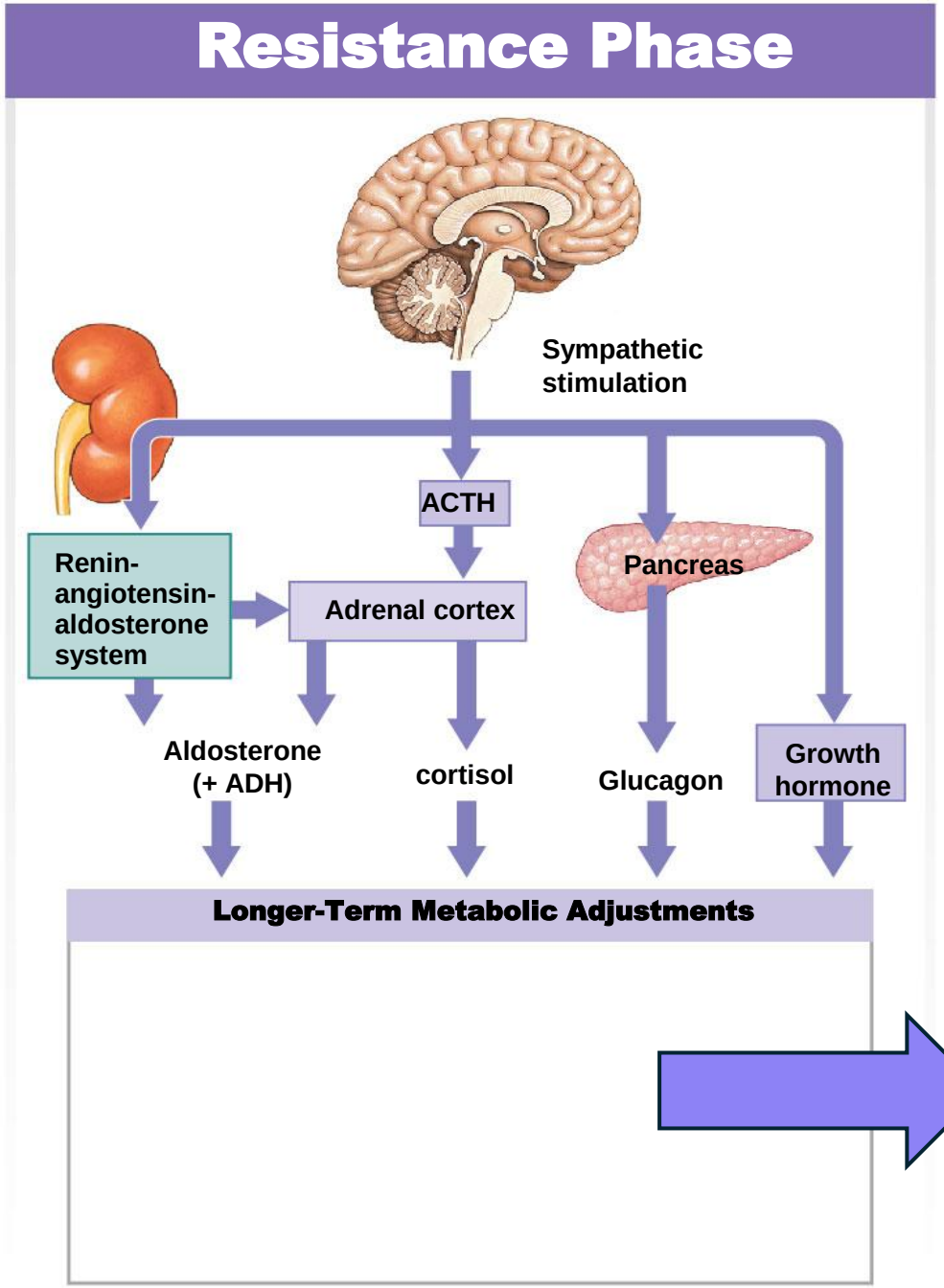


These responses can also be triggered by emotions or other psychic stimuli.

Responses that are going to help you to survive physical threats (seconds to hours)

- Increased alertness and ability to focus
- Dilated pupils
- Increased heart rate, cardiac output and BP
- More blood flow to heart, skeletal muscles
- Increased respiratory rate and O_2 consumption
- Smooth muscle in airways relaxes
- Reduced bloodflow to kidneys and gut
- Increased breakdown of glycogen in muscle
- Mobilization of liver glycogen >> ↑ BGL
- Increased sweating

Resistance Phase



Longer term responses (hours, weeks, months)

- Breakdown of proteins and fat to provide substrates for liver to produce new glucose (**gluconeogenesis)**
  - cortisol, glucagon, GH (fat only)
- Switch in metabolism of many tissues to using lipids as energy source ‘spares’ available glucose for the brain
- Increased BGLs
- Conservation of sodium and water but loss of potassium.

Exhaustion Phase

Duration, symptoms and outcome will Vary by individual and depending on the particular type of stress

- **Exhaustion of protein and lipid reserves**
  - energy reserves finally depleted
  - Structural integrity of tissues compromised

- **Inability of maintain acceptable blood glucose concentration**
  - Hypoglycemia in starvation
  - Insulin resistance in ‘chronic mental or emotional stress’

- **Failure to maintain adequate fluid and electrolyte balance**

- **Cardiovascular damage due to prolonged elevation in blood volume, BP, BGL etc**

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