ENDOCRINOLOGY

Dr.AZZA SAJID ALKINANY

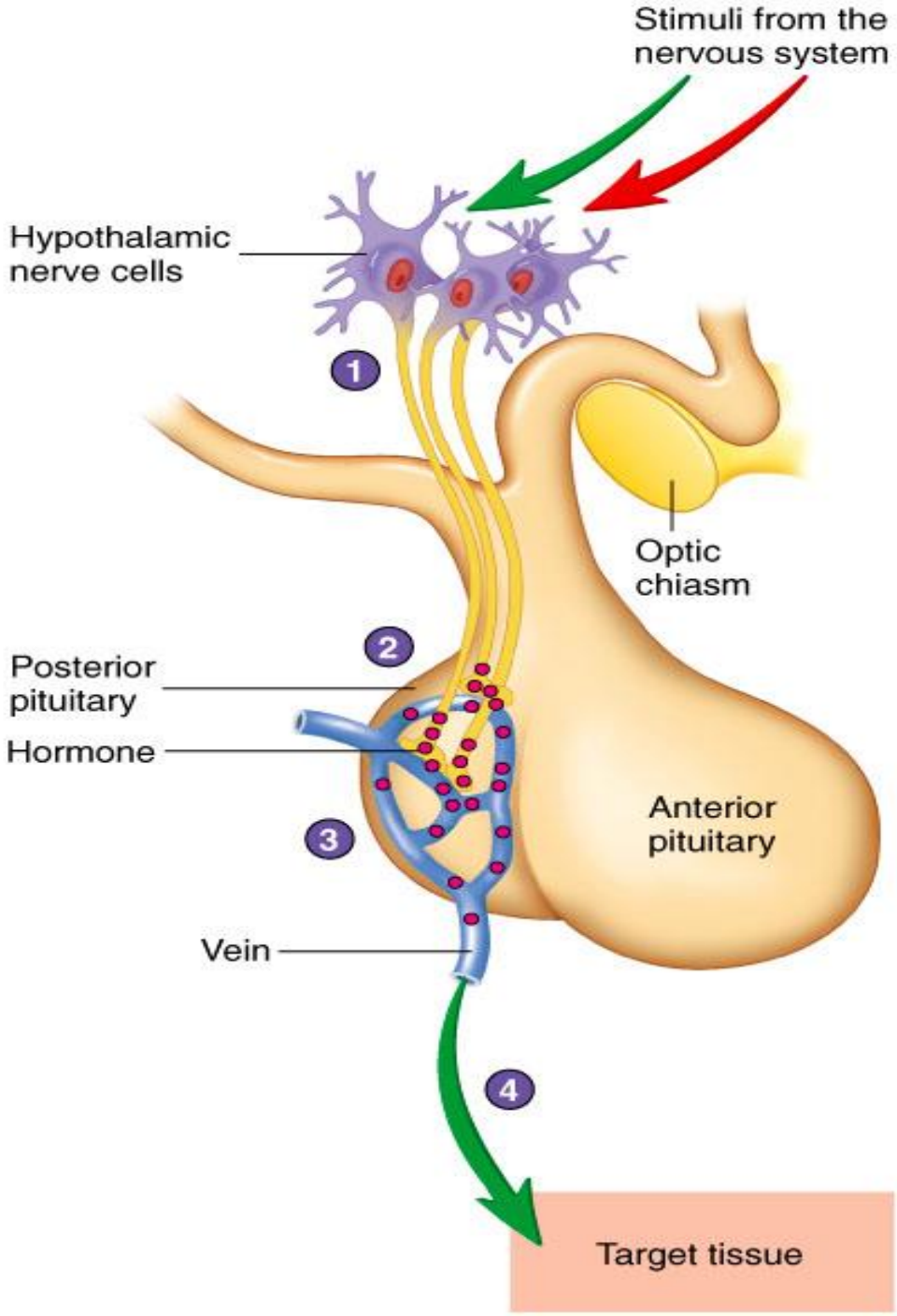
2nd STAGE

1. Stimuli within the nervous system stimulate hypothalamic nerve cells to produce action potentials.

2. Action potentials are carried by axons of nerve cells to the posterior pituitary. The axons of nerve cells store hormones in the posterior pituitary.

3. In the posterior pituitary gland, action potentials cause the release of hormones (*red balls*) from the axons into the circulatory system.

4. The hormones pass through the circulatory system and influence the activity of their target tissues (*green arrow*).



THE RELATIONSHIP AMONG THE HYPOTHALMUS,POSTERIOR PITUITARY AND TARGET TISSUES .

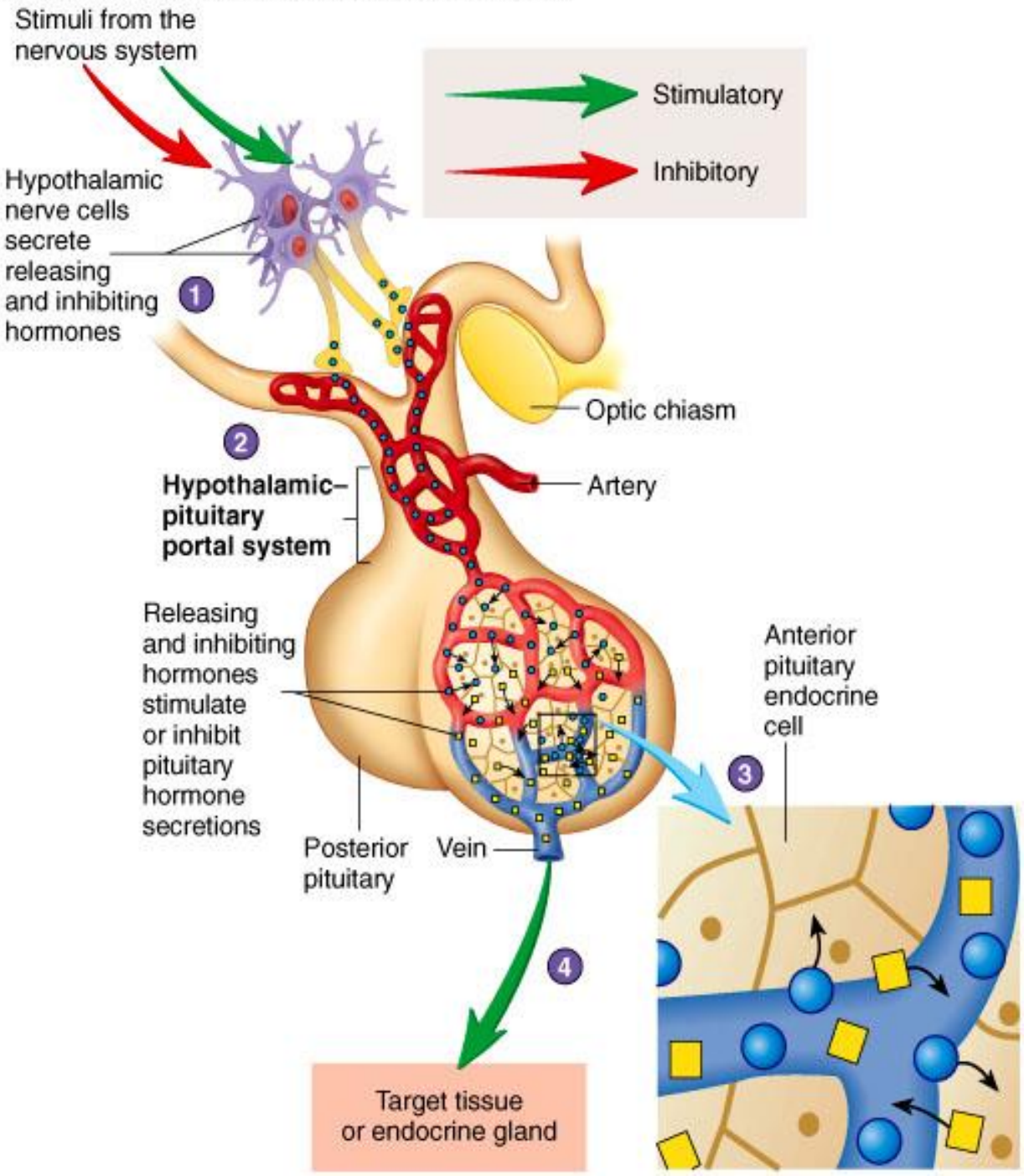
The posterior pituitary does not produce its own hormones, but **stores and releases neurohormones** that it receives from the **hypothalamus**. These neurohormones are transported through modified axons in to the posterior pituitary, where the hormones are stored in the axon endings. When needed, they are then released from the axons into blood capillaries.

1. Stimuli within the nervous system cause releasing and inhibiting hormones (*blue balls*) to be secreted from nerve cells of the hypothalamus.

2. Releasing and inhibiting hormones pass through the hypothalamic–pituitary portal system to the anterior pituitary.

3. Releasing and inhibiting hormones leave capillaries, bind to membrane-bound receptors, and influence the secretion of hormones from anterior pituitary cells.

4. Anterior pituitary hormones (*yellow squares*) are carried in the blood to their target tissues (*green arrow*), which, in some cases, are other endocrine glands.



THE RELATIONSHIP AMONG THE HYPOTHALMUS,ANTERIOR PITUITARY AND TARGET TISSUES .

The anterior pituitary is controlled by the **hypothalamus**, which is connected to it by **blood portal system**. The modified neuron in the hypothalamus release neurohormones into the portal capillaries and the neurohormones are then carried by the portal vein to the anterior pituitary. The **neurohormones** may be of 2 types: **releasing hormone** stimulate the release of a specific hormone (thus TSH releasing hormone controls the release of TSH); **inhibitory hormones** prevent the release of specific hormone

hormones of anterior pituitary gland:

1-Growth hormone or somatotropin

It is a protein.

- 1-stimulates growth in most tissues
- 2-increases amino acids uptake and protein synthesis .
- 3-increases breakdown of lipids release of
- Free fatty acids for energy .
- 4-increases glycogen synthesis and increases blood glucose level .

- GH play important role in regulating blood
- nutrient level after a meal and during fasting period.
- Low blood glucose level and stress stimulate secretion of GH .
- High blood glucose cause decreased secretion of GH .
- GH secretion rhythm occurs: daily peak level of GH correlated with deep sleep .
- Decreased blood glucose causes increased
- Secretion of GH .
- Increased blood glucose causes decreased secretion of GH .

Pathological conditions &disorders

- Pathological conditiond are associated with abnormal GH secretion ,in general hyposecretion or hypersecretion are the result of tumor in hypothalamus ,pituitary ,synthesis of abnormal GH and lack of receptors in the target tissues .

1-Chronic hyposecretion of GH in infant and children cause **DWARFISM .**

2-Chronic hypersecretion of GH lead to **gigantism (acromegaly)** .

2-Thyroid stimulating hormone (TSH):

- A glycoprotein
- Stimulates thyroid gland to synthesize and secrete of thyroid hormones .
- TRH ⟶ TSH ⟶ THYROID HORMONES
- TSH is controlled by TRH from the hypothalamus and thyroid hormones from thyroid gland .

3-Adrenocorticotropic hormone (ACTH) :

- Peptide hormone
- Stimulates the secretion of cortisol from the adrenal cortex .
- ACTH and MSH bind to melaoncytes in the skin pigmentation .

- CRH → ACTH → CORTISOL

4-Melanocyte stimulating hormone (MSH) :

- Bind to membrane bond receptors on skin melanocytes and stimulate increase secretion nelanin in the skin .
- 5-Prolactin :
- A protein
- Play important role in milk production in the mammary gland of lacting females .
- Enhance progesterone secretion of the ovaries after ovulation .Unknown in male .
- Prolactin is controlled by PRH and PIH .

6-Gonadotropins hormones

- Glycoprotein hormone .
- Promote the growth and function of gonads(ovaries and testes)
- The 2 major important hormones are:
- Luteinizing hormone (LH)
- Follicle stimulating hormone (FSH)
- Stimulate the production of gametes sperms in the testes ,oocytes in the ovaries

LH ,FSH control the production of reproductive hormones:

- 1-Estrogen and progesterone in the ovary
- 2-testosteron in the testes .
- LH and FSH are controlled by the hypothalamic releasing hormones (GnRH)

- GnRH → LH and FSH → estrogen ,teststeron

Calcitonin mechanism
The parafollicular cells of the thyroid gland detect the increase in blood Ca^{2+} levels.

Increased calcitonin secretion by the parafollicular cells results.

Decreased breakdown of bone matrix by osteoclasts results in the decreased release of Ca^{2+} from bones.

PTH mechanism
The parathyroid gland cells detect the increase in blood Ca^{2+} levels.

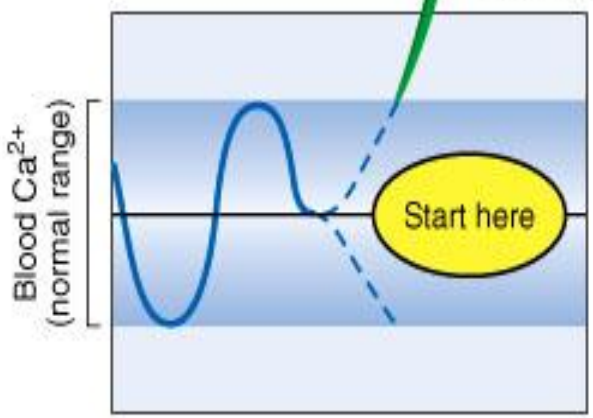
Decreased PTH secretion from the parathyroid glands results.

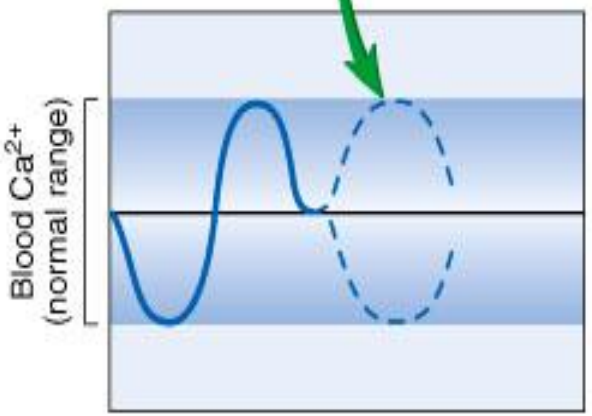
- Decreased breakdown of bone matrix by osteoclasts results in the decreased release of Ca^{2+} from bones.
- Decreased reabsorption of Ca^{2+} by the kidneys results in increased Ca^{2+} loss in the urine.
- Decreased synthesis of active vitamin D by the kidneys results in decreased Ca^{2+} absorption from the small intestine.

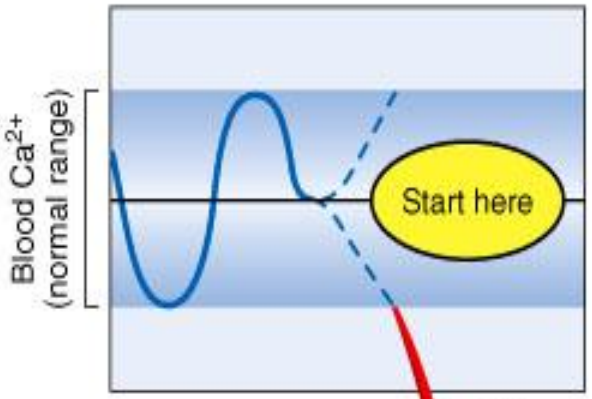
Blood Ca^{2+} levels increase.

A decrease in blood Ca^{2+} levels occurs because fewer Ca^{2+} enter the blood than leave the blood.

Follow the green arrows when blood Ca^{2+} increases.







Follow the red arrows when blood Ca^{2+} decreases.

Blood Ca^{2+} levels decrease.

PTH mechanism
Parathyroid gland cells detect the decrease in blood Ca^{2+} levels.

Increased PTH secretion from the parathyroid glands results.

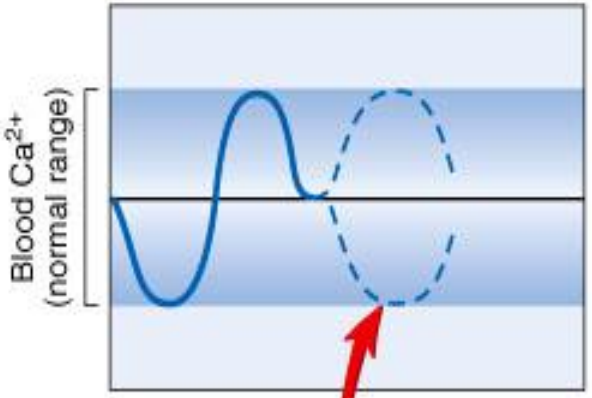
Calcitonin mechanism
Parafollicular cells of the thyroid gland detect the decrease in blood Ca^{2+} levels.

Decreased calcitonin secretion by the parafollicular cells results.

- Increased breakdown of bone matrix by osteoclasts results in the increased release of Ca^{2+} from bones.
- Increased reabsorption of Ca^{2+} by the kidneys results in decreased Ca^{2+} loss in the urine.
- Increased synthesis of active vitamin D by the kidneys results in increased Ca^{2+} absorption from the small intestine.

Increased breakdown of bone matrix by osteoclasts results in the increased release of Ca^{2+} from bones.

An increase in blood Ca^{2+} levels occurs because more Ca^{2+} enter the blood than leave the blood.



Blood Ca^{2+} homeostasis is maintained.

Adrenal glands.

Found above the kidneys. Each gland consists of an outer cortex and an inner medulla.

Adrenal medulla.

Secretes **epinephrine** and the almost identical **norepinephrine,** as a result of emotional stress e.g. anger, excitement or fear. They prepare the body for physical action. Note: the sympathetic system uses norepinephrine as the neurotransmitter in its synapses.

The effects of epinephrine are:

Increases blood glucose above normal (provide extra energy for muscle contraction) by stimulating breakdown of glycogen in the liver and fat in adipose tissue.

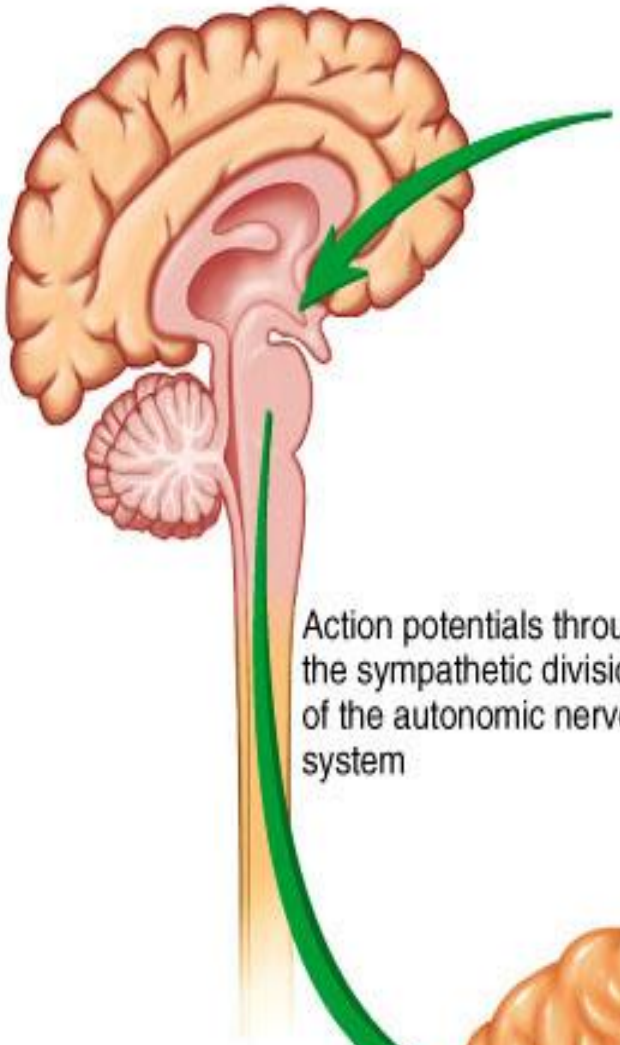
Increase blood flow and thus oxygen supply **to muscles** by:

increasing heart output (pump blood faster and bigger contractions);

vasoconstricting (reducing the blood flow) in the arterioles to the skin and gut, but expanding blood flow to the muscles.

Increasing arterial blood pressure (so blood moves faster), by contracting smooth muscles in the arteries.

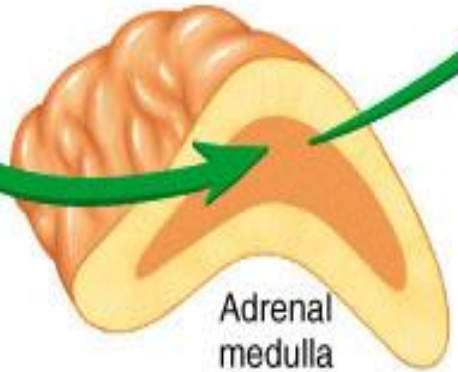
Increasing the metabolic rate of skeletal and cardiac muscles and the nerves (so they work faster



Hypothalamus stimulated by

- Stress
- Physical activity
- Low blood glucose levels

Action potentials through the sympathetic division of the autonomic nervous system



Adrenal medulla

Increased epinephrine and norepinephrine secretion

Target tissue

- Increases release of glucose from the liver
- Increases release of fatty acids from fat stores
- Increases heart rate
- Decreases blood flow through blood vessels of internal organs and skin
- Increases blood flow to skeletal muscles and the heart
- Decreases function of visceral organs
- Increases blood pressure
- Increases metabolic rate in skeletal muscles

Adrenal cortex.

This produces steroid hormones, which enter the cell to attach to receptors inside the nucleus. The main hormones are:

Cortisol. This is a hormone produced in response to stress and controlled by ACTH from the pituitary. Its main effects are on blood glucose and the immune system.

Blood glucose is increased during stress such as fasting. As glycogen reserves run down, cortisol stimulates the breakdown of fat and excess aminoacids to glucose. In extreme cases, it will also breakdown proteins to aminoacids.

Immune system: cortisol suppresses inflammation and other immune responses. Thus the synthetic equivalent, cortisone, is used to suppress allergies and auto-immune responses (see immune lectures).

Aldosterone. This helps regulate **blood sodium**, by increasing sodium absorption into the body. Indirectly, it also affects the water balance of the body (increasing sodium, increases the osmotic pressure of the blood, so water is sucked out of the tissues into the blood).

Thus, when there is a **low blood pressure**:

Pressure receptors in the **kidney** trigger release of the enzyme **renin** which catalyses

the **blood protein angiotensinogen → angiotensinI → angiotensin II**

Angiotensin II controls blood pressure by:

Causing **vasoconstriction** of capillaries, so blood is squeezed out of the capillaries

back into blood circulation (more blood circulating → higher blood pressure).

Stimulate **secretion of aldosterone** by the adrenals. Aldosterone increases blood

sodium, so water is sucked out of the tissues back into the blood circulation

↓

more blood volume

Aldosterone increases blood sodium by:

Increasing reabsorption of sodium ions in the **kidne**

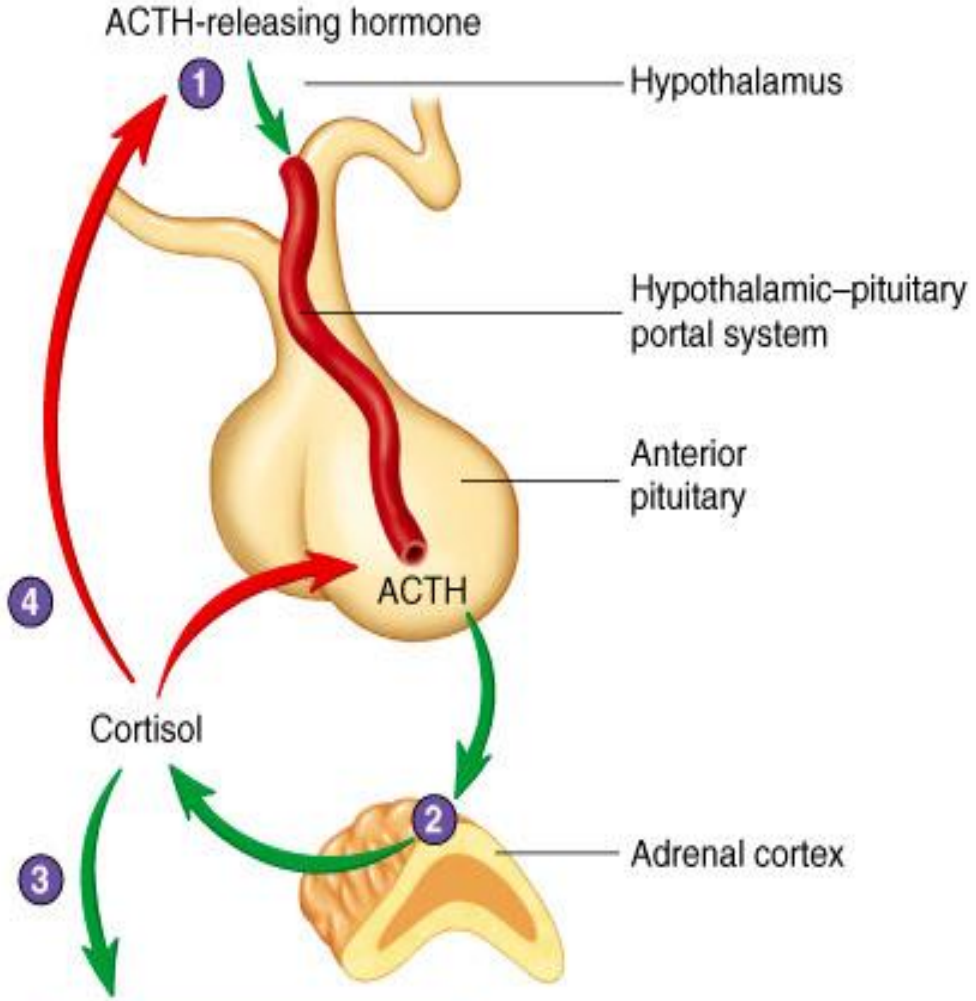
by speeding up Na+/ K+ pumps (note more K+ is excreted as a result).

Increasing absorption of sodium ions from the **gut** (ileum and colon).

Reducing sodium loss from **sweat glands**

Stimulatory

Inhibitory



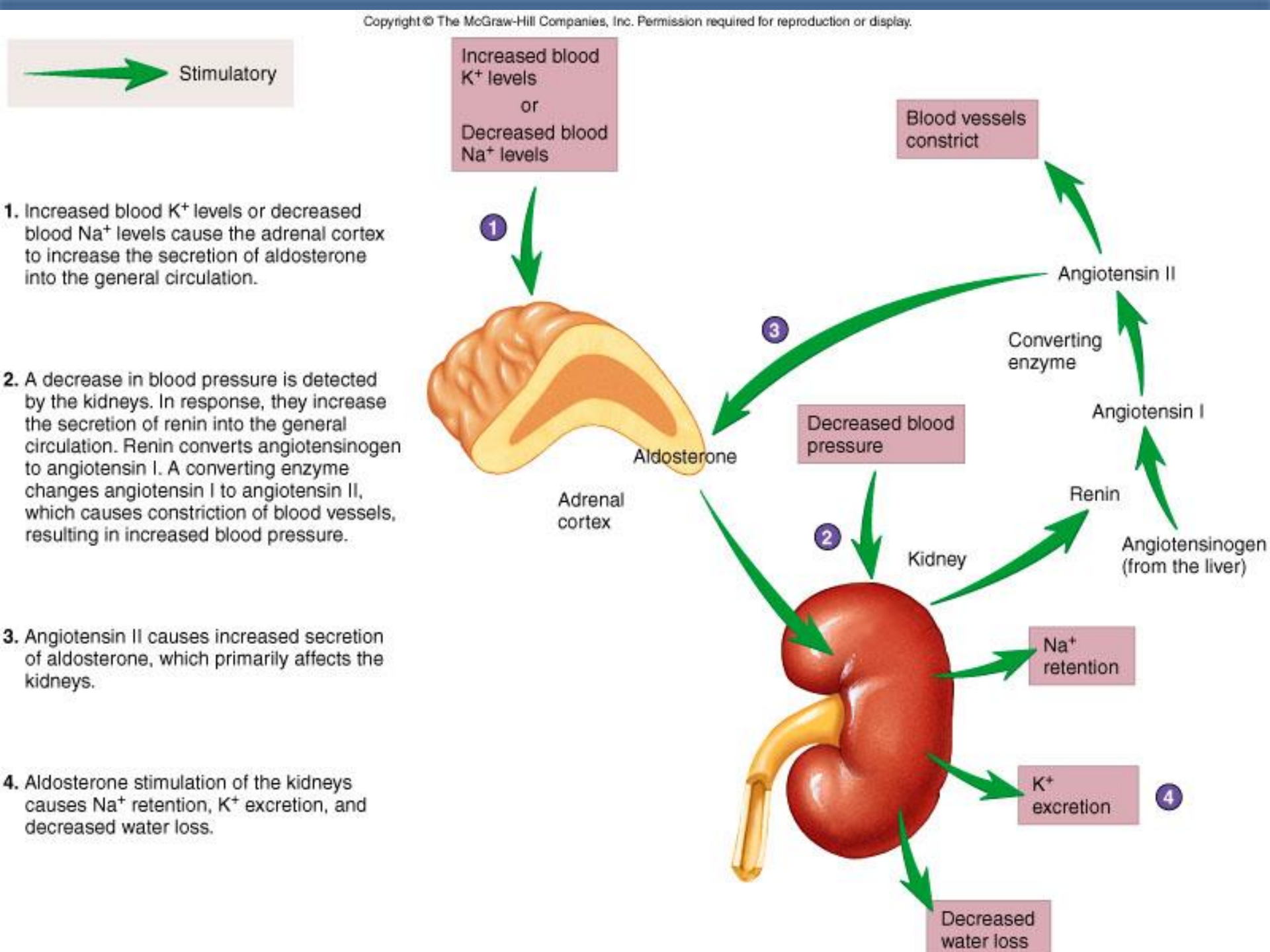
1. In response to stress or low blood glucose, ACTH-releasing hormone passes from the hypothalamus through the hypothalamic–pituitary portal system to the anterior pituitary. The releasing hormone binds to and stimulates cells that secrete ACTH into the general circulation.

2. ACTH acts on the adrenal cortex and stimulates the secretion of cortisol into the general circulation.

3. Cortisol acts on its target tissues to increase protein breakdown and increase blood glucose.

4. Cortisol acts on the hypothalamus and anterior pituitary to decrease ACTH secretion.

Target tissue
- Increases fat and protein breakdown
- Increases blood glucose levels
- Has anti-inflammatory effects



1. Increased blood K^+ levels or decreased blood Na^+ levels cause the adrenal cortex to increase the secretion of aldosterone into the general circulation.

2. A decrease in blood pressure is detected by the kidneys. In response, they increase the secretion of renin into the general circulation. Renin converts angiotensinogen to angiotensin I. A converting enzyme changes angiotensin I to angiotensin II, which causes constriction of blood vessels, resulting in increased blood pressure.

3. Angiotensin II causes increased secretion of aldosterone, which primarily affects the kidneys.

4. Aldosterone stimulation of the kidneys causes Na^+ retention, K^+ excretion, and decreased water loss.

and bicarbonates in to the duodenum, the pancreas also contains patches of endocrine tissue known as the **Islets of Langerhans**. These secrete 2 hormones controlling blood sugar: **insulin** and **glucagon**, which **maintain blood sugar at a level of 100mg glucose/ 100ml blood**.

Insulin (from b cells) is continuously produced, but production increases when there is high blood glucose. It thus decreases blood glucose by:

Encouraging all cells to take up more glucose out of the blood (note cells cannot take up glucose without insulin present).

Stimulates **liver** to convert glucose g glycogen.

Stimulates **adipose tissue** to convert glucose g fat.

Acts on **satiety center** of the hypothalamus so that you no longer feel hungry and so stop eating more sugar.

Glucagon (from a cells) is only produced when blood glucose falls below 70 mg/ 100ml. It increases blood sugar by acting on the **liver** to break down glycogen g glucose; breakdown spare aminoacids g glucose.

Glucose is the main source of ATP for cells, especially for the nervous system. Maintenance of blood sugar is thus an essential part of homeostasis (maintaining constant conditions in the body).

When blood glucose falls, your body will:

1st reduce insulin production.

Then **secrete glucagon** (but insulin still continues in opposition to glucagon).

The **secrete somatostatin** from g cells in the Islets. This is a paracrine hormone inhibiting insulin production.

If you continue fasting and use up all your glycogen, then glucagon can no longer work and you will switch over to **cortisol**, breaking down 1st fat and later protein.

Note that other hormones raise blood sugar above normal (and so are not controlling it): **epinephrine** increase blood sugar by breaking down fats and proteins; **growth hormone** stimulates fat breakdown instead of protein breakdown.

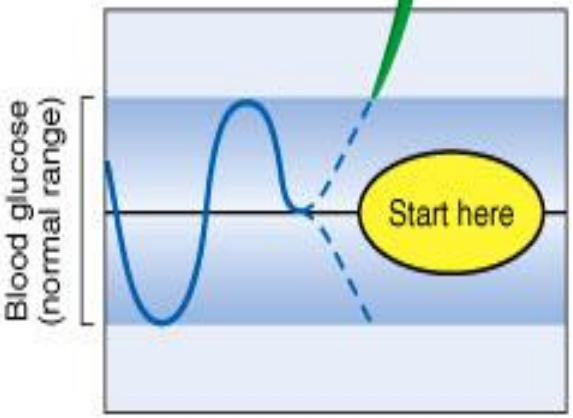
- An increase in blood glucose is detected by the pancreatic islet cells.
- Increased parasympathetic stimulation of the pancreas is associated with digestion of a meal.

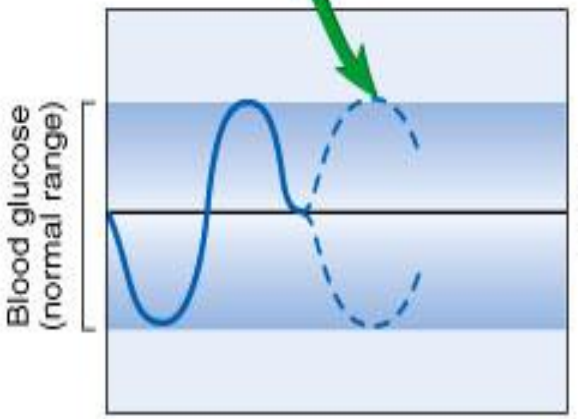
Increased secretion of insulin results from increased blood sugar and parasympathetic stimulation.

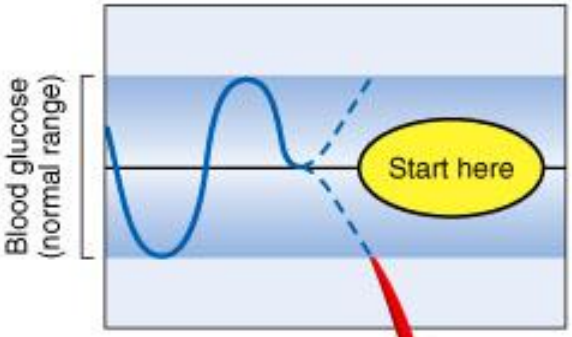
- Insulin stimulates the increased uptake of glucose by most tissues (exceptions include the brain, which does not depend on insulin for glucose uptake).
- Excess glucose is converted to glycogen, which is stored in skeletal muscle and liver.
- Excess glucose is converted to fat (triglyceride) and stored in adipose tissue.

A decrease in blood glucose levels results from the increased movement of glucose into cells.

Follow the green arrows when blood glucose increases.







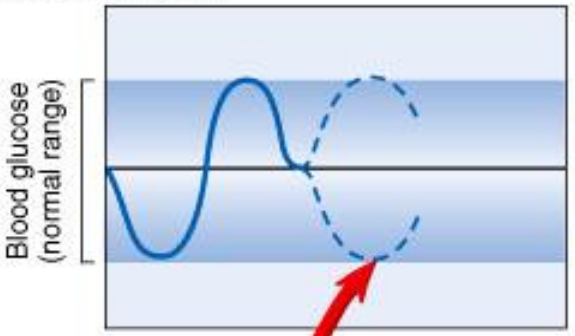
Follow the red arrows when blood glucose decreases.

- A decrease in blood glucose is detected by the pancreatic islet cells.
- Increased sympathetic stimulation of the pancreas is associated with physical activity.
- Increased epinephrine release from the adrenal medulla is associated with physical activity.

Decreased secretion of insulin results from decreased blood sugar, sympathetic stimulation, and epinephrine.

- Decreased insulin results in decreased uptake of glucose by most tissues, which makes glucose available for use by the brain.
- Glycogen is broken down to glucose by the liver, which releases glucose into the blood.
- Glucose is synthesized from amino acids by the liver, which releases glucose into the blood.
- Fat (triglyceride) is broken down in adipose tissue, which releases fatty acids into the blood. The use of fatty acids by tissues spares glucose usage.
- Fatty acids are converted by the liver into ketones, which are used by other tissues as a source of energy.

An increase in blood glucose results from the decreased movement of glucose into most tissues and the release of glucose from the liver.



Diabetes mellitus is due to insulin problems. There are 2 types:

Type 2 = Non-insulin dependent. Lack of insulin receptors on target cells means that although insulin is normal, cells cannot take up glucose and die. This form of diabetes is associated with extreme overweight (and thus prolonged over-consumption of glucose and so prolonged excessive insulin production damaging receptors). In developed countries, it is one of the fastest expanding diseases - USA alone has 0.5million new cases / year. Although the results can be dangerous (affects vision and decreases immunity, could even result in limb amputation), it is easily controlled by dieting).

Type 1 = insulin dependent. This is a genetically controlled (and thus inherited) auto-immune disease in which the pancreas has insufficient b cells (due to destruction by antibodies) and so produces insufficient insulin. This means that:

Blood glucose is excessively high and exceeds the kidney threshold (see

excretion), resulting in excretion of glucose in the urine.

Insulin is required for cells to take up glucose (it assists in transport), so cell

death occurs and the satiety center of the hypothalamus cannot record the

blood glucose. The person thus keeps eating sugar, further boosting blood

glucose and thus excretion. As cells switch to fat and protein metabolism as an

alternative to glucose, the body wastes away.

Treatment requires insulin injections throughout life.