Endocrinology

Prof. Dr. Nermeen Atef Helmy

Hormone : Is the secretion of any endocrine gland is called " HORMONE " which means to stimulate. This name is not exactly explain the nature of the endocrine secretions as some of them stimulate the function while other inhibit the same action.

Hormones are organic chemical substances which are classically divided, according to their composition, into 2 groups; **nitrogenous and steroids.**

Hormones can induce their effect when present. in very small amounts.

The hormone Cycle

A) Synthesis Hormone is synthesized by specific cell type which should be physiologically capable for complete functional activity to produce the specific hormone. The blood reaching the producing cells containing the building units of the hormone is a must. For example, the building stones of thyroid hormones are the amino acid tyrosine and iodine. The thyroid tissue (thyroid epithelium) has the ability to trap iodine from the circulation and accumulate it in the gland. This capacity is called iodine trap. Inside the thyroid cells, this trapped iodine is converted into active one by oxidative enzymes as peroxidase. Formation of the thyroid hormones (T3 and T4) takes place due to utilization of active iodine for iodination of the amino acid tyrosine as follows :

Tyrosine + Iodine (active)→ MIT

MIT + Iodine (active) → DIT

MIT + DIT → t3

DIT + DIT → t4

B- **Storage**:

- Some hormones are stored inside follicles (vesicles) located among the same producing cells such as the thyroid gland in which the thyroid hormones combine with a protein (globulin) to form an inactive thyroprotein (thyroglobulin) which is stored inside the thyroid follicles.
- Other glands like anterior pituitary, adrenal, gonads ... etc.) store their hormones intracellularly in the form of protein - bound hormone. Degranulation of such cells indicates the release of the hormone (s).
- The posterior pituitary (pars nervosa) represents unique example for storage of what is known as posterior pituitary hormones as the actual site of secretion for these hormones is the hypothalamus (paraventricular and supraoptic nuclei).
- T4 is considered a depot for the potent T3. Demonoiodination takes place in the circulation. T3 is 10 times potent more than that of T4.

C- **Release**:

It means the secretion of the hormone to the body fluids mainly blood. The endocrine glands as an important regulators for many biological activities in the body are under careful regulation for their endocrine output. Regulation of the hormone secretion depends .upon several .mechanisms; One of the simplest is the metabolic concentration of the hormone(s) itself or substances influenced by the hormone in the circulation.

D) Transport:

The majority of hormones are transported to their targets via blood. Even in of local or tissue hormones, besides they induce their action at their site of production, they also have a generalized effect.

In the circulating blood, it bound to plasma proteins (albumin or globulin) which tend to restrict the hormonal activity. This pound form of the hormone is biologically inactive. At the cells of the target, the molecules are released from their binding proteins and become free; in order to exert their action at the intracellular level of the target.

Recycling:

- After degradation of the hormone, a part of its building stones is excreted outside the body; while another part returns back to the site of hormone synthesis in order to share in the formation of new molecule of the hormone. For example, a part of iodine, which is released during inactivation of thyroid hormones, is excreted by the kidneys and bile while another part is trapped again by the thyroid tissue to be used for synthesis of thyroid hormones.

The Pituitary Gland

Anatomy:

This gland lies in the fossa of the upper surface of the sphenoid bone which is callead sella turcica. It is attached to the base of the brain (hypothalamus) by means of pituitary stalk (infundibulum). The pituitary gland consists of a

- glandular part (adenohypophysis): the glandular part is further subdivided into pars tuberalis of unknown function, pars distalis (anterior pituitary) and pars intermedia.
- the nervous portion (neurohypophysis): composed of pars nervosa and the infitndibulain.

pars distalis
(anterior pituitary)

Hormones of the pars distalis are classified into metabolic (STH, TSH, ACTH and LTH) and gonadotropic hormones (FSH, LH and LTH).

1- Somatotropic hormone (STH) or Growth hormone:

This hormone regulates normal growth and development in young animals as it is responsible for retention of inorganic elements necessary for formation of soft and hard tissues as well as nitrogen and water. In addition, it stimulates formation of ribosomes and RNA synthesis leading to protein formation. Thus, STH is important for normal growth and composition of bone and muscles. Also, the hormone plays an important role to stimulate cellular growth and division as well as it increases the mass of internal organs specially liver, intestines and lymph nodes.

Hypofunction of STH, particularly in Youngs, leads to a condition known as **dwarfism** which is characterized by symmetrical retardation of growth accompanied usually by normal mental and reproductive capacities.
On the other side, over production of STH before puberty results in **gigantism** which is manifested by increased length and width of bones as the hormone retards calcification and closure of ossification centres. In this respect, the mass of the internal organs as well as the animal weight increase significantly.

Increase after puberty, a condition called acromegaly takes place which is characterized by enlargement of the flat bones particularly the facial accompanied with enlargement of the joints. Moreover, **the diabetogenic effect** accompanied with increased STH has now been recognized as STH secretion for long periods inhibits glucokinase enzyme and destroys the already present beta cells. The aftermath of these sequences lead to hyperglycemia and even glucosuria .

Control of Secretion of STH is under continuous control of **hypothalamus** which secretes STH-RH reaching the pituitary gland through the portal circulation leading to STH release. Also, Somatostatin hormone is produced by the hypothalamus to inhibit synthesis and secretion of STH .

2- Thyroid stimulating hormone (TSH)

This hormone activates all functions of the thyroid gland as it:

1- stimulates growth of thyroid tissue by hyperplasia and hypertrophy leading to formation of multiple large follicles.

2- Activates the uptake of iodine and synthesis of T3 and T4.

3-Activates the proteolytic enzyme inside the lumen of the follicle leading to hydrolysis of the thyroglobulin into free T3 and T4.

4- Increases the blood supply of the thyroid gland

- **TSH is considered fat mobilization factor and a connective tissue stimulator.**

Over TSH production leads to mobilization of fat from its depots and these sites are replaced by connective tissue formation

- Exophthalmos due to replacement of fat in eye pad with CT

- Conversion of the corpus luteum into corpus albicans.

3- Adrenocorticotrophic hormone (ACTH):

-This hormone controls the activity of the adrenal cortex particularly zona fasticulata.

-In mammals, ACTH has a melanocyte stimulating activity leading to coloration and pigmentation of the skin.

- ACTH has a similar effect like glucocorticoids, so it could be used instead of cortisone or cortisol.

Control

ACTH is under continuous control of the hypothalamic **ACTH-RH**.

-In case of over production of ACTH the hypothalamus produces an inhibiting hormone to ACTH which is known as **ACTH-IH.**

4) Prolactin (PRL):

This hormone exhibits both metabolic and gonadotropic activities.

Functions:

1- **In female mammals:**

- It initiates and maintains milk secretion on condition that the mammary gland is previously developed, under the effect of other hormones, for complete functional activity.

- **Stimulates the growth of corpora lutea leading to secretion of progestins mainly progesterone.**

4) Prolactin (PRL):

This hormone exhibits both metabolic and gonadotropic activities.

Functions:

2- In male and female pigeon and doves:

- The hormone stimulates crop milk formation as prolactin increases food intake of the parents and causes increased development of the alimentary tract and liver resulting in enhanced growth and the digested extra-food intake is utilized for the formation of crop milk.

-Prolactin also stimulates cellular proliferation of the mucosal lining of the lateral pouches of the crop. When such cells become peripherally situated. the blood supply is inadequate leading to detachment and degeneration of the cells which constitute the majority of crop milk.

Over Production in male and female mature birds and mammals for long period

leads to atrophy of the gonads as it increases the production of sex hormones which inhibit the gonadotropins production.

5- Gonadotropic Hormones

1) **Follicle stimulating hormone (FSH):**

Functions:

1- In females: it stimulates growth and development of the Graafian follicles leading to secretion of estrogens; a function which necessitates the presence of balanced amount of luteinizing hormone (LH).

2- In males: the hormone is well known as gametogenic hormone as it stimulates the process of spermatogenesis if present with balanced amount of interstitial cell stimulating hormone (ICSH).

2- **Luteinizing hormone (LH}:**

Functions:

1- In female mammals and birds: LH stimulates the process of ovulation and corpus luteum formation.

Also, it inhibits the luteolytic effect of oxytocin. LH augments the stimulating action of FSH on the Graafian follicles.

2- In the male: this hormone is known as interstitial cell stimulating hormone (ICSH) as it stimulates the Leydig cells of the testis to secrete the male sex hormones (androgens mainly testosterone).

Control of Gonadotropin secretion:

1- The hypothalamus: **It secretes gonadotropin hormone releasing hormone (GnRH) which regulates type and released amount of gonadotropins from the pituitary gland**

- **When the pulse frequency and amplitude of GnRH are rapid and multiple this call the release of LH**
- **while decreased frequency and amplitude promote the FSH release.**

Control of Gonadotropin secretion:

2- Ovarian hormones:

- **Estrogens** have a tripple threshold effect on pituitary gonadotropins:

    Low estrogens level: stimulates both synthesis and release of FSH resulting in elevation of its level in the circulation.

    High level of estrogens, Within physiological limits: inhibits synthesis and release of FSH and permits the secretion of the already formed LH.from pars distalis.

    Abnormal high estrogens level: (as in case of cystic ovaries .or administration): it inhibits synthesis and release of both FSH and LH, a case which may lead after a long period to atrophy of the gonads.

Control of Gonadotropin secretion:

2- Ovarian hormones:

- Progestins

Small amounts of for short period in ovaries previously treated with estrogens: stimulates the release of FSH with traces of LH.

Higher levels of progestins: inhibit the secretion of both gonadotropins particularly LH leading to inhibition of ovulation and corpus luteum formation.

The persistence of corpora lutea (of the estrous cycle or those of the pregnancy) in domestic animals specially cows and buffaloes is considered one of the serious problems causing infertility asthe large amounts of progestins inhibit the release of gonadotropins leading to a serious irregularity of the estrous cycle.

3- Inhibin: is a non-steroidal gonadal protein produced by:

-The granulosa cells of the Graafian follicles specially the mature ones.

-The corpus luteum of some species (rat, woman and pig)

-The placenta of rabbit and human are considered propoable sites of inhibin production.

-In male, Sertoli cells are the main source of inhibin production

lower concentrations of inhibin suppresses only FSH (synthesis and release) while higher levels of the hormone inhibit both FSH and to a lesser effect LH.

III - Posterior pituitary (Pars nervosa)

(neurohypophysis):

- It acts as a store for the hormones secreted from the hypothalamus.
- The neurosecretion of hypothalamic neurons (supraoptic and paraventricular nuclei) transported to posterior pituitary where it stored until released to blood.

Antidiuretic hormone (ADH)

Functions:

1. It promotes reabsorption(facultative reabsorption) of water from the collecting ducts of the kidney (facultative reabsorption 15% of glomerular filtrate).
2. High concentrations of antidiuretic hormone cause widespread constriction of arterioles, which leads to increased arterial pressure.

Control:

1. **Increase in osmotic pressure** — **stimulate osmoreceptor (specialized neurons) in hypothalamus** → **Stimulate neurosecretory neurons to produce ADH.**

2. **Decrease blood pressure**:→ Stimulates ADH secretion.

3. **Decrease in blood volume** : Loss of 15 or 20% of blood volume by hemorrhage results in massive secretion of antidiuretic hormone.

4. Nausea, vomiting, excessive sweating→ Stimulate ADH secretion

- **Hypofunction** : depress water reabsorption lead to excessive loss of water in urine (polyurea) and thirst sensation (diabetes insipidus).

Oxytocin hormone (Pitocin)

Called neurohypophyseal hormone as a neurohumeral reflex controls its secretion

Physiologic Effects of oxytocin:

a-It stimulates contraction of the uterus, which is previously primed by oestrogen leading to parturition.

b-It controls let down of milk by its action on the myoepithelial cells which surround the alveoli in the mammary gland.

c-It helps the suction of spermatozoa by stimulating antiperistaltic movements in the Fallopian tube.

d- it is secreted locally in C.L in non pregnant animal to induce involution of C.L

Control of Oxytocin Secretion:

(1) Neuroendocrine control (Suckling, Coitus, The act of labor)

Spinal reflex arc→ Brain→ Release of hypothalamic oxytocin

Thyroid Gland

Physiological anatomy and histology:

- The thyroid gland **in mammals** is formed of two lobes connected together by isthmus which is a band of the thyroid tissue.
- The gland is located on either sides of the lateral aspect of the trachea at the point of attachment to the larynx.
- **In birds, fish, reptiles** and **amphibia** the thyroids consist of two separate lobes.

- The gland is surrounded by two connective tissue capsules, from the inner connective tissue septa emerge to divide the gland into lobules which contain thyroid follicles (vesicles) of variable size.
- These follicles are supplied with rich network of blood capillaries.
- Sympathetic nerves enter the lobules in association with blood capillaries. These nerves regulate only the blood supply of the gland.
- **In case of normal thyroid (euthyroid),** the thyroid follicle is lined by a single layer of cuboidal cells. The lumen contains considerable amount of thyroprotein (stored hormone).
- **Subfunctional activity (hypothyroidism):** the vesicles become enlarged than the normal state, the epithelial cells become flattened and the amount of colloid (thyroglobulin) increases.
- **In hyperthyroidism**, the cells are columnar in shape and the amount of colloid decreases than normal as well as the lumen of the follicle becomes narrow. The basal surface of the thyroid epithelial cells is in contact with blood capillaries.

- **By electron microscope,** it was found that some of the endothelial cells of blood capillaries become thick and large to form a new cell type known C- cells (parafollicular cells).
- These cells produce a hormone called **calcitonin or thyrocalcitonin.**
- In most of mammals, this hormone is produced from the thyroid gland but in birds, reptiles, fishes and amphibia the C cells aggregate and form a separate endocrine gland known as the **ultimobranchial gland** which produces the calcitonin hormone.

Hormones of the thyroid gland:

1- Thyroid hormones (T3 and T4).

2- Thyrocalcitonin.

3- Thermothyrin (Heat - reducing hormone).

Function of T3 and T4:

1- At cell level:

a- Under physiological conditions (euthyroid): T3 and T4 stimulate the release of oxidative enzymes from the mitochondria (as they increase the number of cristae and make them fragile) leading to liberation of energy.

- A part of energy is used for supplying the cells with energy required for their vital processes.
- The remaining part of energy is stored in the form of high energy - containing bonds (like ATP). This stored energy is further utilized for the synthesis of RNA and consequently protein synthesis leading to stimulate the growth.

This action of the thyroid hormones is considered as anabolic one

b- In hypothyroidism: The energy produced by oxidation is lesser than that required by the tissues; therefore there is a continuous exhaustion of the stored energy and by time, this condition may affect protein synthesis and growth.

c- In hyperthyroidism : All the energy produced by Oxidation is lost in the form of CO_2, H_2O and heat, thus it is of catabolic action accompanied with wasteful loss of energy.

2) On metabolism:

a- Within physiological limits (Euthyroid): T3 and T4 promote protein synthesis due to formation of ATP and increase of nitrogen retention in the body → thyroid hormones promote growth and consequently considered anabolic hormones.

b- Hypothyroidism:

- It is usually accompanied with reduced number of mitochondria resulting in decreased quantity of oxidative enzymes in the cells.
- The oxygen utilization of the liver, kidneys and muscles decreases significantly.

- The basal metabolic rate becomes lower as much as 50 % than that of the normal animals.
- The rate of sugar absorption through the intestine is inhibited.
- Protein synthesis is also decreased and retardation of growth takes place.
- The cholesterol level in blood is inversely related to the activity of thyroid gland → **the thyroid activity is lowered** → Cholesterol level increases and generalized arteriosclerosis is common in long standing cases.
- Hypothyroidism also diminishes excretion of calcium and phosphorus from the body.

The effect of hypothyroidism is catabolic.

C- Hyperthyroidism:

- Extra-energy production without efficient storage and utilization- of energy. (wasteful loss of energy in the form of heat)

-The number of mitochondria and the quantity of the cellular oxidative enzymes increases.

- Oxygen utilization by the liver, kidneys and muscles increases. The basal metabolic rate increases as much as 50 % than normal. The rate of glucose absorption increases.

- Glucogenolysis is stimulated leading to reduced liver and muscle glycogen.

- Hyperglycaemia and glucosuria occasionally occur.

- Fat stores are mobilized to supply the extra-energy and the blood cholesterol is decreased.

- Mineral metabolism is also impaired as the excretion of calcium and phosphorus in the urine and feces is increased.

- Moreover, due to the enhanced metabolism the vitamin requirement increases (specially vitamins A).

- As energy is lost without being used for protein synthesis, <u>the plasma proteins concentration and the protein content of the liver and muscles decreases</u>. → the nitrogen balance becomes negative

3) On growth:

a) lack of thyroid hormones on growth differs according to the age of the animal. **In young animals** (sheep, goat, horse, rabbit and rat) and human, hypothyroidism results in a condition known as **cretinism** which is characterized by:

- Asymmetrical retardation of growth, the external and internal gentalia are like infants and when the animal reaches maturity, the secondary sexual characters will not appear.
- Retardation in the proliferation of epiphyseal cartilage, delay in the appearance of ossification centers, weak development of skeletal muscles.
- Retention of excess fluid in the body are recorded in cretin. Moreover, the tongue is enlarged and protrudes between thickened lips.
- The skin is coarse, dry and the hair is scanty. The head becomes larger in size and the neck

- **In case of adult animals**, hypothyroidism leads to a condition comparable to **myxedema** in humans which is manifested by:

- Subcutaneous edema, weakness of the muscular activity.
- Bradycardia, the ECG becomes of low voltage, the gonads undergo slight atrophy and the secondary sexual characters are depressed.

b- Hyperthyroidism results in retardation of growth due to accelerated protein catabolism, decreased plasma proteins and inhibition of protein synthesis.

5) **On reproduction:**

- The thyroid gland is more active at estrus as compared to the other stages of the estrous cycle.
- During pregnancy, the thyroid becomes more active at the late stage.
- Hypothyroidism in females is accompanied with degeneration of the ova leading to irregular estrous cycle and low fertility Silent heat among cattle and buffaloes represent a great problem due to hypoactivity of the thyroid gland.
- In males, hypothyroidism leads to impair the process of spermatogenesis and consequently the semen quality becomes poor. In ram and bull, summer sterility is a common case due to deficiency of T3 and T4.

6) **On the nervous system**:

- **Hypothyroidism** results in depression of neuron functions and the excitability of the nervous system decreases

↓

The affected animal becomes dull, sluggish and sleepy.

- **In hyperthyroidism** the excitability of the nervous system increases

↓

The animal becomes anxious, irritable and its reflexes are exaggerated as well as the reaction time is reduced.

7- On the gastrointestinal tract:

- **Hypoactivity of the thyroid gland:**

constipation, hypophagia, decreased gut motility and the absorption of glucose is reduced.

- **In hyperthyroidism**,

diarrhea, polyphagia, increased gut motility and accelerated absorption of glucose

8) **Cardiovascular system**:

- **Deficiency of T3 and T4**

- Decreases the cardiac output and the blood flow
- Bradycardia takes place
- Enlargement and degeneration of the cardiac muscle
- The arterial blood pressure becomes subnormal.
- If the deficiency is prolonged, **generalized arteriosclerosis** takes place.

- **In hyperactivity of the thyroid gland**

- The cardiac output and the arterial blood pressure increase.
- Tachycardia develops due to : a- Thyroxin stimulates directly the rhythmicity of the SAN, b- The increased metabolism produces peripheral vasodilatation leading to increased venous return and consequently the heart rate accelerates (Bainbridge's reflex).

9- Other effects of thyroid hormones:

- Hypothyroidism results in anemia (usually of Microcytic and hypochromic type). This anemia is due to T3 and T4 affect protein synthesis.
- On the respiratory system, deficiency of thyroid hormones in the blood decreases the depth and rate of respiration accompanied with weakness of the respiratory muscles.
- Thyroid hormones are essential for normal healing of wounds and bone fractures. Moreover, tha.t increase the resistance of the body against infection.

Control of Thyroid Gland

1) Nervous control:

This type of control may be direct of indirect.

- **Direct nervous control** means stimulation of the nerve supply of the thyroid gland resulting in increased its blood supply leading to enhance the activity of the cells to produce more thyroid hormones
- **Indirect nervous control** means stimulation of the nerve supply of the anterior lobe of the pituitary gland resulting' in secretion of TSH-RH which stimulates the thyroid gland

2) Hormonal control:

TSH

- The role of TSH on the thyroid gland was previously mentioned.
- The secretion of TSH is regulated by :

a) The feedback mechanism

b) Environmental conditions :

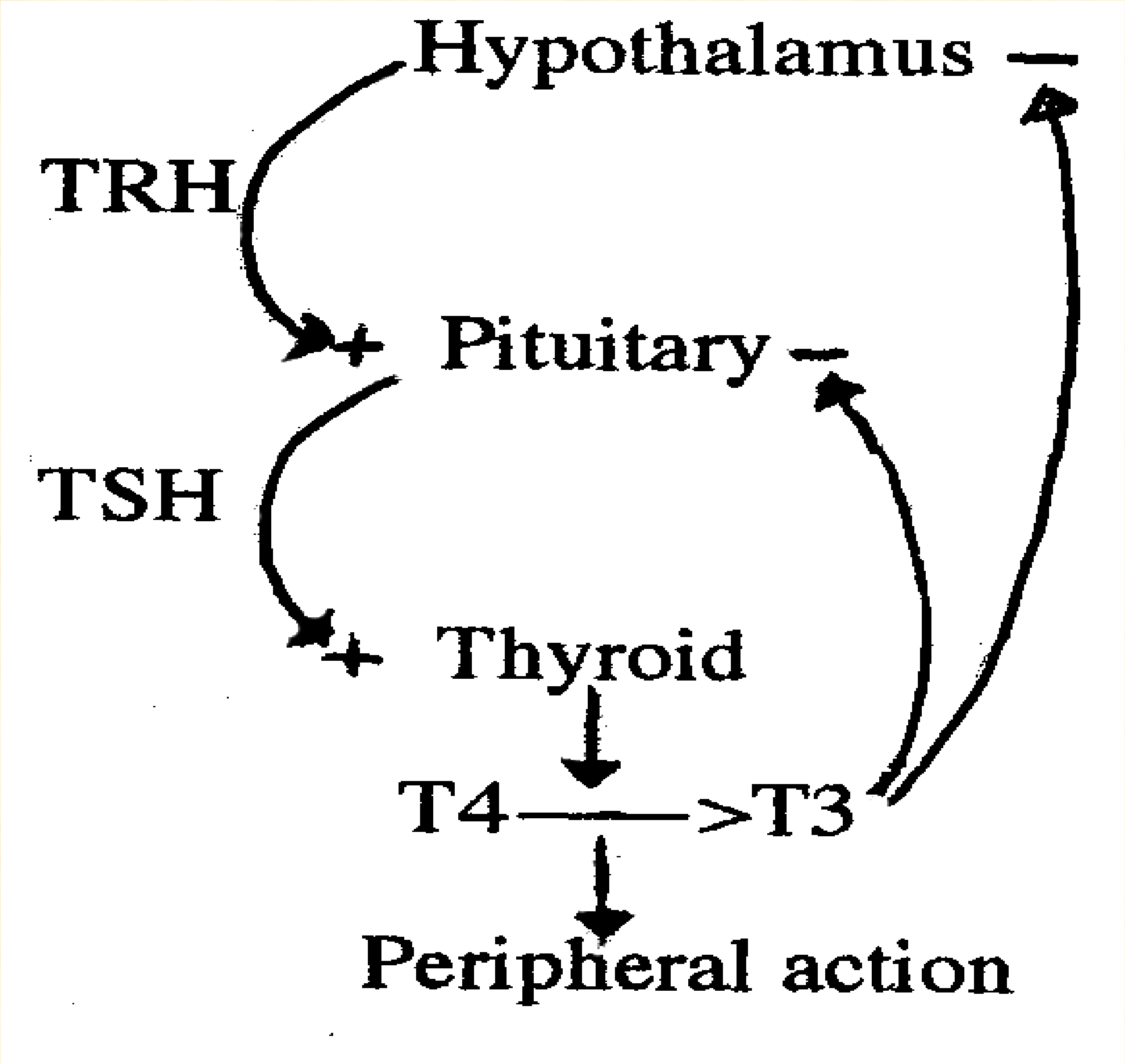
Cold and / or light → **stimulate the hypothalamus to produce** → **TSH-RH**

Transported to the anterior pituitary via the hypothalamo-hypophyseal portal circulation present in the pituitary stalk

↓

Release of TSH which activates the thyroid gland.

High environmental temperature inhibits the release of TSH-RH and stimulates the release of TSH-IH from the hypothalamus resulting in inhibition of the release of TSH and consequently inhibition of the thyroid gland.


Hypothalamus
—
TRH
+
Pituitary
—
TSH
+
Thyroid
T4 ——>T3
Peripheral action

3) Chemical control:

Some chemical substances have the capacity to **block the phases of synthesis of thyroid hormones** → Induce goiter (they are called goitergenic compounds)

The most famous goitergenic compounds are:

a- Potassium thiocyanate and potassium perchlorate: They block the iodine trap and prevent the thyroid tissue from the uptake of iodine.

b- Thiourea: They block the oxidative enzymes (thyroid peroxidase) resulting in prevention of conversion of iodine to active one.

c- Sulphonamides administration: In animals these compounds prevent the iodination of amino acid tyrosine.

4) Goitrin:

Many flowering and vascular plants (cabbage, sprouts) contain **progoitrin** that can be enzymatically converted into a potent antithyroid compound called **goitrin**.

Absorbtion of sufficient quantities of goitrin

Cooking these plants normally destroys the enzymes that convert progoitrin to goitrin; but progoitrin itself is not affected

- Synthesis of thyroid hormones is impaired and hypothyroidism accompanied with goiter takes place.

5) The effect of other hormones:

- Oxytocin and vasopressin of the posterior pituitary
- Relaxin (which is produced by the ovaries and placenta during late pregnancy)

Activate all functions of the thyroid gland.

Goiter

Goiter is an enlargement of the thyroid gland which is not malignant and uninflammatory.

It may be associated with

- **Hypothyroidism (simple or colloidal goiter)**
- **Hyperthyroidism (Exophthalmic goiter)**

1) Simple goiter:

Causes:

- **Iodine deficiency (soil)**
- **Goiterogenic substances**
- **Goitrin**
- **Formation of antibodies to thyroglobulin**

→ Lowering T3 an T4 → **increased release of TSH from the anterior pituitary (feedback mechanism). Over production of TSH leads to enlargement of the thyroid gland (goiter).**

In this type of goiter the histological picture of the thyroid follicles resembles that of hypothyroidism.

2) Exophthalmic goiter

Causes:

a- Over production of TSH as in tumours of gland.

b- Long-acting thyroid stimulating substance (LATS):

- which can activate the thyroid gland of several species of animals
- It is one of the cause of hyperthyroidism.
- This substance is separated from serum of hyperthyroid individuals and always bound with gamma globulin fraction of the serum proteins.

❖ This type of goiter is usually accompanied with very high level of TSH → **Protrusion of the eye ball (exophthalmos)**

Why?

- The microscopic picture of the thyroid follicles in exophthalmic goiter is similar to that of hyperthyroidism.

Thyrocalcitonin (Calcitonin)

Action of the hormone:

- Thyrocalcitonin lowers the calcium (Ca +) in the blood.

-The hormone granules are stored within the cells.

- Degranulation of these cells indicates release of the hormone into circulation.

3- Control of the hormone :

a) When calcium. (Ca) level in the blood rises than the normal level (hypocalcaemia); it stimulates C-cells to release thyrocalcitonin.

b) Glucagon hormone increases the secretion rate of the thyrocalcitonin.

Thermothyrin
(Heat reducing hormone

- In case of danger due to rise in body temperature, the thyroid gland produces a hormone called thermothyrin.

-This hormone decreases oxygen consumption and heat production of the living organism in order to maintain the body temperature within the physiological limits.

THE PARATHYROID GLAND

Physiological anatomy and histology:

- In mouse, cat and man: the parathyroids are embedded within the thyroid tissue.
- In other mammals such as goat, rabbit ....etc: they are separated glands located near to the thyroid.
- In case of birds, there are two parathyroids which are separated from the thyroid gland.
- The parathyroid gland contains two cell types:

  - chief cells (principal) → **responsible for parathonnone production**

  - oxyphil cells: does not have an active function in the biosynthesis of the hormone

- **Storage** of parathormone molecules takes place within the cytoplasm of the chief cells.
- Degranulation of such cells indicates the release of the hormone into the circulation:

Actions of the parathormone:

- The parathyroid hormone is considered as hypercalcaemic agent as its primary role is to increase the calcium (Ca++) level and lowers that of phosphorus in the blood.
- This action is due to :

1- Parathormone accelerates the absorption of both calcium and phosphorus from the small intestine; but to lesser extent than vitamin D does.

2- It acts on the skeletal tissue (bone and teeth) by drawing calcium and phosphorus from them and pour them into the blood stream.

This action is due to parathormone converts the insoluble forms of calcium such as calcium carbonate and triphosphate of the skeletal tissue into soluble forms like calcium citrate and lactate which are poured into blood.

3- Parathormone increases the reabsorption of calcium from the renal tubules and excretion of phosphorus.

Effects of hyperparathyroidism

A) The calcium level in the blood increases and may reach up to 22 mg %.

B) The phosphorus level in the blood decreases (down to 2 - 3 mg %).

C) Calcium deposition takes place in the soft tissues like heart, brain and kidneys. This effect is due to the increased level of calcium in the blood plasma.

D) The calcium is drawn from the skeletal tissue leading to the appearance of cavities in the shaft (diaphysis) of long bones. This condition is called generalized osteitis fibrosa cystica.

E) The increased calcium level in the blood plasma affects the cardiac muscle by stimulating the cardiac systole.

The effect of Hypoparathyroidism

A) The calcium level in the blood decreases down to 4 - 5 mg %.

B) Phosphorus level in the blood plasma increases up to 10 - 15 mg %.

C) The decreased calcium level in the blood plasma results in inhibition of the cardiac systole.

D) Tetany

- Normal calcium level in the blood plasma is important for the maintenance of the functional activity of the neuromuscular junction and to prevent the continual excitability due to external continual stimuli.

- In hypoparathyroidism,:

calcium level in the blood decreases → **increase the excitability of the neuromuscular junction.**

↓

The animal becomes sensitive to any external stimulation and responds by series of muscular contractions (convulsions) and tremors allover the animal body

- Other symptoms such as loss of appetite and stiff gait are also involved in such cases.
- The condition may involve (specially in dogs) persistent contractions of the laryngeal and intercostal muscles as well as the diaphragm followed by paralysis of the affected muscles and the animal dies due to asphexia unless it is treated with calcium compounds at the early stages of hypocalcaemia. These symptoms are **known as tetany.**

Adrenal gland

or suprarenal gland

(birds and mammals)

Adrenal medulla

- The central part
- Functionally related to sympathetic nervous system.
- It secretes epinephrine (80%) and nor epinephrine (20%).

Adrenal cortex

- Essential for life.
- It secretes different groups of hormones (corticosteroids).
- Adrenal cortex Bilateral removal----→ death with circulatory collapse.

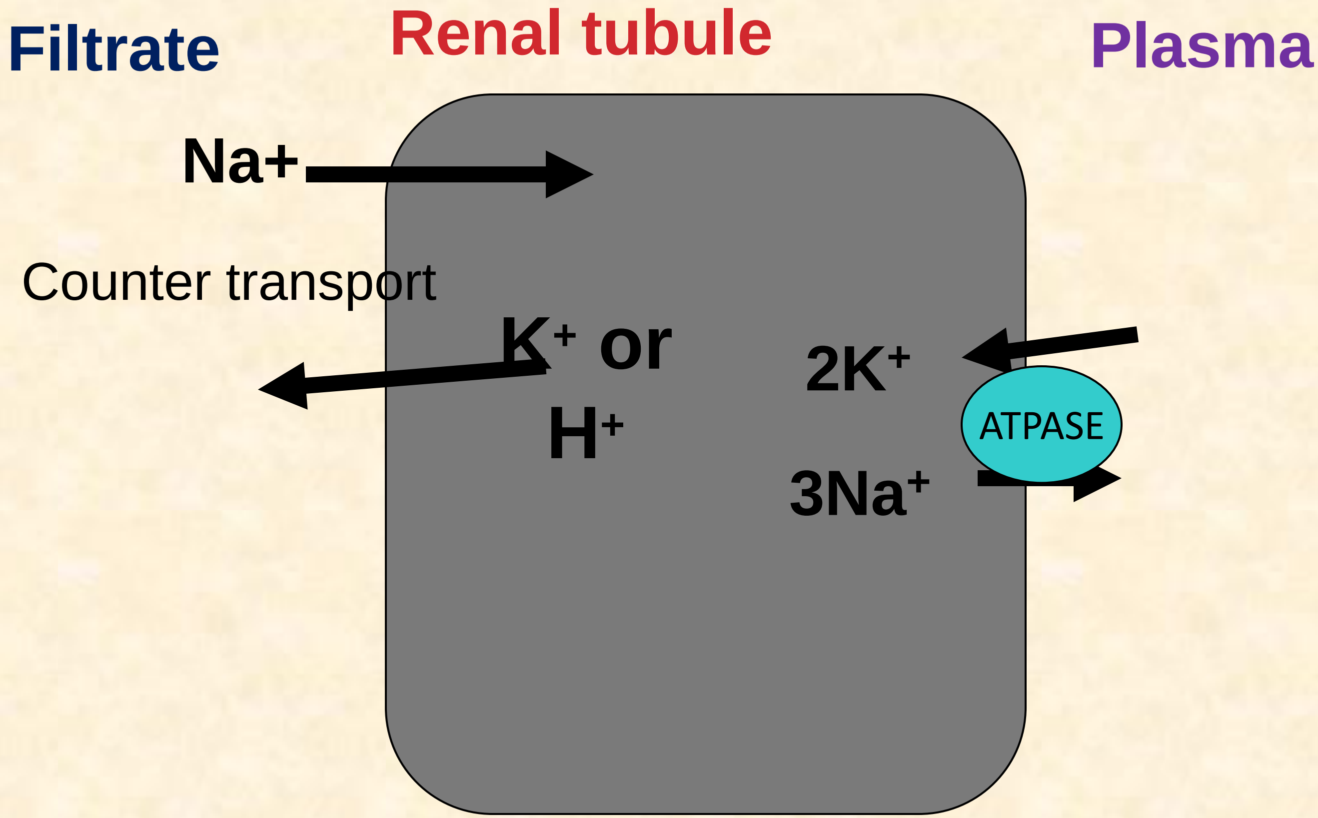
Adrenal cortex

- **Zona glomerulosa 15% of the mass----→ mineralocorticoids.**
- **Zona fsiculata 50% of the mass----→ glucocorticoids.**
- **Zona reticularis 7% of the mass----→ sex steroids**

Mineralocorticoids:

- **This term is because they affect electrolytes of extracellular fluids (Na^+ and K^+), so they are responsible for maintaining <u>Na^+ & K^+ homeostasis.</u>**
- **Mineralocorticoids are acutely critical for maintenance of life, as removal of the adrenal glands can lead to death within just a few days.**
- **The principal steroid with mineralocorticoid activity is aldosterone.**

Functions



On the luminal surface----→ increase number of Na+ channels that facilitates movement of Na+to intracellular.

N.B: Na+ is reabsorbed by ionic exchange with either H+ or K+ compete with ceah other for exchange with Na+ ion (maintaining acid base balance.

- **N.B**: Na+ is the main ion extracelluar, K+ is the main ion intracellular. So it is important to save Na+ and excrete K+.
- **N.B**: positive charge of Na+ cause positive co-transport of negative ions (CL^-) ----→ creates osmotic pressure difference----→ that move water through membrane (obligatory reabsorption for 85% water content of glomerular filtrate as solvent so regulate water balance.

Control of Mineralocorticoid secretion

1. Increase K+ level even than Na+ ----→ stimulate aldosterone secretion (because K+ increase is a dangerous process (hyperkalemia) that affect contractility of the cardiac muscle).
2. Renin angiotensin system.
3. Effect of Na+ concentration and ACTH (usually minor in controlling aldosterone secretion.

- ACTH----→ because both cortisol and aldosterone share their function to certain degree.

Glucocorticoids:

-They are named so because their effect is specific on glucose metabolism.

-Cortisol and corticosterone are the major ones.

-In mammals----→ cortisol.

-In birds, mice, rat ----→ corticosterone.

Functions

I) On carbohydrate:

1. Has antiglucagon effect because it inhibit phosphorylase → **Favor storage of glycogen (liver)**

2. Has anti-insulin effect because it inhibits glucokinase → **Decrease uptake of glucose by the cell**
Decrease rate of glucose utilization.
↓

Excess cortisol----→ gluconeogenesis----→ hyperglycemia----→ steriod diabetes.

II) On protein:

- Mobilization of A.As from extrahepatic tissue mainly from muscles →

A.As are available for gluconeogenesis in liver.

III) On fat:

- Mobilization of F.As from muscles and also from adipose tissue (lipolytic effect) →

These F.As----→ gluconeogenesis.

- Oxidation of F.As ----→ ketone bodies (ketogenic effect).

- Despite F.As mobilization, **excess cortisol develop** a peculiar type of **obesity** with excess deposition of fat in face (moon face), in trunk (buffalo hump) and abdomen instead of hips)

IV) Anti- inflammatory action:

1- It induces vasoconstriction

2- It diminishes permeability of capillary walls

} Prevent formation of inflammatory exudate, local oedema and redness

3- It inhibits proliferation of fibroblasts and connective tissue formation→ inhibition of cellular response to inflammation and retardation of granulation tissue formation.

V) On Immune system:

- Causes atrophy of lymphoid tissue and destruction to already formed lymphocytes → Lymphopnea

- It **suppresses antibody production** by lymphocytes

↓

Suppress immune system so used in organ transplantation medication.

VI) On blood formed elements:

-It induces lymphopenia, eosinopenia, neutrophilia.

VII) Anti-allergic effect:

- Suppress histamine production.

Effect of hyper-adrenocorticism

*(or excessive administration of glucocorticoid for prolonged period as a drug)***:**

1-Metabolic disorders:

-Steroid diabetes.

- Excessive protein catabolism→ Muscle weakness and thin skin

- Peculiar type of obesity = Moon face and pendulous abdomen.

2-Inhibition of bone formation as a result of suppression of calcium absorption.

3- Delayed wound healing.

4-Effect on blood cells:

-Lymphopenia → due to atrophy of lymphoid tissue and destruction of already present lymphocytes

- Eosinopenia→ due to depression of production from bone marrow

-Neutrophilia→ on the expanse of other types of cells.

5-Peptic ulcer due to excessive gastric secretion (both acid secretion and pepsin)

Control

(1) Feedback mechanism:

- Positive feedback is mediated by:

- Any type of physical or mental stress:

e.g., taking an examination, recovering from a broken bone, running away from an invading army, mild starvation. For human males, there is even considerable stress associated with shopping!!).

- ↓↓ glucocorticoids in circulation.

N.B: Glucocorticoids are secreted in response to ACTH from the anterior pituitary. ACTH is itself secreted under control of the hypothalamic peptide CRH.

- Negative feedback is mediated by:

  - ↑↑ glucocorticoids in circulation

(2) Diurinal variation:

In pig and mare the rhythm of glucocorticoids output is highest in the morning (4 – 10 a.m) , rises during sleep and become lowest during the afternoon and early evening.

3- Sex steroids:

A. Androgen hormone: which represent 10% of circulating androgen in male and about 50% in female.
B. Small amount of estrogen + progesterone.

B- Glucocorticoid deficiency:

1- Decrease cortisol reduce mobilization of protein and fat from the tissues ----→ depress other metabolic functions.

2- Decrease cortisol ---→ make the patient unable to tolerate stress.

3-Decrease cortisol (increase ACTH) --------------→pigmentation in mucous membrane and skin.

Adrenal medulla

- It forms the core of adrenal gland
- It can be considered modified sympathetic ganglia.
- Sympathetic stimulation ---→ epinephrine (80%) and nor epinephrin (20%).
- epinephrin---→ anxiety, fright, fleet.
- Nor epiphrin---→aggressiveness (fight+ attack in wild animal).
- So ratio differ in species.

Catecholamine receptors on the surface of the target cells:

- The effect of epinephrine and norepinephrine are initiated by their binding to adrenergic receptors on the surface of target cells

Receptor	Effectively Binds	Effect of Ligand Binding
$Alpha_1$	Epinephrine, Norepinphrine	Increased free calcium
$Alpha_2$	Epinephrine, Norepinphrine	Decreased cyclic AMP
$Beta_1$	Epinephrine, Norepinphrine	Increased cyclic AMP
$Beta_2$	Epinephrine	Increased cyclic AMP

- Circulating epinephrine and norepinephrine released from the adrenal medulla have the same effects on target organs as direct stimulation by sympathetic nerves, although their effect is longer lasting

Effects of catecholamines:

1) **On cardiac muscles:**↑↑ rate and force of contraction (this is predominantly an effect of epinephrine acting through beta receptors).

2) **On blood vessels:** norepinephrine, in particular, causes widespread vasoconstriction, resulting in increased resistance and hence arterial blood pressure. ⟹ to provide glucose for energy production

3) **On bronchioles:** dilatation of bronchioles that assists ventilation

4) **On carbohydrate metabolism:** promote breakdown of glycogen in skeletal muscle

5) On fat metabolism: Increases lipolysis to provide fatty acids for energy production in many tissues and aids in conservation of dwindling reserves of blood glucose.

6) On the eye: Dilatation of the eye pubil to Accommodate for low ambient light

7) On metabolic rate: Increases metabolic rate, oxygen consumption and heat production

8) On GIT: Inhibition of gastrointestinal secretion and motor activity

Control of catecholamines:

1- Stimulation of **acetylcholine** release from preganglionic sympathetic fibers innervating the medulla → Stimulate catecholamine release.

2- Stressors:

- Many types of "stresses" stimulate such secretion, including exercise, hypoglycemia and trauma.

Islets of Langerhans

- **Pancreas**
  - **Islets of Langerhans**
    2% of pancreaic tissue
    - **Beta-cells**: **Insulin**
    - **Alpha-cells**: **Glucagon**
    - **Delta-cells**: **Somatostatin**
  - **Acini**
    - Digestive secretion.

Insulin

Physiological effects:

1) On Carbohydrate metabolism:

Has hypoglycemic effect …….(How?)

1- cause glucose uptake and storage in liver cells through:

- enhancing glucose uptake by liver cells by glucokinase.

2- Inhibiting phosphorylase enzyme → prevent glycogenolysis.

3- increasing activities of enzymes that promote glycogen synthesis (phosphofructokinase and synthetase)

4- Accelerating intracellular glucose oxidation.

The net effect increase glycogen in liver.

2) On Protein metabolism:

Insulin prevents degradation of protein and fat→ stimulates growth indirectly.

3) On cell repair and healing of wounds:

Insulin is essential for cell repair and wound healing. Deficiency of insulin is usually associated with prolonged time necessary for healing.

c) Effect on growth:

Insulin stimulate growth indirectly as it prevents degradation of protein and fat.

Control of insulin secretion

1. **Through chemical feed back mechanism (glucose level).**

Positive caused by	Negative caused by
- Hyperglycemia - Increased blood concentrations of other fuel molecules; amino acids and fatty acids	Hypoglycemia

2.Some hormones that either have direct action, or potentiate glucose stimulus (glucagon, GH, cortisol, adrenalin).

3. Autonomic:

A- parasympathetic ----→ stimulate insulin release.

B- sympathetic ----→ inhibit insulin release, which potentiate the hyperglycemic action of adrenaline.

4. Some chemicals (e.g., alloxan)→ Destroys β- cells

5. Some Sulphonamides: → Stimulates insulin secretion

Glucagon

Physiological effects:

1) On carbohydrate metabolism (Hyperglycemic):

Has hyperglycemic effect …….(How?)

1- It enhances **glycogenolysis** in liver.

2- It activates hepatic **gluconeogenesis** (= formation of glucose from non hexose substrate such as amino acids and fatty acids)

3- It accelerates intracellular glucose oxidation.

2) On Protein and fat metabolism:

1- It enhance transformation of amino acids into glucose (gluconeogenesis).

2- It enhance lipolysis of triglyceride in adipose tissue

Control of Glucagon secretion:

1) Feedback mechanism:

- Positive feedback

  Decrease blood glucose below its fasting level----→ increase glucagon secretion

  Exercise (exercise induces depletion of glucose)

- Negative feedback is mediated by:

  - Hyperglycemia.

(2) Somatostatin hormone → inhibits glucagon release.