Summary of the functions of the hormones:

Metabolism	Anabolism and catabolism , the rate of synthesis and degradation of carbohydrates, proteins, and lipids.
Reproduction	No reproduction without hormones, no sperms without testosterone, no ovum without estrogen and progesterone. Hormones control the development of sex organs, secondary sexual characteristics, gametogenesis, and menstrual cycle.
Digestion	Hormones control the digestive processes including the GIT motility, secretion of digestive enzymes, bile, gastric acid and bicarbonate.
Blood circulation	Regulate blood pressure by altering cardiac output, also affects blood vessels either vasoconstriction or vasodilatation, also hormones affect the blood volume by the control of the water content of the body (water excretion by the kidneys)
Transport of substrates	Transport of substrates such as glucose , amino acids, lipids, minerals, gases, blood cells, water, and hydrogen ions (PH regulation)
Defense against pathogens	Regulate immune system responses, including leukocyte activation, inflammation, antibody production and fever
Growth	All stages of growth are affected by hormones, not one hormone but more than one hormone affects the growth. Hormones control cell division and differentiation
Stress responses	hormones regulate the body's response to stresses
Behavior	hormones control sexual and social behavior, estrogen in females and testosterone in males

Chemistry of hormones:

In physiology we classify hormones into 3 categories:

1- Proteins: Mainly the hormones are proteins. Proteins are either small molecules or large molecules (below or above 20 amino acids).

2- Amino acid derivatives: catecholamines (adrenaline, noradrenalin and dopamine) and Thyroid hormones (T3,T4).

3- Steroids: two types: adrenal cortex hormones and sex hormones.

(vitamin D from skin or diet enter in the synthesis of steroids)

Regulation of hormones secretion:

A) Feedback control (usually) :-

The relationship between the response and stimulus is called *feedback control*.

Two types:
1- Negative feedback control: If the response decreases the stimulus.

Negative feedback control occurs in three loops:

1- Ultra short loop: e.g. Hypothalamus secretes hormone and the hormone affects the hypothalamus (autocrine).

2- Short loop: e.g. Hormone from pituitary affects the hypothalamus.

3- Long loop: e.g. Thyroid hormone affects hypothalamus.

2- positive feedback control: If the response increases the stimulus.

Example: the response is secreting oxytocin, the stimulus is the sucking of an infant. More and more sucking results in more and more oxytocin, and this continues till the process ends.

Another example: in delivery: more and more uterine contraction results in more and more oxytocin till the process ends.

When the process ends the oxytocin release stops. If it continues then the release of oxytocin will turn into destructive process.

So feedback controls the relation between the response and the stimulus.

The [stimulus – response] could be:

a) Hormone - hormone (the stimulus is a hormone and the response is a hormone)

b) Substrate - hormone e.g. Glucose-insulin

c) Mineral - hormone e.g. Calcium - parathyroid hormone

*Hormones which are released in regular bases, their secretion is regulated by feedback control.

B) Neural control (sometimes) :-

In which the release of the hormones is stimulated by substances from neurons.

Example: in pain, emotion, sexual excitement, fright, injury and stress.

so all these can modulate hormone secretion through neural mechanism .

e.g. adrenalin, acetylcholine, dopamine, serotonin ...etc

C) Chronotropic control :-

This control is related to time, duration, season, or stage of development. The secretion of those hormones is genetically dictated .

Example: the growth hormone:

* The secretion of the growth hormone shows two phenomena: **sleep-wake cycle and diurnal rhythm** (the secretion of growth hormone during the 24 hours).

So it is higher at 12 mid noon and 12 mid night, and in between there is variation.

*The secretion of growth hormone is either in pulses or oscillation.

Menstrual rhythm: in the menstrual cycle in females there is the ovarian cycle which lasts about 28 days and have 3 phases: follicular phase, ovulation phase, and luteal phase.

In ovulation phase two hormones are high: estrogen and LH.

In luteal phase : progesterone and estrogen.

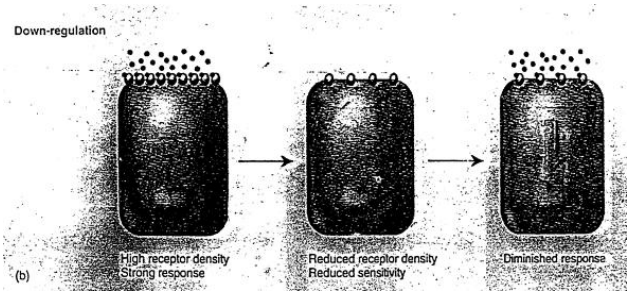
*The secretion of these hormones is genetically determined.

Seasonal rhythm: mostly seen in mammals where some hormones are high just in spring or winter or summer or autumn. Also secretion of these hormones especially sexual hormones and gonadotropin hormones is genetically encoded.

Developmental rhythm: secretion of growth hormone during childhood, puberty, adulthood, and old age, there is variation in secretion of growth hormone during all these stages.

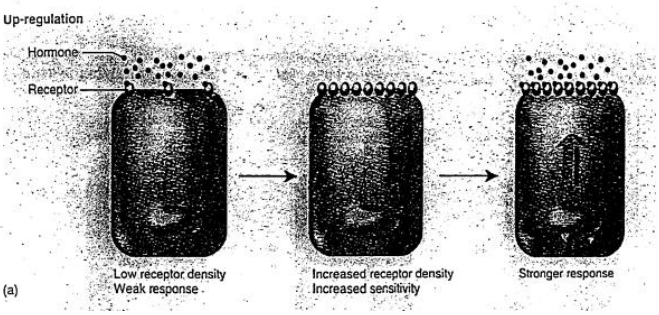
Down regulation and up regulation of the receptors:

In the picture: The number of the receptors is decreased, and the concentration of the hormone is relatively high, but because the receptors number is low the hormone doesn't function properly. This is down regulation.



Example: many old obese individuals have high concentration of insulin but still there is high concentration of glucose which means that insulin doesn't function properly because of the low number of the receptors or the decreased affinity.

Now these individual are advised to have exercise and control their meals and to retain there weight to the normal, after that and within short time, the



number of receptors increases as well as the affinity of the receptors towards the hormone increases. This is called up regulation.

So cells can regulate the number of their receptors as well as the function.

**Exposing the cells to an input of hormone for sustained period of time results in decreased number of receptors for that hormone per cell.

Example: Most probably, the reduction of the number of receptors on adipose tissue or muscle or liver or other cells in the body is because of the exposure of these cells for a long time to high concentration of insulin.

So when there is high insulin concentration and low receptors the cells don't respond to the high insulin concentration. This is called diabetes mellitus [we will take this later when the doctor explains the pancreas]

**Exercise: there are many types of exercise, the best in energy expenditure are cycling then swimming, but these are not practical. The most practical exercise is walking; the best of walking is to walk 6km/hour for about one month. If you are an organized person you will get your weight to normal -if your weight was close to normal-, because insulin starts functioning properly.

So cells can increase the number of the receptors and affinity of the receptors and can decrease them.

** when there is down regulation, most probably the receptors sink down inside the cell, or synthesis of receptors decreases, or both, and in up regulation the opposite happens.

Chemical castration or chemical therapy:

Gonadotropin releasing hormone from hypothalamus affects anterior pituitary which secretes FSH and LH. These two hormones affect the testes to produce testosterone which becomes dihydrotestosterone. This produces prostate cancer.

Continuous injection or administration of gonadotropin releasing hormone → after some time cells in the anterior pituitary don't respond to this hormone, consequently concentration of testosterone decreases and dihydrotestosterone also decreases.

Desensitization; homologous desensitization and heterologous desensitization:

*When the Cells of the anterior pituitary (gonadotrophs) are under continuous administration of gonadotropin releasing hormone they don't respond properly to it, this is called desensitization of the receptors. So the cells also can regulate the sensitivity or the response of the receptors to the hormone.

Example: when you are exposed for a long time to a specific smell you will be no longer able to smell it (the receptors are desensitized).

If the exposure of the cell to a hormone had a desensitizing effect on a further action by that same hormone then it is *homologous desensitization*.

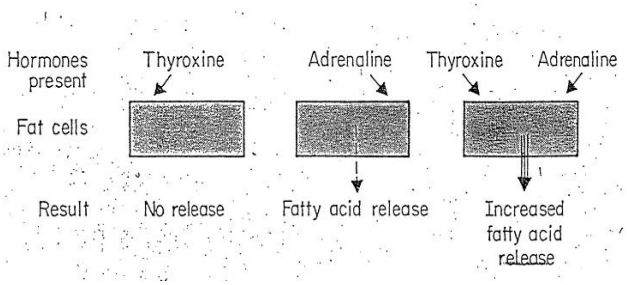
But if the exposure of the cell to one hormone had desensitizing effect with regard to action of different hormone then it is *heterologous desensitization.*

[The doctor asked us to search for more information about the types of desensitization, http://en.wikipedia.org/wiki/Homologous_desensitization]

Hormonal interactions:

Hormones don't function separately, there is interaction between hormones.

1- permissive action:



These are fat cells affected by thyroxin > no result.

Same cells affected by adrenaline > little fatty acids released .

Thyroxin then adrenaline > proper function.

(Thyroxin either increases the number of the receptors or increases the affinity of the receptors to adrenaline or both.)

2- synergistic effect:

The effects of two or more hormones complement each other in such a way that the target cell responds effectively to the sum of the hormones involved.

So Lactogenic hormones, galactokinetic hormones, galactopoietics hormones, mammogenic hormones, these hormones function together to produce best results, they complement each other.

3-Antagonistic effect:

A hormone opposes the action of another on the same target cell.

Example: parathyroid hormone increase PTH and calcitonin decreases it.

Another example: Insulin decreases glucose level and glucagon increases it.

Mechanism of the action of hormones:

A) production of cAMP:

Protein hormones are large molecules , they can't penetrate the cell membrane or nuclear membrane, they need receptors, these receptors are in the cell membrane.

*For the hormone to function it first needs a receptor and a second messenger.

*The hormone binds to the receptor → activates G protein in the cell membrane → G protein is composed of 3 subunits (alpha, beta, gamma) , alpha subunit binds to GTP and splits→ activates adenylate cyclase .

*Hormone receptor activates lets say 100 G proteins, and then adenylate cyclase activates 1000 ATP so we get 1000 cAMP. If there is a lot of cAMP , they activate an enzyme which leads to chemical response.

*some hormones that produce cAMP: ACTH, Angiotensin, Calcitonin, Catecholamines,… .

** Catecholamines are small molecules (1 amino acid) so why they don't diffuse through the membrane?

1- because they have to make a fast action.

2- because they don't have channels to enter the membrane through.

B) Activation of phospholipase C:

Some of the protein hormones produce two second messengers. They need calcium to function; therefore they have to produce a second messenger that increases calcium which is by activating phospholipase C.

Phospholipase C cleaves PIP2 into DAG for the activation of enzymes, and IP3 to increase calcium.

C) Diffusion into the cells:

The amino acid derivatives (except catecholamines like adrenaline) and steroid hormones diffuse into the cells, and bind their receptors inside the cell; either in the cytoplasm or in the nucleus.

They bind to the receptors affecting the DNA; producing mRNA then physiological response.

*Progesterone and estrogen: these are steroids but sometimes we need fast action, therefore they have receptors in some cells in the cell membrane as to function immediately. We conclude that the action of the hormones that bind to receptors inside the cells is delayed action.

*Hormones that are not put in these 3 classes are exceptions like: insulin which is different in the receptor and the second messenger, and nitric oxide that has cGMP as a second messenger.

…….

"إن قاعدة النجاح الأولى التي تعلو على أية قاعدة أخرى هي امتلاك الطاقة. فمن المهم معرفة كيفية تركيز هذه الطاقة وترويضها وتوجيهها على الأشياء الهامة، بدلا من تبديدها وتشتيتها على الأشياء التافهة وغير المجدية"

مايكل كوردا