Faculty of medicine
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Synopsis in Medical Physiology

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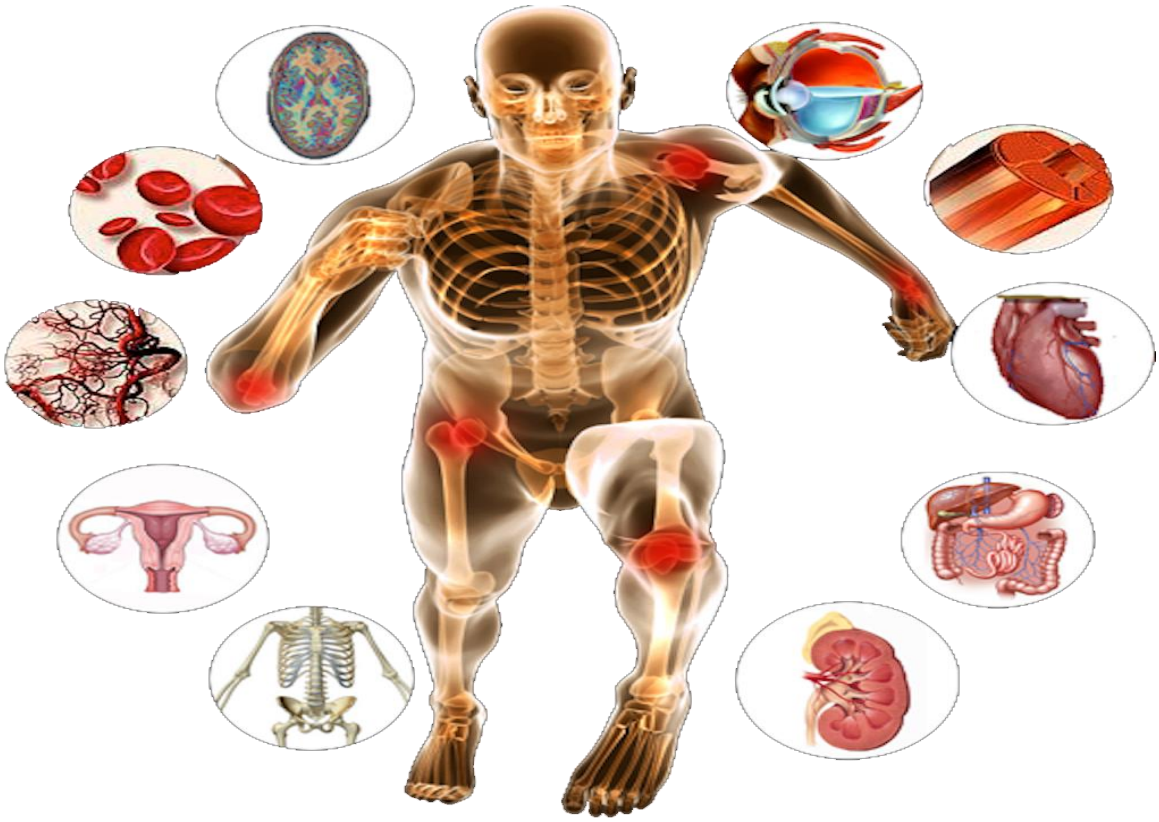

For

First Year Pharmacy Students
Second Semester

Synopsis in Medical Physiology for Pharmacy Students

Book II

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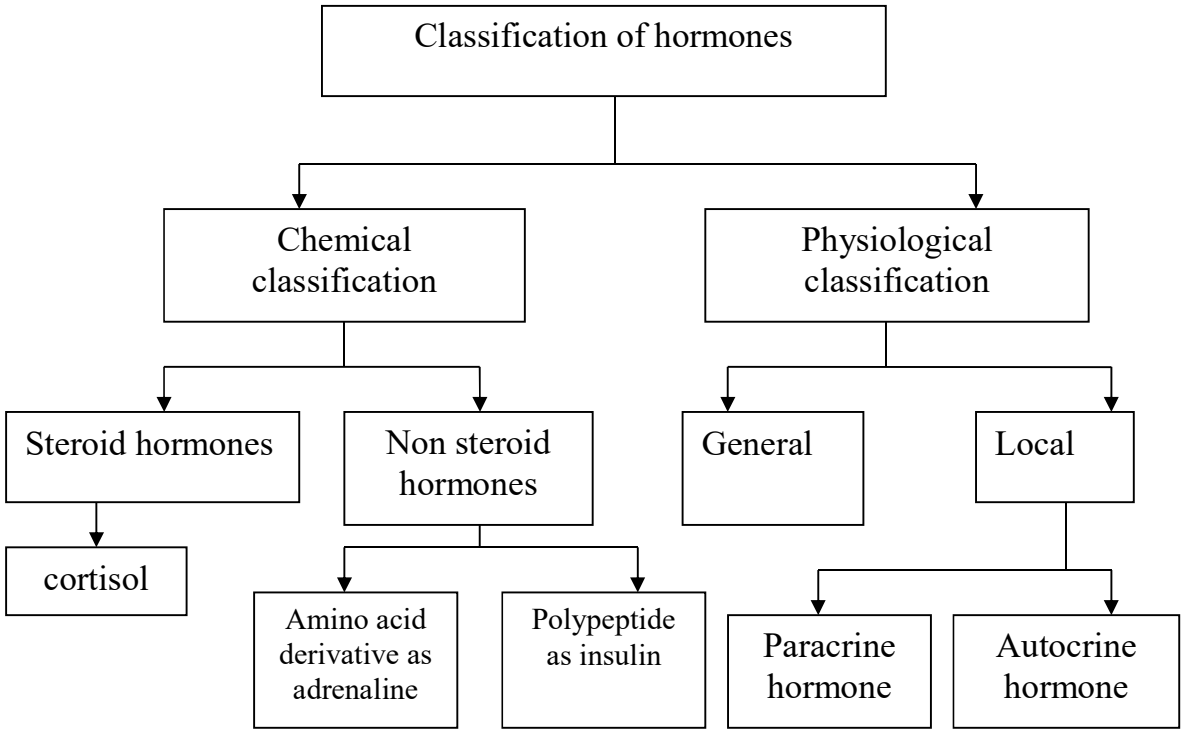
Contents

General endocrinology

The endocrine glands are ductless glands. They pour their secretion directly into the blood.

A hormone is a

1. Chemical substance that is secreted from the endocrine cell or group of cells.
2. It is secreted in minute amounts.
3. It is poured into the blood stream from which it circulates to reach the body fluids.
4. It controls the function of other body cells.



An endocrine hormone is a hormone that is secreted from an endocrine cell to circulate into the blood and the body fluids to act on distant body cells.

A paracrine hormone is a hormone that is secreted from an endocrine cell to circulate into the blood and the body fluids to act on nearby body cells, e.g. gastrin which is secreted from the antral cells of the stomach to act on the nearby gastric glands.

An autocrine hormone is a hormone that is secreted from an endocrine cell to circulate into the blood and the body fluids and acts on the same cell that already secreted it, e.g. interleukin secreted by the WBCs to activate their defence functions.

The neuro-endocrine integration

The haemostatic function is achieved through the integration of the nervous and the endocrine system. The 1st reacts rapidly by a nervous mechanism which lasts for a short duration of action e.g. the reflex action while the 2nd reacts slowly by a hormonal mechanism which lasts for a longer duration of action.

Evidence for the neuro-endocrine integration:-

1. The thyroid hormones are critically important for the growth and development of the nerve cells.
2. The hypothalamus controls the secretion of the pit. Trophic hormones which controls the growth, development and secretion of all other endocrine glands.
3. The hypothalamus secretes the posterior pit. Hormones which are the ADH and oxytocin.
4. The posterior hypothalamic nuclei are considered as a highest sympathetic centre which stimulates the greater splanchnic nerve for the secretion of the adrenal medullary hormones.

The mechanism of hormone action

1-The 2nd messenger mechanism:-

1. It is specified for the non-steroid hormones, which are either amino acid derivatives or frank polypeptides so that they are less lipid-soluble; they cannot cross the cell wall membrane so that their receptors are located on the cell wall membrane.
2. The hormone binds to its receptor site on the outside of the cell wall membrane; this in-turn stimulates a sub-cellular protein called the G protein.
3. The G protein stimulates an enzyme called the adenyl cyclase which converts the ATP into c AMP. It is the c AMP which is the power bottom of the cell where it can induce the following actions:-
    a) Change of the cell wall permeability.
    b) Enzyme activation or sometimes inhibition.
    c) Induction of muscle contraction or relaxation.
    d) Induction of glandular secretion.

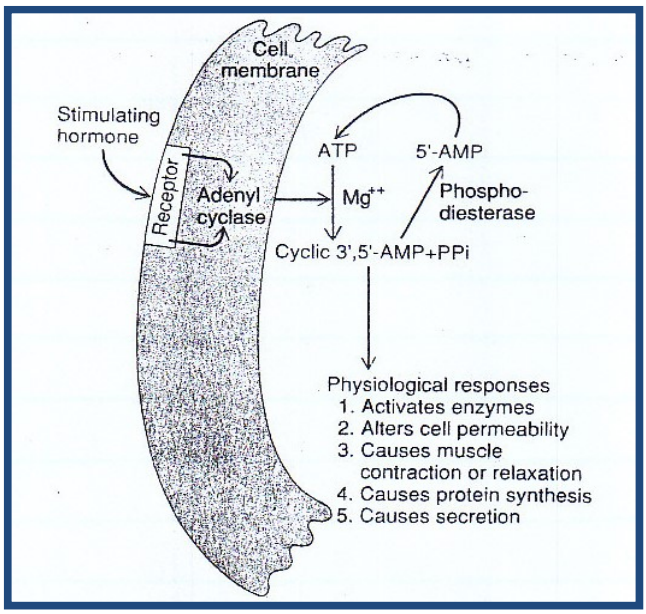


Fig. (1) the 2nd messenger mechanism

4. The hormone is designated the 1st while the c AMP is designated is the 2nd messenger
5. The phosphodiesterase enzyme inactivates the cAMP into the 3,5 AMP, terminating the hormone actions. The phosphodiesterase enzyme inhibitors are a group of chemical compounds that prevent the inactivation mechanism and extends the hormone actions. They include xanthines as aminophylline and coffee & sildenafil.

2- Induction of transcription and translation:-

It is specified for the steroid hormones which are more lipid soluble so they can cross the cell wall membrane bind to a cytoplasmic receptor forming together a mobile hormone receptor complex (MHRC).
The MRC crosses the nuclear membrane, into the DNA where it stimulates the process of transcription of the m RNA which crosses into the cytoplasm where it is translated by the r RNA forming a polypeptide chain.
This polypeptide chain could be an enzyme, a receptor or a contractile protein that mediates the hormone action.

Point of view	The 2nd messenger mechanism	The transcription and translation mechanism
1. The type of hormone	Non steroid	The steroid
2. Lipid solubility of the hormone	Non soluble	Soluble
3. Crossing of the cell wall membrane	No crossing	There is crossing
4. The site of the hormone receptor	Outside the cell wall	In the cytoplasm
5. The mobility of the hormone receptor complex	Fixed	Mobile
6. Crossing of the nuclear membrane	No crossing	There is crossing
7. Role of G proteins	The key player of the mechanism	No role at all
8. Role of cyclic compounds	The key players	No role at all
9. Role of PDE	The key inactivator	No role at all.

10. Role of PDEI	Stimulation	Has no effect at all
11. The latent period	Short	Longer
12. The duration of action	Short	Longer

N. B. For the thyroid hormones the receptors lie on the DNA itself. So that the thyroid hormones pass through the cell wall and the nuclear membranes to combine to their receptor site on the DNA to induce the process of transcription and translation.

General physiological properties of hormones:-

1. They are secreted in a very low concentration.
2. The rate of their secretion is determined by the body needs.
3. Factors stimulating the secretion of one hormone inhibit the antagonistic one.
4. Hormones are inactivated and then excreted, thus they differ from enzymes
5. Hormones have little effect on their secreting glands.
6. The hormone effects on the target tissue depends on
    a) The amount of the hormone secreted.
    b) The number and affinity of the hormone receptor in the tissue.
7. Sometimes the effects of the hormone persist after its clearance from the blood.

General Scheme for the Endocrine Hormones

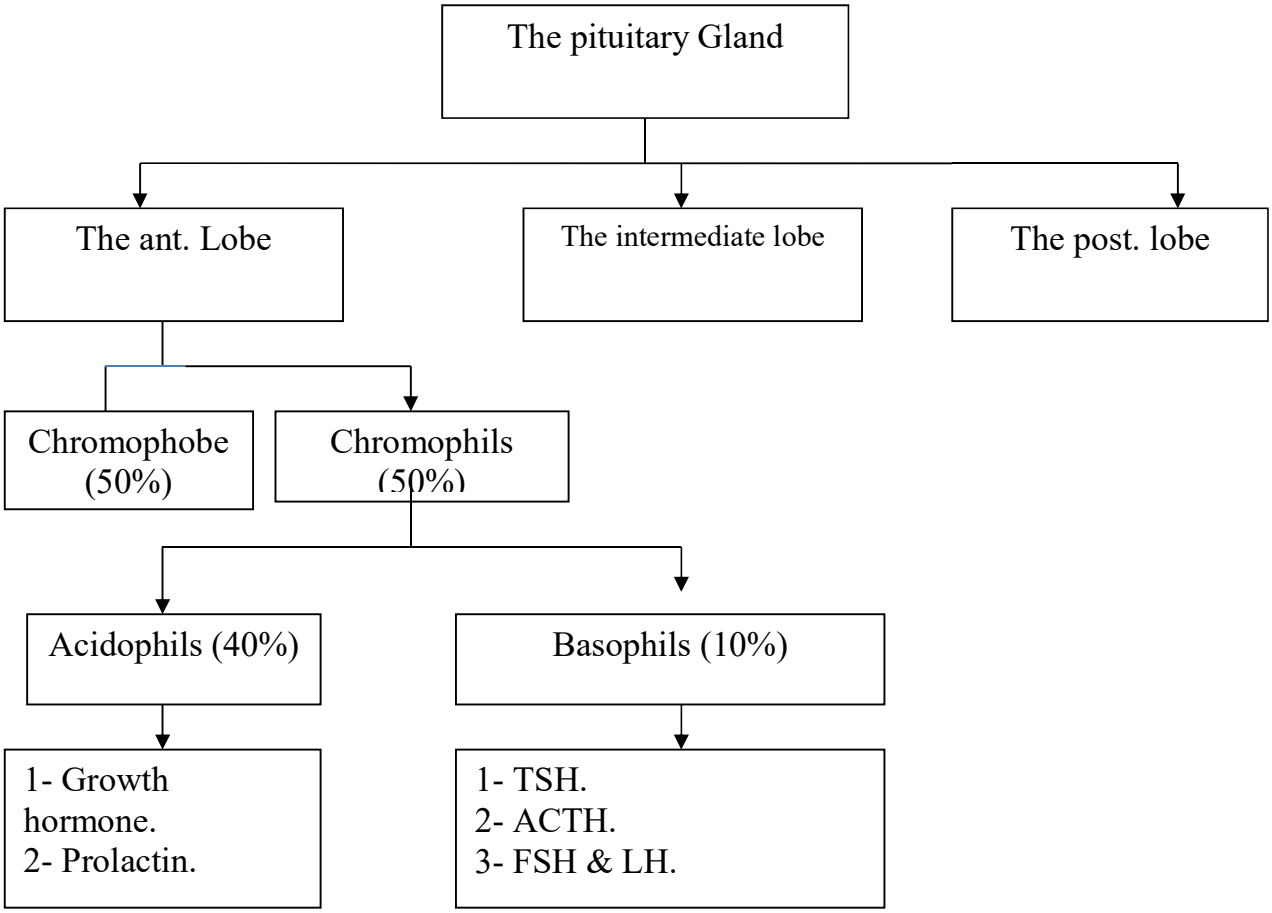
I-The metabolism:-	
a- Source	The secreting cell or the gland.
b- Chemistry	Whether it is a steroid or a non-steroid hormone.
c-Synthesis	
d-The carrier protein	It is mostly globulin and then it comes the albumin.
e-Catabolism	It is inactivated in the liver and the kidney to be secreted in urine and stool
II- The actions	
a-The mechanism	If it is a steroid hormone then it will be the transcription and translation otherwise it will be the 2nd messenger mechanism.
b-The actions	Hormones are classified into the organic and the inorganic type according to their main site of action; where organic hormones act on the

	organic metabolism while the inorganic hormone act on the metabolism of minerals as Ca & Na **A) The organic hormones:-** They extract the energy either from the breakdown of one of 2 sources; CHO on one side and lipids & may be proteins on the opposite side. If they are extracting energy from CHO then they are called ***hypoglycaemic*** hormones, they spare lipids and proteins. They have the following general actions:- **CHO metabolism:-** 1. They stimulate glucose uptake by the peripheral tissues. 2. They stimulate glycolysis and CAC. and inhibit gluconeogenesis. 3. They stimulate glycogenesis and inhibit glycogenolysis **Lipid metabolism:-** 1. They stimulate lipogenesis and inhibit lipolysis. 2. They decrease the level of FFA and ketone bodies. **Protein metabolism;-** 1. They stimulate protein synthesis and inhibit protein catabolism. 2. They decrease the level of the free amino acids in the blood. If they extract energy from lipids; then they spare CHO and burn lipids (and may be even proteins in case of cortisol).They are called ***hyperglycaemic*** hormones; they exert the exact opposite effects to what is mentioned above as follows: **CHO metabolism:-** 4. They inhibit glucose uptake by the peripheral tissues. 5. They inhibit glycolysis and CAC. and stimulate gluconeogenesis. 6. They stimulate glycogenolysis and inhibit glycogenesis.

	Lipid metabolism:- 3. They stimulate lipolysis. and inhibit lipogenesis 4. They increase the level of FFA and ketone bodies. **Protein metabolism;-** 3. They inhibit protein synthesis and stimulate protein catabolism. 4. They increase the level of the free amino acids in the blood. **B) The Inorganic hormones:-** they regulate the level of the inorganic ions in the blood by controlling their absorptive and excreting mechanisms.
III- The control	**A) The organic hormones:-** They are controlled by the following systems:- 1. The hypothalamus: it is connected to the ant. Pit. gland by the hypothalamo-hypophysial portal vessels through which it secretes a number of releasing and inhibiting factors that regulate the activity of the ant. Pit. gland 2. The ant. Pituitary gland: it secretes a number of trophic hormones; a specific one for each target gland to stimulate its growth, vascularity and hormone synthesis & secretion. They are the thyrotrophic(TSH), the adrenocorticotrophic(ACTH) and the gonadotrophic hormones (FSH& LH) 3. The feedback mechanism: when the level of a specific hormone is increased in the blood then this hormone will inhibit its secreting mechanisms through:- *a-A long loop –ve feedback* inhibition; an inhibitory effect

	upon the hypothalamus and the pit. Gland. *<u>b- A short loop –ve feedback</u>* inhibition through which the ant. pit. itself inhibits the hypothalamus preventing it from secreting the releasing factors 4. The effect of stress: all stressors activate the hypothalamus which in turn stimulates the ant. Pit. gland to release its trophic hormones which activate the target glands. 5. The effect of other factors as drugs and the biological clock: **B) The inorganic hormones:-** They are regulated by the level of the inorganic ion they control.
IV- The disturbances	They are either 1ry where the defect is in the gland itself or 2ry where the defect is in the ant. Pit. Gland. ***In 1ry hyper-function of a certain gland there will be decrease of its pit. trophic hormone & v.v. in its 1ry hypo-function.*** ***In 2ry hyper-function of a certain gland there will be increase of its pit. trophic hormone & v.v. in its 2ry hypo-function.***

The pituitary gland



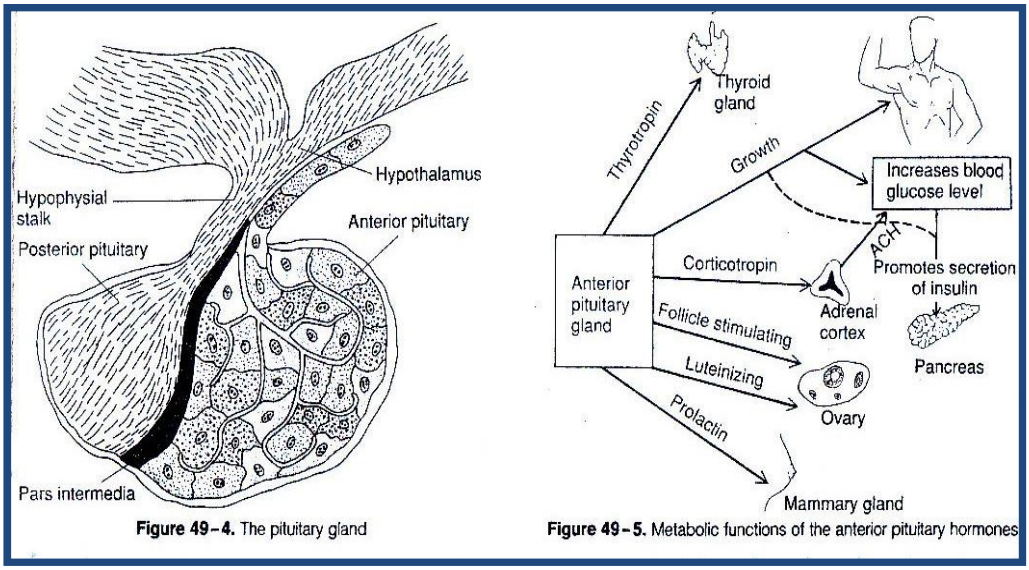


Fig (2) The anterior pit. gland

Growth hormone

[I] Metabolism:-

a- Source:-

Acidophils of the ant. pit. they are also called the somatotropes.

b- Chemistry: - a polypeptide chain.

c- The carrier protein: - it has a little affinity to be carried by the plasma proteins.

d- Catabolism :- in the liver.

[II] Actions:-

-The mechanism of action: - it acts in a steroid hormone like manner where it stimulates protein synthesis by the process of transcription and translation.

- Actions:-

A) Stimulation of the linear growth through the following actions:-

1. Stimulation of cartilaginous growth at the epiphysis of long bones through:-
    a. Stimulation of collagen formation.
    b. Stimulation of chondritin sulphate formation.
2. Stimulation of chondrocytes & their conversion into osteocytes.
3. Stimulation of the osteocytes.
4. Stimulation of ca uptake.
5. Stimulation of protein deposition.

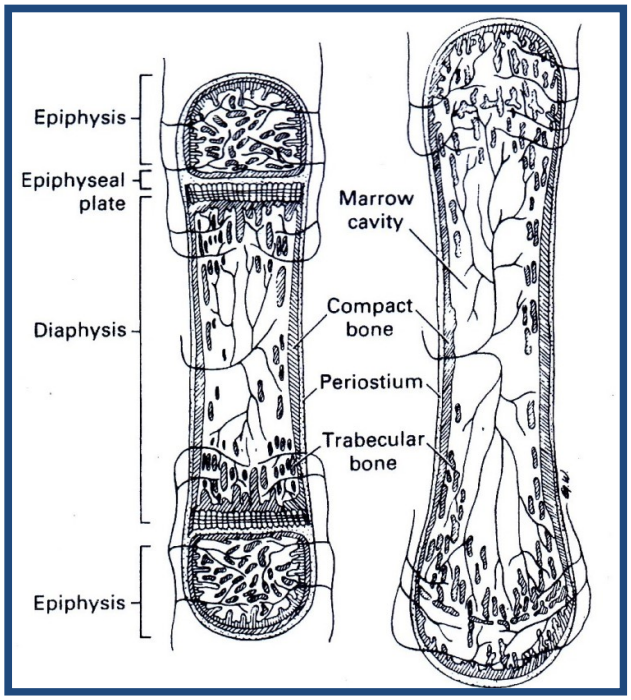


Fig (3) the typical bone and site of GH action

-The mechanism: - the somatomedins; the sulfation factors or the insulin like growth factors; IGFs:-

1. Growth hormone stimulates the liver to synthesize and secrete what is called the somatomedins which are small molecular weight proteins which mediate the effects of the growth hormone at the level of the cartilage and bones.
2. The most important of them is the somatomedin C or the IGF I.

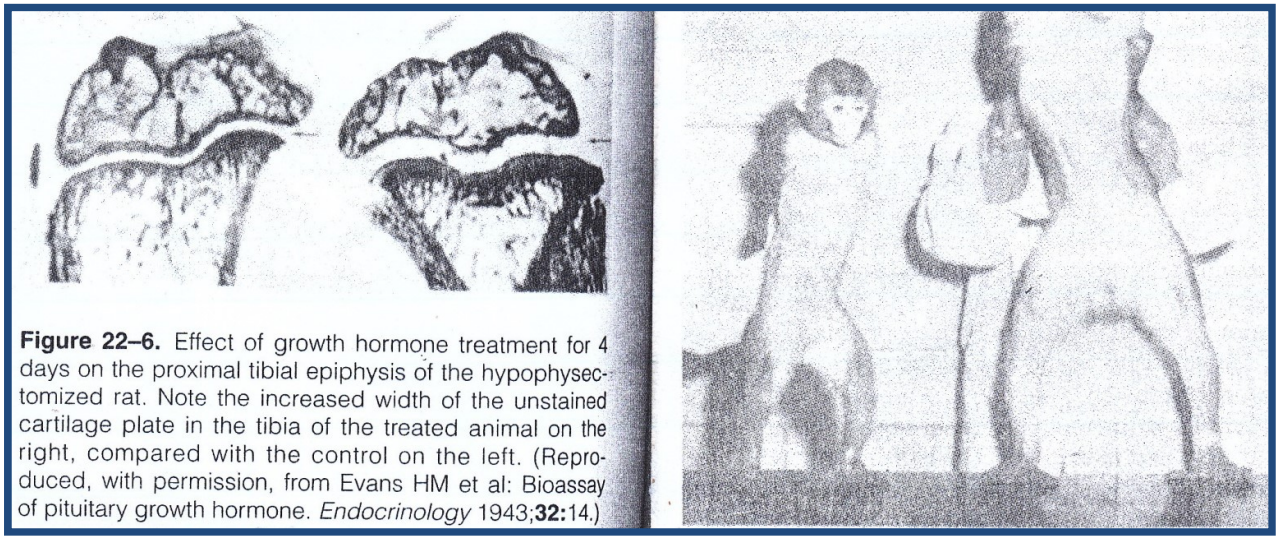


Figure 22–6. Effect of growth hormone treatment for 4 days on the proximal tibial epiphysis of the hypophysectomized rat. Note the increased width of the unstained cartilage plate in the tibia of the treated animal on the right, compared with the control on the left. (Reproduced, with permission, from Evans HM et al: Bioassay of pituitary growth hormone. *Endocrinology* 1943;**32:**14.)

Fig (4) the effect of GH on the epiphysis

3. They have some insulin like actions as stimulation of glycolysis and lipogenesis.

B) Stimulation of the visceral and soft tissue growth:-

1. Stimulation of the growth of muscles and viscera.
2. Stimulation of the RBCs production
3. Lactogenic effect.
4. Increase of the plasma and the interstitial fluid volume.

C) Metabolic effects:-

It is a hyperglycaemic hormone so ;-

The metabolic aspect	Stimulation	Inhibition
The CHO metabolism	Glucose absorption from the GIT. Gluconeogenesis. Glucagon secretion Glycogenolysis.	Glucose uptake by the peripheral tissues by inhibition of the hexokinase enzyme. Glycolysis Glycogenesis
The lipid metabolism	Lipolysis Increase the level of FFA. Increase the level of ketone bodies.	Lipogenesis.
The protein metabolism	Protein synthesis. Amino acid uptake by the cells. Transcription and translation.	Protein catabolism

The mineral metabolism	Ca absorption from the GIT	Na & K excretion from the kidneys.

[III] Control of secretion:-

A) The role of the hypothalamus:-

The hypothalamus secretes growth hormone releasing (GHRF) and inhibiting (GHIF) factors.

The GHIF is also known as the somatostatin.

Stimulants for the GHRF	Stimulants for the GHIF
Exercise and stress	
Hypoglycaemia	Hyperglycaemia
Hyperaminoacidaemia	Hyperaminoacidaemia
Hypofattyacidaemia.	Hypofattyacidaemia.
Hypoketonaemia.	Hyperketonaemia
NREM sleep.	REM sleep
Oestrogen	Androgens and cortisol.

B) The feedback regulation:-

1- Short loop –ve feedback where the increased level of GH decreases the secretion of the GHRF and increases the secretion of GHIF.

2- Long loop –ve feedback where the increased level of somatomedins inhibits the secretion of the GHRF and stimulates the secretion of GHIF.

[IV] Disturbances:-

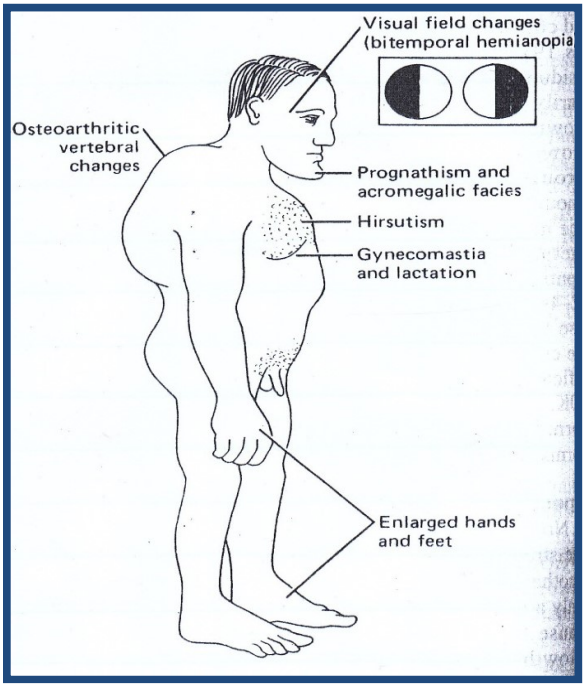
[A] The pit. Hypo function:-

Point of view	Dwarfism	Panhypopituitirism
Incidence	Before puberty	After puberty
Causes	Pituitary hypo-function due to tumours or surgical removal	Pituitary hypo-function due to due to craniopharyngeoma or a postpartum haemorrhage. In the latter it is called Sheehan's syndrome.
Physiological changes	1. Symmetric retardation of the linear growth. 2. Symmetric retardation of the soft tissue growth. 3. Crowded facial features 4. Normal mentality 5. Normal sexuality 6. There may be associative hypothyroidism 7. There may be associative hypocorticism.	1. There is rapid onset senility or what is called precocious senility. 2. Loss of the body and the scalp hair. 3. The skin becomes dry and wrinkled. 4. The muscles becomes atrophic 5. There is loss of teeth 6. There is mental retardation.

		7. There severe pallor 8. There is hypogonadism 9. There is hypothyroidism 10. There is hypocorticism

[B] The pit. Hyper-function:-

The point of view	Gigantism	Acromegaly
Incidence	Before puberty	After puberty
Cause	Pituitary hyperfunction mostly due to tumours	
The physiological changes 1-The bones;-	1. There is marked elongation of the long bones due to continued growth of bones at the epiphyseal line. 2. A gigantic may reach 2 meters height. 3. The ratio between the upper and the lower body segments is less than the normal figure of 1.	1. There is marked thickening of the long bones due to deposition of bony tissue under the periosteum. 2. There is hypertrophy of the flat; the short or the acral bones as follows;- 3. The skull:- a) There is overgrowth of the supra-orbital bridges. b) Enlargement of the nose. c) Prognathism; enlarged protruded mandible. 4. The hands and feet are broad and thick. 5. The vertebral column:- 6. There will be kyphosis.
2- The soft tissue	1. There will be symmetrical overgrowth of the soft tissue. 2. There will be symmetrical overgrowth of the muscles; in the early stages they are strong but later they become weak as they don't run parallel to the bone growth.	
3- The compression changes	1. Hypogonadism in males and females 2. Gynaecomastia 3. Headache 4. Bi-temporal hemi-anopia	

	 Fig (5) acromegaly
4- The metabolic changes	Hyperglycaemia and glycosuria

Prolactin or Mammotrophin

[A] Metabolism:-

1-Source:-It is secreted from the acidophils of the ant. Pit called the lactotropes.

2- Chemistry: - it is a polypeptide.

[B] Actions:-

(I) Actions on the breast:-

1- Stimulation of milk synthesis and secretion; stimulating the formation of fat, lactose and the milk casine.

2- It doesn't act during the period of pregnancy although its secretion is gradually increased during it but it waits for the withdrawal of estrogen and progesterone after the delivery of the placenta. The breast should be primed by the actions of these 2 hormones.

3-Estrogen stimulates the growth of the stroma and the ductal system of the breast while progesterone stimulates the growth of the acini.

(II) Actions on the gonads:-

It inhibits the secretion of the hypothalamic gonadotrophin releasing hormone from the hypothalamus; inhibiting the secretion of pit. gonadotrophin stopping the gonadal function.

[C] Control of secretion:-

In the normal ordinary conditions the hypothalamus secretes both the prolactin releasing and inhibiting factors but the dominance is for the inhibitory one, so there is continuous inhibition of prolactin secretion. Certain conditions reverse this dominance where they stimulate the secretion of prolactin releasing factor from the hypothalamus; these are:-

1-Pregnancy
2-Suckling
3- Conditioned reflexes as seeing or hearing a crying baby.
4- Stress and exercise

[D] Disturbances:-

Hyperprolactinaemia:-

1. There is hypogonadism and may be even infertility.
2. There are gynaecomastia and may be galactorrhea.
3. There is osteoporosis.

The post. Pit gland

Point of view	The anti-diuretic hormone; ADH	Oxytocin
[I]Metabolism:- 1- Source	The supra-optic nucleus of the hypothalamus.	The paraventricualr nucleus of the hypothalamus
2-chemistry:- 3- Carrier proteins:- 4- Catabolism:-	The hormones are bound to a carrier protein called Neurophysin I&II respectively. They are enclosed in the secretory granules known as the Herring's bodies. They are transported down the hypothalamohypophyseal stalk to be store in the post. Pit to be released on the body needs. Cleavage of the hormone from the binding carrier protein occurs during the transport mechanism. They are both polypeptides. They have loose binding capacity with globulins. In the liver then they are excreted by the kidneys. Oxytocin is broken down by the oxytocinase enzyme.	
[II] Actions 1- The mechanism of	c AMP	

action 2- The actions:- A- The kidneys:-	It has a very potent anti-diuretic action through widening of the pores in the walls of the collecting ducts. Its receptors in the kidneys are called the V2 receptors.	It has a weak anti-diuretic action.
B- The plain muscles:- 1-In the wall of the blood vessels:-	It is very potent vasoconstrictor through the V1-a type of receptors in the wall of the blood vessels.	It is weak vasoconstrictor
2- In the wall of the viscera:-	It causes contractions of the hollow organs as the uterus and the intestines.	It causes contractions of the 1. The myoepithelial cells of the mammary glands→ the milk let down reflex. 2. The uterus during sexual intercourse. Labour & after labour for the separation of the placenta and uterine involution. 3. The plain muscles of the epididymis and the vas deference to help the ejaculation.
[C] The metabolism:-	It has a hyperglycaemic effect through stimulation of the ACTH and an anti-insulin action through the V1 type of receptors.	
[III] control	It is secreted in the following conditions:- 1. Hyper-osmolarity of the plasma in case of dehydration 2. Hypovolaemia as in case of haemorrhage 3. Stress as surgery and	It is secreted in all conditions that necessitate its secretion as sexual intercourse, labour and suckling.

	pain 4. Drugs as morphine and nicotine increase ADH while ethanol decrease it	
[IV] Disturbances	Diabetes insipidus This is polyuria due to defective secretion or function of the ADH (nephrogenic diabetes insipidus). The following changes occur 1. Polyuria 2. Polydipsia. 3. Hypo-vitaminosis of water soluble vitamins. 4. An increase of the BMR.	

The thyroid gland

It secretes the following hormones

1- The tyrosine derivatives; T3 & T4 from the follicular a cells.
2- The polypeptide chain calcitonin.

Thyroid hormones; T3&T4

[I] Metabolism:-

1-Source: - they are secreted from the follicular A cells.
2-Chemistry: - they are iodinated derivatives of the amino acid tyrosine.
3-Synthesis;-they are synthesized in the following manner:-

1. Active iodide uptake by the iodide pump.
2. Oxidation of the iodide ion into the iodine element.
3. Iodination of tyrosine to form the mono-iodo-tyrosine and the diiodotyrosine.
4. Coupling of the iodinated compounds to form T3 and T4

4-Storage: - they are stored inside the follicles in the form of thyroglobulin.
5-Secretion:- which is carried out by pinocytosis then proteolysis of thyroglobulin to release the hormone.
6- The rT3; the reverse T3:-
it is formed in the peripheral tissues that contain a deiodinase enzyme converting the T4 into T3.
7- Carriage :- they are carried in the blood by the plasma proteins as follows;

1. Thyroid binding globulin 65%
2. Thyroid binding prealbumin25%
3. Thyroid binding albumin 10%.

8- Catabolism and excretion:- by oxidative de-amination and conjugation with glucuronic acid.

The point of view	T3	T4
1. Affinity to the plasma protein binding	One time	Ten times
2. Affinity to the nuclear receptor binding	More	Less
3. Latent period	6 hours	3 days
4. Duration of action	2-5 days	2 weeks
5. Potency	4 times potent	One time potent

[II] Actions:-

1-The mechanism of action:- stimulation of transcription and translation through nuclear receptors.
2-Actions:- they are called the machinery hormones as they stimulate each and every physiological function in the human body.

A) Stimulation of growth and development:-

1- They are essential for the growth and development; physically, sexually and most important mentally.
2- They stimulate skeletal growth through a synergistic action with GH.
3- The skeletal growth is more dependent on the thyroid hormones than soft tissue growth.
4- They stimulate brain development in the 1st few years of life.
5- Hypothyroidism is associated with growth retardation while hyperthyroidism is not associated with overgrowth but with metabolic hyperfunction

B) The metabolic effects:-

1- The cell metabolism:-

a) Stimulation of anaerobic and aerobic energy production
b) Increase the number and the size of mitochondria.
c) Stimulation of oxidative phosphorylation
d) Stimulation of the Na-K pump
e) In thyrotoxicosis there is uncoupling of oxidation and phosphorylation so there will be excess heat production.

2- The protein metabolism:-

a) In normal physiological levels they stimulate the protein anabolism.
b) In hyperfunction they stimulate protein catabolism causing wasting and muscle atrophy.
c) In hypofunction they stimulate synthesis of an abnormal type of proteins called the mucopolysaccharides.

3- The CHO metabolism;-

They stimulate all aspects of CHO metabolism leading to hyperglycaemia.

4-The lipid metabolism:- as long as they are hyperglycaemic then they extract energy from the breakdown of lipids.

a) Stimulation of lipolysis
b) Increase the level of FFA
c) Increase the level of ketone bodies
d) Stimulation of the breakdown of cholesterol and phospholipids.
e) Inhibition of lipogenesis

6-Vitamins:-

a) They increase the body needs of vitamins.
b) They increase the conversion of carotenes into vit.A

C) Effects on different body systems:-

a) Cardiovascular system:-
    1. Stimulate all cardiac properties.
    2. Increase of the heart rate and the COP.

3. Peripheral vasodilation due to the increase of the BMR.
4. Increase of the SBP and the pulse pressure with decrease of the DBP.

b) Respiratory system:- they increase the rate and depth of respiration.

c) Gastrointestinal system:-
1. They increase the appetite
2. They stimulate the secretory and the motor function of the GIT.

d) Central nervous system:-
1. They increase the level of excitability of the CNS.
2. They decrease the total reflex time
3. They are essential for the high intellectual functions of the CNS.

e) The endocrine glands:-
They stimulate the secretion of insulin parathormone and cortisol

f) The blood: - they stimulate the production of the RBCs.

[III] Control of secretion:-

1. The role of the hypothalamus:- it secretes the thyrotrophin releasing and inhibiting factors.
2. The role of the pit. gland:- it secretes the thyrotrophin or the thyroid stimulating hormone; TSH.
3. The role of the feedback mechanism:-

a) When the level of the thyroid hormones is increased they inhibit the hypothalamic releasing factor, stimulate the hypothalamic inhibiting factor, thus they decrease the secretion of the thyrotropin (long loop –ve feedback).

b) The ant. Pit. thyrotropin inhibits the hypothalamus in the same way; the short loop –ve feedback

4. The effect of drugs:-

a) Inhibitors of the iodide pump; as thiocyanates and perchlorates.

b) Inhibitors of iodination; as propylthiouracil.

c) Iodides:- they affect the thyroid secretion in the following way:-
1. Normal iodide supply→ normal hormone secretion.
2. Mild decrease of the iodide supply→ compensatory enlargement of the gland; goitre.
3. Marked increase or marked decrease of the iodide supply to the gland results in suppression of secretion. The inhibitory effect of the marked decrease of iodide is due to lack of the raw material while the inhibitory effect of the marked increase is due to a –ve feedback effect on the hypothalamus and the ant. pit. due to intial excess secretion of the hormone.
4. The Wolf-Chaikoff effect: - high iodine supply will result in suppression of the gland. Lugol's iodine solution is

given just for 2 weeks prior to any operative procedure on the toxic enlarged thyroid to induce atrophy of the gland.

5. The effect of stress :-
    a) Cold stressors are the specific stimulus for the thyroid gland, through stimulation of the thyrotrophin releasing factor and TSH.
    b) Excitement, on the other hand inhibits the thyroid function

[D]Disturbances:-

-Disturbances in the childhood period; cretinism:-

It is due to deficient thyroid hormones in the childhood period.

Physiological changes:-

a) Retardation of the physical growth:-
    1. There is inhibition of the skeletal growth.
    2. Short stature
    3. Delayed eruption of teeth
    4. Delayed closure of fontanels.
    5. Delayed sitting and walking.
b) Retardation of the sexual growth:- in the form of infertility.
c) Retardation of the mental growth:-
    1. The cretin is always idiot.
    2. There is defective speech.
    3. There is incontinence of urine and stool.
d) Special features:-
    1. Swollen eye lids with narrow palpebral fissure due to excess formation of the mucopolysaccharides.
    2. Enlarged protruded tongue
    3. Protuberant abdomen with umbilical hernia.

Point of view	Cretinism	Dwarfism
The cause	Thyroid hypofunction	GH insufficiency
Mentality	Retarded	Normal may be even supernormal
Sexuality	Retarded	Normal
Physical growth	Retarded but bones are more affected	Retarded but bones and soft tissue are equally affected
The face	Ugly coarse features	Fine nice baby or doll face.

-Disturbances in adults:-

Point of view	Hypo-function or Myxoedema	Hyper-function or thyrotoxicosis
A) cause	1-Primary :- 1. Atrophy 2. Inflammation 3. Irradiation 4. Autoimmune disease. -TSH is elevated. 2- Secondary:- due to failure of TSH secretion	1- Primary:-Grave's disease is an auto-immune disease where the lymphocytes produce an abnormal type of IgG called thyroid stimulating immunoglobulin (TSI). TSI has a similar action to TSH but with:- -longer duration of action, -No response to the –ve feedback. -Can cross the placenta. -Less potency. 2-Secondary due to excess secretion of TSH.
B-Pathophysiological changes:-		
1-BMR	Decreases down to -40% with cold intolerance.	Increases up to 100% with hot weather intolerance.
2-CHO	Hypoglycaemia with an increase of the liver and the muscle glycogen content.	Hyperglycaemia with a decrease of the liver and the muscle glycogen content.
3- Fat	Hypercholesterolemia with atherosclerotic changes	Hypocholesterolaemia Hypotriglyceridaemia and hypophospholipidaemia
4-Protein	Formation of an excess amount of mucopolysaccharides; myxoematous tissue which is retained under the skin causing non-pitting type of oedema.	Protein catabolism in the form of muscle wasting and osteoporosis.
5-Vitamins	Hypercarotenaemia Hypovitaminosis A which results in night blindness.	Deficiency of all vitamins.

6-The cutaneous changes **7- The facial changes**	The skin is dry cold and yellow. There is non-pitting oedema. Puffy eye lids. There is loss of the outer 1/3 of the eye brow.	The skin is sweat, hot and flushed. There is palmer erythema. There is exophthalmos due to the formation of the exophthalmos producing substance; another IgG formed by the lymphocytes, causing the following:- 1. Retro-orbital oedema 2. Degenerative changes in the extra-ocular muscles 3. Sympathetic stimulation.
8- The body systems	All the physiological parameters of the body systems are increased.	All the physiological parameters of the body systems are decreased.
• **CVS**	Decrease of all the cardiovascular parameters as the heart rate, COP, ABP with slow circulation.	Increase of all the cardiovascular parameters as the heart rate, COP, ABP with rapid circulation. There is marked rise of the SBP and drop of the DBP with large pulse volume.
• **CNS**	Decrease of the level of excitability, poor memory, slow thinking, hyporeflexia and hypersomnia.	Increase of the level of excitability, irritability, hyperreflexia and insomnia
• **Respiratory system**	Decrease of the rate and depth of respiration.	Increase of the rate and depth of respiration.
• **GIT** • **Blood** • **Reproduction**.	Decrease of the appetite Constipation Weight gain Anaemia Infertility	Increase of the appetite Diarrhoea Weight loss 2ry type of polycythaemia Infertility

Calcium homeostasis

1. The total body calcium content is 1200-1400 gm
2. 995 is present in the bones and teeth.
3. 1% is present in the ECF& ICF.
4. The plasma calcium level is 10 mg %, 40% of it is non-diffusable while 60% is diffusible. 10% in the form of Ca citrate and 50% are in the form of the ionisable form.

Factors affecting the serum ionized Ca level:-

1. The phosphate level:

There is an inverse relation between the serum Ca and phosphate ions. The product of their multiplication is a constant at the constant ph and is called the SOLUBILITY PRODUCT.

2. The pH:- acidosis increases the level of serum Ca ions while alkalosis decreases it.
3. Hormones:

There is one single Ca lowering hormone called calcitonin.
There are 2 raising ca hormones called parathormone and vit.D.

Physiological significance of the ca ions;-

1. It has a structural function in bones and teeth.
2. It is a catalyst for coagulation
3. It is essential for the neuromuscular junction where it is responsible for the normal excitability, the release of the transmitter and the excitation contraction coupling.
4. It is essential for the endocrine function where it is necessary for the hormone release and its actions.
5. Cell metabolism.

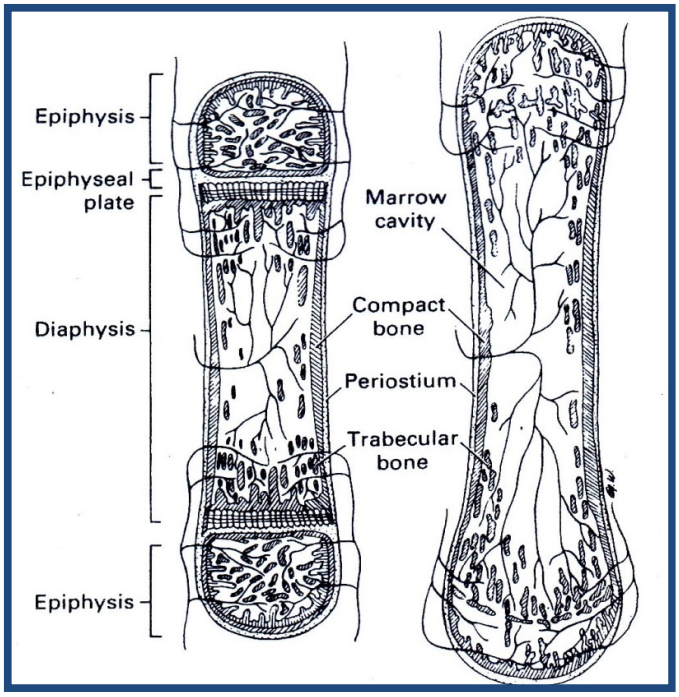
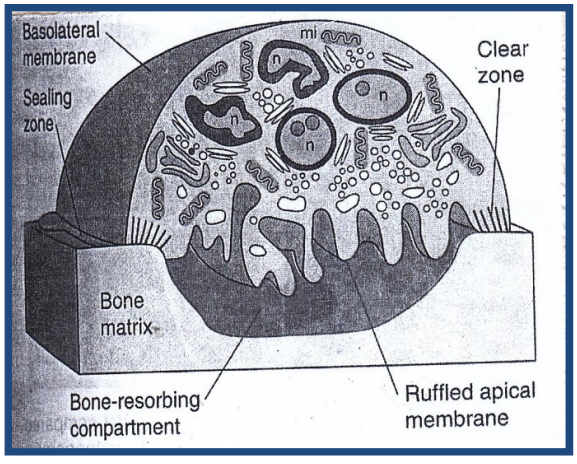
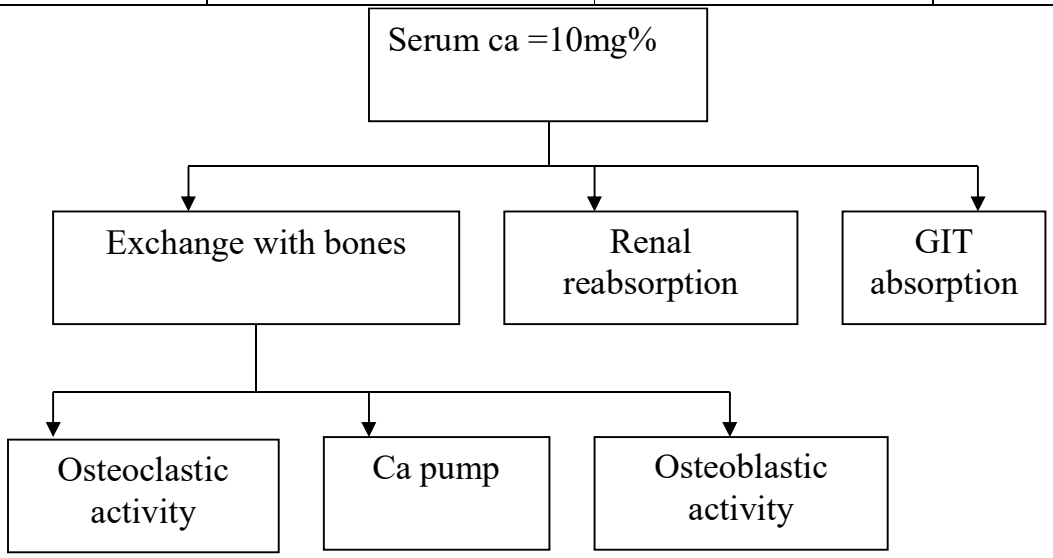


Fig. (6) The structure of a long bone.

The point of view	Calcitonin	Parathormone	Vit. D
[I]Metabolism:- 1-Source:-	The para-follicular C cells of the thyroid gland.	The chief or the dark cells of the parathyroid gland	1-dietary; in milk& egg yolk. 2- synthesis:- 7dehydrocholesterol is transformed in the skin by the UV rays into cholecalciferol. In the liver the latter is transformed into 25(OH) cholecalciferol. In the kidneys, under the effect of the parathormone the latter is transformed into the active form of vit.D or the 1-25(OH) Cholecalciferol.
2- Chemistry	Polypeptide chain		A steroid hormone
[II] The actions:- 1- The mechanism of action:-	Second messenger mechanism  Fig. (7) Bone resorption		Transcription and translation to induce the synthesis of the following proteins:- 1-Ca binding protein; calbidin. 2-The Ca-ATPase. 3-The alkaline phosphatase.

2- The actions:- a) on the bones:-	1-Inhibition of the osteoclasts. 2-Stimulation of the osteoblasts. 3- On the long run calcitonin decreases both cellular activities having an insignificant effect on bones	1-Stimulation of the osteoclasts. 2-Inmhibition of the osteoblasts.	The normal small physiological dose of vit. D induces bone calcification while the large toxic dose induces decalcification.
b) on the kidneys:-	Increases the renal. excretion of both Ca and PO4	Decreases the renal excretion of ca. Increases the renal excretion of PO4.	
c) on the GIT:-	Decreases Ca absorption	Increases the absorption of Ca through an increase of vit.D.	Increases the absorption of ca from the intestine through stimulation of protein synthesis of the above mentioned proteins.
[III] Control:- 1-Ca: 2-PO4: 3- Others	Direct relationship. Inverse relationship. GIT hormones increase it	Inverse relationship. Direct relationship Sympathetic stimulation increase it	Inverse relationship. Direct relationship



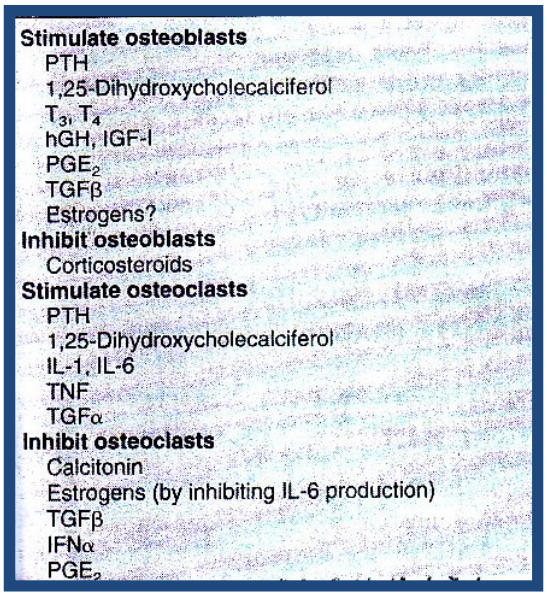


Fig. (8) factors affecting the osteoclastic and the osteoblastic activity

Hypocalcaemia

-Causes:-

1. Hypoparathyroidism
2. Hypovitaminosis D
3. Alkalosis
4. Hyperventilation
5. Hyperphosphataermia
6. Relative dietary hypocalcaemia as in pregnancy and lactation

-Physiological effects:-

A) Increase of the neuromuscular excitability leading to the following:-

1. Clonic and tonic convulsions of the skeletal muscles
2. Colic and spasm of the smooth muscles in the respiratory airways and the GIT.
3. Arrhythmias.

B) Failure of coagulation but this is not the cause of death, asphyxia is the actual cause of death.

Tetany:-

It is the increase of the neuromuscular excitability due to hypocalcaemia.

The point of view	The manifest type of tetany	The latent type of tetany
Serum Ca level	Less than 6 mg%	More than 6 mg %
Tetanic manifestations	Occur during rest:- 1. Clonic and tonic convulsions of the skeletal	1-Occur during stress and exercise. 2- Tetanic

	muscles 2. Colic and spasm of the smooth muscles in the respiratory airways and the GIT. 3. Arrhythmias 4. Obstetrician or the achucheur's hand; there is flexion of the wrist and the MP joints, extension of the IP joints and adduction of the thumb.	manifestations can be provoked as follows:- a- The Chevostek's test; where there are ipsilateral facial twitches on tapping on the facial nerve. b- Trouseau's test where there will be carpal spasm on occlusion of the circulation in the upper arm

The suprarenal cortex

It consists of 3 zones; glomerulosa, fasiculata and reticularis.
Zona glomerulosa secretes the mineralocorticoids; the most important of which is aldosterone.
Zona fasiculata secretes the glucocorticoids; the most important of which is cortisol.
Zona reticularis secretes the sex hormone androgen.

Aldosterone hormone

[I]Metabolism:-

1- Source:- the zona glomerulosa of the suprarenal cortex.
2- chemistry: - steroid in nature.
3-Carrier protein: - 50% of the hormone is circulating freely.
4-Catabolism: -
-It is reduced into di- then tetra-hydro-steroid then conjugated with glucoronic acid to be excreted in urine and the foecal matter.
-Transformed into 17 keto-steroid.

[II] Actions: -

-Actions: - it is sodium retaining and potassium depleting.
A) On the kidneys:-

1. Stimulation of Na re-absorption in exchange for K or H excretion in the DCT.
2. Secondary increase of cl and water re-absorption.

B) On the sweat and the salivary glands: -
It stimulates Na re-absorption in exchange for K excretion in the ducts of the glands.
C) On the GIT:-
It stimulates Na absorption in exchange for K excretion in the small intestine.
-The mechanism of action: - as steroid hormones, it stimulates protein synthesis forming the aldosterone-induced protein (AIP).
AIP produces the following effects

1. Increase of the number and the activity of the Na-K pump molecules.
2. Increase of the ATP-ase activity.

[III] Control:-

A) The ECF k^{+}:-
Hyper-kalaemia is the most potent stimulus for the release of aldosterone hormone.
B) The ECF Na:-
Hypo-natraemia is the most frequent stimulus for the release of the hormone. It stimulates it through the following mechanisms:-

1. Stimulation of the rennin angiotensin system due to hypovolaemia and renal ischaemia.
2. Hyponatraemia is always associated with hyperkalaemia.
3. Direct action on the zona glomerulosa.
4. Stimulation of the ant. pit. to release aldosterone releasing hormone (ASH)

C) The ACTH: - it has a permissive effect on the z.glomerulosa.

Hyperaldosteronism:-

A) The 1ry type (Conn's syndrome) is due to a tumour in the z Glomerulosa

Pathophysiological changes:-

1. Hypernatraemia but NO OEDEMA due to the aldosterone escape phenomenon where there is an increase of the GFR and the rate of tubular flow in the kidney where aldosterone cannot stimulate Na re-absorption in the DCT.
2. Hypervolaemia
3. Hypertension
4. Hypokalaemia leading to hyperglycaemia, renal damage and hyperpolarization of the muscles.
5. Alkalosis leading to tetany.

B) The 2ry type is due to:-

-Heart failure due to stimulation of the rennin angiotensin system by renal ischaemia.

-Liver cell failure due to lack of the hormone inactivation.

-Renal cell failure due to stimulation of the rennin angiotensin system by renal ischaemia.

-THERE IS OEDEMA at the early stage of the disease.

Cortisol

[I]Metabolism:-

1- Source: - from the Z. Fasiculata.

2-Chemistry: - it is a steroid hormone.

3-carrier protein:-

75% is bound to the corticosteroid binding globulin or what is called the transcortin

15% is carried by the albumin.

10% is free.

4- Catabolism as aldosterone.

[II]Actions:-

-The mechanism of action: - transcription and translation.

- (i) Physiological actions:-

-Induced by the endogenously secreted normal hormone level.

-They are all metabolic and exclusively hyperglycaemic actions.

1-CHO metabolism:-
It inhibits glucose uptake by the peripheral tissues.
It stimulates gluconeogenesis through stimulation of the gluconeogenic enzymes.
2-Protein metabolism:-
It is an extra-hepatic catabolic but intra-hepatic anabolic where it stimulates al steps of the protein synthesis.
3-Lipid metabolism:-
It stimulates lipolysis, increases the level of FFA and ketone bodies.

(ii) Pharmacological actions:-

1. Anti-stress where it increases the blood sugar, FFA and amino acid levels.
2. Anti-inflammatory; where it inhibits the enzyme phospholipase which is responsible for the formation of the arachidonic acid which gives rise to the inflammatory mediators; prostaglandins and leukotrienes.

   Thus, cortisol inhibits the following:-
   a) Capillary vasodilation
   b) Leukocytic migration
   c) T cell activation
   d) Lysis of the lysosomal membranes.
   e) Prostaglandins induced fever and pain.
3. Anti-allergic:- it may block the antigen antibody reaction or it may prevent its consequences.
4. Anti-shock where it raises the ABP.
5. Haematological:-
   a) Stimulation of erythropoeisis.
   b) Stimulation of the production of the platelets.
   c) Inhibition of the esinophil production.
   d) Inhibition of T lymphocytic production
   e) Inhibition of IgG production
6. Cardiovascular system:-
   a) Hypernatraemia
   b) Hypervolaemia
   c) Hypertension
   d) Oedema
   e) Hypokalaemia
   f) Alkalosis
   g) Sensitize the vascular walls to circulating amines.
   h) In crease the capillary fragility due to weak capillary wall collagen and rise of the capillary hydrostatic pressure..

[III] Control of secretion:-

1- The role of the hypothalamus; where it secretes the corticotrophin releasing and inhibiting factors.
2- The role of the ant. pit.; where it secretes the corticotrophin or the ACTH.
3- The feedback regulation:-

Excess cortisol will inhibit the corticotrophin and its releasing factor.

4- The effect of stress; where it stimulates the hypothalamus which in-turn secretes the corticotrophin releasing factor to stimulate the release of the corticotrophin
5- The effect of the circadian rhythm; where cortisol secretion is increased in the early morning and decreases in the late evening.

[IV] Disturbances:

Cushing's syndrome

-It is hyper-function of the z.fasiculata either due to excess secretion of the ACTH (2ry) or a tumour of the zone itself (1ry).

-Pathophysiological changes:-

1-CHO metabolism:-

There is hyperglycaemia, glucosuria and steroid diabetes which may mount up to diabetes mellitus.

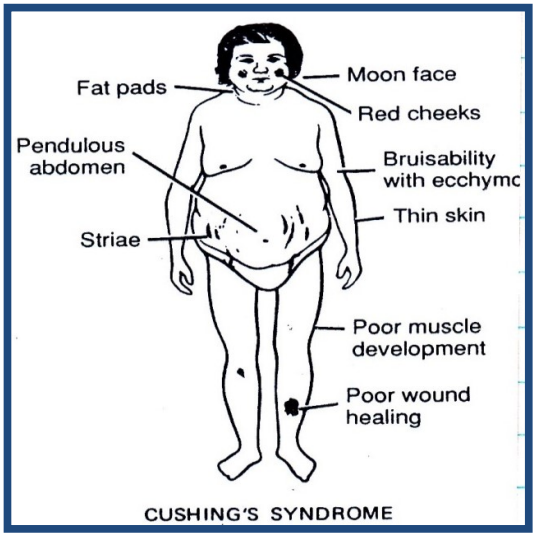


Fig. (9) Cushing's Syndrome

2-Protein metabolism:-

There is excess [protein breakdown leading to

a) Skin changes in the form of purple striations, bruises and delayed healing of wounds.
b) Wasting and muscle atrophy.
c) Osteoporosis and kyphosis
d) Hyper-calcaemia and renal damage

3- Fat metabolism:-

There is excess lipolysis in the lower half of the body with excess lipogenesis in the upper half i.e. in the trunk & head and neck regions, leading to what is called the lemon stick appearance or the bufflo hump and moon face .

4- The body systems :-

a) The blood:-

1. Polycythaemia

2. Thrombocytosis
3. Esinopenia
4. Lymphocytopenia.

b) <u>CVS:-</u>

1. Hypernatraemia
2. Hypervolaemia
3. Hypertension
4. Hypokalaemia
5. Alkalosis
6. Oedema
7. +ve Hiss test; increased capillary fragility

c) Hairsuitism.

Hypo-function of the suprarenal cortex
Addison's disease

It occurs due to damage of the suprarenal cortex by TB or an auto-immune disease.

<u>A) Hypoaldosteronism:-</u>

1. Hyponatraemia
2. Hypovolaemia
3. hypotension
4. Hyperkalaemia
5. acidosis

<u>B) Hypocorticism:-</u>

1. Decrease of the basal metabolic rate
2. Decrease of the energy production
3. Hypoglycaemia
4. Hypotension
5. Easy fatigability
6. Muscle weakness
7. Failure of water diuresis
8. Increase of the ACTH and MSH leading to bronzed colouration of the skin
9. Addisonian crisis; hypotension and shock on exposure toi stressors

D) <u>Hypogonadism</u>

The adreno-genital syndrome

The affected age	Males	Females
Before puberty	Pre-coscious puberty:- 1. Excess musculinization 2. Precocious male sexual characters; as facial hair, deep	Pseudohermaphroditism:- 1. 1ry sexual organs of a female but the external genitalia are of that of a male. 2. Enlarged labia simulating

	voice and acne	the scrotum 3. Enlarged clitoris 4. Undescended vagina 5. Atrophy of the uterus and the ovaries
After puberty	Un-noticed	**Virilism.:-** 1. Musculinization 2. Hairsuitism 3. Enlarged larynx 4. Deep harsh voice 5. Male body built 6. Atrophy of the breast 7. Amennoehea 8. Sexual desire to the same sex

The endocrine pancreas

The ilets of Langerhans contain the following type of cells:-

1. Alpha cells secreting Glucagon hormone
2. Beta cells secreting insulin hormone
3. Delta cells secreting somatostatin hormone
4. Theta cells secreting the pancreatic polypeptide.

Insulin

[I]Metabolism:-

1-Source: - beta cells of the Ilets of Langerhans.

2-Chemistry: - it consists of 2 polypeptide chains A& B linked together by a disulphide bridge.

3-Biosynthesis: -

The ribosomes of the RER synthesise the pre-pro-insulin which is converted into pro-insulin by the SER then to insulin and C peptide by the Golgi apparatus.

4-Secretion:-

-On depolarization of the beta cells there will be ca influx which stimulates the process of exocytosis of the secretory insulin- containing granules.

-There are 2 phases for insulin secretion; the rapid phase within 2-5 minutes which releases the already stored hormone and the slow phase within 15 min. which include synthesis then release of the hormone.

5-Carriage: - free

6- Catabolism:- in the liver and kidneys and other target tissues through reduction by hepatic insulin glutathione trans-hydrogenase cleaving into A and b chains.

[II]Actions:-

1-The mechanism of action:-

A) The tetramer insulin receptor:-

1. The insulin receptor is a tetramer formed of 2 alpha and 2 beta subunits.
2. The alpha subunit is totally extracellular.
3. The beta subunit is trans-cellular and its cytoplasmic portion contains a kinase enzyme.
4. When the insulin molecule binds to the alpha subunit→ activation of the kinase enzyme of the beta subunit→ auto-phosphorylation of the tyrosine residue on the beta subunit → phosphorylation or dephosphorylation of other cellular proteins.

B) The glucose transporters:-

These are membrane proteins which are responsible for the facilitated diffusion of glucose through the cell wall membranes.

Seven types are known, designated from GLUT-1 to GLUT-7.

GLUT-4 is the one which is insulin dependent.
GLUT-4 is present in the skeletal muscle, heart and the adipose tissue.
GLUT-4 is normally located in the cytoplasm of the cell, when insulin activates its receptor then GLUT-4 moves to be inserted into the cell wall membrane to transport the glucose molecule by a facilitated diffusion mechanism.

Transporter	Site	Function
GLUT-1	Brain- RBCs- kidneys	Basal glucose uptake
GLUT-2	Liver- small intestine- kidneys	Transport thropugh membranes
GLUT-3	Brain –kidneys	Basal glucose uptake
GLUT-4	Heart- skeletal muscle and the adipose tissue	Insulin stimulated glucose transport
GLUT-5	Jejunum- sperm	Transport of fructose
GLUT-6	----------	None
GLUT-7	Liver	G6P transporter in the ER

Actions:- it is a frank hypoglycaemic hormone

1-CHO metabolism:-

1. Stimulation of the glucose uptake in the skeletal muscle, heart and the adipose tissue.
2. The non- insulin dependent glucose uptakers are the brain, RBC, GIT, kidneys and the liver.
3. Stimulation of glycolysis; it is the key stimulant hormone e for the G6PD.
4. Stimulation of glycogenesis in the muscle
5. Inhibition of glycogenolysis by inhibition of the phosphorylase enzyme.
6. Inhibition of gluconeogenesis through inhibition of the release of the amino acids from the extra-hepatic tissues.

2- The protein metabolism:-

1. Stimulation of the protein synthesis and inhibiton of protein catabolism.
2. Stimulation of the amino acid uptake
3. Stimulation of the process of transcription and translation

3- The lipid metabolism;-

1. Stimulation of lipogenesis.
2. Inhibition of lipolysis through the inhibition of the hormone sensitive lipase.

4-The minerals:-

1. Stimulation of K uptake by cells together with glucose
2. Stimulation of the Na-K pump.

5-Growth and development;-

1. it stimulates the cellular proliferation and differentiation.
2. It has a synergistic effect with the GH.

[III] Control:-

Stimulants	Inhibitors
Hyperglycaemia	Hypoglycaemia
Hyperaminoacidaemia	Hypoaminoacidaemia
Hyperfattyacidaemia	Hypofattyacidaemia
Hyperketonaemia	Hypoketonaemia
GIT hormones as gastrin	Somatostatin
General hyperglycaemic hormones as cortisol	General hormones as adrenaline and nor-adrenaline; as they are potent inhibitors for the hormone
Parasympathetic or beta adrenergic stimulation	Alpha adrenergic stimulation
Hyperkalaemia and hyponatraemia	Hypo-kalaemia and hyper-natraemia
Beta cell stimulants as sulfonylureas	----------

Glucagon

It is secreted from the alpha cells of the Ilets of Langerhans.
It is a polypeptide chain
It acts through the cAMP mechanism.

Actions: - it is a frank hyperglycaemic hormone

1. Stimulation of glycogenolysis.
2. Stimulation of gluconeogenesis.
3. Stimulation of lipolysis.
4. Positive inotropic.
5. Cholagogue
6. Stimulation of secretion of the GH.

-Control of secretion:-

Stimulants	Inhibitors
Hypoglycaemia	Hyperglycaemia
Severe muscle exercise	Somatostatin.
Hyperaminoacidaemia	Hypo-aminoacidaemia
Beta adrenergic and vagal stimulation	Alpha adrenergic stimulation

Somatostatin

It is secreted from the delta cells of the pancreatic ilets of Langerhans.
It is a polypeptide chain
It decreases the secretion of insulin, glucagons& GH.
It inhibits the GIT functions.
It is stimulated by any rise of blood sugar, amino acid, fatty acid or the GIT hormones in the blood.

Blood glucose homeostasis

It is the maintenance of the blood glucose level within the normal physiological range where the fasting blood sugar ranges between 80-110 mg% and the 2nd hour post-prandial never exceeds 140mg%.

Mechanisms of blood glucose homeostasis:-

1- The role of the liver:-

After meals 2/3 of blood sugar is converted into glycogen by the liver to be converted back to glucose in between meals by the process of glycogenolysis.

During starvation the liver maintains the blood sugar level in the 1st 18-24 hours through the process of glycogenolysis then it starts the process of gluconeogenesis.

2-The role of hormones:-

-The following hormones are considered hyper-glycaemics or anti-insulins;-

1. Adrenaline which stimulate glycogenolysis.
2. GH which stimulate gluconeogenesis.
3. Glucagons, cortisol and thyroxine all of which stimulate the processes of glycogenolysis and gluconeogenesis

-The hypoglycaemic hormones are insulin and the insulin like growth factors, IGF

Significance of blood sugar homeostasis:-

1. The brain, retina and the germinal epithelium cannot tolerate hypoglycaemia.

2. Hyperglycaemia is always associated with
   a) Cellular dehydration, polyurea with loss of fluid and electrolytes in urine
   b) Hyperfattyacidaemia, hypercholesterolaemia with atherosclerotic changes in the blood vessels

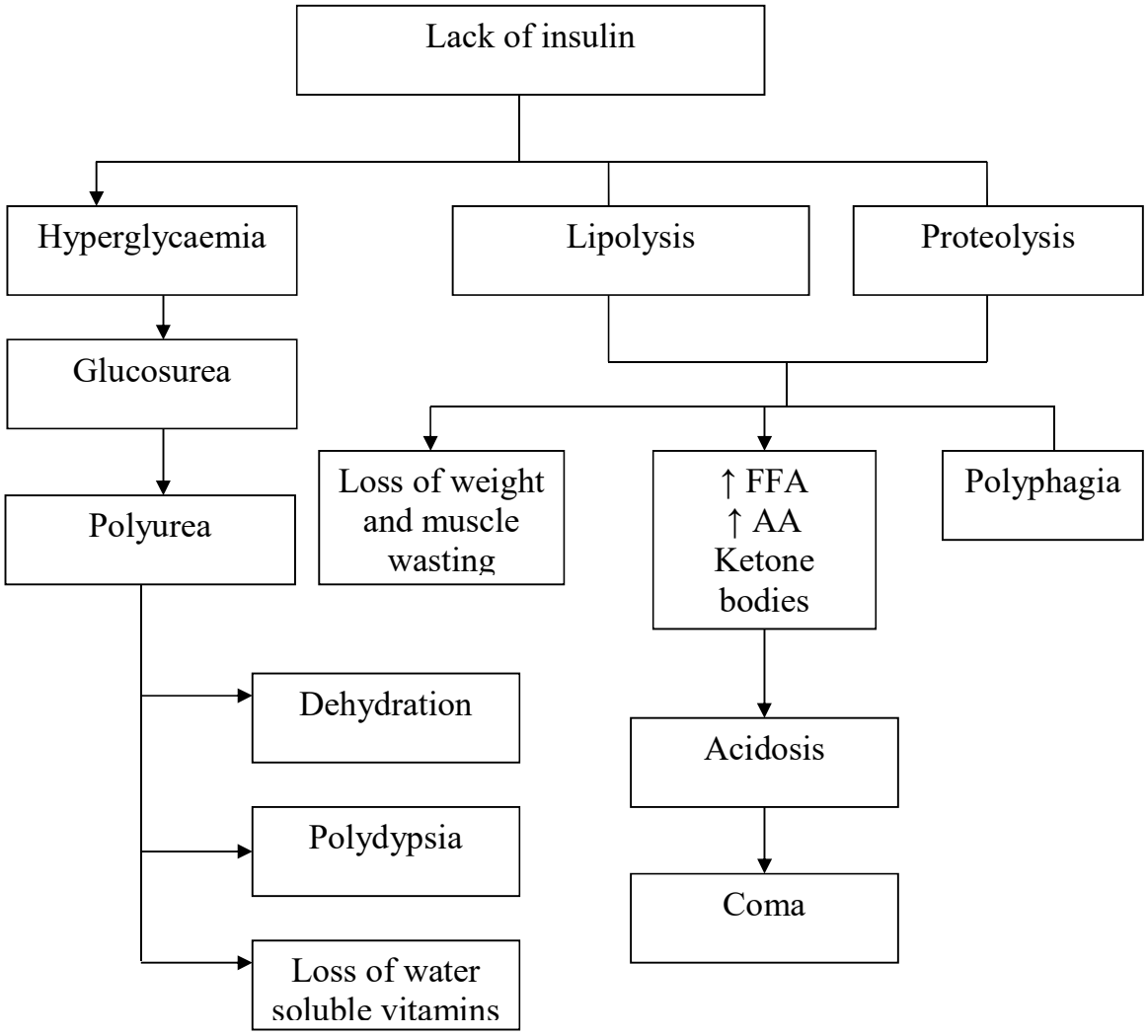
Disturbances of the blood glucose homeostasis

Diabetes Mellitus

1. It is permanent hyperglycaemia due to insufficiency or inefficiency of insulin, sometimes both causes may be present.
2. Diabetes is classified into 2 major categories; the insulin dependent (IDDM) and the non-insulin dependent (NIDDM) types.
3. IDDM: - the main pathophysiology here is lack of insulin secretion due to damage of the beta cells of the pancreas either due to viral, bacterial or autoimmune disease.
4. NIDDM: - the main pathophysiology here isb the development of insulin receptor resistance due to what is known as the receptor down-regulation phenomenon.

The point of view	IDDM	NIDDM
Cause	Damage of the beta cells	Receptor resistance
Age of incidence	Less than 35 years	More than 35 years
Family history	Negative	Positive
Obesity	Negative	Positive
Role of insulin therapy	Mandatory	Obsolete EXCEPT in stressful situations as infections and surgery
The main line of treatment	Insulin; life long	Diet + exercise Glucose sensitizers as metformin Beta cell stimulants in late stages of the disease.

Pathophysiology of diabetes mellitus



Hypoglycaemia: -

1. It is mostly iatrogenic, due to the intake of a hypoglycaemic drug such as insulin or a beta cell stimulant that is not followed by food intake.
2. Rarely, it is due to hyper-insulinim.
3. It passes through the following stages:-
    a) The stage of sympathetic over-stimulation; where the blood sugar level drops below 70 but still higher than 50 mg %. There is tachycardia, hypertension, hyperventilation, Mydriasis, large pulse volume, marked sweating and very cold extremities.
    b) The stage of brain excitement; where the blood sugar level drops below 50 but still higher than 2o mg%. There are convulsions of both types tonic and clonic.
    c) The stage of paralysis; where the blood sugar drops below 20mg5 where there is paralysis of the brain centres and finally death

Some organs with an endocrine like activity

These organs are:-

A) **The kidneys** which secrete the following hormones:-
    1. Rennin:-
        a) It is secreted from the JGC.
        b) Is stimulated by hypo-volaemia, hypotension, hyponatraemia and sympathetic stimulation.
        c) It produces the following functions;-
            1. Arteriolar vasoconstriction.
            2. contraction of the mesangeal cell leading to decrease of the GFR
            3. Increase of the aldosterone, ADH,ACTH and norepinephrine secretion
    2. Erythropoietin
    3. Active form of vitamin D.
    4. Prostaglandins.

B) The heart:- which secretes the atrial natriuretic peptide (ANP):-
    1. it is a polypeptide that is secreted from the atrial muscle cell in response to stretch.
    2. It antagonizes the Rennin angiotensin II system where it:-
        a) Decreases the vascular reactivity.
        b) Decreases the aldosterone secretion
        c) Decreases the ADH secretion.

d) Relaxes the messangeal cells→ increase of the GFR
e) Decreases na re-absorption from the DCT..

C) <u>The respiratory system</u>: where it secretes heparin, Angiotensin I converting enzyme and prostaglandins.

D) **<u>The liver</u>;** which secretes the following:-

1. Somatomedins
2. Erythropoietin
3. The 25 (OH) cholecalciferol.
4. Prostaglandins.

E) <u>The GIT</u>:- see the physiology of the GIT.

F) <u>The skin</u>:-which secretes the cholecalciferol

G) <u>The pineal body</u>: - which secretes melatonin.

Physiology of Reproduction

The male reproductive system

The male reproductive system consists of 1ry and 2ry sex organs; the 1ry sex organ is that one responsible for the formation of the sperms which is the testicles. The 2ry sex organs are those which share in the sexual function; they include the epididymis, vas deference, the prostate and the seminal vesicles.

Physiology of the testicles:-

A cross section of the testicle shows that it is divided into compartments; each of which contains a long coiled tubule called the somniferous tubule, which is surrounded by a CT stroma. A cross section of the tubule shows that it is an ordinary tubule lined with a layer of germinal epithelium and large intervening cells called the Sertoli cells; the germinal epithelium is responsible for the process of sperm production while the cells of Sertoli are responsible for associative functions.

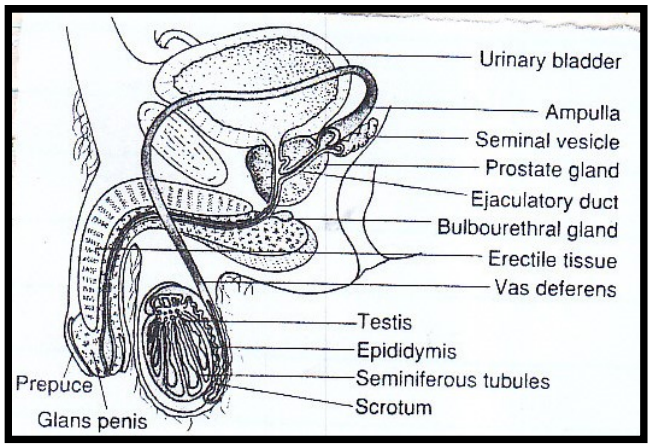


Fig. (10) the male genital system

Functions of Sertoli cells:-

1- Nutrition of the sperms.
2- Washing of the sperms.
3-Endocrine function; secreting the following substances:

a) Mullarian inhibitory factor.
b) Androgen binding protein.
c) Inhibin which is responsible for inhibition of the FSH hormone.
d) Aromataze enzyme which is responsible for the formation of estrogen needed for the completion of the process of sperm production.

Functions of the germinal epithelium:-

It is responsible for the production of mature sperms.
The process occurs through a meiotic preceded and followed by mitotic divisions.

Steps of spermatogenesis:-

1-1st mitotic division: it transforms the spermatogonia into 1ry spermatocytes.
2- Meiotic division; transforming the 1ry into 2ry spermatocytes.
3- 2nd mitotic division transforming 2ry spermatocytes into spermatids.
4-Spermiogenesis; a process to maturate the spermatids into mature sperms.It is carried pout by the Sertoli cells.

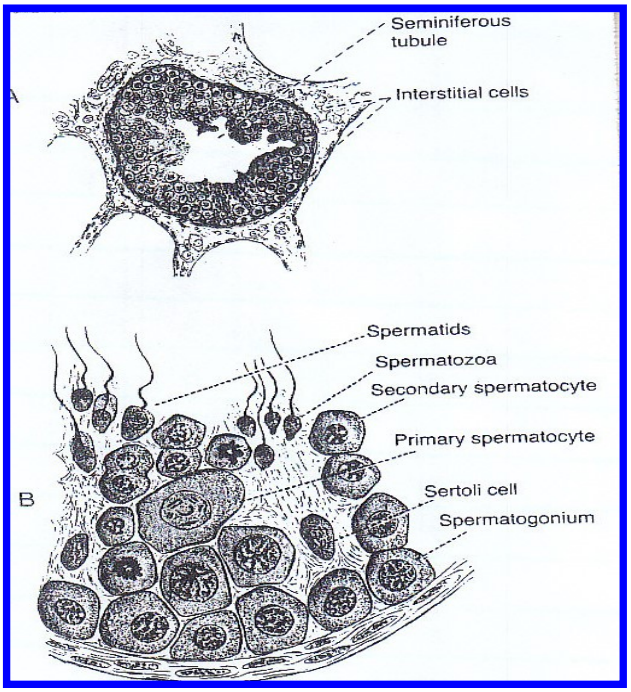


Fig. (11) the process of spermatogenesis

Factors affecting the process of spermatogenesis:-

A-Hormonal factors:-They are hormones which are stimulants for sperm production; they are:

a) LH: Leutinizing hormone which stimulates the interstitial cells of Leydig to secrete the testosterone hormone.
b) Testosterone hormone; secreted from the interstitial cells of Leydig to stimulate the meiotic division of the 1ry spermatocytes into 2ry spermatocytes.
c) FSH: Follicle stimulating Hormone which stimulates the Sertoli cells to mature the spermatids into mature sperms; the process of spermiogenesis.
d) Oestrogen; formed by aromatization of some of the male androgen to complete the process of spermatogenesis.
e) Other nonspecific hormones as GH, thyroxine and ACTH; they are metabolic stimulants.

B-Non hormonal factors: they include the effect of temperature, diet and toxic agents.

1-The effect of temperature:-

-Spermatogenesis occurs at a lower temperature of 34°C.

-This low temperature is guaranteed by the testicular thermostat which is composed of:-

a- Thin skin allowing the continuous loss of excess heat.

b- There is no subcutaneous fat in the scrotum, so there is no heat retention.

c-The scrotal skin is surrounded all around by air allowing continuous heat loss.

d-The Dartos muscle reflex:-
In hot weather, it is relaxed so the testicles are suspended downwards, allowing more heat loss.
In cold weather, it is contracted lifting the testicles upwards towards the scrotum, causing some heat retention.
e- The counter-current exchange mechanism in the vascular system of the testicles.
-Hot or cold showers will inhibit the process of spermatogenesis.

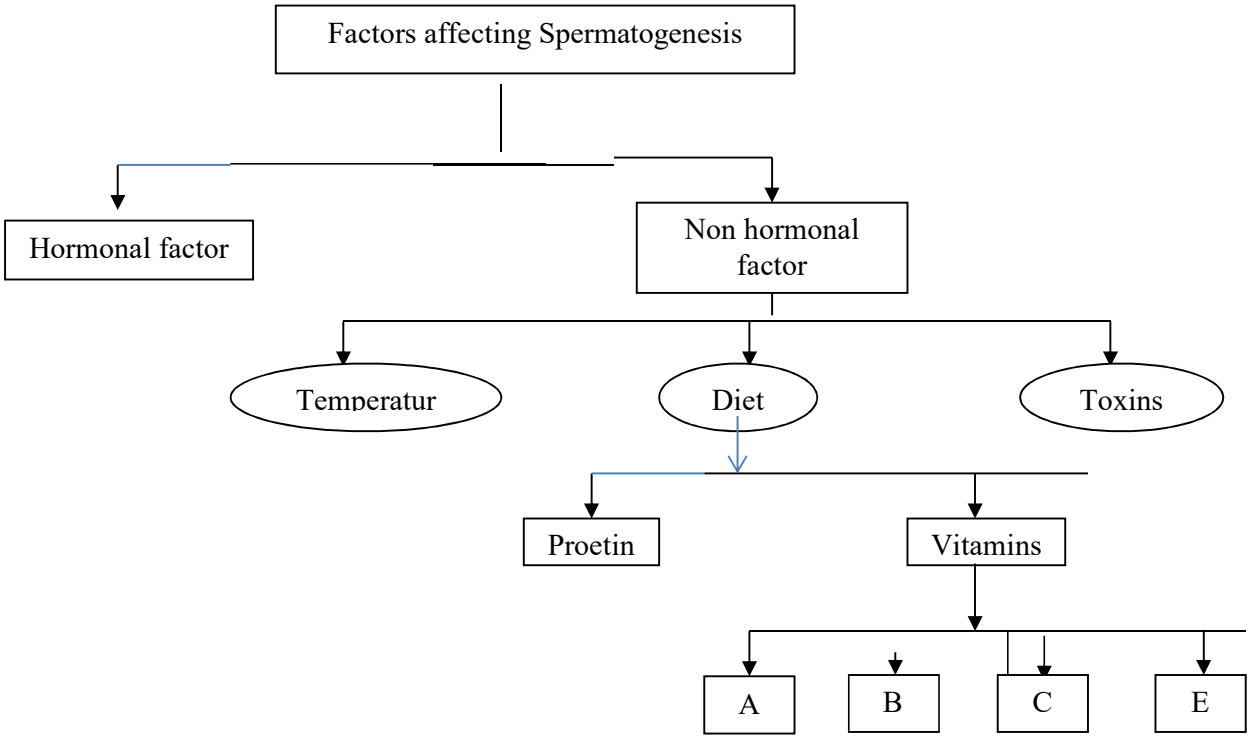
2-The effect of diet:-

Diet should contain the following nutritive elements;
a- Proteins of high biological value; containing the essential amino acids.
b- Vitamins:

I. Vitamin A which is essential for the integrity of the germinal epithelium.
II. Vitamin B complex which is needed for the cell and nucleic acid division.
III. Vitamin C which is needed as an antioxidant scavenging free radicals resulting from mitotic and meiotic divisions.
IV. Vitamin E which is proved to be an antisterility factor in rats.

3-The effect of toxins and irradiation:-

-Some drugs and toxins can pass into the testicular epithelium damaging it.
-X rays can also damage the testicular tubules.



The blood testis barrier:-

-It is a histological barrier that separates the testicular environment from the blood.

-It is formed of the tight junctions between the Sertoli cells.

-Functions of the blood testis barrier:

1. Prevention of the access of foreign toxins to the testicles.
2. Prevention of access of the antigenic sperm products into the general circulation.
3. Maintain the composition of the testicular environment at a constant condition.
4. Keep the osmotic gradient of the testicular fluid in favour of continuous supply of nutrients into the testicles.

The interstitial cells of Leydig:-

-They are present in the stroma surrounding the testicular seminiferous tubules.

-They secrete testosterone under the stimulant effect of the LH.

Testosterone hormone

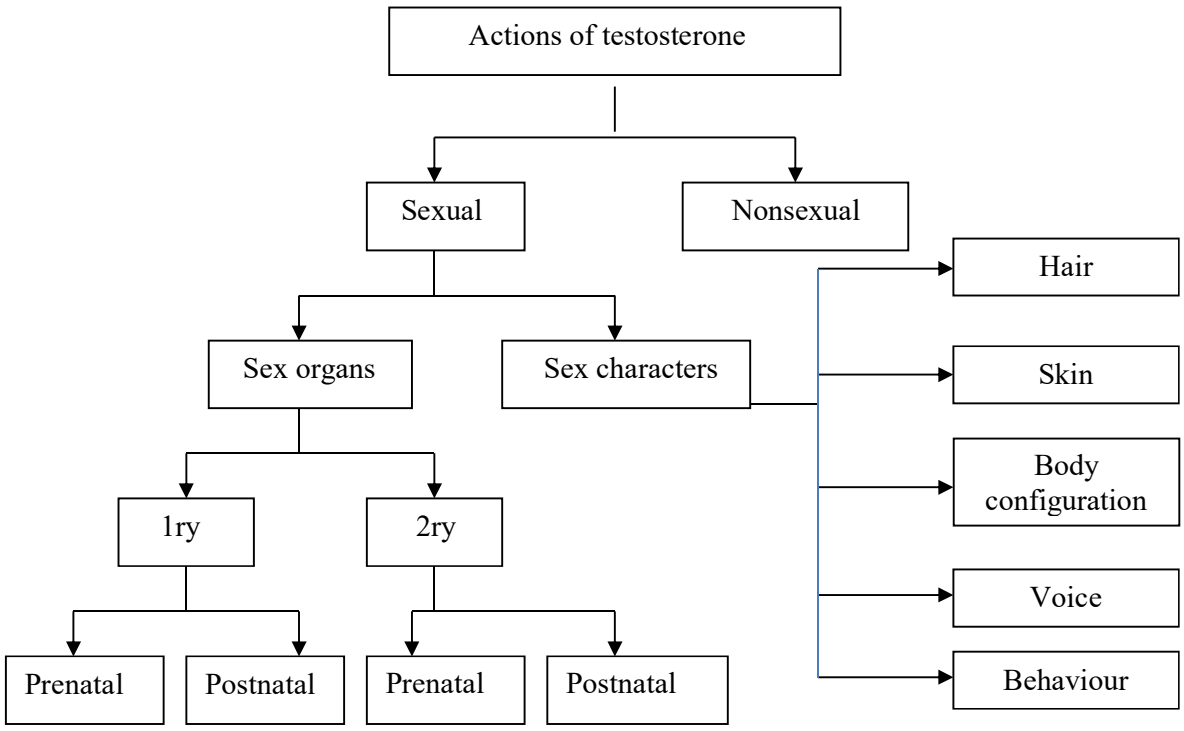
(I)Metabolism:-

a) Chemistry:-Steroid hormone.
b) Secretory cell:-The interstitial cell of leydig.
c) Carrier protein:- 65% is bound to gonadal globulin.
33% is bound to albumin.
2% remains free.
d) Catabolism: Reduced into dihydrotestosterone which is more active, then fixed into the male genitalia.

(II)Actions:-

a-Mechanism of action:-induction of transcription and translation.

b-Actions:-



A) Nonsexual actions:-

1- General metabolic stimulant.

2- Stimulant of eryhropoeisis.

3-Protein anabolic, increasing the bulk of muscles and the density of bones.

B) Sexual actions:-

1-Sex organs:-

-It is responsible for the testicular descent into the scrotum in the last trimester of the intrauterine life.

-At puberty it is responsible for the stimulation of spermatogenesis.

-It is responsible for the formation of the male 2ry sex organs and inhibition of the formation of the 2ry female sex organs.

2-Sexual characters:-

a- Hair:-

-It is responsible for the masculine hair distribution in the face, chest and the pubis.

In the pubis the hair takes a triangular shape with the apex upwards reaching the umbilicus.

-It is responsible for temporal recession of hair on both sides of the skull, but it is not responsible for baldness.

b- Skin:-it becomes thick, resistant with excess sebaceous secretion.

c- Body configuration:-

-Muscles are bulky; bones are more dense, larger and thicker.

-It causes widening of shoulders and narrowing of the pelvis.

d-The voice is harsh due to hypertrophy of the vocal cords.

e-The behaviour is more aggressive.

(III)Control of the hormone secretion:-

-Testosterone hormone ids under the control of L H

-LH is a glycoprotein that is secreted from the leutotrophes of the ant.pit.

-LH is under the control of the following:-

1. The hypothalamus which secretes a gonadotrophin releasing factor which stimulates secretion of the LH.
2. Feedback control:- Rise of the LH or the testosterone hormone results in a feedback inhibition of the hypothalamic gonadotrophin releasing factor.

The female reproductive system

-The 1ry sex organ in the female genital system is the ovaries which are responsible for the production of the oocytes

-The 2ry sex organs include all other organs which share in the sexual function; as the uterus, the fallopian tubes, cervix and the vagina.

-Normally, there are regular cyclic changes that take place in the female genital system, every month; this is the female sexual cycle.

-The female sexual cycle include the following:-

A. The ovarian cycle.
B. The uterine cycle.
C. The cervical cycle.
D. The vaginal cycle.
E. The mammary cycle.

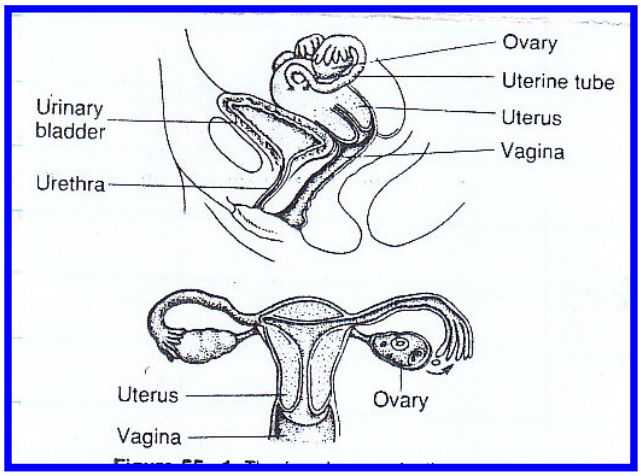


Fig. (12) the female genital system

The ovarian cycle

-These are changes that occur in the ovaries every 28 days.
-They are responsible for the production of the female gametocytes which are called the oocytes.
-It consists of 3 phases; the follicular, the ovulation and the luteal phases.

A-The follicular phase:-

1-Th ant.pit.gland, by the age of puberty, secretes large amounts of FSH (follicle stimulating hormone) which acts upon 6-12 ovarian follicles to stimulate their growth and development.
2-Under the effect of the FSH, the following changes occur in these follicles:

a. Proliferation of the granulosa cell layer.
b. Formation of a protective double layer around the follicle; composed of an internal cellular layer and external fibrous coating layer. The internal cellular layer is called theca interna while the external one is called theca externa.
   The theca interna layer is similar to the granulosa cell layer and secretes steroid hormones.
   The theca externa is a highly vascular CT.
c. The granulosa cell layer secretes a fluid rich in oestrogen, the fluid collects in a number of cavities, so the follicle is called the vesicular.
d. The cavities coalesce together forming one single large cavity, pushing the cellular mass containing the ovum, to the opposite side of the follicle, which is now called the Graffian follicle.

3-The LH supports the FSH induced changes.

Follicular atresia:-

-It is one protective mechanism to ensure the selection of the healthiest ovum for the process of fertilization.

-The healthiest follicle secretes the largest amount of oestrogen, it is the fastest in growth and development and it synthesizes the largest number of FSH receptors on its surface. Thus, it attracts most of the hormone secreted by the ant.pit .depriving all other follicles from it. It is this follicle which is rapidly growing while all others become atrophic.
-When it reaches its final stage of growth and development, its oestrogen starts to induce a –ve feedback effect on the FSH secreted from the ant. pit, decreasing the FSH secretion with more and more atrophy of all other follicles.

B-The stage of ovulation:-

-It occurs at the 14th day of regular cycle.
-On the 12th day of the cycle, there is a sharp increase of the LH secretion (6-10 folds); an LH surge; which finalizes the growth and development of the Graffian follicle to be ready for fertilization.
There is also a double folded increase of the FSH secretion to complete the whole process of maturation.

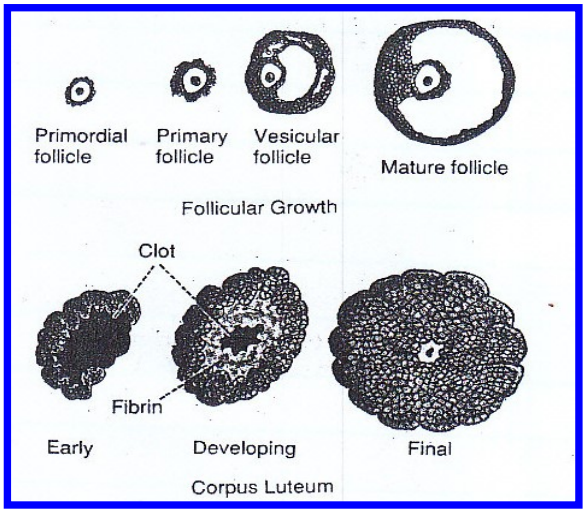
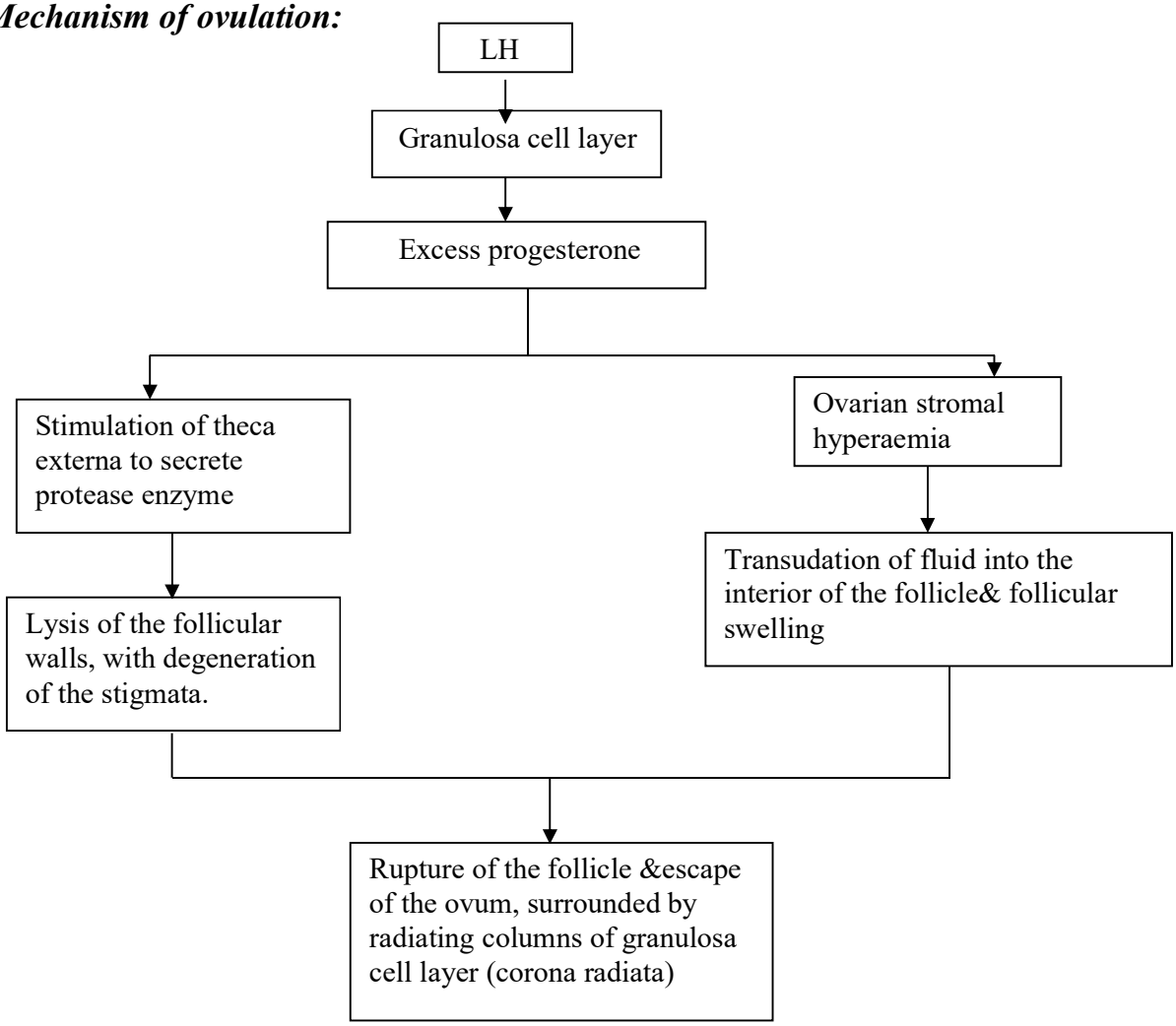


Fig.(13) the follicular phase

-Mechanism of ovulation:



C-The luteal phase:-

-The cellular mass remaining in the ovary after ovulation is called the corpus luteum.

-The corpus luteum consists of the granulosa cells which are now filled with lipoid material giving them a yellow coloration, hence the name luteum.

-The corpus luteum secretes the following hormones:-

1- Large amounts of progesterone and estrogen.

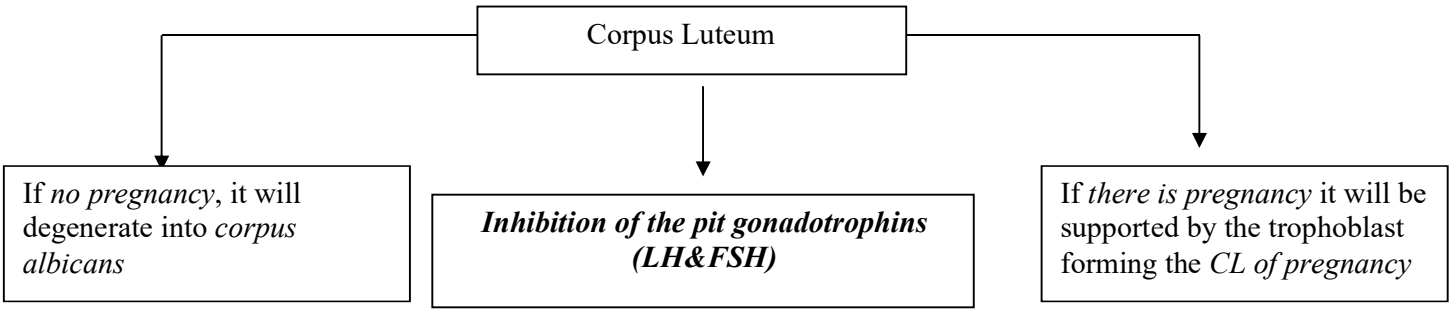
2-Moderate amounts of the hormone called inhibin.

3-Relaxin and little androgen

-Fate of the corpus luteum:-

1-Corpus luteum continue to secrete progesterone and oestrogen which support the uterine endometrium and at the same time inhibits the ant. pit. secretions of gonadotrophins which supports the corpus luteum.

2-If pregnancy occurs; the trophoblastic cells in the wall of the uterus replace the ant.pit. and start to secrete gonadotrophins, which maintain the structure and function of the corpus luteum. In this case it continues to function till the end of the 3rd month of pregnancy when the placenta is formed. This is called the corpus luteum of pregnancy.
3-If pregnancy did not occur; there will be neither the trophoblastic tissue in the wall of the uterus, nor the pit. Gonadotrophins, so the corpus luteum will degenerate into the corpus albicans (the fibrous white body).



The uterine cycle

-These are cyclic changes that occur regularly in a cyclic manner every 28 days.
-The 1st menstrual cycle is called menarche; it is a landmark of puberty.

-Functional histology of the endometrium:

The uterine endometrium consists of 2 layers; the superficial one which is supplied by the spiral arteries and is shed during menses, it is called stratum functionale. The 2nd layer is the deep layer which is supplied by the basal arteries and is not shed during menses.

A-The destructive, the menstrual or the bleeding phase:-

1-It coincides with the degeneration of the corpus luteum. It starts on the 1st day of the cycle.
2-On sudden degeneration of the CL there will be sudden drop of the oestrogen and progesterone levels leading to sudden vasoconstriction of the spiral arteries supplying the superficial layer. There will be ischemia and necrosis of this layer; cells release their contents of metabolites which dilate these arteries leading to blood gushing.
3-This phase may last up to 6 days. The volume of blood may reach up to 30 ml; it is non-clotted due to the presence of the fibrinolysin.

B-The proliferative, the follicular or the estrogenic phase:-

-It coincides with the follicular phase of the ovarian cycle.
-Oestrogen secreted from the ovarian follicles induces proliferative changes in the endometrium which include the following:-

1. Increase of the number of the stromal cells.
2. Growth of the glands and the blood vessels into the endometrium.

3. Endometrial thickness may reach up to 8 mm.

-It starts on the 5th day of the cycle

C-The secretory, luteal or the progestational phase:-

-It coincides with the luteal phase of the ovarian cycle.

-It starts on the 14th day of the cycle.

-The luteal progesterone induces the following changes:-

1. The endometrial glands much markedly increase in number and size and become loaded with secretions.
2. The endometrium becomes very highly vascular, its thickness reaches up to 16 mm

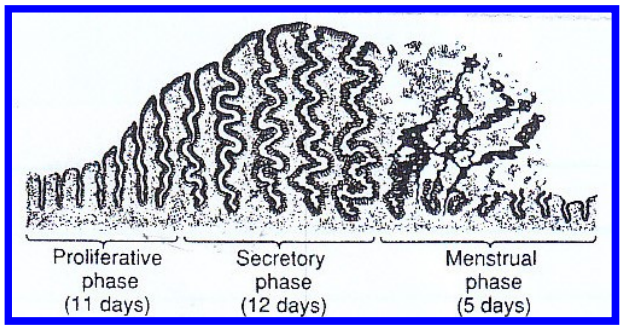


Fig. (14) the menstrual cycle

3. -If pregnancy occurs then the trophoblastic cells secrete gonadotrophin (LH&FSH) which support the CL till the end of the 3rd month of pregnancy where the placenta is formed.

-If pregnancy did not occur then the CL will degenerate (due to drop of the pit. gonadotrophins), leading to a sudden drop of the oestrogen and progesterone levels→ vasoconstriction of the spiral arteries with shedding of the superficial layer of the endometrium.

The cervical cycle

-These are cyclic changes in the cervix that aim to prepare the female genital system to the possibility of pregnancy.

A-The follicular or the estrogenic phase:-

Follicular oestrogen makes the cervical mucous very thin and highly alkaline; characters that highly suits the sperms and facilitate the process of fertilization.

B-The luteal or the progestational phase:-

The luteal progesterone makes the cervical mucous very thick and highly acidic; characters that don't suit the sperms at all and the process of fertilization very difficult. This is to prevent a 2nd fertilization of the same ovum.

The vaginal cycle

A-The follicular or the estrogenic phase:-

Oestrogen induces keratinization of the vaginal epithelium.

B- The luteal or the progestational phase:-

Progesterone induces epithelization, leukocytic infiltration.

The mammary cycle

A-The follicular or the estrogenic phase:-

There is proliferation of the stroma, and only the ductal NOT THE ACINAR system of the glands.

B- The luteal or the progestational phase:-

There is proliferation of the acinar system with maximum degree of vascularization.

Hormonal control of the female sexual cycle

1-In the ant. pit.gland, at puberty, there is release from a feedback inhibitory mechanism, hence it starts to secrete large amounts of its gonadotrophic hormones; FSH&LH.

2-In the ovary; **FSH** acts on the ovaries to stimulate growth and formation of the mature graffian follicle. This follicle secretes large amounts of estrogen which induces e following effects:-

1. On the ant.pit→inhibition of the FSH secretion.
2. On the uterus:-→the follicular or the proliferative changes of the uterine cycle.
3. On the cervix:-→thin alkaline mucous secretion.
4. On the vagina:-→cornification of the vaginal epithelium.
5. On the breast:-→proliferation and vascularization of the stroma.

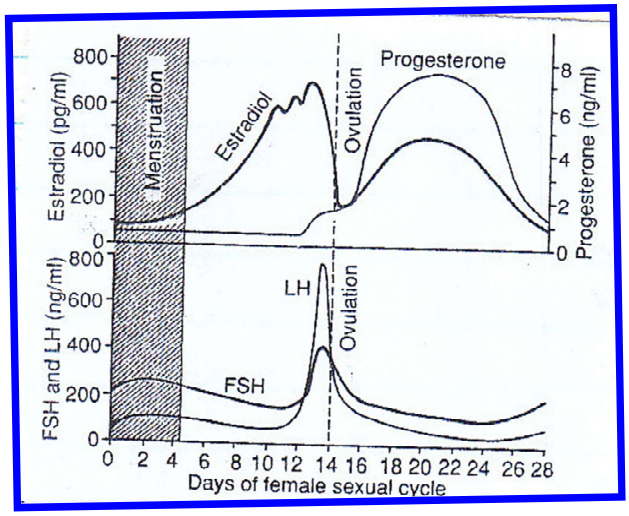
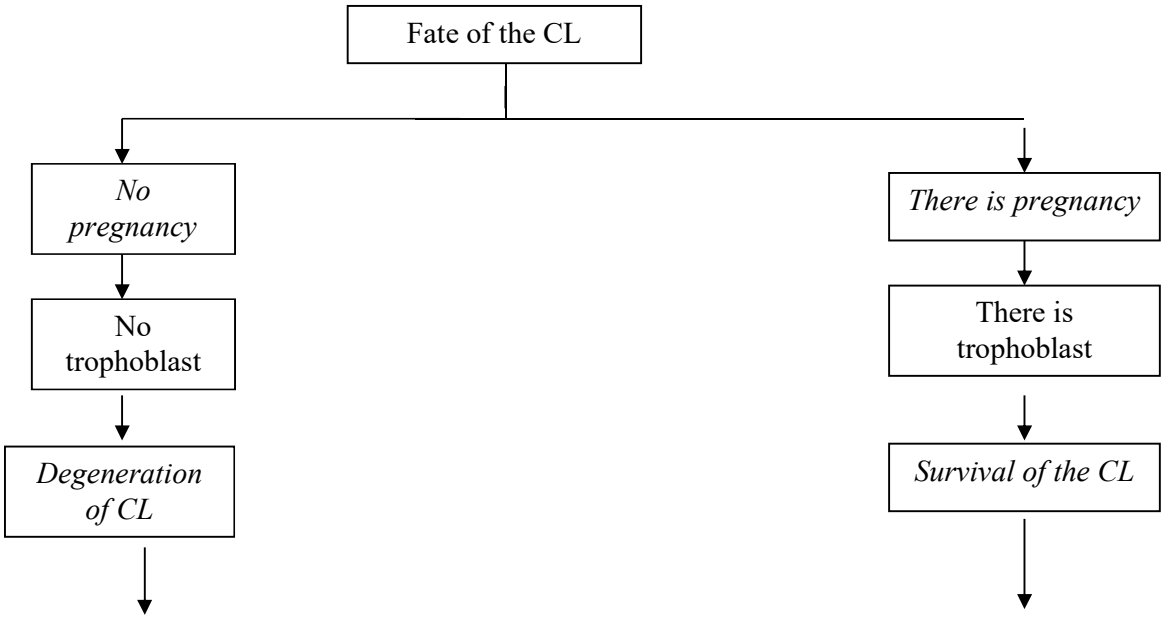


Fig. (15) The hormonal profile during the female cycle

3- In the ovary; the **LH** secreted form the ant.pit. induces ovulation; leaving the corpus luteum inside the ovary. The corpus luteum secretes large amounts of progesterone which induces the following changes:-

1. On the ant.pit→ inhibition of the LH secretion.
2. On the uterus:-→ the luteal or the secretory changes of the uterine cycle.
3. On the cervix:-→ thick acidic mucous secretion.
4. On the vagina:-→ epithelization and leukocytic infiltration of the vagina.
5. On the breast:-→ proliferation of the acini of the breast.

4-The end of the story depends on the destiny of the corpus luteum; whether it will degenerate in case of *no pregnancy* or it will survive in case of *pregnancy*.



The Ant.Pit.	1-Release of the ant.pit. from luteal inhibition. 2-Start of release of FSH and a new cycle begins.	-Continued inhibition of the ant. pit., no gonadotrpophin hormone secretion; no further cyclic phenomenon.
The Uterus	1-Drop of estrogen and progesterone level. 2-Destructive or bleeding phase takes place, followed by a new follicular then secretory phase (NEW CYCLE).	-Continued endometrial growth under the effect of luteal hormones; so there will be no bleeding→ missed menstrual period=PREGNANCY.
The Cervix	-As the new cycle restarts; there will be cyclic cervical changes; follicular then secretory.	-Maintained progestational cervical changes.
The Vagina	-As the new cycle restarts; there will be cyclic vaginal changes; follicular then secretory.	-Maintained progestational vaginal changes.
The breast	-As the new cycle restarts; there will be cyclic mammary changes; follicular then secretory.	-Maintained and progressive mammary changes.

The anovulatory cycles:-

-These are short cycles that are not associated with ovulation due to the following causes:-

1- Decreased secretion of LH hormone.

2- Down regulation of LH receptors on the surface of the mature Graffian follicle.

-It occurs in the early cycles following puberty and the late ones preceding the menopause.

Sure evidence of ovulation:-

1. Detection of pregnandiol which is the metabolic end product of progesterone in urine.
2. The basal body temperature chart.
3. Endometrial biopsy showing the secretory endometrium.
4. Cervical biopsy showing hick acid mucous with –ve Spinbarkeit test.
5. Vaginal smear showing epithelial proliferation and leukocytic infiltration.
6. Ultrasonic identification of the CL.
7. Laparoscopic examination of the ovaries and identification of the corpora lutea.

-Mechanism of menstruation in the anovulatory cycles:-

1-The mature Graffian follicle continue to secrete oestrogen which supports the uterine endometrial proliferation and vascularization.

2-The very high levels of oestrogen starts to produce a –ve feedback effect upon the ant.pit. gland leading to sudden drop of FSH secretion which is the main stimulus for the graffian follicle to continue growth and oestrogen secretion.

3-The sudden drop of FSH lead to another drop of oestrogen level with vasoconstriction of the endometrial spiral arteries leading to menstruation.

The endocrine function of the ovaries; the female hormones

The point of view	**Oestrogen**	**Progesterone**
[I]Metabolism:- 1-Source:-	-Ovarian follicle. -Adrenal cortex. -Placenta.	-Corpus luteum.
2-Chemistry:- 3-Carrier protein:-	-Steroid hormone. -Albumin and globulins.	
4-Catabolism	-In the liver, is conjugated into glucoronate and sulfate then excreted in urine and stool	-In the liver is converted into pregnandiol, and then excreted in urine.
[II]Actions:- -Mechanism of action:-	-Induction of transcription and translation.	
-Actions:- *A)Sexual organs:-* 1-Uterus and the	-Proliferative changes of	-Secretory changes of the glandular

fallopian tubes.	the glandular and vascular tissue. -Ecbolic for the uterus.	tissue and vascularization. -Tocolytic for the uterus.
2-Cervix:-	-Thin alkaline mucous secretion.	-Thick acidic mucous secretion.
3-Vagina:-	-Hypertrophy and cornification.	-Epithelization and WBCs infiltration
4-Breast:-	-Proliferation of the stroma, ducts and fatty tissue.	-Alveolar proliferation.
B)Sexual characters:-	Feminizing up on hair, skin, body configuration, voice and behaviour.	-No effects on the sexual characters.
C)Non sexual actions:	1-Protein anabolic.	1-Mild protein catabolic.
	2-Salt and water retention.	2-Salt and water retention, however in excess level it competes with the endogenous aldosterone leading to water loss.
	3-Maturation of ossification centres.	3-Thermogenesis through either stimulation of the heat gain centre or a permissive action on thyroid hormones.
	4-Vasodilator and hypocholesterolaemic.	4- Vasodilator and hypocholesterolaemic.
[C]Control:- 1-The hypothalamus:-	-Secretes the FSH releasing factor.	-Secrets the LH releasing factor.
2-The ant.pit.	-Secretes the FSH which stimulates the oestrogen secretion.	-Secretes the LH which stimulates progesterone secretion from the corpus luteum.
3-The feedback mechanism	a-Ordinary –ve feedback. b-A +ve feedback mechanism occurs just prior to ovulation where the	
	Increased oestrogen stimulates FSH secretion to complete the growth of the follicle.	Increased progesterone stimulates LH secretion (LH surge) to induce ovulation.

Pregnancy and lactation

Fertilization

1-The process of fertilization takes place in the mid portion of the fallopian tubes.

2-The ovum remains viable for about 24 hours while the sperm can remain viable for a much longer period up to 72 hours.

3-The sperm should pass through a process of capacitation that takes place in the female genital tract before getting up into the uterus and the fallopian tubes; it include the following changes :-

a) Wash out of different metabolic waste products that are inhibitory to the sperm. This wash out is carried out by the uterine and fallopian tube fluids.
b) Removal of the cholesterol cover that is present over the acrosome ; the acrosomal cap.
c) Thinning out of the membrane of the head of the sperm, so that it becomes more permeable for Ca ions which are essential for the whiplash motion of the sperm and the release of the acrosomal enzymes which are proteolytic for the corona radiata.

4-Steps of fertilization:-

a) The sperms secrete ample amounts of proteolytic enzymes as hyaluronidase that erodes the layer of corona radiata .
b) Many sperms attack while only one succeeds to pass through the corona radiate and the zona pellucida.
c) Once one sperm succeeded to penetrate, a number of changes occur to prevent another penetration by another sperm; otherwise the ovum will be fertilized twice, will die off.
d) Only the head of the sperm passes into the interior of the ovum, transformed to the male pro-nucleus which will unite with the female pro-nucleus forming the zygote.
e) The zygote takes about 3-4 days to reach the uterine cavity, and then wonder all around inside it for another 3-4 days. During this trip, it continues to multiply, forming the morula and finally the blastocyst.

5-Implantation:-

a) The blastocyst is implanted in the dorsal wall of the uterus; which is the normal site for implantation. Its outer trophoblastic cells secrete proteolytic enzymes that convert the endometrium in the area of implantation into a stromal area called the decidua.
b) The blasto-cyst is surrounded by an inner layer of cytotrophoblast and an outer layer of syncytiotrophoblast. The embryo starts to grow on one side while the decidua on the opposite one leading to the formation of the conceptus; the pregnancy sac.

-Functions of the HCG:-

1- Stimulation of the corpus luteum to secrete large amounts of progesterone and oestrogen which are responsible for continuous growth of the endometrium.

2- Stimulation of the testicular descent from the abdominal cavity into the scrotum in male embryos.

Function of the placenta

The placenta stands for nearly all body systems of the embryo, it stands for the lungs, the kidneys, the liver, the immune system and the endocrine glands.

1-Respiratory function of the placenta:-

-The foetal deoxygenated blood enters the placenta inside the umbilical arteries.

-The pO2 of the foetal venous blood is about 15 mmHg while the maternal blood pO2 is 50 mmHg, so oxygen diffuses from the maternal side of the placenta to its foetal side.

Fig. (7) the placenta

-The pCO2 of the foetal blood is about 2-3 mmHg higher than that of the maternal blood so that CO2 diffuses from the foetal side to the maternal side of the placenta.

-The oxygenated blood leaves the placenta inside the umbilical veins.

2-Metabolic functions of the placenta:-

a. CHO metabolism:-
   - Storage of glycogen.
   - Glycogenolysis.
   - Transport og glucose by simple diffusion in early pregnancy hen by facilitated diffusion in late pregnancy.

b. Protein metabolism:-
   - Active uptake of amino acids.
   - Albumin passes more easily tan globulin.

c. Fat metabolism:-
   - Passive diffusion of fatty acids from the maternal side to the foetal side.

d. Minerals and vitamins:-
   - Na, K and Mg pass by simple diffusion from the maternal side to the foetal side, but Ca is actively uptaken by the foetus.

3-Excretory function of the placenta:-

Waste products of the foetal side pass to the maternal side of the placenta.

4-Immune functions of the placenta:-

a. It is impermeable to toxins.
b. It is impermeable against bacteria..

c. It is permeable to antitoxins (immunoglobulin).The anti- Rh antibody can cross the placenta but the antibodies of the ABO system cannot as they are of the Ig M group.
d. It is impermeable to viruses EXCEPT the following:-
    - The Pox group of viruses; small and chicken pox.
    - The Measles group of viruses; german and classic measles.
    - The Herpes group; simplex and zoster.
    - The Rabies group.
e. Most drugs can cross the placenta.

5-Endocrine functions of the placenta:-

The placenta secretes HCG, human chorionic somatomamotrophin, oestrogen, progesterone and relaxin.

The endocrine function of the placenta

1-Human chorionic gonadotrophin (HCG):-

-It is secreted as a partial replacement of the pit. gonadotrphins which are suppressed by the placental oestrogen and progesterone.
-It stimulates the descent of the testicles from the abdominal cavity to the scrotal; one during the last trimester of pregnancy.

2-Human chorionic somatomamotrophin (HCS):-

-It is also called as human placental lactogen.
-It is started to be secreted on the 5^{th} week of pregnancy.
-It stimulates the mammary growth and development in the moher.
-It has weak growth hormone like actions in the mother as it has:-

- Protein anabolic action.
- Hyper-glycaemic action.
- Hyperfattyacidaemic action

3-Estrogen and progesterone:-

- During pregnancy Estrogen secretion is increased by about 30 times, while progesterone by 10 times.
-They are secreted from the trophoblastic layer of the placenta.
-They exert the same ordinary functions on the female genital system.
-Estrogen stimulates the growth and development of the foetus.
-Progesterone stimulates decidual proliferation for the nourishment of the foetus.

4-Relaxin hormone:-

-It is secreted from the placentas to relax the symphysis pubis, the uterus and the cervicovainal passages.

5-Other hormones:-

It also secretes TSH and endorphins.

Labour
Parturition

It is the process of delivery of the baby, by the end of the pregnancy period.

The normal duration of pregnancy is 270 days from the day of fertilization, or 284 days from the 1st day of the last menstrual period.

Mechanism of labour:-

-By the end of pregnancy, certain hormonal and or mechanical changes occur to induce uterine contractions with expulsion of the foetus and the contents of the pregnancy sac.

A) The hormonal changes:-

1-The estrogen/progesterone ratio:

During the 3rd trimester it starts to increase stimulating uterine contraction.

2-The oxytocin theory:

During the 3rd trimester the posterior pituitary secretes large amounts of oxytocin which in turn stimulates uterine contractions.

Also the response of the uterine muscle to the hormone is increased resulting in stronger uterine contractions, by the end of the normal pregnancy.

3-The foetal hormone theory:-

By the end of the normal pregnancy the foetal endocrine glands secrete large amounts of hormones which are stimulants for the uterine contractions; where te pit. gland secrete excess amounts of oxytocin and the adrenal cortex large amounts of cortisol.

Also the foetal membranes secrete large amounts of prostaglandins which are potent ecbolics for the uterine muscle.

B) The mechanical theory:-

-By the end of normal pregnancy the pregnancy sac reaches an ample size which can stimulate a number of mechanisms leading to uterine contractions as follows:-

a- Stretch of the uterine wall:-the ample-sized foetus stretches the wall of the uterus resulting in uterine contractions.

b- Stretch of the cervix:-by the end of pregnancy the head reaches full size resulting in cervical stretch which in turn stimulates the uterine contractions.

C) The integrated mechanohormonal theory:-

1-By the end of pregnancy, the pregnancy sac reaches an ample size which stimulates uterine contractions either through a direct effect on the wall of the uterus or through a reflex action originating through the cervical stretch.

2-With uterine contractions the head descends downwards resulting in more cervical stretch, with more uterine contractions pushing the head more downwards.
3-The cervical stretch by the head results in a reflex stimulation of oxytocin secretion which in turn augments uterine contractions, which push the head more downwards leading to more cervical stretch with more secretion of oxytocin and more forceful uterine contractions until the head, is delivered.
4-During the 3rd trimester the uterus is under many contracting forces; higher estrogen and oxytocin level with increased sensitivity to both of them.

Lactation

-For lactation to occur, it must be preceded by the following:-

1-Growth of the mammary glands:-

A- At puberty through the effect of oestrogen, progesterone and GH.
b- Gestational growth at the time of pregnancy; by oestrogen, progesterone and HCS.

2-Milk secretion:-

-This is the function of prolactin which stimulates milk synthesis and secretion.

3-Milk let down reflex.

Touching the nipple results in stimulation of the lateral spinothalamic tract which in turn stimulates the hypothalamus. The hypothalamus stimulates the post.pit. gland to secrete more oxytocin which in turn stimulates the myoepithelium cells around the mammary acini to contract evacuating milk.

Puberty

-It is the timing at which sexual maturation occurs.
-It occurs at the age of 12 in girls and 14 in boys.

-Mechanisms of puberty:-

Several theories have been introduced to explain the occurrence of puberty, they include the pituitary feedback theory, the hypothalamic neurotransmitter theory and the opioid theory.

1-The pituitary feedback theory:-

a-During the childhood period the pituitary gland is said to be supersensitive to the very low levels of sex hormones secreted by the adrenal cortex, so that it secretes very low levels of FSH and LH hormones. Thus, the gonads are not active during this period.

b-By the time of puberty and for unknown reason this super sensitivity fades away, the pituitary gland recovers from this inhibition of the adrenal sex hormones and start to secrete increasingly large amounts of FSH and LH.

c-Under the stimulating effect of the FSH and LH, the ovaries and the testicles start to grow and upgrade their function, this is what is called puberty.

2-The hypothalamic neurotransmitter theory:-

-Normally there is a group of transmitters released from the hypothalamus that stimulate the secretion of FSH and LH from the ant.pit.gland. These transmitters include dopamine and nor-epinephrine.

-By the time of puberty there is marked increase of the release of these transmitters from the hypothalamus, which in turn stimulates the secretion of larger amounts of FSH and LH.

-Under the effects of these gonadotrophic hormones, the gonads start to upgrade their function.

Stages of puberty:-

1-Telarche:-Development of the breast.

2-Pubarche:-development of the axillary's and pubic hair.

3-Menarche:-the 1st menstruation.

4-Adrenarche:-increase of the level of adrenal androgen.

Abnormalities of puberty:-

1- Precocious puberty which may be false or true.

2-Delyed puberty, where there is failure of ovulation till the age of 17 and for boys it is failure of spermatogenesis till the age of 20 years.

3-Absent puberty, where there is no puberty at all.

Menopause

-It is the timing at which there is cessation of the gonadal functions.

-The average age is 50-55 years.

-Cause:-It is depletion of the primordial follicles from the ovaries with secretion of relatively higher amounts of androgen from the ovarian and the adrenal interstitium.

-Manifestations:-

1-Estrogen deficiency causes osteoporotic, vasomotor and pelvic atrophic changes.

2- Psychic changes.

Contraception

1-Physiological or the rhythm method:-by abundance of sexual intercourse 4 days before and 3 days after the expected date of ovulation.

2-Contraceptive pills:-they contain oestrogen and progesterone which are taken daily till the 21st day of the cycle inhibiting the secretion of the pit. FSH and LH.

3-The intrauterine devices (IUDs) they prevent he process of implantation

Physiology of Gastrointestinal system

General considerations

-The digestive and absorptive functions of the gastrointestinal system depend on a variety of mechanisms that soften food, propels it down and mix it with different secretions of the gastrointestinal (GIT) system and this is achieved through a variety of secretomotor functions of different parts of the digestive system and its accessories such as the liver and the pancreas.

-Functional anatomy:-

The organization of the different layers of the wall of the GIT is illustrated in the following figure;

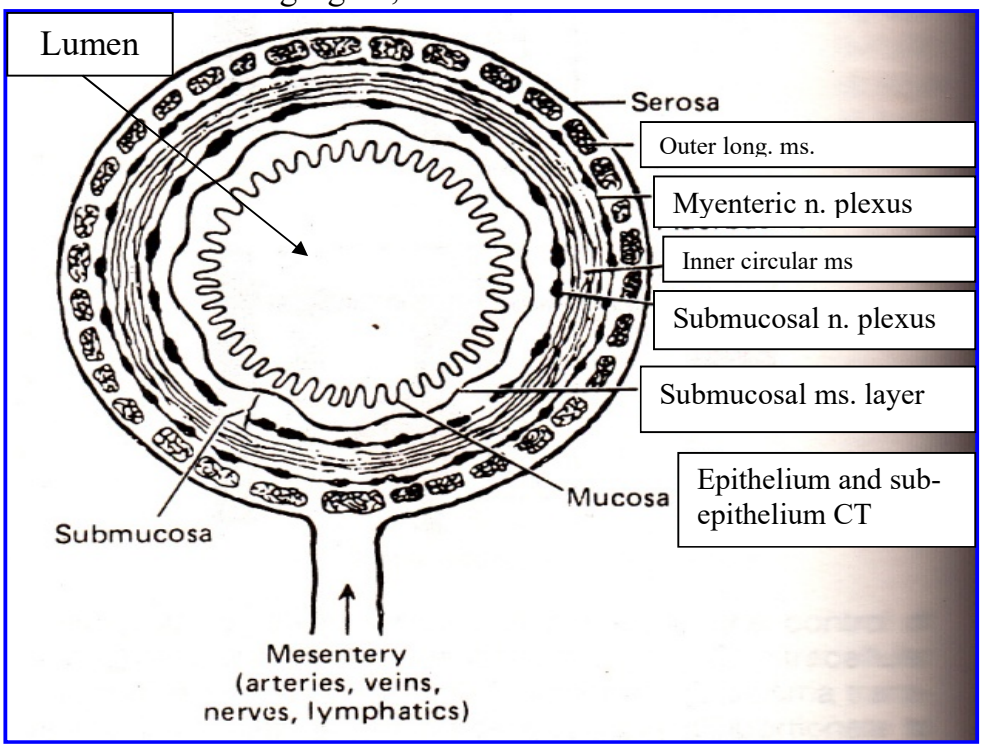


Fig (15) the wall of the gastrointestinal tract

-The enteric nervous system:-

- There is a couple of nerve plexuses in the wall of the gastrointestinal (GIT) system that regulate its major 2 functions; secretions and motility.
- The Meissner's or the submucosal nerve plexus which regulates the activity and function of submucosal glands; the secretory function.
- The Auerbackh's or the myenteric nerve plexus which is located in the muscle layer and is concerned with regulation of the motor activity of the muscle layer in the wall ; the motor function.

The salivary secretion

-A normal person secretes about 1.5 liters of saliva/day with a ph of about 7.

-The human salivary glands:-

There are 3 pairs of glands in the human being; the parotid (serous), the sub-mandibular (mixed) and the sub-maxillary (mucinous).

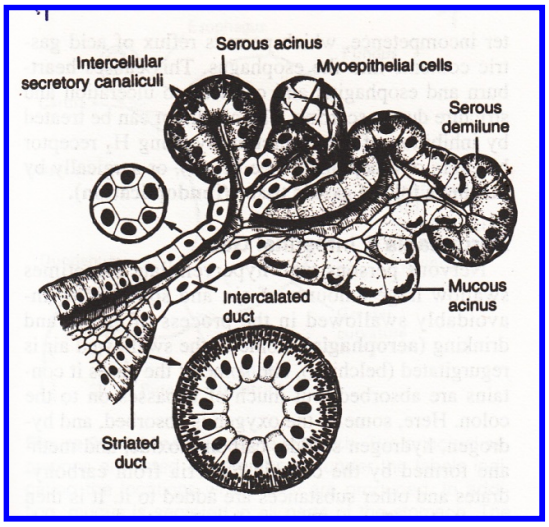


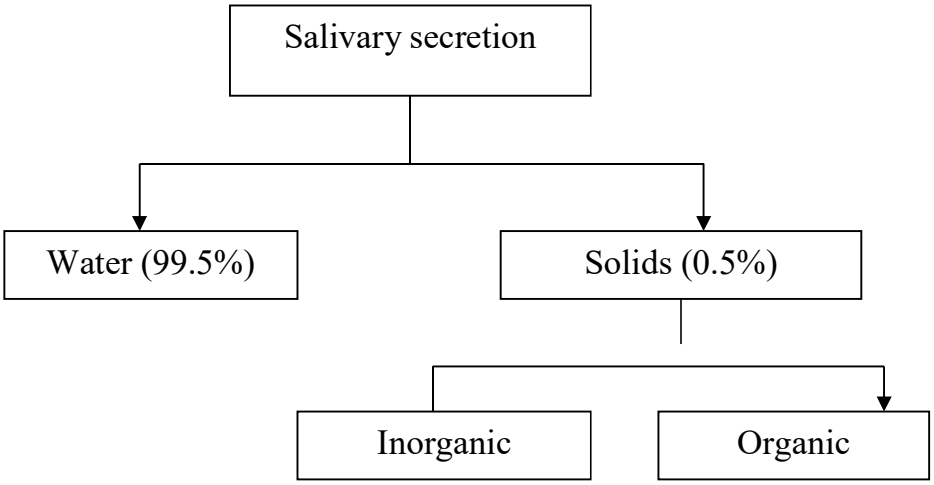
Fig (16) the salivary acini

-Composition of saliva:-

1- Water; representing about 99.5% of the salivary secretion.

2-Solids; representing 0.5%; which are subdivided into organic and inorganic:-

a) The organic components are mainly mucin, ptyalin, lysosomes and IgG.
b) The inorganic components are mainly Na, K, Cl& HCO3.



-Types of salivary secretion:-

a) <u>The 1ry salivary secretion:</u>
-This is the secretion of the salivary acini, it contains mucin and ptyalin and it is highly rich in Na, Cl&HCO3.
b) <u>The 2ry salivary secretion</u>:
-This is the secretion that comes out of the salivary ducts.
-Inside the ducts the 1ry secretion is modified so that Na, Cl& HCO3 are reabsorbed in exchange for the excretion of K. This occurs under the effect of aldosterone hormone.

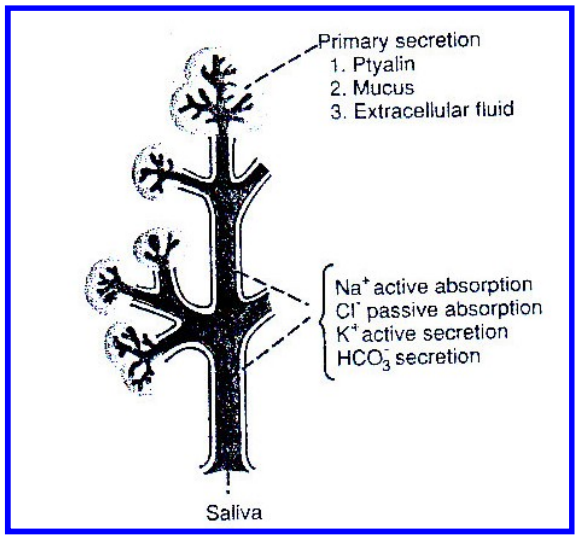


Fig (17) Types of salivary secretion

The mechanisms of salivary secretion:-
Salivary secretion is an active and not a passive filtration mechanism.

<u>The autonomic regulation of the salivary glands:-</u>

a) <u>The sympathetic supply</u>; which arises from the LHCs of the upper 2 thoracic segments, relay in the superior cervical sympathetic ganglion.

-Sympathetic stimulation produces vasoconstriction and a trophic type of secretion which is highly viscid, scanty with little water content.

b) <u>The para-sympathetic supply:-</u>

The chorda tympani nerve supplies the submandibular and the sublingual glands. It arises from the superior salivary nucleus in lower pons, pass through the facial nerve trunk to relay in the submandibular ganglion.

The lesser superficial petrosal nerve supplies the parotid gland, it arises from the inferior salivary nucleus, in the upper medulla pass through the glossopharyngeal nerve trunk and relays in the otic ganglion

- Parasympathetic stimulation produces vasodilation and a copious type of secretion which is watery, profuse& rich in ptyalin.

Point of view	Sympathetic stimulation	Parasympathetic stimulation
1-The blood supply	Vasoconstriction	Vasodilation
2-Type of secretion	Viscid	Watery
3-Water content	Less	Larger
4-Enzyme content	Little	Larger
5-Mucin content	Rich	Little
6-Type of secretion	False	True
7-Name of secretion	Trophic	Watery

-The nervous control of salivary secretion:-

Point of view	The unconditioned salivation	The conditioned salivation
1-Nature	Inborn reflex	Acquired reflex
2-The stimulus	Mechanical or chemical stimulation of the taste buds.	Seeing, hearing or even thinking of food.
3-Role of learning	No role at all	They play a major role
4-Role of the cortex	No role at all	It plays a major role.
5-The centre	The salivary nuclei and not the cerebral cortex	

-Functions of saliva:-

1. ***Articulation:***
   It facilitates speech through lubrication of the tongue and the buccal mucosa.
2. ***Buffering:***
   It maintains the ph of the mouth cavity constant by the buffers it contains; mucin, HCO3 and phosphates.
3. ***Cleaning:***
   It mechanically clears and cleans the mouth cavity.
4. ***Digestion:***
   It facilitates the digestion of CHO through its ptylin enzyme content.
5. ***Excretion:***
   It is a route for the excretion of many heavy metals as arsenic.
6. ***Facilitation of deglutition:***
   It lubricates the food bolus making it easier to be swollen.
7. ***Facilitation of taste sensation:***
   It dissolves the food materials.
8. ***H2O regulator:***
   It is decreased on dehydration
9. ***H2O solvent:***
   It is a route for administration of many drugs e.g. coronary vasodilators.

Mastication

-It is the grinding of large food particles into smaller ones.

-Functions of mastication:-

1-it is essential for digestion of food especially fibres.
2-It is essential for deglutition.
3-It augments salivary secretion.
4-It helps taste sensation.

Swallowing (Deglutition)

-It is the passage of food from the mouth to the stomach passing through the pharynx and the oesophagus.
-It starts voluntary by putting the food particles up on the tip of the tongue then continues reflexly.

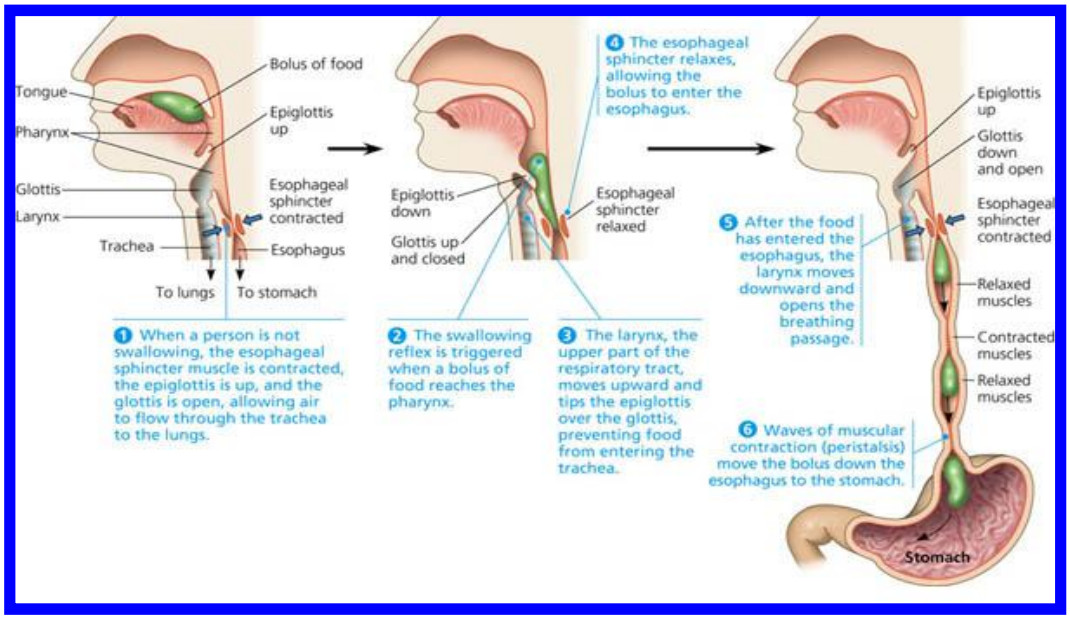


Fig (18) the act of swallowing

-It consists of 3 phases; the buccal, the oesophageal and the gastric phases.

A-The buccal phase:-

-It is a voluntary phase.
-It starts by placing the food bolus on the dorsum of the tongue.
-The tip of the tongue is elevated and the dorsum is depressed, so that the bolus slides backwards to the back of the tongue.
-The bolus is squeezed and rolled up backwards towards the pharynx.

B- The pharyngeal phase:-

-It is an involuntary phase.
-The bolus touches the swallowing receptor area; the anterior tonsillar pillar as it passes from the mouth to the pharynx.

-The swallowing receptor area sends afferent impulses via the glossopharyngeal nerve, to the swallowing centre which is located in the medulla oblongata.
-The swallowing centre sends efferent impulses to the cranial nerve nuclei V, IX, X& XII.
-This leads to waves of peristalsis passing through the pharynx, by successive contractions and relaxations of the superior, middle and inferior constrictors of the pharynx.
-A group of reflexes occur to prevent the passage of the bolus to the upper respiratory passages as follows:-

1. Reflex approximation of the posterior tonsillar pillars to prevent the passage of the un-masticated food or large particles to the pharynx.
2. Reflex elevation of the soft palate to close the post. nares to prevent the passage of the bolus to the nose.
3. Reflex elevation of the epiglottis to close the larynx to prevent the passage of the bolus to the interior of the larynx
4. Reflex approximation of the vocal cords to shut the interior of the larynx.
5. Reflex apnea.
6. Reflex relaxation of the upper oesophageal sphincter to allow the passage of the bolus into the oesophagus.

C-The oesophageal phase:-

-The oesophagus is a muscular tube, which wall is formed of striated muscle fibres in its upper 1/3, smooth muscle fibres in its lower 1/3 and a mixture of both in the middle 1/3.
-The upper 1/3 is supplied by the vagus nerve; the lower 1/3 is supplied by the local enteric nerve plexuses of the GIT.
- When the bolus enters into the oesophagus, peristaltic contractions occur in the oesophagus to push it downwards in to the stomach.
-When the bolus reaches the lower oesophageal sphincter it relaxes to allow its passage into the stomach. The lower oesophageal sphincter is the last 2-3 cm of the oesophagus which is tonically contracted between meals to prevent the reflux of the gastric contents into the oesophagus. It is constricted by gastrin but relaxed by vasoactive intestinal peptide (VIP).
-Achalasia is a condition where there is failure of the lower oesophageal sphincter to relax on arrival of the bolus to the lower end of the oesophagus.
Gastroesophageal reflux: it is the entry of the gastric contents into the lower end oesophagus due to incompetence of the lower oesophageal sphincter.

Physiology of the stomach

Functional anatomy of the stomach

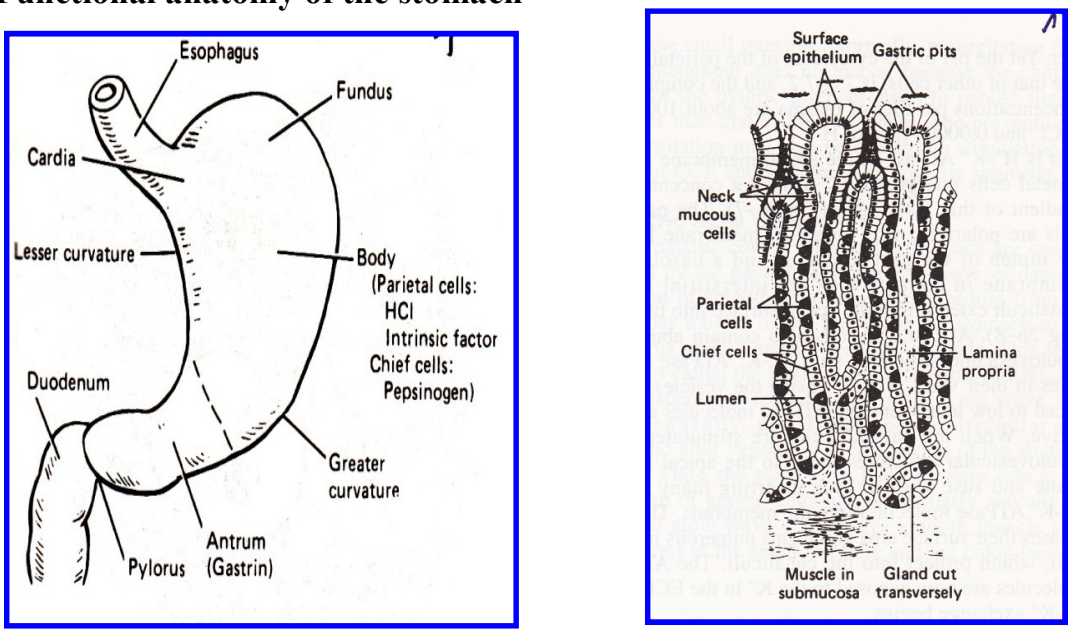


Fig (19) Regional anatomy and histology of the stomach

General functions of the stomach:-

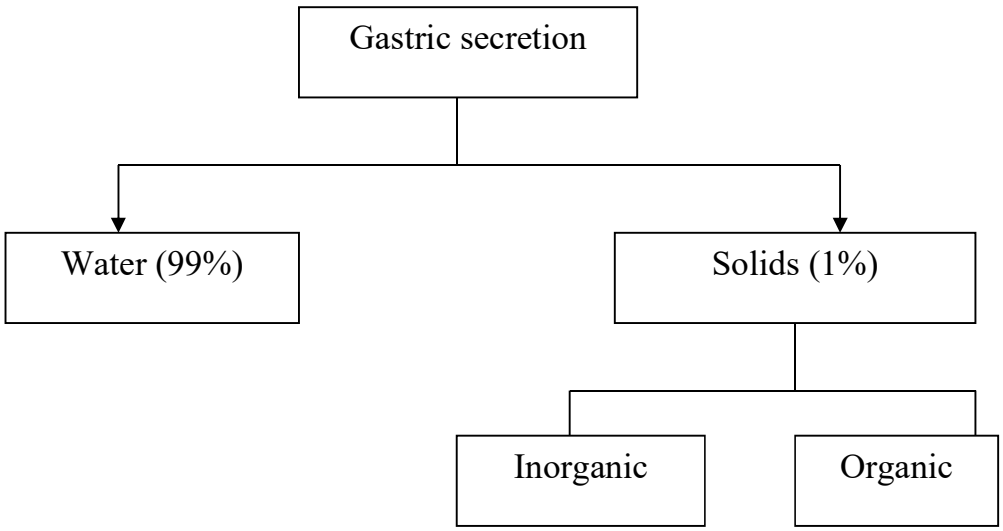
1. Storage of food.
2. Digestion of the protein content of food.
3. Piecemeal evacuation of the partially digested food.
4. Sterilization of food by its acid content.
5. Secretion of the intrinsic factor which is essential for the absorption of vit.B12.
6. Facilitation of defecation through the gasterocolic reflex.
7. Absorption of small amounts of water and ethanol.

<u>The gastric secretion:-</u>

-It has a volume of about 2.5 litres and a pH of about 1.

-It has the following important components:-

1. The gastric HCl.
2. Pepsinogen enzyme.
3. Mucous.
4. The intrinsic factor.



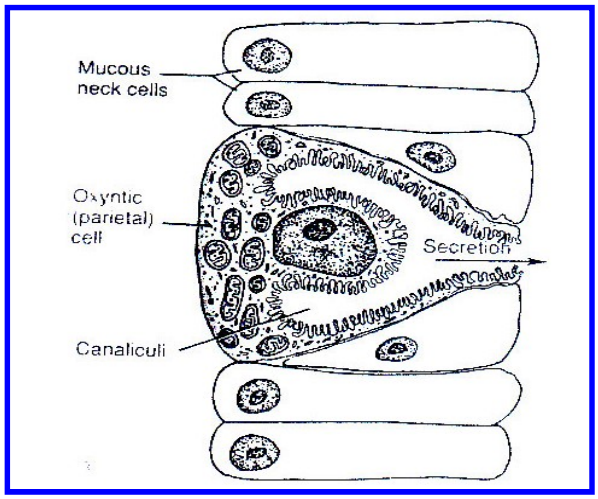


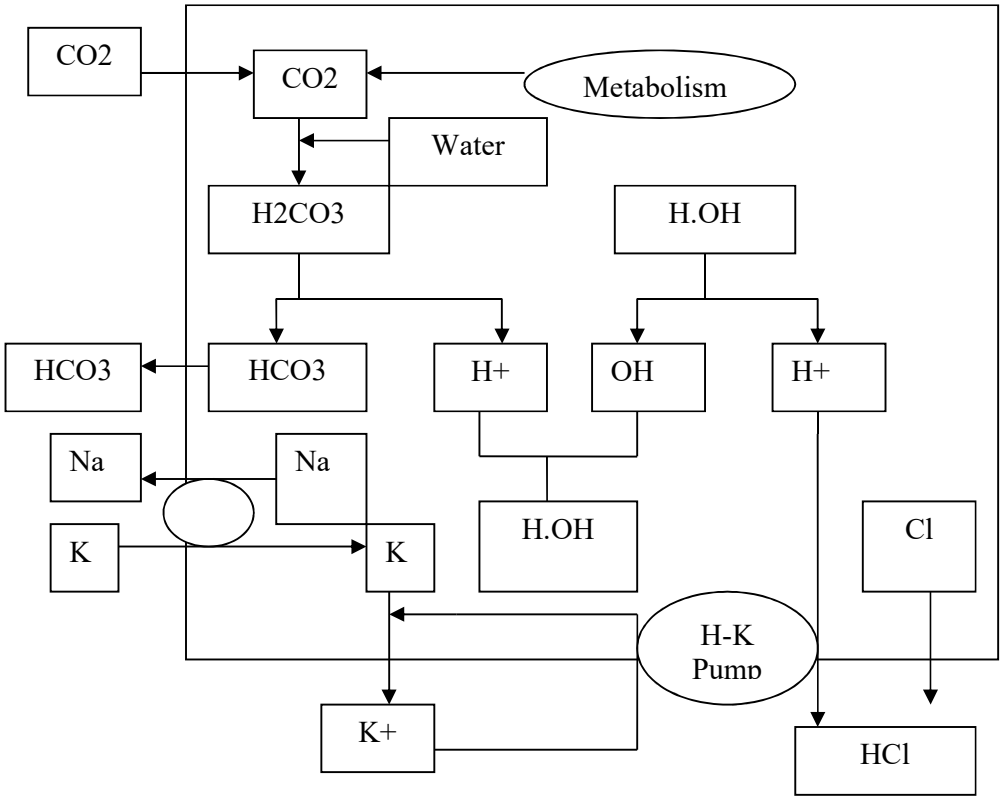
Fig (20) the oxyntic cell

1-The gastric HCl:-

-It is secreted from the oxyntic or the parietal cells.

-Steps of synthesis of gastric HCl:-

1. Inside the parietal cell, CO2 combines with water to form carbonic acid.
2. Carbonic acid dissociates into H+ and HCO3 which diffuses to the interstitial fluid and then to the blood in the general circulation.
3. Water inside the cell dissociates into H+ and OH^- groups which combines with H+ from the carbonic acid to form water. H+ of water diffuses into a lateral canaliculus in exchange for K+. Cl diffuses from the extra-cellular in to the intracellular fluid then to that para-cellular canaliculus where it combines with H+ to form gastric HCl.



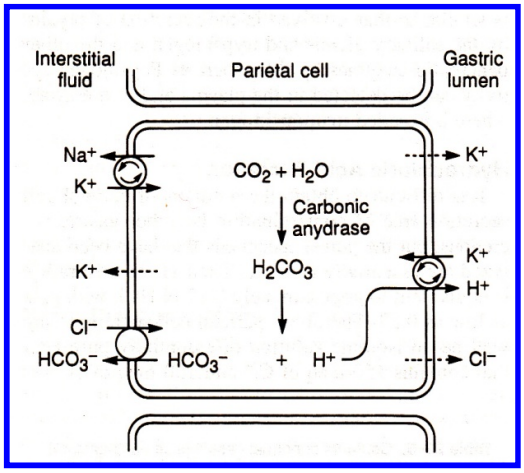


Fig (21) steps of gastric acid synthesis and secretion

-The mechanism of gastric HCl secretion:-

It is stimulated through the activation of one or more of the following receptors:-

1. Muscarinic receptors; which are stimulated by A.ch. and blocked with atropine. They act through an increase of the intracellular Ca.
2. Histaminergic receptors; type 2 which are stimulated by histamine and blocked by cimitidine or ranitidine. They act through an increase of the cAMP.
3. Gasrinergic receptors which are stimulated with gastrin. They increase the intracellular Ca.

The increase of the intracellular Ca and cAMP activate a protein kinase which in turn activates the H-K ATPase pump.

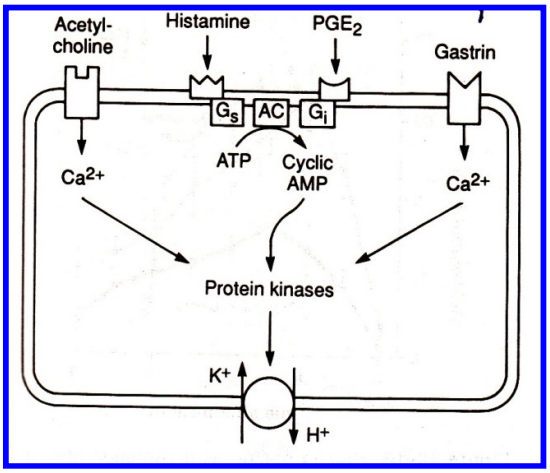


Fig (22) Receptors which stimulate gastric acid secretion

-The post-prandial alkaline tide:-

It is a rise in the bicarbonate content& pH of blood after the ingestion of meals due to the diffusion of the bicarbonate anion into the general circulation as a side product of gastric HCl synthesis.

-Functions of the gastric HCl:-

1. Absorption of calcium and iron.
2. Antibacterial action.
3. Bile secretion stimulant; Cholerhetic.
4. Coagulation of milk.
5. Digestion of proteins through :-
    a) Activation of the protein digesting enzyme; pepsinogen into pepsin.
    b) Supply of the optimum pH for the action of pepsin.
    c) Hydrolysis of the protein molecules to be easily digested.
6. Emptying regulator of the stomach; through the enterogastric reflex.

2-Pepsinogen enzyme:-

-There are 2 types of pepsinogen; type I and type II.

-Type I:-

1. It is the main type.
2. It is secreted from the *chief or peptic* cells in body and fundus.
3. Its secretion is linked to the gastric HCl secretion.

-Type II:-

1. It secreted in small amounts.
2. It is secreted by the *mucous* cells in the body, fundus and the antrum.

3. Its secretion is not linked to the gastric HCl secretion.

-The gastric mucosal barrier:-

It prevents the auto-digestion of the gastric mucosa by the acid and pepsin enzyme despite that they are digesting proteins in the chyme.

It consists of the following:-

1. The resistant nature of the surface mucosal cells in the stomach.
2. A layer of thick and alkaline mucus that covers the gastric mucosa.
3. The tight junctions between the gastric mucosal cells.
4. The normal secretion of intra-mucosal acid lowering prostaglandins by the COX enzyme type I.

3-Mucous:-

-There are 2 types of mucous; thick and thin.

-Thick mucous is secreted by the mucous cells lining the entire surface of the stomach; it is thick, insoluble, viscid and alkaline.

-Thin mucous is secreted by the mucous neck cells of fundal and corpal glands, it is thin, soluble and less viscid.

Point of view	Thick mucous	Thin mucous
1-Source	The surface mucosal cells	The mucous neck cells of the fundal and corpal glands.
2-Site	All over gastric mucosa	
3-Water solubility	Insoluble	Soluble
4-characters	Highly viscid and alkaline	Less viscid and less alkaline.

4-The intrinsic factor:-

-It is a glycoprotein in nature that is secreted from the parietal or the oxyntic cells. It facilitates the absorption of vit.B12 from the terminal ileum.

The gastrin hormone

-It is the gastric stimulating hormone; it stimulates all functions, growth and vascularity of the stomach.

-The secreting cells:-

1-The G cells in the lateral wall of the antral glands in the antrum.

2-The TG cells in the stomach and the small intestine.

-Functions of gastrin;-

1. Stimulation of gastric secretion.
2. Stimulation of gastric motility.
3. Stimulation of gastric growth and vascularity.
4. Stimulation of the endocrine and exocrine pancreatic secretions.
5. Motor to the lower oesophageal but inhibitory to the ileocecal sphincters.

-Control of secretion:-

Stimulants	Inhibitors
1-Peptides	1-High gastric acidity
2-Antral distension	2-Secretin, VIP& GIP.
3-Vagal stimulation	3-.Sympathetic stimulation
4-Anger and hostility	4- Fear and depression

The storage function of the stomach

The stomach can store up to one litre of chime without any change of the intragastric pressure, this is due to:-

1- The plasticity of the stomach.

2- The receptive relaxation character.

3- The Law of La Place; which states that the intra-gastric pressure is directly proportionate to the tension in the wall but inversely proportionate to the radius. With food entry into the stomach there is an increase of its radius but little increase of the tension in walls.

The gastric movements

1-Tonus rhythm; the tonic contractions:-

-These are continuous mild to moderate contractions in the fundus area.

-Their main function is to maintain the intra-gastric pressure constant.

2-The receptive relaxation:-

-With food intake, there is reflex relaxation of the lower oesophageal sphincter and the fundus of the stomach to allow an easy and free passage of the food bolus into the stomach.

3-The peristaltic movements:-

-They started in the middle of the stomach as weak contraction rings that spread towards the pyloric antrum. They gain force as they approach the antrum, they may even obliterate the gastric lumen when they reach the antrum.

-When they reach the antral area they may proceed as follows;-

1. They may spread backwards in an upward direction toward the fundus squeezing and squirting the chyme back to the gastric lumen to be properly digested; this is the RETROPUlSIVE MOVEMENT.
2. They may spread forwards in a downward direction toward the duodenum squeezing and squirting the chyme into the duodenum as it was properly digested in the stomach; this is the PROPUlSIVE MOVEMENT.
3. The pyloric region is converted to an isolated chamber in which these peristaltic contractions are acting strongly for proper digestion of chime.

4-Hunger contractions:-

-These tetanic strong contractions that are produced by summation of the tonic ones.
-They occur in the body of the stomach.
-They continue for 1-3 minutes resulting in pain sensations.
-They occur after 12-24 hours of fasting, reach the maximum intensity in 3-4 days then subside later on.
-Mechanism:-
Hypoglycaemia stimulates the hypothalamic feeding centre which in turn stimulates the medullary vagal nucleus. The vagal nucleus increases the frequency of the tonic contractions; they are summated to form the titanic hunger contractions.

-Factors affecting the gastric motility:-

A) Dietary factors:-

1. The volume of food:
   -Moderate or even marked distension of the stomach stimulates gastric motility and emptying.
   -Over-distension of the stomach leads to an opposite effect.
2. The type of food:-
   -CHO is the fastest to be evacuated from the stomach followed by proteins and then lipids.
   -Fats delay gastric evacuation through stimulation of both the enterogastric reflex and the secretion of the enterogastrone hormones. It includes secretin, cholecystokinin, GIP&VIP (Vasoactive intestinal peptide).
3. The consistency of food:-
   -Fluids are the fastest to be evacuated followed by semisolids and then solids.

B) Duodenal or gastrointestinal factors:-

1. The enterogastric reflex.
2. The enterogastrone hormone.

C) Nervous factors:-

-Anger and hostility stimulate gastric evacuation.
-Fear and depression inhibit gastric motility.

D) Drugs and chemicals:-

-Ethanol, bicarbonates and dopaminergic blockers stimulate gastric emptying.
-Amphetamine inhibits gastric emptying.

Vomiting

-It is the expulsion of the gastric contents throughout the oesophagus, pharynx and the mouth into the exterior.
-THE STOMACH IS ABSOLUTELY PASSIVE DURING THIS ACT.
-The act is carried out through a centre of vomiting that is located in the medulla oblongata. This centre is connected to the cranial nerve nuclei V, VII, IX, X & XII. It is also connected to the AHCs supplying the diaphragm and the muscles of the anterior abdominal wall.
-In close contiguity to the vomiting centre there is a chemically stimulated area called the chemoreceptor trigger zone (CTZ).

-Mechanism of vomiting:-

1-The stage of nausea:-

-It is a psychological feeling associated with widespread cholinergic transmission in the form of sweating, salivation, hypotension and reflex tachycardia.
-The stomach is fully relaxed, the LES is closed but there may be anti-peristalsis movements that drive the duodenal contents into the stomach.

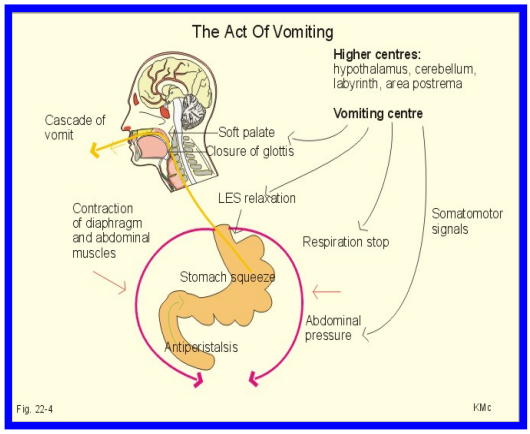


Fig (23) the act of vomiting

2-The stage of retching:-

-A series of forceful intermittent contractions of the diaphragm and the ant. abdominal wall muscles.
-These contractions squeeze the stomach and force the abdominal oesophagus and the cardiac portion of the stomach into the chest cage, but the LES still contracted well and closed.

3-The stage of evacuation:-

-Contractions of the diaphragm and the ant. abdominal wall become more strong and more frequent, they increase the intra-abdominal pressure very markedly.
-The gastric incisura becomes contracted and all of a sudden the LES is opened, the fundus is relaxed and the high intra-abdominal pressure squeezes the gastric contents to the exterior.
-During the upward passage of the gastric contents to the mouth, the same group of reflexes that naturally occur with swallowing, take place also here to prevent the passage of the vomitus material into the respiratory passages.

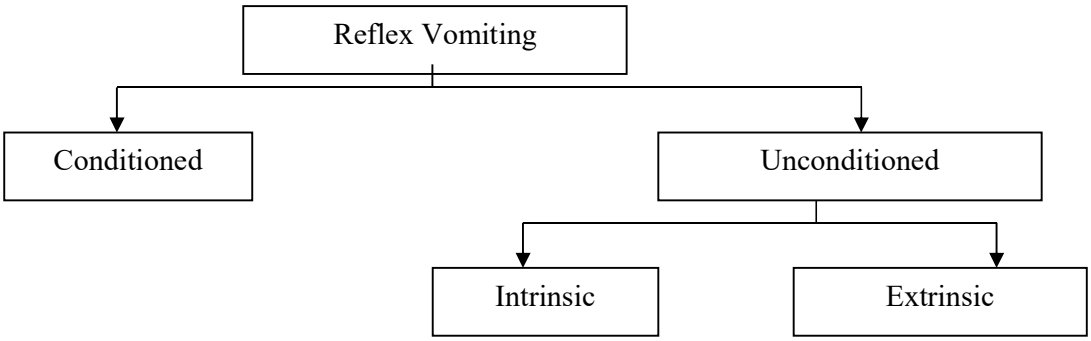
-Causes of vomiting:-

A) Central vomiting: - due to stimulation of the vomiting centre or the CTZ.

-Direct stimulation of the vomiting centre may occur in cases of meningitis or tumours compressing it.

-Stimulation of the CTZ may occur by chemical substances as drugs e.g. morphine or by the rise of urea and creatinine in case of renal failure.

B) Reflex vomiting:-



1-The conditioned reflex vomiting; it occurs on seeing, smelling, or even thinking of something nauseating..

2-The unconditioned vomiting which occurs on stimulation of afferent nerves connected directly to the vomiting centre. It may be intrinsic if their receptors lie inside the GIT or extrinsic if the receptors lie outside the GIT.

-The intrinsic unconditioned vomiting occurs in case appendicitis, gastritis, peptic ulceration and intestinal obstruction.

- The extrinsic unconditioned vomiting occurs in case of myocardial infarction, renal stones or inflammations.

The exocrine pancreatic secretion

-The exocrine pancreatic juice is about 1.5 litres /day with an alkaline pH of about 8.

-The pancreatic juice is of 2 types; the enzymatic or the acinar and the watery alkaline or the ductular secretion.

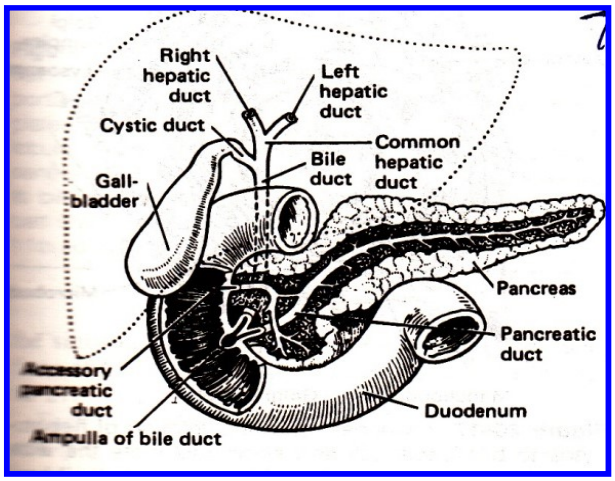


Fig (24) the hepatobiliary system and the pancreas

-Composition of the pancreatic juice:-

1- Water.

2-Electrolytes: - as Na, K, Ca, Cl& HCO3

3-Enzymes which include:-

a) Trypsinogen and chemotrypsinogen.
b) Ribonuclease and deoxyribonuclease.
c) Pro-carboxypeptidase and pro-elastase.
d) Lipase, cholesterol esterase and phospholipase A.
e) Alpha amylase.

1) The pancreatic proteolytic enzymes are secreted in the inactive state as there is no glandular protective mechanism from auto-digestion.
2) These enzymes are activated only inside the duodenal lumen by an intestinal enzyme called the enterokinase. It 1st activates trypsinogen into trypsin which in turn activates all other enzymes.
3) Some of trypsinogen is activated inside the pancreatic ducts, so that an anti-trypsin is secreted there to prevent any auto-digestional activity.
4) With obstruction of the common pancreatic duct, there will be an increase in the level of the activated trypsin inside the pancreatic ducts. Trypsin activates phospholipase A which acts on the biliary lecithin converting it into lysolecithin; a toxic substance which disrupts the pancreatic and the surrounding fatty tissue; a condition that is known as acute pancreatitis which is usually fatal.

Control of the pancreatic secretion:-

A) The nervous control:-

-It accompanies the cephalic and the gastric phases of gastric secretion.

-Vagal impulses stimulate the acinar enzymatic secretion which remains inside the acini.

B) The hormonal control:-

1-The secretin hormone:-

-It is secreted by the S duodenal and jejunal cells.

-It is released in response to the contact of gastric HCl with the duodenal mucosa.

-Functions:-

1. Stimulation of the ductular alkaline watery secretion of theb pancreas.
2. Stimulation of bile secretion (Cholerhetic)
3. Stimulation of the bicarbonate secretion from the Bruner's glands in the duodenum.
4. Inhibition of gastric secretion and motility.
5. Contraction of the pyloric sphincter.

2-The cholecystokinin hormone:-

-It is secreted from the duodenal and the jejunal mucosal cells.

-It is secreted in response to distension of the duodenum with fats, peptones and acid.

-Functions:-

1. Stimulation of the acinar enzymatic secretion of the pancreas.
2. Contraction of the walls of the gall bladder and relaxation of the sphincter of Oddi leading to the evacuation of bile (Cholagogue)
3. Augmentation of the action of secretin up- on the pancreas.
4. Stimulation of the intestinal secretion and motility.
5. Inhibition of the gastric secretion and motility.

The biliary secretion

-Bile is the secretion made up by the liver cells.

-The liver secretes about one litre of alkaline bile daily.

-If there is no chyme to be digested in the small intestine, the sphincter of Oddi will be closed and bile will regurgitate up into the gall bladder to be stored there.

-Whenever there is chyme in the intestine to be digested then the same sphincter of Oddi will be relaxed and bile will flow from the gall bladder into the small intestine to share in the process of digestion.

-Composition of bile:-

1-Water: 97.5%

2-Solids: - 2.5%

a) Organic constituents:2% :-
    1. Bile salts.

2. Bile pigments.
3. Cholesterol
4. fatty acids
5. Lecithin

b) Inorganic constituents 0.5% as Na, K, Ca & HCO3

Point of view	Hepatic bile	Cystic bile
1-Colour	Golden yellow	Dark yellow or brownish
2-pH	Highly alkaline (7.8)	Less alkaline (7)
3-Water	97.5%	88%
4-Specific gravity	Lower (1008)	Higher (1050)
5-The bicarbonate content	More	Less

-The bile salts:-

-There are 2 types of bile salts; the 1ry and the 2ry ones.

The 1ry bile salts;--These are the sodium and potassium glycho and tauro salts of the cholic and chenodeoxy cholic acids.

-By enumeration they are:sodium glycocholate , sodium taurocholate, sodium glychochendeoxycholic and sodium taurochendeoxycholic acid.

The 2ry bile salts:-

-They are synthesized in the large intestine by the action of the intestinal bacteria which reduce the cholic into the deoxycholic acid and also convert the chendeoxycholic into the lithocholic acid.

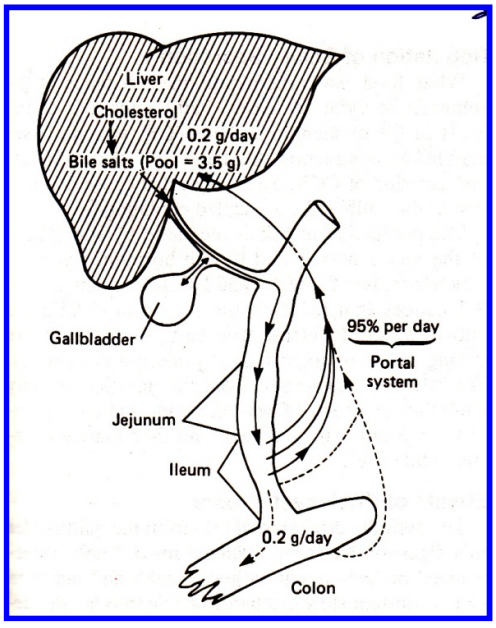


Fig (25) the hepatobiliary system and the enterohepatic circulation of bile

Functions of the bile salts:-

1) **Digestion of lipids:-** they facilitate the process of lipid digestion through the following mechanisms;-
   a. Emulsification of fat: - they break the large fat globules into smaller ones.
   b. Activation of the pancreatic and the intestinal lipases.
2) **Absorption of lipids:-**
   -They form a water soluble compound when they bind to phospholipids; a compound that is known as the micelle. This compound carries the free fatty acid or cholesterol in its interior then ferries them across the parietal watery film lining the small intestinal wall.
3) **Cholesterol solvent** action where they prevent the formation of cholesterol stones.
4) **Cholerhetic action;** where they stimulate the secretion of bile from the liver cells.
5) **Peristaltic stimulant.**
6) **Anti-putrefactive** action where they facilitate digestion and absorption of lipids which if undigested will inhibit the proteolytic enzymes resulting in putrefaction of proteins.

Factors affecting secretion of the bile salts:-

1-The nervous factor; where vagal stimulation stimulates while sympathetic inhibits the formation of bile by the liver.
2-The hormonal factor; where secretion stimulates the secretion of bile.
3-The blood supply; where bile secretion is directly proportionate to the hepatic blood flow.
4-The bile salts; they have a direct stimulant effect up on the secretion of bile form the liver cells.

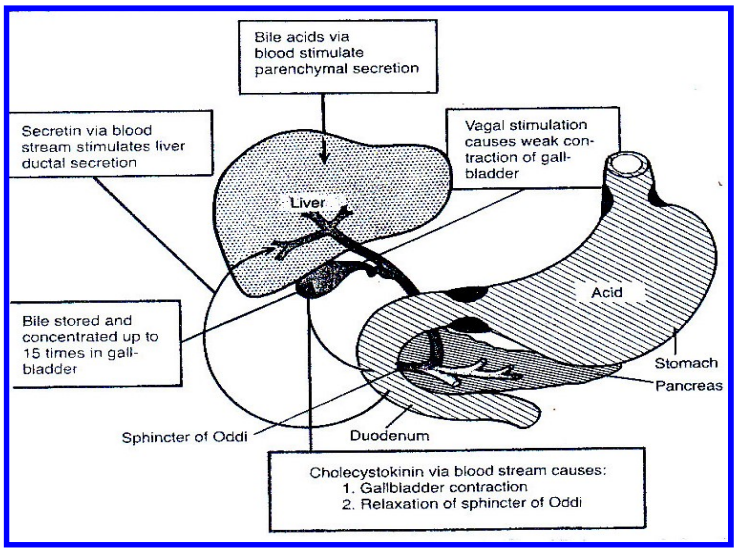


Fig (26) Cholerhetics

The gall bladder

Functions of the gall bladder:-

1- Storage of bile.
2- Concentration of bile; 10 times the bile is concentrated by water absorption.
3- Decrease of the intra-biliary pressure.
4- Acidification of bile through the bicarbonate absorption.
5- Mucous secretion of about 20 ml /day.
6- Evacuation of bile.

The gall bladder evacuators:-

These are called the cholagogues.
1- Nervous; as vagal stimulation and parasympathetic inhibition.
2- Hormones as CCK.
3-Drugs as MgSO4.

Point of view	Cholerhetics	Cholagogues
1-The nervous factor	Vagal stimulation	
2-The hormonal factor	Gastrin and secretin	CCk
3-The chemical factor	The bile salts	MgSO4
4-Others	The hepatic blood flow	

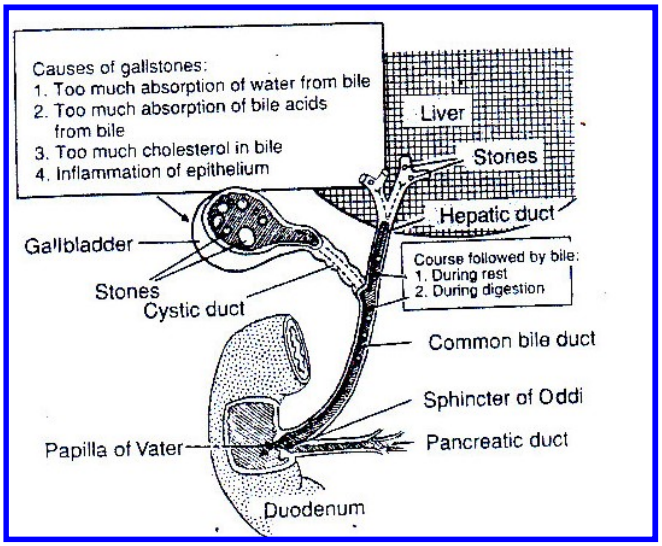


Fig (26) causes of gall stones

The bile pigments

Metabolism of the bile pigments:-

1. They are the end product for the breakdown of the haemoglobin content of the RBCs.
2. Haemoglobin is broken down into the haem and the globin parts.

3. Haem is further cleaved into iron and protoporphyrin, while the globin fraction is broken down into the constitutive a.a. which pass to the general protein metabolic pool.
4. The haem fraction is transformed into biliverdin then reduced into bilirubin.
5. Bilirubin is carried in plasma upon the plasma protein albumin; this fraction is called the free, indirect, the unconjugated or the haembilirubin.
6. The free, the unconjugated or the haembilirubin is uptaken b y the liver cells to be conjugated with sul;furic or glucoronic acids forming the conjugated, the direct, the conjugated or the cholebilirubin.
7. The liver excretes the cholebilirubin through the common bile duct into the small intestine
8. In the small intestine, cholebilirubin is converted into urobilinogen by the intestinal bacteria.
9. 75% of the intestinal Urobilinogen is transformed into another pigment; the Stercobilinogen which is excreted ion the foecal matter to be oxidized on exposure to the air into a dark brown pigment called the Stercobilin, which gives the stool its dark brown coloration.
10. The remaining 25% of the Urobilinogen is reabsorbed from the intestine through the enterohepatic circulation where 20% of it is re-excreted into the intestine while just 5% is filtered through the kidneys into urine to be oxidized on exposure to air into urobilin.

<u>-The Van Den Berg reaction</u>

a) The direct reaction: the Van den Berg reagent +the conjugated bilirubin→ pink colour
b) The indirect Van den Berg reaction; the pink colour appears only after addition of alcohol to the mixture.
c) The biphasic Van Den Berg reaction; the pink colour deepens after addition of alcohol.

Alcohol dissociates bilirubin from the carrier albumin molecules.

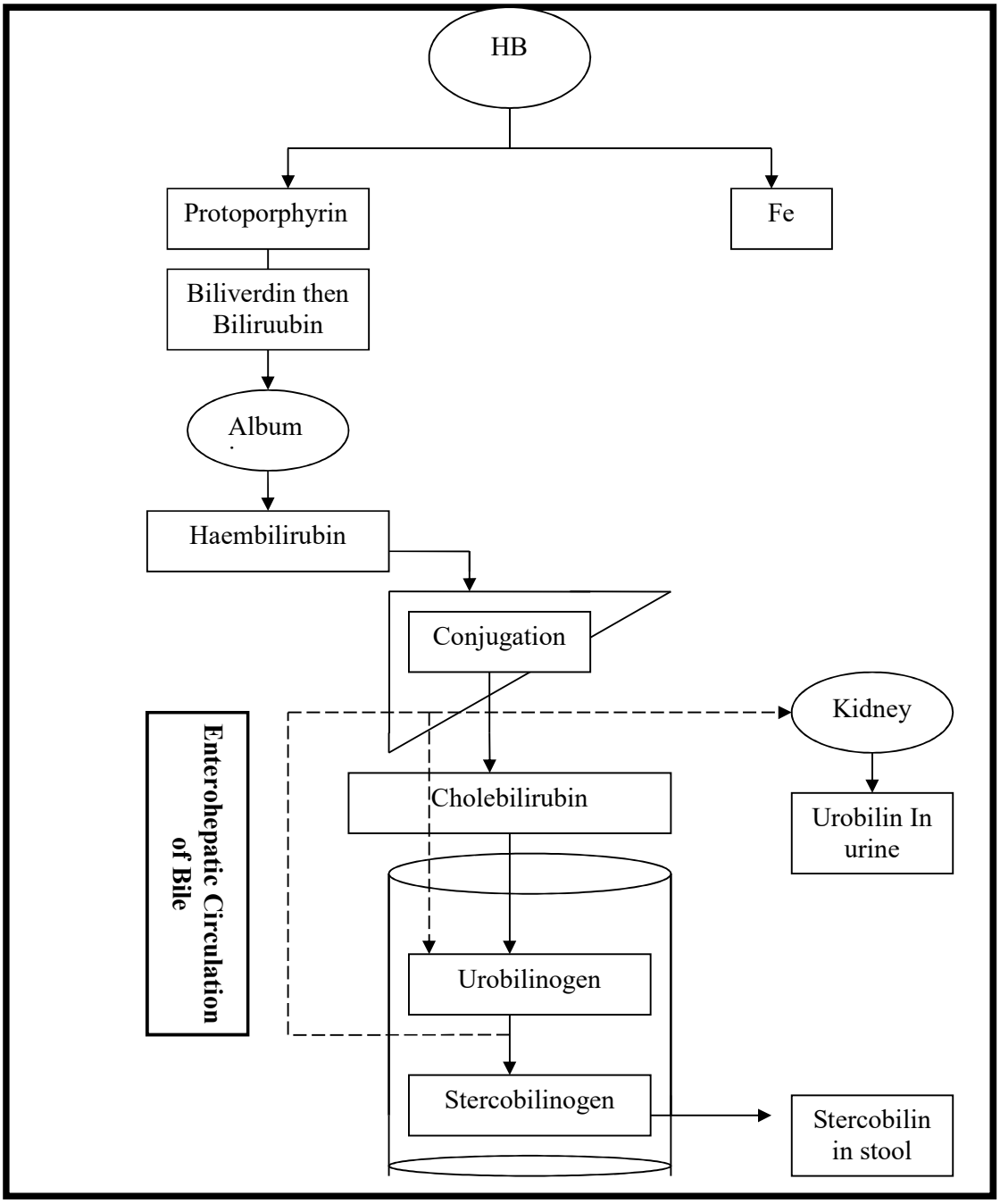


Fig (27) metabolism of Bile pigments

Jaundice

-It is defined as yellowish colouration of the skin and mucous membranes due to high level of bile pigments in the plasma and the interstitial fluid.

-The normal serum bilirubin is 0.8- 1.2 mg%

The point of view	The prehepatic or haemolytic jaundice	The hepatic jaundice	The post-hepatic or the obstructive jaundice
A-Cause	Excess haemolysis of the RBCs	Liver disease	Biliary obstruction
B-The haematological changes:-			
1-The liver functions.	Normal	Impaired	May be impaired.
2-Haemolytic anaemia.	Present	Absent.	Absent.
3-The pigment in blood	Haembilirubin	Both types.	Cholebilirubin.
4-The Van DenBerg reaction.	Indirect	Biphasic	Direct.
5-The presence of bile salts.	Absent	Present(+)	Present (++)
C-The urinary changes:-			
1-Colour	Normal	Dark	Very dark
2-The foam test.	White foam	Yellowish foam	Dark yellowish foam.
3-The urinary pigment.	None	Cholebilirubin (+)	Cholebilirubin (+++)
4-The bile salts	Absent	Present (+)	Present (++)
D-The stool			
1-colour	Very dark	Pale	Very pale
2-The bile pigment.	Stercobilinogen(+++)	Stercobilinogen but less than the normal amount	Absent
E-General changes:-			
1-The depth of colouration.	Mild	Moderate	Marked
2-Itching and bradycardia.	Absent	Absent	Present
3-Digestion and absorption of fat	Normal	Partially impaired	Markedly impaired

The small intestine

1-The intestinal secretion is made up of mucous and digestive juice.
2-The mucous is secreted from the Bruner's glands in the 1st few centimetres of the duodenum and also from the goblet cells over the mucosal surface of the small intestine.
4-The digestive juice is secreted from the intestinal glands. It is about 1 litre/ day with a pH of about 7-7.5.the digestive enzymes are present in the cellular brush border of the mucous cells, when the cells are desquamated their enzyme content get mixed with the alkaline juice.

Digestive function in the small intestine:-

(A) CHO digestion:

1-Starch and glycogen are digested into maltose, malotriose and α limited dextrins.
2-Maltose and malotriose are digested into glucose.
3-The α limited dextrins are digested into glucose.
4-Lactose is digested into glucose and galactose.
5-Sucrose is digested into fructose which is further converted into glucose.

(B)Proteins; they are digested by the peptidases into amino acids.

(C)Lipids:

-Digestion of lipids starts in the stomach by the lingual lipase.
-The gastric phase is of a little importance for the digestion of lipids.
-The most important phase is digestion by the pancreatic lipase.
-Trilycerides→ diglycerides→ monoglycerides→glycerol

Absorption in the small intestine:-

(A) CHO absorption:

-It occurs in the duodenum and the jejunum.
-Glucose and galactose are absorbed by 2ry active transport mechanism using a symport carrier together with Na. This is the Na-glucose co-transport or Na-glucose symport carrier mechanism.
-Fructose is absorbed by facilitated diffusion.
-Pentoses are absorbed by simple diffusion.
-The maximum absorptive capacity for glucosec120 gm/ hour.

(B) Protein absorption:-

-It occurs in the jejunum and the 1st part of the ileum.
-L-amino acids are absorbed by a Na co-transport mechanism.
-D-amino acids are absorbed by passive diffusion.
-In infants there may occur absorption of whole protein particles but it declines with age.

(C) Absorption of lipids;-

1-The miscells ferry their cholesterol and free fatty acids content across the unstirred watery layer to the brush border of the mucosal cells, releasing their content of fatty acids into the cells.

2-Inside cells the following occurs:-

a) Short chain fatty acids pass as such to the portal blood.
b) Long chain fatty acids and some cholesterol are re-estrified .
c) The intra-cellar newly formed TG and cholesterol esters are coated by protein and phpospholipids by golgi complex to form the chylomicrons which will pass to the lymphatics.

(D)Absorption of water and electrolytes:-

1-Na it is absorbed by 3 mechanisms; uniport, symport and antiport.

-The uniport carrier is an active Na pump from the lumen to the blood.

-The symport is a co-transport mechanism with glucose, galactose or L-amino acids.

-The antiport mechanism is the absorption of Na in exchange with H+ excretion.

2-K is absorbed by simple diffusion or active transport.

3-Cl and HCO3:-

a) Large amounts are absorbed together with Na in the duodenum and jejunum.
b) In the ileum and colon Cl is actively reabsorbed in exchange for HCO3.
c) Also in the ileum and the colon there is an active Cl pump into the lumen that is stimulated by cAMP. In cholera there is intracellular accumulation of cAMP which in-turn produces massive Cl secretion into the lumen with associating severe diarrhea. The diarrhea is painless as it is not due to the stimulated peristaltic rush.

4-Water: is absorbed by osmosis following the absorption of electrolytes and nutrients.

(E) Absorption of vitamins;

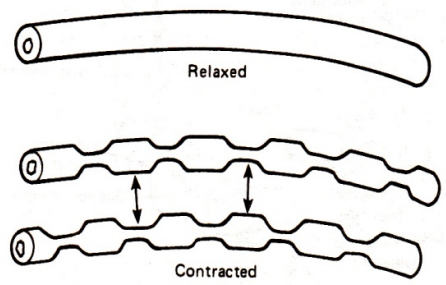
1-Water soluble vitamins EXCEPT vit.B12 are absorbed rapidly in the jejunum. B12 is absorbed through the terminal ileum together with the intrinsic factor.

2-Fat soluble vitamins are absorbed by simple diffusion from the duodenum and jejunum.

Factors affecting absorption in the small intestine:-

a) Adequate blood flow.
b) Adequate lymph flow.
c) Proper digestion.
d) Proper motility of the GIT.
e) The physicochemical properties of the substance that is to be absorbed.

The intestinal movements

The type of movement	Origin	Criteria	Function
1-Segmentation movement	Myogenic	1-Series of constrictions occur at regular intervals in a portion of the small intestine dividing it into ovoid segments. 2-At the middle of each segment there occurs another constriction and the old one disappears. 3-The cycle is repeated at a frequency of 12/ min. in the duodenum and 8/min. in the ileum. 4-It is controlled by the basic electric rhythm. 	1-Mixing or chopping of chime. 2-Squeezing the lymph and the blood vessels. 3-Facilitation of absorption.
2-The peristalsis movement	Neurogenic through local axon reflex	1-It consists of peristaltic waves traveling at a speed of 0.5 – 5 cm / sec. 2-It dies off after few seconds. 3-It is evoked by :- a) Intestinal distension with chime. b) The gasteroenteric reflex: gastric distension leads to reflex stimulation of the intestinal peristalsis. c) Hormones as CCK.	1-Mixing of chime with the digestive juice. 2-Propulsive action. 3-Facilitation of absorption.
3-The peristaltic rush	Neurogenic; vagal and local axon reflex	1-It is a strong peristaltic wave traveling rapidly for a long distance. 2-It occurs in response to strong irritation. 3-It causes diarrhoea.	Rapid proper emptying of the intestinal lumen.

4-The antiperistaltic movement.	Neurogenic; local axon reflex	1-Duodenum 2-Ileum	1-Proper digestion 2-Proper absorption.
5-Movement of the villi	It is a hormonal dependant movement; villikinin and bile.	It consists of shortening and elongation of the villi	It facilitates the absorption

-The ileocecal sphincter:-

It is the last few cms of the ileum, with a thick muscular coat.

The large intestine

-<u>Functions of the large intestine:-</u>

1. Defecation
2. Digestion of fibres in animals.
3. Excretion of heavy metals as Mg and arsenic.
4. Absorption of water and electrolytes.
5. Synthesis of :-
   -Vitamins as vit. K and vit. B complex.
   -Toxic materials as histamine and tyramine.
6. Secretion of mucous.
7. Storage of the foecal matter.

<u>Movements of the large intestine:-</u>

<u>1-The haustration movements:-</u>

They are exactly the same as the segmental movements of the small intestine but with outwards bulge of the dilated portions leading to the formation of what is called the haustrae.

<u>2-The propulsive movements:-</u>

a) The peristaltic movements:-where the haustration movement spreads anal-wards.
b) The mass movement:-
   1. It propels the faecal matter from the transverse to the sigmoid colon.
   2. A ring contraction is formed, the next 25 cm of the large intestines contracts as one unit squirting its contents into the distal segment of the colon.
   3. The mass movement is completed within 30 seconds.
   4. A series of this type of movement occurs in the colon after breakfast and extends up to 20 minutes.
   5. It is triggered by the gastrocolic and the duodenocolic reflexes.

The large intestinal bacteria:-

1. The Beneficial bacteria:-they have the following functions

-Synthesis of vitamin K, histamine, biotin and folic acid.
-Stimulation of IgG and IgM production in the wall of of the intestine.

2. The non-beneficial bacteria:
-They consume vit. C,B12 and choline.
-They produce cholesterol.
-They produce histamine, tyramine and ammonia. The latter is absorbed by the liver clearing it from blood.

Defecation

It is the act of reflex emptying of the contents of the rectum and colon.

Mechanism of defecation:-

1-The unconditioned spinal defecation:-

A-Distension of the rectum→ stimulation of the stretch receptors in the rectal walls→ afferent impulses via the pelvic nerve to the sacral defecation centre (S2, 3& 4).

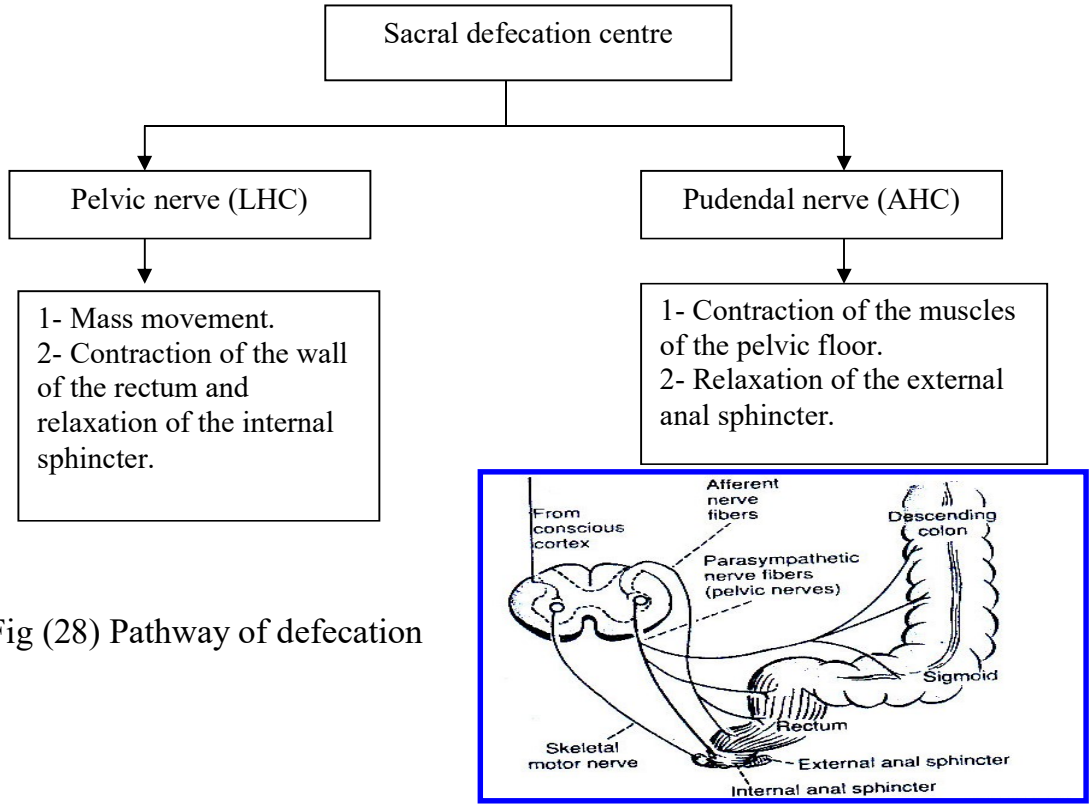


Fig (28) Pathway of defecation

B- Passage of the foecal matter inside the anal canal will stimulate more contractions of the wall of rectum and the pelvic floor with more relaxation of the external sphincter.

2-The conditioned spinal defecation :-

-If the conditions are not suitable for defecation to take place then the cerebral cortex will inhibit the spinal defecation centre.

-If the conditions are suitable then the cortex will facilitate the reflex through stimulation of the AHCs of the levator ani, diaphragm and the muscles of the ant. abdominal wall increasing the intra-abdominal pressure for better evacuation.

The liver

-The liver is the 2nd largest organ after the skin; it is also the largest endocrine gland.

-Functions of the liver:-

A) Metabolic functions:-

1. CHO metabolism: It shares in glucose homeostatic mechanisms; as glycogenolysis and glycogenesis.
2. Protein metabolism; through synthesis of plasma proteins, except gamma globulins, de-amination and inter-conversion of amino acids besides the urea cycle where it converts ammonia into urea.
3. Fat metabolism; as β oxidation of fatty acids and synthesis of cholesterol, lipoproteins& phospholipids.
4. Vitamins; where it sotres vitamins A, D, B12.
5. Minerals; where it stores iron and copper.
6. Heat production

B) Secretory functions: they secrete bile salts.

C) Excretory functions: they excrete the bile pigments.

D) Haematological functions :

1. Blood reservoir.
2. Synthesis of plasma proteins except gamma globulins.
3. Erythropoeitic function; by synthesis of the globin part of haemoglobin, storage of iron & copper and secretion of erythropoietin.
4. Coagulative function; by formation of prothrombin.

E) Defense function by the Kupffer cells.

F) Detoxifying function for toxins and drugs.

Metabolism

A calorie is the amount of heat that raises the temperature of one Kg of water 1 ° C from 15 to 16° C.

The heat value of food:-

The physical heat value: - it is the amount of heat produced by complete oxidation of food outside the body and is measured by the bomb calorimeter.

The physiological heat value: - it is the amount of heat produced by complete oxidation of food inside the body. The physiological and the physical heat values of either CHO or fats are exactly the same as they are completely burnt down in the body into CO2 and water. The physiological heat value of proteins is less than their physical one because in the body they are incompletely burnt down

The basal metabolic rate; BMR

The metabolic rate is the amount of energy that is liberated per unit time by the metabolism of food.

The basal metabolic rate: -

Is the metabolic rate under the normal resting physiological conditions i.e. complete physical, mental and psychological rest.

It is 40 calorie/ m^2 / hour.

Values within ± 15% of that normal standard are considered normal.

Factors affecting the BMR;-

A) Physiological factors:-

1. Age: in infants it is 25 but in adults it is 40 calorie/ m^2 / hour.
2. Sex; it is higher in males than females.
3. Pregnancy; it is increased in pregnancy by about 30% due to excess secretion of T3 and T4.
4. Exercise: it increases the BMR.
5. Emotions: they increase the BMR.
6. Meals and the nutrition state: it is decreased in the malnutrition states and increased with diet especially proteins.
7. Sleep: it decreases the BMR by about 10% due to drop of the muscle tone.
8. Climate: it is lower in hot weather but higher in cold weather.
9. Race: it is lower in the Chinese.

B) Pathological factors;-

The item	Factors increasing	Factors decreasing
1. The pituitary gland	Hyperpituitrism	Hypopituitrism
2. The thyroid gland	Hyper-thyroidism	Hypo-thyroidism
3. The adrenal cortex	Hypercorticism	Hypocorticism
4. The adrenal medulla	Pheochromocytoma	----------

5. The body temperature	Hyperthermia; where rise of the body temperature by 1 raises the BMR by 15%	Hypothermia; where the drop of the body temperature by 1 decreases the BMR by 15%
6. Organ failure	Heart failure due to hypoxia of the tissues.	1-Shock. 2-Renal failure.
7. Others	1-Diabetes insipidus to compensate for the heat loss in urine. 2-Leukaemia due to the excess tissue breakdown	1-Starvation.

C) **Chemical factors: -**

Factors increasing	Factors decreasing
1-Thyroid hormones	1-Thyroid inhibitors
2-Sympathomimetics	2-curare

The specific dynamic action; SDA

1. It is the rise of the metabolic rate 2ry to the ingestion of food.
2. The metabolic rate increases one hour after and reaches a maximum after 3 hours of the ingestion of food.
3. The SDA is of 2 types:
   a) The 1ry is the mandatory energy expenditure to stimulate CHO, protein or fat metabolism.
   b) The 2ry SDA is the actual rise of the BMR due tothe stimulated metabolism.

Factors affecting the SDA:-

a) Type of food; where proteins have the highest SDA as they stimulate the BMR with about 30% increase above its basal level. Fats are 6% while CHO are only 4% stimulants.
b) Quantity of food.
c) The external temperature: where the highest SDA of proteins occur at a temperature of 35° C. A decrease of the external temperature decreases the SDA of proteins which has a very high significant value in cold weather.

Body temperature

The normal body temperature ranges between 36- 37.5° C, this is the core temperature.

The rectal temperature is higher 0.5 ° C.

The axillary temperature is lower0.5 ° C.

Physiological variations in the body temperature;-

1- The effect of age; it is a little bit increased in the old age.
2- Timing of the day; it is a little bit higher in the after-noon than in the early morning.
3- The effect of the cyclic phenomenon; as the female sexual cycle where it is increased by the time of ovulation due to the release of progesterone.

Methods of heat production and heat loss:-

Heat production	Heat loss
1-The basal metabolic rate	1-Radiation to non contact objects by the electromagnetic waves
2-The SDA	2-Conduction to the contact objects.
3-The muscle tone	3-Convection to air.
4-Shivering	4-Evaporation of the sweat and the insensible perspiration
5-Lipolysis	----------
6-Heat gain from the environment	----------

Factors affecting heat loss:-

1. Temperature gradient; the higher the gradient the more heat will be lost.
2. Humidity; it decreases the heat loss.
3. Air currents: they increase the heat loss.
4. Clothes; the number of the layers , the type of the clothes and their compactness

The hypothalamus and body temperature regulation:-

The hypothalamus contains the following centres for the regulation of the body temperature:

1. The heat gain centre which is located in the posterior nuclei.
2. The heat loss centre which is located in the anterior nuclei.
3. The set point value centre which detects any changes of the body temperature away from the normal values by comparing the information from the thermo-receptors to the set point.

The hypothalamus can thus activate heat gain or heat loss mechanisms as follows;

Item	The heat gain	The heat loss
1-The muscle tone	Increase of the muscle tone	Decrease of the muscle tone
2-Shivering	Shivering due to stimulation of the primary motor centre for shivering in the post. Hypothalamus.	----------
3-Sympathetic stimulation	Sympathetic stimulation leading to coetaneous v.c., erection of hair to trap air and lipolysis for energy production.	Stimulation of cholinergic transmission to the sweat glands leading to excess sweat secretion.
4-Hormones	Release of TSH and excess thyroxine which stimulate lipolysis and heat production	Decrease of the TSH and thyroxine secretion.
5-Coetaneous circulation	Vasoconstriction due to sympathetic stimulation	Vasodilatation due to;- Inhibition of the sympathetic discharge. Local BK released from the sweat glands. Local axon reflex. The direct effect of heat.
6-Appetite	Increase of the appetite.	Decrease of the appetite
7-Panting	----------	Increased in non-sweating animals

Physiology of sweating

The sweat glands are of 2 types; the exocrine and the apocrine glands.

Item	The exocrine	The apocrine
Distribution	All over the body	The axilla, the inguinal and the genital areas.
The nerve supply	Cholinergic sympathetic	Adrenergic sympathetic.
Functions	Regulation of the body temperature	Sweat secretion with characteristic odour in relation to sexual intercourse

Stimulants for sweat secretion;-

1. High environmental temperature
2. High humidity
3. Physical exercise
4. Emotions
5. Sleep
6. Central stimulation of the sweat centre by asphyxia

Effects of the excessive sweating:-

1. Dehydration
2. Hyponatraemia
3. Hypotension.
4. Heat exhaustion and collapse.

Disturbances of the body temperature

1- Hypothermia;-

The heat production is less than the heat loss.
There is drop of the BMR, no shivering and depression of the CNS.
It is a reversible condition.

2-Hyperthermia or the heat stroke:-

Heat production is more than the heat loss.

Causes:-

1. Severe muscle exercise
2. High protein diet especially in a hot and humid environment.
3. Hyperthyroidism.

3-The sun stroke: - it is a state of hyperthermia due to damage of the heat loss centre on direct exposure of the skull to direct sunrays.

The main line of management of both heat and sun strokes is increase heat loss mechanisms by immersion in cold water and in severe cases in ice cold water.

4-Fever:-

It is the rise of the body temperature due to bacterial or viral antigens.

The mechanism:-

Both types of antigens trigger the leukocytes to release the interleukin I which stimulate the formation of prostaglandin E_2. The latter raises the hypothalamic set point so the hypothalamus stimulates the heat gain and inhibits the heat loss mechanisms.

The management relies on decreasing that elevated set point by cold foments and anti-prostaglandins. When the elevated set point drops the hypothalamus recognizes that the body temperature is higher than the set point so that it starts to stimulate the heat loss mechanism that is why fever drops on occurrence of sweating.

Physiology of Nutrition

The process of food intake is regulated by the following 2 hypothalamic centres; the hunger or the feeding centre in the lateral hypothalamus and the satiety centre in the ventromedial hypothalamus.

Factors affecting food intake;-

1. The body temperature;

   Cold weather stimulates the heat gain mechanisms including feeding.
   Hot weather produces the opposite effects.
2. Conditioned reflexes:-

They may be excitatory or inhibitory
They act through the amygdalla and the pre-frontal nuclei.
Amygdalla is responsible for sorting out the type of flood you like or dislike.

3. Unconditioned reflexes:-

The oral metering reflex; on chewing or swallowing there will be stimulation of oral receptors that will inhibit the hypothalamic feeding centre.

The GIT metering: on distension of the stomach or the intestine with food, mechanoreceptors in the walls send afferent impulses via the vagus nerve to inhibit the feeding centre.

4. The chemical composition of the blood;-

Hyperglycaemia, hyper-fattyacidaemia or hyper-aminoacidaemia will all inhibit the feeding centre.

5. Hormones and drugs:-

Insulin, glucagons or CCK stimulate the feeding centre
Amphetamine on the other hand inhibits it.

Obesity

It is the excess deposition of fat due to excess energy input than the energy output.

Causes of obesity:-

A) Dietary habits; where there are faulty feeding habits in the childhood period including the quality and the quantity of food.
B) Abnormal regulation of the feeding process; which is mostly psychogenic.
C) The physical habits; a sedentary life style decreases the energy output.
D) Hereditary causes which may be genetic, dietary or psychic.
E) Hypothalamic causes; as lesions in the ventromedial nucleus.
F) Endocrinal causes; as Cushing syndrome.

Diagnosis of obesity;-

1- Determination of the skin thickness where 50% of the body fat is stored under the skin.

2- The total body weight in relation to age, sex and height, where it should not exceed a 20% surplus of the standard or the ideal body weight.

3- The body water where it constitutes 75% of the fat free body weight.

Management of obesity:-

- Reduction of the energy input; with a negative caloric balance of about 1000 cal/day is needed.
- Increase of the energy output; by regular exercise.

- Drugs as amphetamine

Starvation

Starvation is the complete abstinence of food intake.

Effects of starvation:-

a) Hunger pains
b) Emaciation and cachexia
c) Depression of the physical, mental, sexual and the glandular activity.
d) Depression of the tissue regenerative power.
e) <u>The metabolic effects:-</u>

A) <u>CHO metabolism;-</u>

- Stimulation of the hepatic glycogenolysis which supplies energy for the 1st 24 hours.
- Later on there will be stimulation of the renal and hepatic gluconeogenesis by GH, glucagon and cortisol.

B) <u>Lipid metabolism:</u>

After the depletion of CHO, fats start to supply energy.
It occurs through the stimulation of lipolysis which increases the level of FFA and ketone bodies.

D) <u>Protein metabolism:-</u>

It passes through 3 stages; the 1st is the stage of adjustment, the 2nd is the stage of the steady phase and the 3rd is the stage of the pre-mortal phase.

<u>The stage of adjustment:-</u>

1. The amount of the excreted nitrogen depends on the source of the energy; if it was the stored glycogen then the excreted N_2 starts low then is gradually increasing. If there is previous protein intake then it will start high to decline later on.
2. The phase lasts for few days.

<u>The steady phase stage:-</u>

1. Here the energy production is the function of both fat catabolism (80%) and protein catabolism (20%).
2. Its duration depends on the amount of the stored fat.

<u>The pre-mortal phase;-</u>

1. It starts when the fat is depleted.
2. Energy is derived from proteins and the urinary N_2 excretion increases till death.

f) <u>The blood changes;-</u>

1. The blood <u>sugar is</u> at the fasting level.
2. The blood <u>amino acids</u> are at the fasting level.
3. There is <u>hyperlipidemia.</u>

4. The blood volume; there is hypovolaemia due to decrease of the RBC, HB and Haematocrite value.
5. Hypoproteinaemia; the plasma proteins decrease leading to oedema
6. The pH: there is acidosis.
7. The electrolyte balance; it remains constant as long as the kidneys and the endocrine glands remain functioning well.

g) The urinary changes:-

1. The N_2 content; as mentioned before.
2. The urine volume depends on the fluid intake.
3. The pH is acidic
4. The electrolyte content; Na & Cl are decreasing while K, S and Mg are increasing. Ca and P are constant

Renal Physiology

The main function of the kidneys is to clean the plasma from any unwanted or harmful materials such as excess salts, toxic material and drugs.

Functional anatomy of the kidney

The functional unit of the kidneys is the nephron and there is about 1.3 million nephrons in each human kidney**.** The nephron is composed of 2 main functional parts ; the glomerulus and the renal tubular system; figure (1) shows the different parts of the nephron.

Nephrons which have their glomeruli in the outer part of the renal cortex are known as the cortical nephrons while those with their glomeruli in the inner "juxtamedullary" cortex are known as the juxtamedullary nephrons. The 1st type has short loop of Henle while the 2nd one has a long loop.

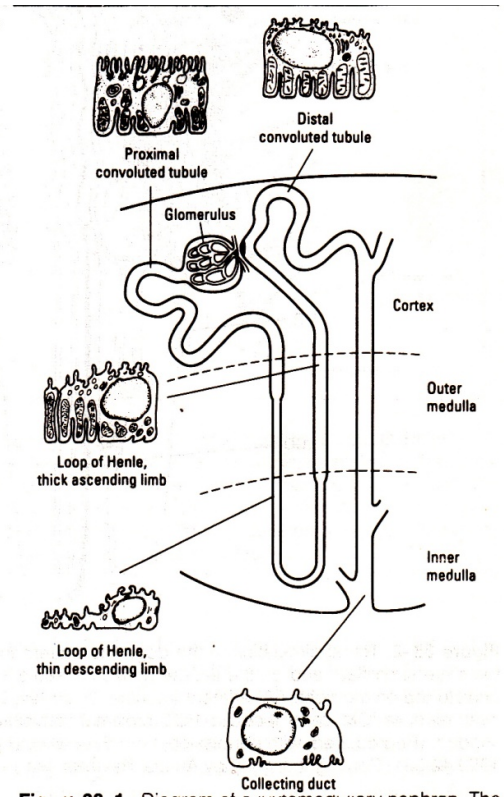


Fig. (29) The nephron and its components.

General functions of the kidney

A) Excretory function; as it excretes any excess amount of:
1. Water
2. Salts
3. [H+]
4. Non-volatile waste products as urea
5. Drugs and chemicals

B) Endocrine function; as it secretes the following:-
1. Rennin; which converts the angiotensinogen into angiotensin I
2. Erythropoietin
3. Active form of vit. D
4. prostaglandins

C) Detoxifying function; as it inactivates any drugs and chemicals.

D) Homeostatic function; as it regulates the following parameters:-
1. The ECF volume and osmolarity.
2. The arterial blood pressure.
3. The acid base balance
4. The electrolyte balance

General criteria of the renal circulation:-
1. It is very rich; 1200 ml/min, constituting about 225 of the COP.
2. It is one type of portal circulation.
3. The glomerular capillary hydrostatic pressure is very high 60mmHg.
4. The glomerular capillary has a very high degree of permeability.
5. There is a high degree of autoregulation.

Physiology of the glomerulus

The main function of the glomerulus is to form the tubular fluid through a process of filtration under high hydro-static pressure, so it is called glomerular filtration or ultra-filtration.

The glomerular filtration rate; GFR:-

It is the rate of formation of the glomerular filtrate by the renal glomeruli. It is 125 ml/min.

The filtration fraction: - is the ratio of the GFR to the effective renal plasma flow; ERPF. It is about 18%.

Factors determining the GFR: -

A) The filtration force:-

There is only one filtering force in the glomerular tuft of capillaries; the glomerular capillary hydrostatic pressure which 60 mmHg.

B) The re-absorption force:-

There are 2 re-absorptive forces; the plasma protein oncotic pressure (32 mmHg) and the Bowman's intra-capsular pressure (18mmHg).

The net force for filtration = 60-(32+18) = 10 mmHg.

C) The permeability of the glomerular membrane:-

The GFR is directly proportionate to the glomerular membrane permeability.

There are pores in the glomerular membrane that allow passage of the molecules less than 7 nm.

Besides, the pores are guarded by a negative charge repelling back any negatively charged molecules, even it their diameter is less than 7 nm as the molecules of albumin so it is not filtered through the normal kidney.

D) The surface area of the glomerular membrane which is controlled by the mesangial cell sphincter; a sphincter at the inlet of the glomerular tuft of capillaries.

Factors affecting the GFR:-

1- **Factors affecting the filtration force:-**

a) Diameter of the afferent arteriole:-

-Vasodilatation of the afferent arteriole increases the capillary hydrostatic pressure which increases the GFR.

b) Diameter of the efferent arteriole:-

-Vasoconstriction of the efferent arteriole increases the capillary hydrostatic pressure which increases the GFR.

- The maximum increase of the GFR could be obtained by vasodilatation of the afferent and vasoconstriction of the efferent arterioles.

2- **Factors affecting the re-absorptive forces**:- these are

a) The plasma protein osmotic pressure; which if decreased in case of hypoproteinaemia, will decrease the re-absorptive force and increase the GFR.
b) The Bowman's intra-capsular pressure: - it is normally 18 mmHg, but when it starts to increase it decreases the GFR and can stop it completely when it reaches 28mmHg.

3- Factors affecting the glomerular permeability:-

-In case of acute nephritis the charge of the pores is lost so that albumin molecules start to be filtered.

-In case of chronic nephritis there is destruction of the membrane barrier leading to massive filtration of albumin.

4- Factors affecting the surface area:-

-The glomerular membrane surface area is controlled by the tone of the pre-capillary sphincter of mesangial cells; when constricted by angiotensin or vasopressin it decreases the surface area and when relaxed by ANP it increases it.

5- The renal blood flow:-

When the rate of the renal blood flow is increased then there will be no good chance for the re-absorption mechanism to take place and the GFR will increase.

6- The mABP:-

Within the range of 80-220 mmHg any change of the m ABP is not associated with any change of the GFR, due to a *tubuloglomerular feedback* mechanism and the renal capsular auto-regulation.

-**The renal capsular auto-regulation:-**

When the m ABP increases then the renal capsule compresses the renal arteries to decrease the renal blood flow to the normal and thus it keeps the GFR at a relatively constant value.

Physiology of the renal tubular system

The proximal convoluted tubule (PCT)

Functions of the proximal convoluted tubule:-

a) Re-absorption of the following:-
   1. Organic molecules as glucose, amino acids and urea.
   2. Inorganic moieties as Na, K, Cl& HCO3.
   3. Water.
b) Excretion of the fo0llowing:-
   1. Metabolic waste products as H+ ions and creatinine.
   2. Drugs as penicillin
c) Synthesis and secretion of ammonia into the tubular fluid

[I]The re-absorptive function of the PCT:-

1-Sodium re-absorption:-

-A fixed ratio 70% of the filtered sodium is re-absorbed from the PCT. This is the glomerulotubular balance.
-Na re-absorption occurs through 2 different routes; the trans-cellular and the para-cellular routes.

2- The bicarbonate re-absorption

1. It occurs in a coupled manner with Na re-absorption.
2. In the tubular fluid NaHCO3 dissociates into Na and HCO3.
3. Na is reabsorbed in exchange for H+ which is excreted into the lumen.
4. H+ binds with HCO3 to form H2CO3
5. H2CO3 dissociates at the luminal border into CO2 and H2O.
6. CO2 diffuses into the inside of the cell to be dissolved in the ICF water to form H2CO3 which rapidly dissociates into H+ and HCO3.
7. H+ is excreted in exchange for Na re-absorption while the HCO3 diffuses with the reabsorbed Na into the interstitium.

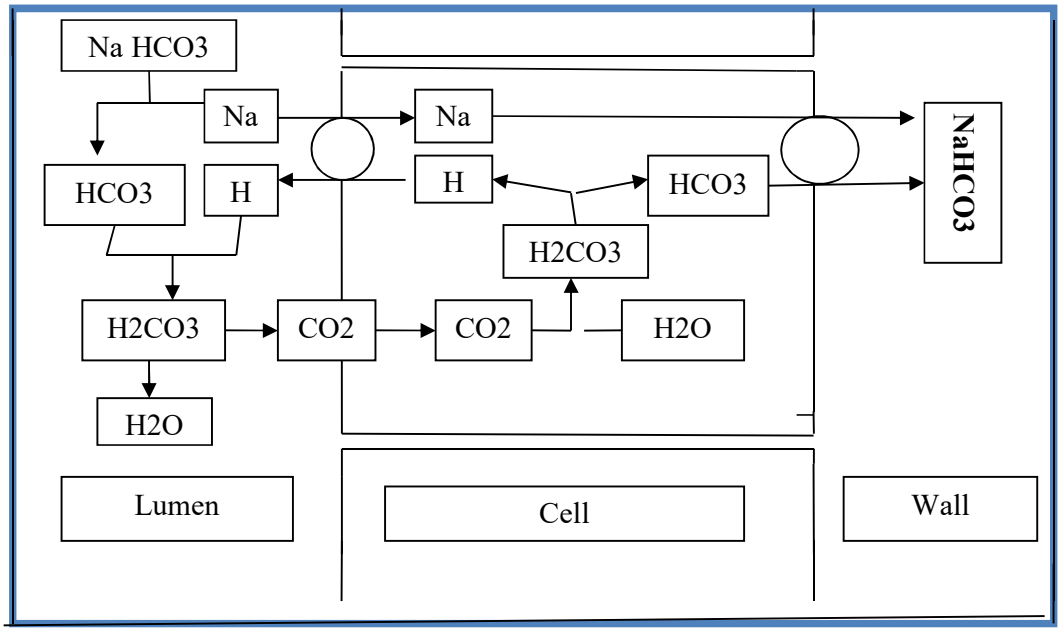


Fig. (30) Na and HCO3 reabsorption in the PCT

3-Glucose re-absorption in the PCT.

1. All over the whole tubular system it is the PCT tubule which can reabsorb glucose. It is the only site of the renal tubular system that contains the Na glucose symport carrier.
2. At the lateral border of the tubular cell glucose is reabsorbed with Na down a concentration gradient for the latter.
3. Glucose re-absorption in the PCT follows the following table:-

Amount of the glucose filtered	Fate
Up to 250 mg/min	Complete re-absorption
250-300 mg/min.	95% is reabsorbed.
300-350 mg/min	80% is reabsorbed.
350-400 mg/min.	65% is reabsorbed.
>400mg/min.	Not reabsorbed at all

4. Any amount of glucose that is not re-absorbed in the PCT will appear in urine.
5. The tubular transport maximum for glucose: - it is the maximum amount of glucose to be reabsorbed by both kidneys in one minute. In males it is 375mg/min while ion females it is 350mg/min.
6. The renal threshold for glycosuria: - it is the minimum level of the blood sugar in the venous blood just above which glucose starts to be excreted in urine

[II]The excretory function of the PCT:-

1-Excretion of H+ ions:-

2-Drugs as penicillin are also excreted by the PCT.

[III]The secretory function of the PCT:-

Secretion of ammonia:-

In the tubular cell ammonia is formed from glutamine by glutaminase enzyme.

At the luminal border it combines with the H+ ion to form the ammonium ion which is then excreted into the tubular fluid.

Physiology of the loop of Henle

Physiology of the DCT

Functions of the DCT:-

1- Re-absorption of Na in exchange for K+ or H+ under the effect of the aldosterone hormone.

2-Bicarbonate re-absorption

3-H+ ion excretion

4- Water re-absorption.

Physiology of the collecting duct

The main function of the collecting duct is to adjust the final volume of urine.

The wall of the collecting duct is impermeable to water.

The ADH can make it water permeable and under the effect of the hypertonic medullary interstitium water can be absorbed in case of body needs.

Mechanisms for concentration of urine:-

1. In cases of hyperosmoarity and hypervolaemia the ADH is released in large amounts from the post. pit.gland.
2. There is gradually increasing hypertonic medullary interstitium which gradually increases water re-absorption from the collecting duct as we go deep and deep into the apex of the medullary pyramid.

Diuretics

A diuretic is any factor or substance that increases the water content of urine, increasing its volume and decreasing its specific gravity.

They are;-

1. Water ingestion decreases the ADH release.
2. Ethyl alcohol decreases the ADH release.
3. Glucose 25% and mannitol they are called osmotic diuretics.
4. Xanthines; as coffee it dilates the afferent arteriole and increase the GFR.
5. CA inhibitors as acetazolamide or Diamox.
6. Aldosterone antagonists.
7. Furosemide or Lasix inhibits the re-absorption of solutes from the thick ascending limb of Henle, making the tubular fluid hyperosmolar with little water re-absorption from the collecting ducts.
8. Acidifying salts; they are now obsolete.

The concept of renal plasma clearance

The renal clearance of any substance is the volume of plasma that is cleared from this substance, by both kidneys, in just one minute.

Determination of the plasma clearance

1- Determination of the amount of the substance that is excreted in urine in just one minute, (A). It equals the volume of urine in one minute (V) multiplied by the urinary concentration of this substance (U)

2- Measurement of the plasma concentration of the substance, (P)

3- Calculation of the clearance (C) according to the following equation:-

$$C = \frac{V \times U}{P} \text{ ml/min.}$$

The significance of the clearance concept:-

1. It is one of the renal function tests.

2. The clearance of inulin or creatinine is used to measure the GFR.
3. The clearance of PAHA is used to measure the renal blood flow.
4. It can explain the way of renal handling of different substances whether filtration and re-absorption or filtration and secretion.

1-The inulin or the creatinine clearance; measurement of the GFR:-

Inulin is freely filtered which means that its concentration in plasma equals that of the GFR

It is neither re-absorbed nor secreted in the renal tubular system so the amount that is filtered equals the amount that is excreted.

The amount filtered = the amount excreted

Glomerular inulin conc. X GFR= Urinary inulin conc. (U) X Volume (V) of urine/min.

As the glomerular inulin conc. equals that of plasma then it could be substituted by it in the equation so

The plasma inulin conc. (P) X GFR = Urinary inulin conc. (U) X Volume (V) of urine/min.

Then it could b e said that;

$$GFR = \frac{U \times V}{P} =$$ The inulin clearance.

The value of inulin clearance:-

a) Measurement of the GFR.
b) Identification of the renal handling of different substances:-
    1. If the clearance of a substance is higher than that of inulin then this substance is filtered then secreted by the renal tubular system.
    2. If the clearance of a substance is lower than that of inulin then this substance is filtered then re-absorbed by the renal tubular system.

Creatinine has the same properties and significance of inulin.

2- The PAHA clearance; determination of the renal blood flow:-

PAHA has got a very important criterion that gives it the advantage of measuring the renal plasma and then the renal blood flow. It is cleared off from the body just by one single circulation to the kidney so;

The amount of PAHA entering the kidneys in one single minute = the amount excreted in urine in one single minute also.

Plasma PAHA conc. X Renal Plasma Flow (RPF) = Urinary PAHA X Volume of urine/min.

$$RPF = \frac{U_{PAHA} \times V}{P_{PAHA}} =$$ The clearance value of PAHA.

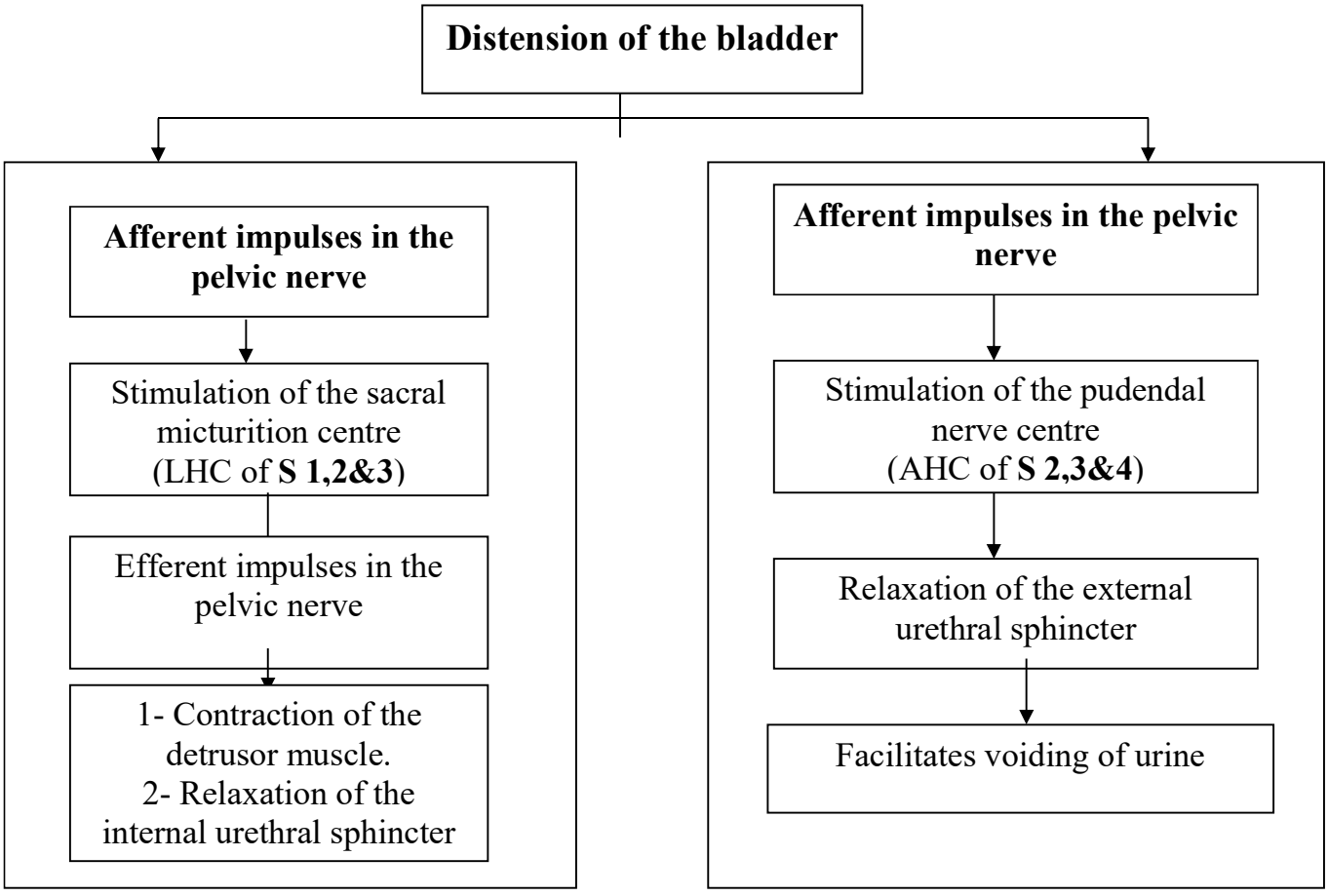
Physiology of micturition

Micturition is a conditioned spinal reflex action that leads to the evacuation of the urinary bladder.

The conditioning of micturition:-

At the age of 2 years it is conditioned by the cerebral cortex where it can facilitate it if the surrounding conditions are suitable or inhibit it if not.

The filling level (ml)	The sensation felt
150-300	The 1st urge for voiding of urine.
400-600	Sense of fullness
600-700	Pain but micturition could be suppressed
At 700	The breaking point for micturition.



The flow of urine in the urethra stimulates mechanoreceptors in its wall to send afferent impulses via the pudendal nerve to stimulate:-

1- The sacral micturition centre leading to more contractions of the detrusor muscle with relaxation of the internal sphincter.
2- The pudendal nerve centre with more contractions of the levator ani with relaxation of the external sphincter.

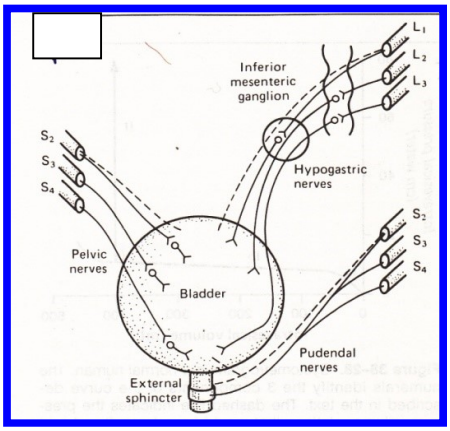


Fig. (31) The pathway of micturition.

Physiology of the Acid Base Balance

The acid base balance

- The normal arterial pH is 7.4.
- The normal venous pH is 7.37.

- **The buffering systems:-**
  A buffering system maintains the pH of its medium at a constant value.
  Any buffering chemical consists of a weak acid and a strong base.
  The pH of the medium is determined according to a balance between the base and the acid fractions of the buffering system, an equation called the Henderson and Hasselbakh's equation as follows:-

$$\text{The pH} = K + \text{Log.}\frac{[\text{Base fraction; } HCO_3]}{[\text{Acid fraction; } CO_2]}$$

- **The alkali reserve:-**
  As a result of metabolism there is continuous production of variable acids which represents a dangerous challenge to the human body.
  The body protects itself from this challenge through a reserve of a strong alkali (HCO_3) in the plasma; the alkali reserve. It constitutes about 55% of the total plasma volume.
  Acidosis is more challenging to the human body because it produces the following effects:
  1. Depression of the cellular energy productive machines and the Na-K pump.
  2. Depression of the cardiovascular system leading to bradycardia, cardiac arrest, ↓ of the COP and generalised vasodilatation with increased capillary permeability.
  3. Depression of the CNS; including the neuromuscular transmission, neural excitability and muscular performance.

- Acidosis is the drop of the alkali reserve with maintenance of the pH at a normal level, while acidaemia is the drop of both.

- Alkalosis and alkalaemia are exactly the opposite of acidosis and acidaemia respectively.

The physiological buffering systems in the human body

They are:-

1. The intra-cellular buffers.
2. The chemical buffers of the blood.
3. The kidneys.
4. The respiratory system.
5. The liver.

A) The role of the intracellular buffers: -

They are the intracellular organic anions as proteinate which can buffers the intracellular [H+]. They include also the intracellular PO^4, SO^4 and oxalates.

B) The chemical buffers in the blood:-

They are: -

a) The carbonic acid / bicarbonate system:

- If an acid is added to the blood stream then it is scavenged by the bicarbonate fraction of the system as follows;

$HCl + NaHCO_3 \rightarrow Na\ Cl + H.OH + CO_2$.

- If an alkali is added to the blood stream then it is scavenged by the carbonic acid fraction of the system as follows;

$NaOH + H_2CO_3 \rightarrow Na.HCO_3 + H.OH$

b) The acid / basic phosphate system:-

- If an acid is added to the blood stream then it is scavenged by the basic phosphate fraction of the system as follows;

$HCl + Na_2\,HPO_4 \rightarrow NaCl + NaH_2PO_4$.

- If an alkali is added to the blood stream then it is scavenged by the acid phosphate fraction of the system as follows;

$Na.\ OH + Na.H_2\,PO_4 \rightarrow Na_2H.PO_4 + H.OH$

c) The plasma proteins.

d) The haemoglobin

- They are actually polypeptide chains or contain polypeptide chains (HB) with a CCOH- terminus and an amine NH2 terminus.
- If [H+] is added then it binds to the CCOH-.
- If an alkali is added then the [OH-] is bound to the amine terminus.
- Besides, HB has another advantage where it contains the histidine amino acid which contains the imidazole group which binds H+.

The most effective and the most ideal buffers are determined down to the following rules:-

1. The effectiveness of the chemical buffer relies on 2 factors; its pKa; the dissociation constant ant its amount in the blood.
2. The carbonic acid / bicarbonate system has a very high amount in the plasma but it has a low pKa. On the contrary, the phosphate buffer has a very high pKa but its concentration is 1/10 of that of the bicarbonate system.
3. The ideal buffer is the protein system which totally has a concentration in the blood of about 20g % and a very high pKa.

C) The role of the kidneys: -

1. The kidneys have a very high potency for the excretion of the H+ ions by both the PCT and the DCT.
2. They both can excrete the H+ in the free and the ionic forms.
3. The PCT can excrete it in the free form down a luminal pH of 6.9.
4. The DCT can excrete it in the free form down a luminal pH of 4.5.
5. For each H ion that is excreted by either of them one Na HCO_3 is reabsorbed into the blood.
6. They can also excrete it the bound form in the form of ammonium ion NH_4+.
7. The DCT is advantageous over the PCT in excreting the H+ as:-
    a) It has a specific uniport pump for the H+ ion excretion.
    b) Its maximum acidifying capacity is 4.5.
    c) It has 3 luminal buffering systems for neutralization of the freely excreted H+.
8. In case of acidosis the kidneys excretes excess H+ and reabsorbs NaHCO3. In alkalosis the reverse occurs.

D) The role of respiration:-

1. There are 2 types of chemo-receptors which are stimulated by any change in the chemical composition of the blood, the central which lies in the medulla oblongata and the peripheral which lies in the aortic and the carotid bodies.
2. The central type is stimulated by any rise of the pCO_2 and the peripheral is stimulated by any drop of pO2, rise of pCO2 and drop of the pH.
3. In case of acidosis they stimulate respiration to increase the washout of CO2; the main source pf H+ in the blood.
4. In alkalosis the reverse occurs.

E) The role of the liver: -

In acidosis the liver stops all metabolic pathways that end in acid formation as glycogenolysis, glycolysis and lipolysis. In alkalosis the reverse occurs with stimulation of Cori's cycle, glycogenesis and lipogenesis.

The Acid Base Disorders

The point of view	Acidosis		alkalosis	
	Respiratory	**Metabolic**	**Respiratory**	**Metabolic**
The pathophysiology	Defective respiratory washout of the CO2	Excess production of acids with expiry of the alkali reserve.	Hyper-active respiratory washout of the CO2	Excessively available alkali reserve
The cause	1-Low environmental oxygen as in high altitudes. 2-Respiratory diseases. 3-Alveol-capillary membrane disease. 4-A-v shunts	1-Excess production of FFA and ketone bodies due to accelerated lipolysis as in:- a- Uncontrolled DM b-starvation, c-prolonged fasting d- Severe prolonged muscle exercise. 2-Excess production of lactic acid due to stimulated anaerobic metabolism as in hypovolaemia due to a-Dehydration b-Severe vomiting c-Diarrhoea d- Burns and haemorrhage. 3-Diamox which prevents the re-absorption of NaHCO3. 4-Addison's disease.	1-Stimualted respiratory centre by a tumour or in case of meningitis or encephalitis. 2- In hysterical personalities.	1-Excess ingestion of alkalis as bicarbonate. 2-Excess ingestion of green leafy vegetables. 3-Mild vomiting. 4- Diuretics other than diamox. 5-Conn's and Cushing's syndromes
Compensatory	1-Stimulation of the renal	Stimulation of respiration to	1-Stimulation of renal	1-Inhibition of respiration.

mechanisms	excretory power for H+. 2-Stimulation of the hepatic mechanisms of Cori's cycle, glycogenesis and urea cycle with inhibition of glycolysis and lipolysis.	wash out the excess CO2	excretion of NaHCO3 with inhibition of renal excretion of H+ ions. 2-Stimulation of hepatic glycolysis, glycogenolysis and lipolysis.	

Physiology Of the Special Sen

Functional anatomy of the eye

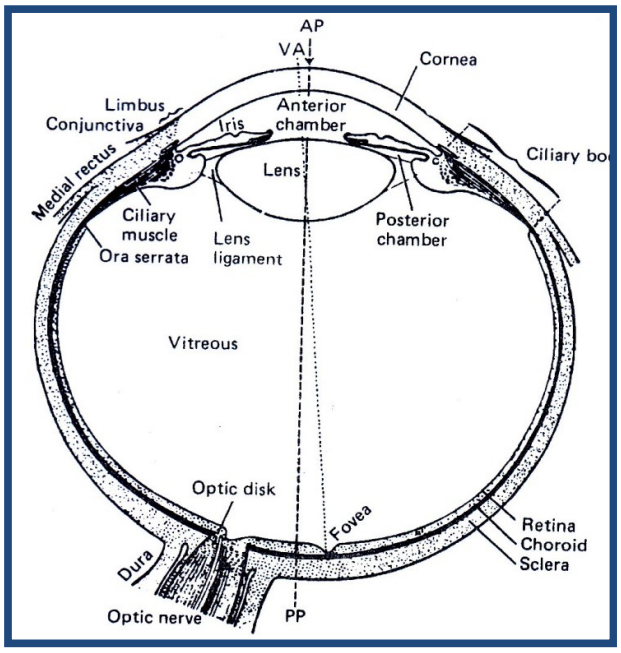


Fig. (32) Functional anatomy of the eye

The lacrimal secretion

-There is one main lacrimal gland in the upper lateral fornix besides there are small numerous glands along the conjunctival fornices.

-The mechanism of secretion:-

Point of view	The unconditioned	The conditioned
1-The stimulus	Irritation of the nasal or the conjunctival mucosa	Psychic and emotional
2-The afferent nerve	The trigeminal nerve	Variable according to the stimulus
3-Role of the cerebral cortex	No role	Necessary
4-The centre	The lacrimal centre in the lower pons	

-The Lacrimal flow:

From the lacrimal gland to the inner canthus to the lacrimal sac, then to the nasolacrimal duct which finally pours into the nose.

The orbicularis occuli helps the flow of tears.

Epiphora is the increase of tears down the cheeks.

The eye lids

Blinking:-

-Functions of blinking;

1. Control of the amount of light that enters the eye.
2. Protection

3. Spreading of tears.

-Types of blinking:-

1-The rhythmic type:-

-It is involuntary.

-It occurs at a rate 10-20/ minute.

-It is due to rhythmic autonomic discharge from the hypothalamus.

-It sweeps the tears to the inner canthus.

-Its rate is decreased by attention.

2-The reflex blinking:-

It is the protective closure of the eye lids due to stimulation of the optic, trigeminal or the cochlear nerves.

3-The voluntary blinking:

It could be for long time and may be bilateral.

The aqueous humour

-It is the clear transparent fluid that fills the anterior and the posterior Chambers of the eye.

-Composition:-

- It is alkaline.
- There is no protein content.
- Glucose and urea are present but in a lower concentration than that of the plasma.
- Vit. C, pyruvate and lactate are present but in a higher concentration than that of plasma.
- It contains the bicarbonate buffer.
- It contains Na Cl

-The mechanism of secretion:-

- It is a process of mixed active secretion and ultra-filtration.
- It is formed at a rate of 2-5 cc/minute.
- There is active secretion of Na followed by passive diffusion of Cl and HCO3 following Na secretion.
- Carbonic anhydrase enzyme plays the same important role for the dissociation of carbonic acid and formation of the active HCO3 radical
- Evidence that it is an active secretory mechanism:-
    1. Na, Cl, Vit. C, pyruvate and lactate concentration in aqueous are higher than that in plasma.
    2. Glucose and urea are lower than those in the plasma.
    3. The isotopic Na studies proved that it is an active secretory mechanism from the ciliary capillaries.
- Cortisol eye drops stimulate its production raising the IOP.

-Drainage of the aqueous humour:-

From the posterior to the anterior chambers, to the irido-corneal angle where it is drained by the spaces of Fontana to the canal of Schlemm then to the aqueous veins then to the ipsilateral venous plexus.

-Functions of the aqueous humour:-

1. Maintenance of the intraocular pressure.
2. Maintenance of the shape of the eye.
3. Maintenance of the normal positioning of the different eye structures in the anterior and posterior chambers.
4. Nutritive to the avascular structures of the eye.
5. Drainage of metabolites.
6. Little role in refraction.

The vitreous humour

-It is a gelatinous material lying between the lens and the retina.

-Functions;-

1. Maintenance of the globular shape of the eye.
2. Maintenance of the normal positioning of the lens and retina.
3. Nutritive to the avascular retina.
4. Drainage of metabolites.
5. Little role in refraction.
6. Plays a role in the genesis of the IOP.

The intraocular pressure

-The normal values: - 15-20 mmHg with 5 mmHg diurnal variation. It is highest in the morning and lowest in the evening.

-It is measured by the tonometer and the technique is called tonometry.

-Regulation of the intraocular pressure:-

This is achieved through the control of the outflow of the aqueous into the canal of Schlemm. When the rate of formation increases then the IOP increases which in turn increases the rate of outflow so the IOP returns to the normal value.

-Significance of the IOP:-

1- Maintenance of the spherical shape of the eye ball.

2- Proper positioning of the refractive media of the eye.

-Glaucoma:-

-It is the rise of the IOP.

-It is of 2 types:-

1. The open angle glaucoma (OAG) where there is excess secretion more than the drainage rate.

2. The closed angle glaucoma (CAG) where there is an obstruction to the outflow of the aqueous, mostly due to inflammation and fibrosis at the irido-corneal angle.

The cornea

-It is the transparent part of the outer layer of the eye.
-Histologically and anteroposteriorly it is composed of the following layers:-

1. The outer stratified epithelium
2. The bowman's elastic membrane.
3. The substantia propria.
4. The Descmet's membrane.
5. The innermost endothelial layer.

-Nutrition and metabolism of the cornea:-

The cornea is an avascular structure that receives the nutrients as follows:-

1. The oxygen is uptaken from the atmosphere.
2. The nutritive elements are taken from the aqueous humour in the anterior chamber.
3. It also receives nutrients from the capillaries of the corneoscleral junction.
4. It is drained by the lymphatics in the substantia propria.

The corneal transparency:-

The anatomical factors	The physical factors
1-The uniform regular arrangement of the epithelium.	1-The same refractive index of all corneal fibres.
2- The uniform regular arrangement of the collagen fibres.	2-The cornea is partially dehydrated by evaporation from the outer epithelium and an endothelial pump that pumps water into the aqueous.
3-There is no blood vessels.	3-Vitamin A where its deficiency leads to xerophthalmia.
4-There is no myelinated nerve fibres	4-Vitamin B_2 where its deficiency leads to corneal vascularisation.

-Functions of the cornea:-

1. Protection by the corneal reflex and absorption of the UV rays.
2. Permeability where it acts as a route for administration of the eye drops.
3. Refraction where it acts as a convex lens which power equals 45 dioptres.
4. Transparent allowing the passage of light rays into the interior of the eye.

-The protective function of the cornea:-

1- The corneal reflex:-

-Touching the lateral aspect of the cornea with a piece of cotton results in reflex blinking. It is one of the superficial reflexes.

2- The pericorneal film of tears.

3- The blinking mechanism.

The sclera

-It is the hard fibrous coat covering the post.5/6 of the eye.

-It is opaque due to the irregular arrangement of the CT fibres and the partial hydration

-It is protective and is the site for the insertion of the extraoccular eye muscles.

The lens

-Functional histology:-

1-The lens is entirely encapsulated.

2-Underneath the anterior capsule there is an epithelial layer that is producing the lens fibres.

3-The old fibres are pushed inwards to become centrally located in the lens while the new fibres remain peripherally placed until they are pushed inwards by the newly formed ones.

-Structure of the lens:-

1- 70% water and 30% solids in the form of proteins as albumin and nucleoproteins.

2- It is an avascular structure which obtains its nutritive elements from the aqueous humour.

-The metabolism of the lens:-

1. It has a very low metabolic rate.
2. Glucose is metabolised both aerobically and anaerobically.
3. The aerobic metabolism depends on :-
   -The flavoproteins; FAD&FADH
   -Glutathione and ascorbic acid.

Causes of lenticular transparency:-

1- The uniform arrangement of the fibres.

2-There is no vessels.

3-There is no nerves.

4- The same physicochemical properties of the protein fibres of the lens.

5- The same refractive index of all the layers.

-Functions of the lens:-

1-Protective for the retina where it absorbs the U/V rays.

2- Refractive function where its power is about 20 dioptres at rest.

3- The near response or accommodation.

-Cataract:-It is lenticular opacification due to lenticular protein denaturation and calcification.

The near response or the accommodation reaction

It is a physiological process which occurs on shifting the gaze to a near object to bring its image exactly on the retina.

It comprises the following changes;-

1. Bilateral miosis.
2. Increased diopteric power of the lens.
3. Convergence of both eyes.

1-The bilateral miosis:-

a) It prevents the entry of excess light.
b) It allows only the central rays to enter the eye, thus it prevents the occurrence of the spherical and the chromatic aberration.

-The spherical aberration:-

The refractive power of the central part of the lens is higher than that of the peripheral part so that central rays are brought to into a focus which is nearer to the lens than that of the peripheral rays leading to blurring of the image.

-The chromatic aberration:-

The peripheral parts of the lens act as 2 prisms which analyse the light into its various colours.

c) It increases the depth of focus. The depth of focus is the distance through which the object can move to and fro in front of the eye without any change of the clarity and sharpness of the retinal image.

2-The increase of the diopteric power of the lens;-

-On near vision the image is initially formed behind the retina so that the lens increases the convexity of the anterior surface. This is done through contraction of the ciliary muscle with relaxation of the zonnule → increased convexity of the anterior surface of the lenticular capsule→ increased convexity of the anterior surface of the lens.

3-Bilateral convergence:-

This is due to contraction of medial recti of both sides.

-Range of accommodation:-

It is the distance between the far and the near point of distinctive vision by accommodation

-Amplitude of accommodation:-

It is the difference between the diopteric power during accommodation and that of rest. It is about 10 D

The errors of refraction

Pont of view	1-Myopia or short sight	2-Hypermetropia or long sight
1-site of the image	Before the retina	After the retina
2-Causes	1-Long antero-posterior diameter of the eye due to stretching of the sclera in a rapidly growing child. 2-Greater curvature of the lens.	1-Short antero-posterior diameter of the eye. 2-Lesser curvature of the cornea.
3-The corrective mechanism	There is no corrective mechanism	Accommodation. However it becomes ineffective with the near point due to the great power of accommodation that is needed to focus the near point.
4-State of the ciliary muscle	Atrophy	Hypertrophic
5-Treatment	Concave lens	Convex lens

3-Asigmatism:-

-Astigmatism means that there is no point.

-It means that light rays are not focused into a point in the retina but into a line, due to difference in the dioptric power in the different plane meridians

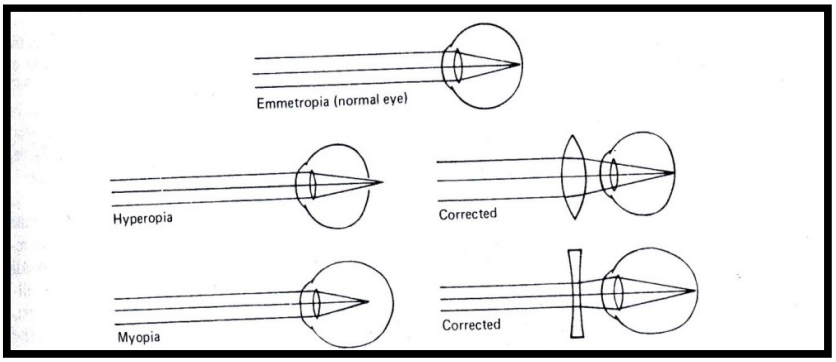


Fig. (33) Errors of refraction and their correction.

-This means that the point is focused into a line and the line is focused to a hallow.

-Causes:-

1. Congenital.
2. Traumatic.
3. Inflammatory.

-Types of astigmatism;-

1. Corneal.
2. lenticular
3. Corneolenticular.

-Correction;-

By the use of a cylindrical lens which is a part of cylinder. It is placed in a manner where its vertical axis is perpendicular to the axis of defective meridian.

4-Presbyopia:-

-This means that the near point of the eye is receding away due to some sort of fibrosis in the zonnule of the lens.

-It corrects a myopic but worsens the hypermetropic eye.

The iris

-It is the anterior part of the middle layer of the eye ball.

-Functions of the iris:-

1. Regulation of the amount of light that enters the eye.
2. Protection of the retina from the U/V rays.
3. It prevents the spherical and the chromatic aberrations

Miosis	Mydriasis
1-Near vision	1-Far vision
2-Light reflex	2-Withdrawal of the light.
3-Light adaptation	3-Dark adaptation
4-Sleep	4-Excitement
5-Parasympathetic stimulation	5-Sympathetic stimulation.
6-Parasympathomimetics as pilocarpine.	6-Parasympatholytics as atropine.
7-Sympatholytics.	7-Sympathomimetics as ephedrine.
8-Horner's syndrome	8-Occulomotor injury.
9- 1st and 3rd stages of anaesthesia	9-2nd and 4th stages of anaesthesia.
10-Toxicity of morphine	10-Toxicity of alcohol.

The light reflex:-

On exposure to light there will be papillary constriction of the directly exposed eye; the direct reflex and also in the other eye which is not directly exposed to light; the indirect or the consensual reflex.

Neurophysiology

Sense of position and movement

Proprioception or kinaesthetic sensation

-It is the ability of identification of the position and direction & rate of movement of the body with the eyes closed.

Point of view	Sense of position	Sense of movement
1-Definition	It is the ability of perception of the position of different body parts in relation to each other.	It is the ability of perception of the rate and direction of movement of different parts of the body.
2-The receptors	1-Touch receptors in the skin. 2-Deep receptors in the SC tissue as Pacinian corpuscle.	Deep receptors in the SC tissue as Pacinian corpuscle.
3-The pathway	The gracile and cuneate tracts	
4-Examination	One limb is put in one certain position and the subject is asked to put the other one in the same position	One limb is moved in a certain direction and e subject is asked to determine the rate and direction of movement

Thermo-receptive sensations

Point of view	Warmth sensation	Cold sensation
1-Receptors	-A specialized type of free nerve endings.	
	They are called Ruffini nerve endings. They are present in spots	They are called Krause's end bulbs. They are present in spots also but they are more in number(2-10 times more than warm spots)
2-The afferent fibres	C fibres	A delta fibres
3-The pathway	The lateral spino-thalamic tract.	
4-The discharge rate -The maximum rate	From 25-50 °C. At 37°C	From10-40°C. At 25°C
5-Adaptation	They are moderately adapting re captors.	
	-They are more rapidly adapting	-They are more slowly adapting
	-On adaptation there is a sense of thermo-neutrality.	
6-Mechanism of stimulation	-Rise of body temperature accelerates the metabolic rate,	-Drop of body temperature decelerates the metabolic rate, decreasing the concentration of

	increasing the concentration of metabolites which stimulates the warmth receptors.	metabolites which stimulates the cold receptors.
7-Functions	-Arousal of warm sensation	-Arousal of cold sensation
	-Information of the hypothalamus about the body temperature to regulate it.	
8-Examination	The skin is touched with test tubes filled with hot and cold saline.	

-The paradoxic cold sensation:-

Cause cold spots are more numerous and more superficial than the hot ones they are more easily stimulated. On exposure to degrees ranging from 45-50°C, false cold sensation arises and may result in cold pressor response of the CVS; tachycardia and hypertension.

-Weber's illusion:-cold objects are felt heavier.

Pain sensation

-Pain is a specific unpleasant sensation that arises due to tissue damage.

-It is a subjective sensation that is associated with measurable physiological changes in the heart rate and the ABP.

-General criteria of pain:-

1. It is a widely distributed sensation that involves the skin, deep structures and the viscera.
2. It is less localized than other types of sensations.
3. Its receptors have the following characteristics:
    a) They are naked or free nerve endings, they are called nociceptors.
    b) They are non-adapting or slowly adapting receptors.
    c) They are stimulated by the products of tissue damage which are released from the cells i.e. intrinsic allogenic substances as histamine, serotonin, AMP, ADP and bradykinin.
    d) They are further classified into mechanosensitive, chemosensitive and thermosensitive types according to the mode of tissue damage.
4. Pain is a specific sensation, the following are the evidences:-
    a) Over-stimulation of the retina does not cause pain sensation.
    b) The pulp of the teeth contains only the free nerve endings so that it is sensitive only to pain sensation.
    c) Pressure on a nerve trunk abolishes all type of sensations except pain.

d) Pressure on a nerve trunk can abolish the fast type of pain but leaves the slow type intact.
e) Some diseases abolish one type of pain sensation leaving the other intact e.g.Tabes Dorsalis abolishes fast but keeps the slow type of pain intact while syringomyelia abolishes pain leaving the fine sensations intact.
f) Analgesics as aspirin blocks one type of pain e.g. the slow type but doesn't affect the fast type of pain.
g) Anaesthetics abolish the fast type of pain leaving the slow type intact.

5. Pain has 3 main qualities; pricking, burning and aching.

1. Pain sensation is carried through the following nerves:-
   - From the thoraco-abdominal viscera by the sympathetic nerves.

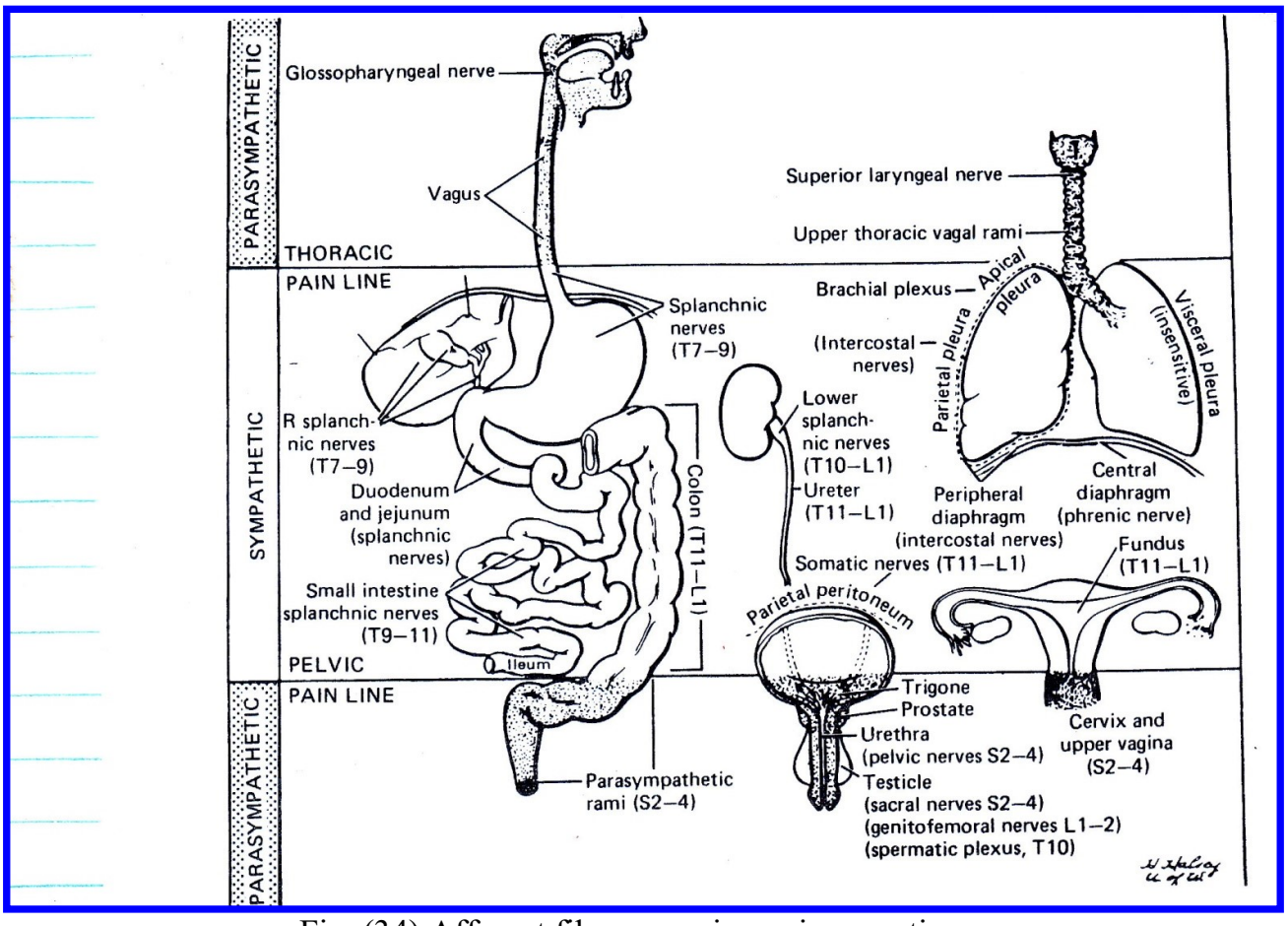


Fig. (34) Afferent fibres carrying pain sensation

   - From pharynx, larynx and trachea by the parasympathetic nerves IX &X.
   - From the pelvic organs by the pelvic nerve.
   - From the central area of the diaphragm by the phrenic nerve.

2. Pain is classically divided into 3 types; superficial (coetaneous), deep and visceral.

Superficial or coetaneous pain

-It is that type of pain that arises from stimulation of pain receptors in the skin.

-It is of 2 types; fast or immediate and slow or delayed pain.

Point of view	Fast or immediate pain	Slow of delayed pain
1-Timing	Immediately after the injury.	Delayed sometime after the injury.
2-Localization	Well localized	Diffuse.
3-Character	Sharp	Dull aching.
4-Type of conducting fibre	A delta	C fibre
5-Blocked by	Hypoxia	Cocaine
6-Effect of Tabes Dorsalis	Lost	Present.

-Cutaneous type of pain is associated with:-

- Somatic effects as flexion withdrawal reflex.
- Autonomic effects as changes of the heart rate or the ABP.
- Emotional effects as anxiety

-The dermatomal divisions of the skin:-

The dermatome is an area of the skin that is supplied by one dorsal horn cell.

Cutaneous hyperalgesia:-

-It is a pathological condition of the skin where non-noxious stimuli produce pain and the already noxious ones produces a more severe type of pain.

-Causes:-

1. Injury of the skin as in burns.
2. Inflammation of the skin.
3. Irritation of the dorsal root.
4. Deep or visceral diseases.

Point of view	Primary hyperalgesia	Secondary hyperalgesia
1-Site	In the injured area and the area of spreading flare.	In the area of health skin all around.
2-The threshold of pain	Decreased	Normal may be even increased.
3-Duration of the lesion	Longer	Shorter
4-Mechanism	*Sensitization* of the pain receptor by the release of intrinsic allogenic substances a histamine.	*Convergence facilitation theory:* -Afferents form both the health and the injured area converge

		on the same DHC. -Impulses from the damaged area facilitates the DHC which give more afferent discharge on arrival of the pain impulses from the healthy area.

Deep pain

-It is the type of pain that results from stimulation of pain receptors in the deep structures as tendons and ligaments.

-Criteria of the deep pain:-

1. It is dull aching or boring.
2. It is poorly localized, may be referred and is carried by the C type of fibres.
3. It is always associated with somatic, autonomic and emotional effects.
4. It is usually associated with cutaneous hyperalgesia.

-Causes of deep pain:-[SITU]

1. Spasm of muscles; it compresses the blood vessels leading to ischemia and pain.
2. Ischaemia due to accumulation of the pain factor which is K, bradykinin and lactic acid.
3. Trauma; as it stimulates the pain receptors in the periostium.
4. Underlying pathology of a deeper structure as in appendicitis.

Visceral pain

-It is a type of pain that results from stimulation of pain receptors in the visceral walls.

-It is the parietal layer of the pleura and the peritoneum that contains the pain receptors.

-It is the parietal layer of the pleura and the peritoneum that is sensitive to pain while their visceral layer is not.

-The parenchyma of organs is not sensitive to pain, including that of the liver, lungs and the brain.

-Criteria of visceral pain:-

1. It may be dull aching or colicky in nature.
2. It is poorly localized.
3. It is usually referred to other sites.
4. It is always associated with somatic, autonomic and emotional effects.
5. It is carried by the C type of nerve fibres.

-Causes of visceral pain:-[DISC]

1. Distension of a hollow viscus.

2. Ischaemia as that of the heart.
3. Spasm as that of the ureter.
4. Compression as that produced by a tumour.
5. Chemical injury as that induced by a peptic ulcer.

Referred pain

-Referral of pain is the feeling of pain sensation in a site other than its original site of production.

-Examples of referral of pain:-

1. Cardiac pain is felt in the area of the left shoulder and the sternum.
2. Ureteric pain is felt in the area of the groin, scrotal and inguinal area.
3. Billiary colicky pain is felt in the area of the right shoulder.
4. Acute appendicitis' pain is felt around the umbilical area.

Theories of pain referral:-

1-The DRG branching theory:

-One dorsal root ganglion divides into 2 branches; one supplies the viscous e.g. the heart and the other branch supplies a piece of the skin.
-Pain impulses from both of the viscous and the skin reach the same DRG, then to the same cortical neuron.
-The cerebral cortex is used to receive pain impulses from the parietal structures as the skin and muscles and from the internal viscera which are protected by the body walls.
-Once up on a time the cerebral cortex receives one pain impulse coming from the viscous, so it perceived it as coming from the skin and parities.

2-The convergence projection theory:-

-The afferent sensory nerves carrying pain sensation from both the skin and the viscous, both converge on the same posterior horn cell (PHC) in the substantia Gelatinosa of Rolandi. .

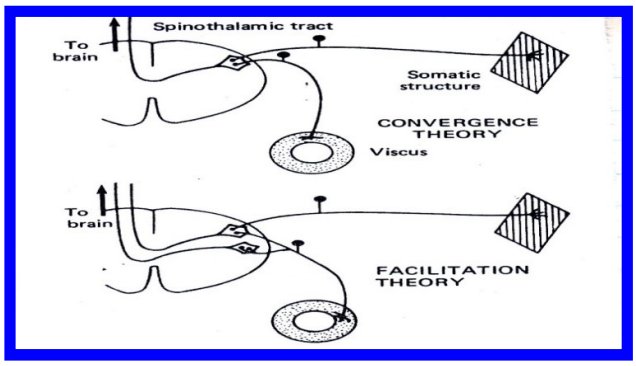


Fig. (35) the convergence projection theory

- The PHC send the pain afferent impulses to the same cortical neuron which is used to pain impulses coming from the parities and not the viscera
-When the viscous send pain impulses to the same PHC and then to the same cortical neuron, the latter perceived it as coming from the skin and parities and not the viscous.

The pain control or pain analgesia system

-Pain is an unpleasant sensation that is associated with a lot of body changes including somatic, autonomic and emotional changes. That is why there is a number of mechanisms that limit the perception of this sensation; this include the following:-

1. High threshold for pain sensation.
2. There is a sensory version of the all or none law which the pain sensation follows which means that if the injurious stimulus is strong enough it will induce pain and if not (minimal) it will not produce the sensation.

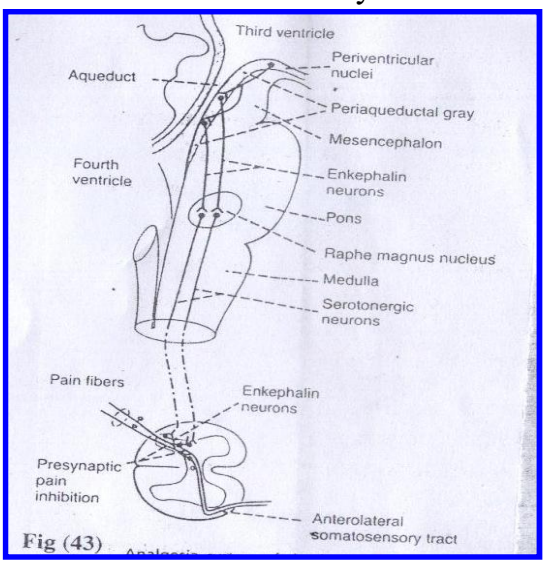


Fig.(36) the pain analgesia system.

3. The pain analgesia or the pain control system.

The Pain analgesia system

-This is composed of the following:-

A- The periaqueductal grey area.
B-The Raphe Magnus nucleus.
C- The pain inhibitory complex.

A)The Periaqueductal grey area:-

1-It is located in the midbrain.
2-They have high opiate affinity.
3-They are activated by the hypothalamus and the limbic system during stress and emotions.
4-Their axons secrete *Enkephalins* and terminate on the Raphe Magnus nucleus.

B) The Raphe Magnus nucleus:-

1-It is located in the lower pons and the upper medulla.
2-Their axons secrete *Seretonin* terminating on the Pain Inhibitory Complex (PIC).

C) The Pain Inhibitory Complex (PIC):-

1-This is a group of short neurons inside the spinal cord. Their axons end on the central ends of the A delta fibres and the C fibres.
2-They secrete Enkephalins.
3-They block pain transmission by pre-synaptic inhibition through Ca channel blockage, they prevent the release of the chemical transmitter for pain from the endings of these A delta and C fibres.
4-The analgesia may last for minutes up to hours.

5-They can block local cord reflexes that follow pain sensation.

-The feedback control of the pain analgesia system:-

When pain impulses enter the spinal cord they ascend from the 2nd order neuron to the thalamus through the lateral spin thalamic tract which give collaterals to the peri-aqueductal grey area which in turn stimulate the Raphe Magnus nucleus and so on.

Significance of the pain analgesia system:-

1. Stress analgesia:-During stressful situations as in wars, the hypothalamus and the limbic system are stimulated sending efferent impulses to activate the peri-aqueductal grey area, Raphe Magnus nucleus and the pain inhibitory complex. They in turn inhibit pain transmission.
2. Explains the subjective variations of pain sensation
3. Explains the voluntary control of pain sensation as in Yougi players

-The gate control theory of pain sensation:-

1- Synapses for pain are considered as gates for pain transmission.

2-These gates are located in the spinal cord, the reticular formation and the thalamus.

3-Pain sensation could be blocked at the spinal gate either by the descending impulses from the pain analgesia system or by competitive inhibiting impulses in the nearby afferents A delta or A Beta fibres. The 1st type can compete with pain using counter-irritation and acupuncture while the 2nd type carrying rubbing or scratching sensation.

Sensations from the Head

-Sensations from the head region are carried by the trigeminal nerve and the sensory root of the 2nd and 3rd cervical spinal nerves.

-An arbitrary line is drawn from the chin, passing through the tragus of the ear and ends at the vertex. In front of this line, the sensations are carried out by the trigeminal nerve, while behind it is the function of the 2nd and 3rd cervical nerves.

Headache

-It is considered as one type of referred pain where pain is felt in the head while its original site is located somewhere else; either inside or outside the cranium or even inside the thoracic or abdominal viscera.

-The original sites of headache:-

1-The intracranial pain sensitive structures:-

1. The cerebral arteries.
2. The venous sinuses.
3. The cranial nerves V, IX& X.
4. The Dura of the anterior and the posterior fossae.

N. B. The intracranial pain insensitive structures:-

1. The brain.

2. The Pia matter.
3. The Arachnoid matter.
4. The falx and tentorium cerebelli.
5. The floor of the middle fossa.

- Pain from structures above the tentorium is referred to the frontal area of the head.
- Pain from structures below the tentorium is referred to the occipital area of the head.

2-The extra-cranial sources of headache:-

1. Sinusitis.
2. Rhinitis.
3. Errors of refraction.
4. Otitis media.
5. Impulses from the thoracic and abdominal viscera.
6. Constipation.

-Mechanisms of the intracranial headache:-

1. Arteries:-dilation, distension and traction.
2. Veins:-traction.
3. Pain sensitive structures:-inflammation.
4. Cranial nerves:-traction or compression by tumours.

Causes of the intracranial headache:-

1-Inflammatory headache:-

-It occurs in case of inflammation of the meninges e.g. meningitis headache.

-It is severe type of headache, surrounding the head all around.

-It also occurs after traction of the meninges as in surgery.

2-Neoplastic headache:-

-It occurs in case of brain tumours due to compression or traction on one of the pain sensitive structures.

3-Low intracranial pressure headache:-

-It occurs in case of lumber puncture if more than 20 ml of the CSF is aspirated.

-It is increased on standing due to vasodilation.

-The treatment is saline injection

4-High intracranial pressure headache:-

-It occurs due to arterial distension.

-It is a pulsating type of headache.

5-Chemical induced headache:-

-It may occur due to histamine, alcohol or the presence of toxins in the blood.

6- The most common cause of headache in adults is psychogenic.

The basal ganglia

-They consist of the following nuclei:-

1- The caudate nucleus.

2- The lentiform nucleus; which consists of 2 further sub divisionary nuclei; ***the putamen and the Globus pallidus.***

N.B. the caudate nucleus and the putamen are sometimes called together the corpus striatum.

3- The amygdaloid nucleus.

4-The claustrum.

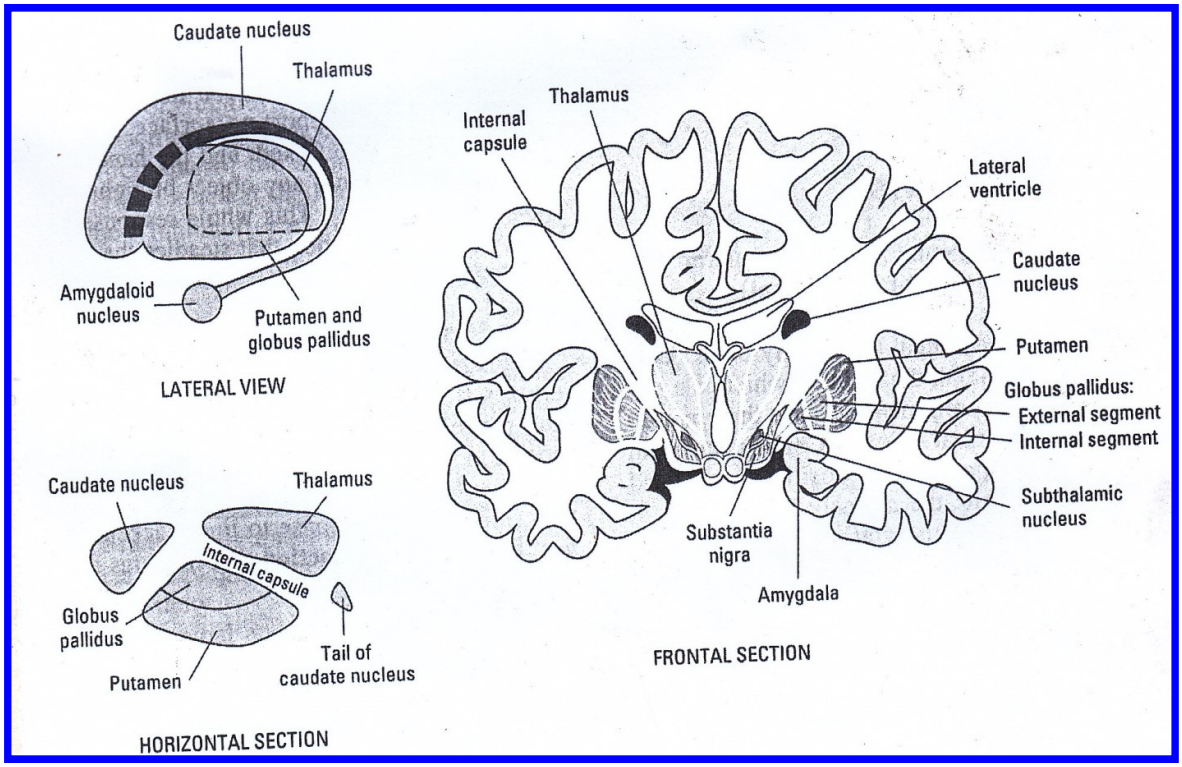


Fig. (37) the basal ganglia

-The neurotransmitters in the basal ganglia:-

They are excitatory as Acetyl choline and norepinephrine or inhibitory as dopamine.

The normal function needs some sort of a balance between the both.

Functions of the basal ganglia:-

1-In the lower animals they act as the 1ry motor area.

2-In humans:

a) They contain the plans and programs of the learned and familiar movements in the putamen circuit.
b) The cognitive function of the caudate circuit:
The caudate circuit can transform the ideas and thoughts into multiple successive patterns of movements.
c) Timing and scaling of movements.

d) The caudate nucleus is excitatory to the muscle tone while the lentiform is inhibitory. Diffuse stimulation of the basal ganglia results in inhibition of the muscle tone.

The Parkinson's disease:

-It is also called paralysis Agitans.

-Manifestations :-(RAT)

(A)Rigidity:-

a) It is hypertonia that is encountered although the movement.
b) It affects flexors more than extensors leading to generalized flexion attitude.
c) It is of 2 subtypes; lead pipe and cog wheal:
   -In lead pipe rigidity the hypertonia is equal although the movement.
   -In cog wheal the hypertonia is NOT equal although the movement.

(B) Akinesia:-

a) It is 2ry to rigidity.
b) The gait becomes short stepping i.e. shuffling gait.
c) The speech becomes slow and monotonus.
d) There is loss of the habitual, associative and expressive movements i.e. the body language is no more existent.
e) There is mask face due to rigidity of the muscles of the face.

(C) Tremors:-

a) They are fine rhythmic oscillatory movements.
b) They occur at a rate of 2-5/sec.
c) They are alternating flexion and extension affecting the distal joints, leading to the appearance of the pill rolling movements of thumb and index fingers.
d) They are static; they disappear during movements and sleep, but increased with emotions.

The hypothalamus

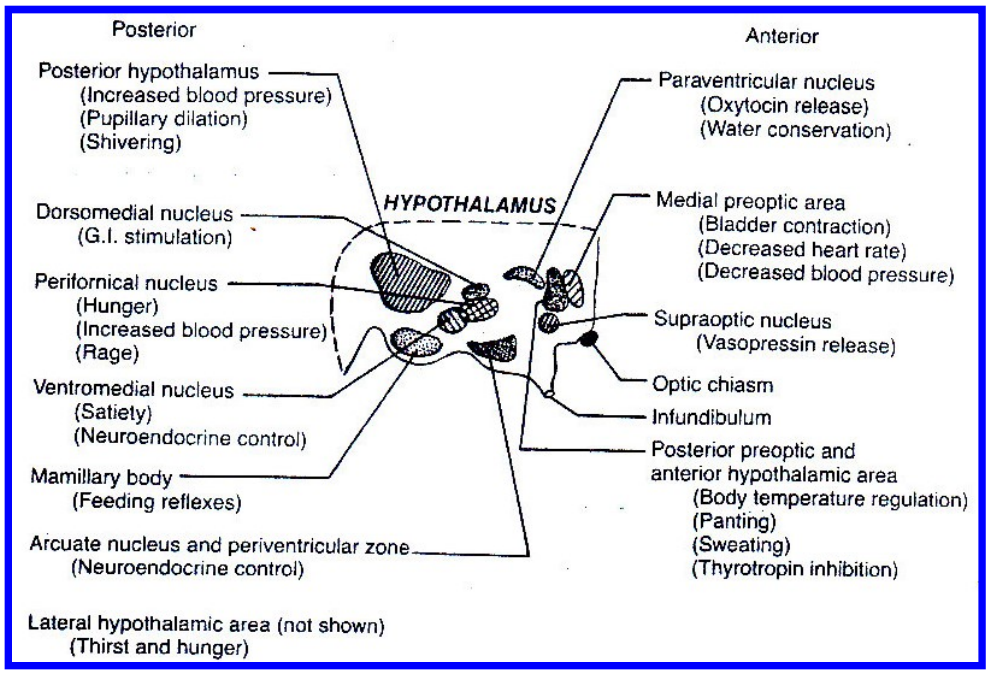


Fig (38) the hypothalamic nuclei

The hypothalamic functions are summarized as follows:-

1. <u>Cardiovascular& Autonomic functions:-</u>

-The post. And lateral hypothalamus are considered as higher sympathetic centres, so on stimulation of these centres they produce sympathetic like effects as tachycardia, rise of the blood pressure and mydriasis.

-The antero-lateral part of the hypothalamus acts as a higher centre for the parasympathetic system , so on stimulation of these centres they produce parasympathetic like effects as bradycardia, hypotension and miosis.

2. <u>Endocrine function:-</u>

A-The hypothalamus secretes releasing and inhibiting factors that controls the release of the trophic hormones of the anterior pituitary gland.

B-The supra-optic and the paraventricular hypothalamic nuclei secrete the antidiueretic hormone and oxytocin which are actually released from the posterior pituitary.

C-On exposure to cold weather the hypothalamus stimulates the adrenal medulla to secrete more adrenaline for energy production.

3. <u>Regulation of body temperature:-</u>

-There are 2 centres or areas in the hypothalamus that regulate the body temperature; the heat gain and the heat loss centre.

-The heat gain centre is located in the dorsomedial nucleus of the hypothalamus.

-It is also called the 1ry motor centre of shivering. On exposure to cold weather it stimulates shivering and the release of thermogenic hormones as adrenaline and thyroxine.
-The heat loss centre is located in the anterolateral part of the hypothalamus; when exposed to hot weather it stimulates sweating and cutaneous vasodilation.

4. Regulation of body weight:-

-There are 2 centres that regulate food intake; the feeding or the hunger and the satiety centres.
-The feeding, the hunger or the weight gain centre is located in the lateral hypothalamus, when stimulated by hypoglycaemia or hyper-insulinaemia it stimulates food intake.
-The satiety centre is located in the medioventral nucleus of the hypothalamus. On stimulation by hyperglcaemia, hypoinsulinaemia, release of GIT hormones and calcitonin it inhibits he feeding process.

5. Regulation of body water:-

-The lateral hypothalamus contains the thirst centre which is stimulated by either hyperosmolarity or hypovolaemia to drive the subject to drink water.
-The supraoptic nucleus of the hypothalamus secretes the antidiuretic hormone which stimulates the absorption of water from the kidneys .

6. Control of sleep:-

-The hypothalamus plays an indirect role in the physiology of sleep where the reticular activating system passes through the posterior portion of the hypothalamus.

7. Control of emotions:-

-The hypothalamus is responsible for the emotional expression, the sense of reward and punishment.
-It is responsible for the fear reaction. The ablation of the ventromedial nuclei results in sham rage reaction.

8. Control of cyclic phenomenon:-

The supraoptic nuclei which are connected to the retina receives information about light and darkness and through which it regulates various rhythmic changes.

-The hypothalamic lesions:-

1-The lateral hypothalamus:
   a) Decreased eating and drinking.
   b) Extreme passivity.

2-The ventromedial hypothalamus:-
   a) Excessive drinking and eating.
   b) Extreme rage.

3-The posterior hypothalamus:-
   a) Decrease of body temperature.

b) Decrease of body activity.
c) Sleep.

4-The supra-optic nucleus:-
This leads to diabetes insipidus.

The Limbic System

-The limbic system comprises a group of nuclei located at the limbus between the old and the new cortex.
-It forms one functional unit together with the hypothalamus.

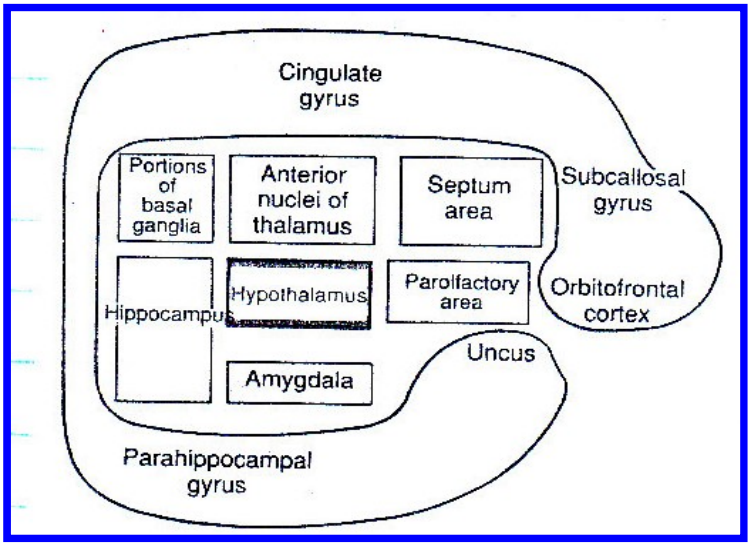


Fig. (39) The limbic system

Functions of the limbic system:-

1. Reward and punishment:

- The reward centre is located in the lateral and ventromedial hypothalamic nuclei.
- The punishment centre is located in periventricular hypothalamic nucleus.
- The reward centre when stimulated produces a state of reward; pleasure and satisfaction.
- The punishment centre when stimulated produces a state of displeasure and fear.
- They are important in:-

a) Behaviour.
b) Memory and learning.

2. Motivation:

-It is the force that drives someone to do something.
-The centre is located in the limbic association area.

3. Behaviour:-

- The amygdaloid nucleus is concerned with sorting out the type of food.

- The sexual behaviour is controlled by the limbic system.

4. Emotions:

- Strong stimulation of the punishment centre leads to rage.
- Strong stimulation of the reward centre; the ventromedial area leads to placidity.
- Fear results from less potent stimulation of the punishment centre.

5. Olfaction:

The limbic system is concerned with perception and discrimination of the variety of olfactory stimuli.

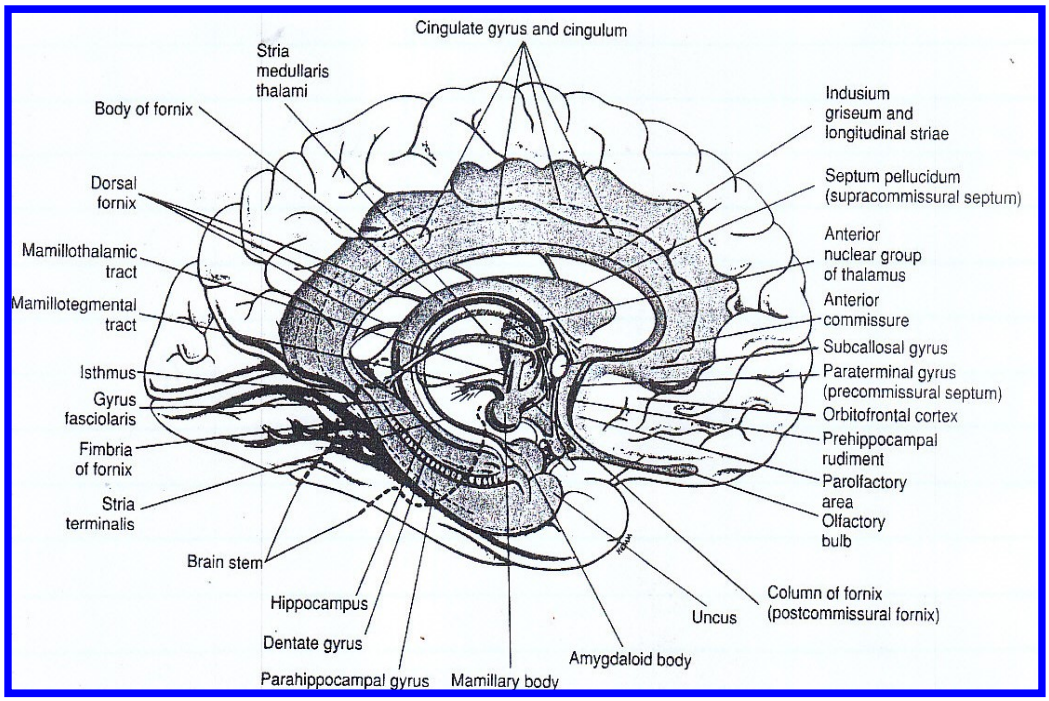


Fig (40) the limbic system

The Reticular Formation

-Definition:-

It is a complex interlacing network of nerve cells and nerve fibres that extends in the central region of the brain stem and the spinal cord.

-Connections:-

It receives afferent connections from the following structures:-

1. Collaterals from the ascending sensory pathways.
2. Collaterals from the auditory, visual and olfactory pathways.
3. The cerebellum, basal ganglia and the cerebral cortex.

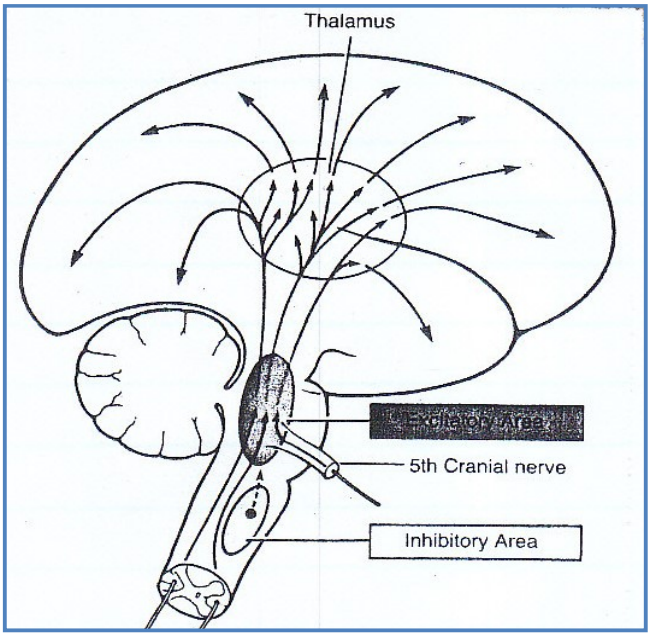


Fig. (41) the reticular formation

-The ascending reticular activating system (ARAS):-

It is a polysynaptic pathway that arises from the reticular formation sending excitatory impulses to all areas of the cerebral cortex.

Functions:-

1. It is responsible for the alert and conscious state.
2. Affects the electrical activity of the brain.
3. Regulation of :-
    a) Attention, emotions and conditioning of reflexes.
    b) The skeletal muscle tone.
    c) The ANS functions.
    d) The sensory input.

-Factors affecting the ARAS:-

Decreased activity	Increased activity
1-Sleep	1-Motor and sensory activity
2-CNS depressants	2-CNS stimulants
3-Tumours	3-Emotions