6th Semester zoology

BSc zoology

PHYSIOLOGY AND ENDOCRINOLOGY

2019 admission onwards

Prepared by

Fathimath Raseena Padikkal

Guest lecturer

Zoology department

CPA College of global studies. puthanathani

SIXTH SEMESTER B.Sc. ZOOLOGY PROGRAMME
ZOOLOGY CORE COURSE – IX [Theory]
PHYSIOLOGY AND ENDOCRINOLOGY
Code: ZOL6B10T
[54 hrs] [3 hours per week] [3 credits]

equipping with excellence

SECTION A: PHYSIOLOGY (36 HOURS)

MODULE 1. Nutrition (5 hrs)

Regulation of digestive activity: Nervous and hormonal control; Ruminant digestion; Nutrition in pregnancy, infant nutrition, breast feeding, composition of breast milk; importance of dietary fibres; Balanced diet; Nutritional disorders: anorexia, acidity, ulcer, flatulence; starvation, fasting and its significance; Obesity: causes and consequences.

MODULE 2. Respiration (6 hrs)

Gaseous exchange and transport of respiratory gases (brief account), Oxygen- Haemoglobin dissociation curve; Respiratory pigments, structure and properties of Hb; Neurophysiological control of respiration; Physiological problems in diving mammals, new-born and aged individuals.

MODULE 3. Circulation (6 hrs)

Blood: functions and composition; Coagulation of blood (Enzyme cascade theory); Clinical analysis of blood, ESR; Haemodynamics; Haemostasis, haemolysis and jaundice, haemoglobinopathies; Blood transfusion and agglutination, aphaeresis. Types of heart; ECG; Common cardio-vascular problems: Abnormal variations in BP, Tachycardia, Bradycardia, Myocardial infarction, heart failure, cerebral hemorrhage and cerebro-vascular accident.

MODULE 4. Osmoregulation and Excretion (6 hrs)

Osmoconformers and osmoregulators; Water conservation in desert forms; Osmotic and ionic regulation in terrestrial, fresh water and marine animals;
Types of excretion, urea cycle; Human kidney: Urine formation with counter-current mechanism and hormonal regulation; Common renal disorders: haematuria, uremia, proteinuria, renal hypertension, nephritis, renal calculi, oedema, acidosis and alkalosis; Dialysis.

MODULE 5. Muscle Physiology (5 hrs)

Structure of vertebrate skeletal muscle: EM structure of Myofibrils and Myofilaments, contractile proteins; Mechanism of muscle contraction: Ultra structural changes (sliding filament theory); physiology, biochemistry and energetics of muscle contraction; energy sources, role of creatine phosphate, cori cycle; Muscle twitch, fatigue, tetany and rigor mortis.

MODULE 6. Nerve Physiology (6 hrs)

Different types of nerve cells; glial cells, giant nerve fibre of crustaceans and cephalopods; regeneration of medullary fibres, neurotrophins; Nerve impulse transmission, synapses and neuromuscular junctions, synaptic transmission (electrical and chemical), neurotransmitters.

MODULE 7. Bioluminescence and Bioelectricity (2 hrs)

Classification of bioluminescence: symbiotic, extracellular and intracellular;
Physiology and significance of light production; Structure and functions of electric organs.

Section B: ENDOCRINOLOGY (18 hrs)

MODULE 8. Invertebrate and Vertebrate endocrinology (12 hrs)

Neuro- endocrine organs and hormones in crustaceans and insects.
Classification of hormones: Amine, peptide and steroid hormones; Endocrine glands in man (hypothalamus, pituitary, thyroid, parathyroid, pancreas, adrenal, thymus, pineal and gastro-intestinal): their hormones and functions (brief account); Hormonal disorders.
Hormones of reproduction: Testes, ovaries and placenta, their hormones and physiological effects; role of hormones in female sexual cycle; hormone related female and male sexual dysfunctions.

MODULE 9. Concept of neurosecretion and hormonal action (6 hrs)

Hypothalamus-hypophysial interactions, hypothalamus releasing and inhibiting hormones and their roles, Neuro-hormonal integration, Neuro-endocrine pathways, Regulation of hormone secretion. Hormonal action :Hormone receptors; Mechanism of action of peptide and steroid hormones; mode of action of insulin and thyroxine; positive and negative feedback regulation.

equipping with excellence
CPA COLLEGE OF GLOBAL STUDIES

equipping with excellence
CPA COLLEGE OF GLOBAL STUDIES

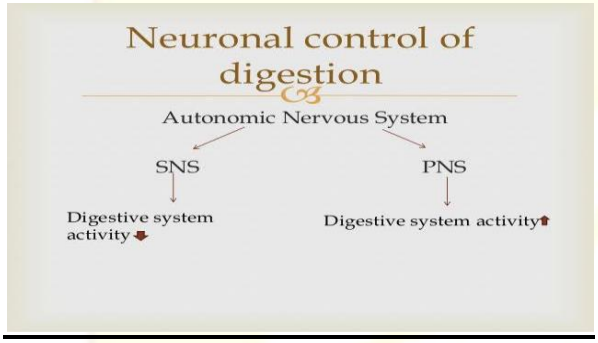
SECTION A: PHYSIOLOGY

MODULE 1. NUTRITION

REGULATION OF DIGESTIVE ACTIVITY

- The digestive activities in the gastro- intestinal tract are under neural and hormonal regulation.

NERVOUS CONTROL OF DIGESTION



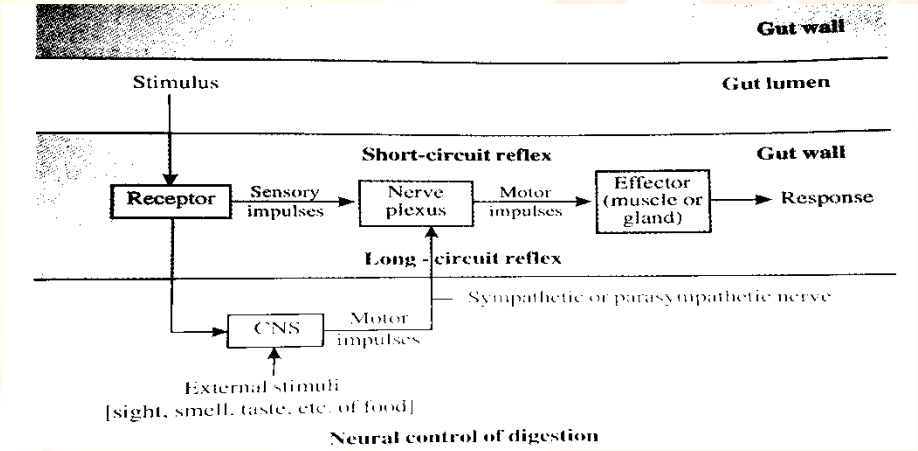
- Gut wall is innervated by *intrinsic* and *extrinsic nerves*
- Intrinsic forms the *enteric nervous system (ENS)*
- ENS consists of 2 plexus :
    - Outer *myenteric plexus*
    - Inner *sub-mucous plexus*

MYENTERIC PLEXUS	SUB – MUCOUS PLEXUS
• Formed by intrinsic nerves	• Formed by extrinsic nerve
• Located in between the longitudinal and circular muscles	• Located in the sub-mucosa
• Controls gastro-intestinal peristaltic movements	• Controls gastro-intestinal secretions

- Extrinsic nerves includes ,

- *Sympathetic systems*
- *Para sympathetic system*

- Extrinsic nerves enter the gutwall and forms synapse with the neurons of *myenteric* and *sub-mucosal plexus*
- Sympathetic innervations : inhibits motility of the gut wall
- Parasympathetic innervations : stimulates motility
- *Basic electrical rhythm (BER)* determines the rhythm and frequency of gastric contraction
- 2 types of reflexes :
  - Short-circuit reflexes : impulses follow a receptor ⟶ nerve plexus ⟶ effector route
  - Long-circuit reflexes : impulses follow a receptor ⟶ CNS ⟶ nerve plexus ⟶ effector route



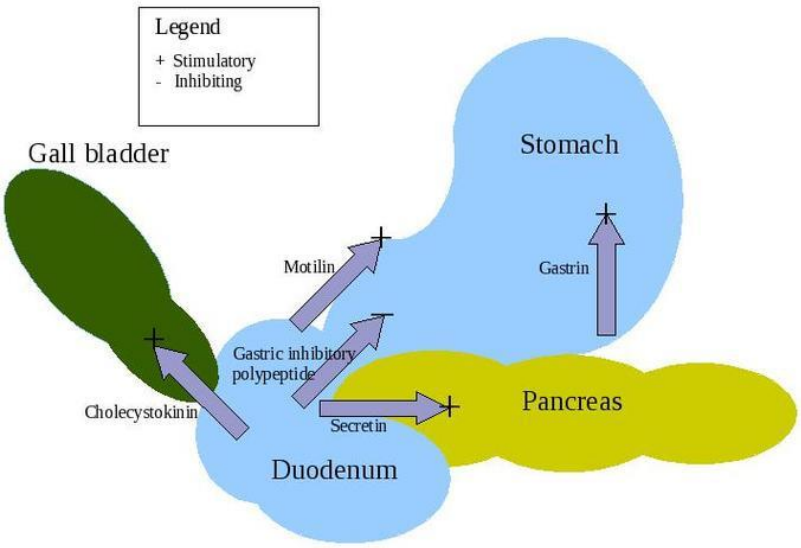
Neural control of digestion

HORMONAL CONTROL OF DIGESTION

5 major hormones that control digestion :

- Gastrin is in the stomach and stimulates the gastric glands to secrete pepsinogen (an inactive form of the enzyme pepsin) and hydrochloric acid. The secretion of gastrin is stimulated by food arriving in the stomach.
- Secretin is in the duodenum and signals the secretion of sodium bicarbonate in the pancreas and it stimulates the secretion of bile in the liver. This hormone responds to the acidity of the chyme.
- Cholecystokinin (CCK) is in the duodenum and stimulates the release of digestive enzymes in the pancreas and stimulates the emptying of bile in the gallbladder.
- Gastric inhibitory peptide (GIP) is in the duodenum and decreases stomach churning in order to slow the emptying of the stomach. Another function is to induce insulin secretion.

- Motilin is in the duodenum and increases the migrating myoelectric complex component of gastrointestinal motility and stimulates the production of pepsin



GASTRO-INTESTINAL HORMONES AND THEIR FUNCTIONS.

- Gastro-intestinal hormones are the hormones secreted by the gastro-intesinal tract.
- They include gastrin, secretin, enterogastrone, cholecystokinin or pancreozymin (CCK or PZ), duocrinin, villikinin, enterocrinin, gastric inhibitory peptide (GIP), vasoactive intestinal peptide (VIP), motilin, chymodenin, etc.

1. Gastrin

- Gastrin is not, in fact, a single hormone, but is a family of at least six structurally similar polypeptides.
- They fall into two chemical groups, namely little gastrin (G-17) and big-gastrin (G-34).
- The former has 17 amino acid residues, and the latter has 34 amino acid residues.
- Gastrin is secreted by the pyloric and duodenal mucosa. *There are two kinds of gastrin, stomach gastrin and intestinal gastrin.
- Gastrin produces excitatory effects and governs the balanced production of HCl.
- It stimulates the secretion of pepsin and HCI,promotes the secretion of HCO, by pancreas and liver, constricts the lower oesophageal sphincter, increases the frequency and velocity of BER, enhances the motility of the gastro intestinal tract, and relaxes pyloric and ileo-caecal sphincters.
- High concentrations of HCI inhibit and low concentrations stimulate gastrin production

2. Secretin

- Secretin is produced by the duodenal and jejunal mucosa. *It counters the effects of gastrin, relaxes the lower oesophageal sphincter, inhibits the secretion of gastric juice, decreases the motility of the GI tract, and stimulates the secretion of primary pancreatic juice, intestinal juice and bile.
- Primary pancreatic juice has low enzyme content, but has high levels of sodium bicarbonate ions.
- This is significant in the neutralisation of chyme.

3. Enterogastrone

- Enterogastrone is secreted by the duodenal and jejunal mucosa.
- It is carried to the stomach by blood stream.
- It inhibits the production of gastric juice and HCl.

4. Cholecystokinin

- Cholecystokinin (CCK), also called pancreozymin (PZ).
- It is secreted by the duodenal and jejunal mucosa.
- It inhibits the secretion of gastric juice, stimulates the secretion of the intestinal juice and the enzyme-rich secondary pancreatic juice, decreases the motility of the GI tract, stimulates the contraction of gall bladder and the discharge of bile, and stimulates the relaxation of the hepatopancreatic sphincter

5. Duocrinin and villikinin

- These are secreted by the duodenal mucosa.
- Duocrinin stimulates the activity of Brunner's glands.
- Villikinin stimulates the movement of villi.

6. Enterocrinin

- Enterocrinin is secreted by the mucosa of jejunum and ileum.
- It stimulates the activity of intestinal digestive glands and thereby increases the production of succus entericus (intestinal digestive juice).

7. Gastric inhibitory peptide (GIP)

- GIP is a peptide hormone.
- It is secreted by the duodenal and jejunal mucosa.
- The presence of glucose and fat in the duodenum induces its production.
- GIP inhibits the secretion of gastricjuice, decreases the motility of the GI tract and stimulates the production of insulin.

8. Vasoactive intestinal peptide (VIP)

- VIP is a polypeptide neurohormone, produced by the vasomotor nerve fibres in the Gl tract.
- It stimulates the secretion of the electrolytes-rich intestinal juice, the gastric secretion of HCI, stimulates the relaxation of the smooth muscles of the intestine, and serves as a peripheral vasodilator.

9. Motilin

- Motilin is a polypeptide hormone.
- It is secreted by the duodenal mucosa.
- It stimulates gas tric secretion and induces the contraction of the smooth muscles of the intestine.

10. Chymodenin

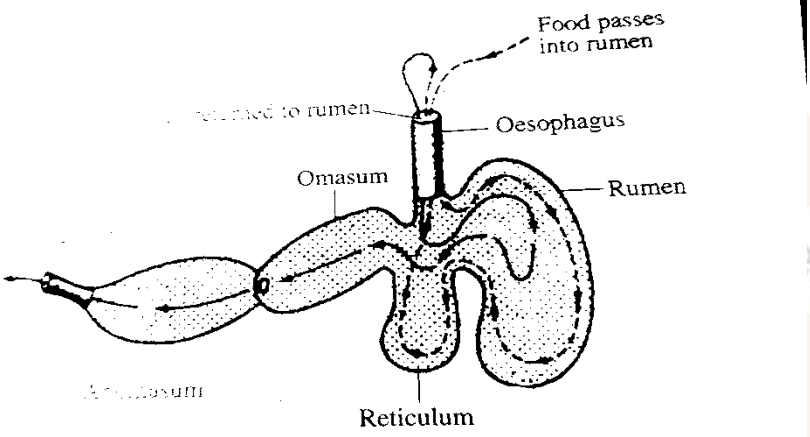
- Chymodenin is a peptide hormone.
- It is secreted by the duodenal mucosa.
- It stimulates the selective secretion of chymotrypsinogen by pancreas.
- Some other hormones are also believed to regulate digestive activity.
- They include bombesin, nearotensin, somatostatin, etc.
- The source of **bombesin** is not known
- It promotes gastric secretion, contraction and emptying of gall bladder and the motility of small intestine.
- **Neurotensin** is secreted by the motor neurons of the enteric nervous system.
- It inhibits the motility of the GI tract.
- **Somatostatin** is a hypo thalamic hormone, which inhibits the pituitary growth hormone.

- It may be brought to the GI tract also where it inhibits the secretion of gastric and pancreatic juices and some gastro intestinal hormones (secretin, motilin, GIP and VIP), decreases intestinal motility, and increases the contractility of gall bladder.

RUMINANT DIGESTION

equipping with excellence

- Ruminants are cud- chewing herbivorous mammals
- They include camels, cattle, sheep, goats, deers, antelopes, gazelles, giraffes
- They have a highly specialized chambered or compound stomach, especially modified for rumination and cellulose digestion
- Ruminant stomach has four chambers, namely rumen, reticulum, omasum and abomasum
- Rumenis the first and the largest chamber of the ruminant stomach
- It harbours symbiotic bacteria, yeasts, and ciliate protozoans, which help in cellulose digestion
- Rumen serves as a fermentation vat, as a centre of cellulose digestion, and also as a storage chamber
- Abomasum is the second largest chamber and it functions as the true digestive stomach
- It secretes digestive enzymes for gastric digestion
- The other chambers do not secrete digestive enzymes
- Rumination, or cud- chewing is a special adaptation for cellulose digestion
- The partly digested food in the stomach is regurgitated re-masticated and swallowed again for final digestion
- In rumination, animal swallows fresh food without proper mastication this food reaches the rumen and remains there for some time
- Heavy fermentation follows and the enzymes secreted by symbiotic bacteria and protozoans break down cellulose
- They will be absorbed directly and utilized by the animal
- Most CO_2 and CH_4 formed during fermentation, will escape by belching
- The partly digested food slowly moves from rumen to reticulum , here it gets into small balls, called cud
- Later, at rest the animal regurgitates cud and swallows it again . this is rumination
- In omasum, most of the water and some salts are absorbed
- Abomasum, the true digestive stomach, secretes digestive enzymes for gastric digestion



Ruminant stomach showing pathways of food movement

NUTRITION IN PREGNANCY

- Pregnancy is just a physiological phase, characterized by rapid growth of both mother and foetus
- During pregnancy, mother and foetus require rich and regular supply of nutrients
- Poor maternal nutrition during pregnancy, may cause the depletion of mother's food reserves and the low birth weight of the baby
- It may also cause the low vitality and premature death of the baby
- Before and during pregnancy, a women needs sufficient nutrients for maintenances, for the development of breasts, uterus and placenta, and also for the formation of the amniotic fluid
- She want to supply enough nutrients for the intrauterine growth and development of the foetus
- A full term pregnant women must gain 10-12 kg of weight
- Underweight of a pregnant women may leads to the small size and low birth weight of the child, such infants are prone ti infectious diseases and has high mortality
- Overweight at the beginning, or during second and third trimester , may leads to ***eclampsia*** (convulsion or coma during pregnancy)
- The recommended weight gain is 1.5 during first 3 months, and 1.5 or a little more during last 6 months.
- Sudden gain or loss of weight during pregnancy is harmful
- Nutritional deficiencies commonly 0ccur with respect to Ca, Fe, phophates and vitamins

- Deficiency of calcium, phosphates and vitamin D hampers the normal development of bones and teeth in foetus
- Iron deficiency leads to low RBC count, low Hb content, and anaemia in mother and child
- Defiency of vitamin K affects blood clotting

Dietary Recommendations

- An extra intake of 300 kcal per day is necessary during second and third trimester of pregnancy
- This could be satisfiedby addition of 35 gms of cereals and 10 gms of sugar or jiggery
- During pregnancy, an increased intake of proteins is essential for the development of placenta and foetus and also for maternal tissues
- An additional intake of 14 gms of protein is sufficient
- This extra protein demand can satisfied by addition of 100 gms of milk and 15 gms of pulses to normal diet
- A normal diet can satisfy fat requirements of foetus. The liver and brain of the foetus contain phospholipids, which are rich in essential fatty acids. So extra intake of fat is required
- A pregnant women requires sufficient supply of calcium, phosphorus, iron, iodine
- Calcium and phosphorus are essential for the strengthening the bones and teeth of developing foetus
- Iron is essential for the formation of haemoglobin, needs 400 mg of iron for formation of haemoglobin, and 250 mg for foetus
- For this additional 8 mg of iron / day is recommended
- Iron is also supplied for the synthesis of thyroxine and also for the prevention of goiter in both the mother and baby
- All vitamins are required in sufficient quantities during pregnancy for normal growth and metabolism in mother and foetus
- Vitamin K is especially important for the formation of prothombin in the baby to prevent haemorrage caused by birth process
- Vitamin D is essential for proper absorption of calcium by foetus from mother
- In pregnant women, 5-6 small feeds with regular intervals are desirable
- Leafy veggies, fruits, and fluids are better
- Rich, highly spiced and fried foods, rich gravies, heavy desserts and excessive salts and condiments must avoided
- Sugar must be substituted by jiggery, since it contains more iron

equipping with excellence
PRO COLLEGE OF GLOBAL STUDIES

Food item	Quantity per day
1. Cereals	475 gm
2. Pulses	55 gm
3. leafy veggies	100 gm
4. other vegitables	40 gm
5. roots and tubers	50 gm
6. milk and milk products	250 gm
7. oils and fats	40 gm
8. fruits	60 gm
9. sugar and jiggery	40 gm

INFANT NUTRITION

- infancy is a physiological important stage in the life of humanbeings
- it is characterized by rapid growth, profound changes in the body composition, biochemical and physiological maturation of body, accelerated internal activities and high BMR
- an infant needs all nutrients in sufficient quantities
- during early infancy, the secretion of pancreatic amylase is very low, the intestinal absorption of fats occurs at a low rate, and synthesis of proteins from aminoacids is most efficient
- the consumption of starch rich food must reduced, and consumption of protein rich food is recommended
- an infant has high needs of calcium, vitamin D, and iron
- calcium is for ossification and strengthening of bones and teeth
- vit. D promotes the intestinal absorption of calcium, and deficiency leads to Rickets
- iron is essential for the formation of blood cells and synthesis of haemoglobin
- the birth-weight of a normal new-born baby gets doubled by the fifth month, and tripled by 12^{th} month, provided all nutrients are available in sufficient amounts
- a lactating mother can successfully breast feed her baby during the first 3 or 4 months
- beyond that period, breast milk alone will not be sufficient and so the baby needs supplementary food supply
- malnutrition impairs the physical growth and health and the mental and intellectual development of the baby and adversely affects its immune powers
- infant in the age group of 0 to 3 months require 120 kcal of energy and 2 gm of protein every day per 1 kg of body weight
- an average mother can produce 420 kcals and 7.2 gm of protein

BREAST FEEDING

- breast feeding is a complete and balanced food for a baby during the first few months of their life
- new born baby depends heavily on breast feeding for some time for its sustenance and growth
- breast feeding is significant in two ways
  - **I.** It supplies the baby almost all nutrients in sufficient quantitiesand transfers to it maternal antibodies to provide immunity against infections
  - **II.** It reduces the chances for mastitis and malignancies in the mother
- Human milk is more watery than the milk of cow, buffalo, goat and sheep
- Its nutritive value is higher than that of cow's or buffalo's milk
- Its major contents includes water (88.5%), fat (3.3%), lactose(6.8%), casein (0.9%), lactalbumin and other proteins (0.4%), and calcium (0.2%)
- Other constituents include fats, vitamins A, B1, B2 and C, Calcium, iron etc
- During first two days after birth, the mother secretes an yellowish fluid, known as ***colostrum,*** it is highly nutritious, and is a rich source of vitamin A and antibodies for baby

Advantages for the baby

1. Breast-milk is a complete and balanced food and it contains all the essential nutrients in the correct propotion required by the body. So far no suitable substitute has been formulated to replace it
2. Human milk is dilute and easily digestible and it forms the most ideal food for the baby during initial days
3. Breast milk supplies the baby not only the essential nutrients but also the maternal antibodies, that protect from infectious diseases
4. Milk allergy, constipation, gas formation and gastro-intestinal discomfort are less common in breastfed babies
5. Breast feeding provides the baby emotional security and a feeling of comfort and well being

Advantages for mother

1. Breast feeding and emptying reduces the risk of mastitis, breast cancer and ovarian cancer
2. Breast feeding reduces size of uterus to its normal size after delivery
3. It delays the resumption of sexual cycle and ovulation
4. It helps to establish a strong bond of love and affection between child and mother

5. Breast feeding provides the mother some relaxed time, free from tensions

Risks of insufficient breast feeding

1. High susceptibility to infectious disease
2. Higher chances for sudden infant death syndrome (SIDS)
3. Growth impairment

equipping with excellence

Composition of breast milk

The major contents of 100 ml of milk				
Contents	Human milk	Cow's milk	Buffalo's milk	Goat's milk
Proteins	1.2 gm	3.3 gm	3.8 gm	3.3 gm
Fats	3.8 gm	3.7 gm	8.5 gm	4.1 gm
Lactose	7 gm	4.8 gm	4.4 gm	4.7 gm
Vitamin A	48 µgm	47 µgm	60 µgm	36 µgm
Thiamine	0.02 mg	0.04 mg	0.05 mg	0.05 mg
Riboflavin	0.04 mg	0.18 mg	0.1 mg	0.12 mg
Vitamin C	4 mg	2 mg	2.5 mg	2 mg
Calcium	33 mg	125 mg	210 mg	130 mg
Iron	0.15 µgm	0.1 µgm	0.2 µgm	0.05 µgm
Caloric value	71 kcal	69 kcal	100 kcal	76 kcal

CHC COLLEGE OF GLOBAL STUDIES

IMPORTANCE OF DIETARY FIBRES

- Dietary fibres, commonly called roughage or bulk, are the polysaccharides and lignin of plant cell walls, which cannot be hydrolysed by the digestive enzymes of animals
- Their major components includes cellulose, hemicelluloses(xylans, mannans, arabinans, galactans), hexosans (fructosans, galactans), lignin, pectic compounds, gums and mucilages
- Cereals, pulses, tubers, green veggies, nuts, fruits etc are rich source of dietary fibres
- In mammals, fibres are believed to be digested by the enzymes secreted by some symbiotic bacteria inhibiting the large intestine
- The dietary sources, rich in fibres include legumes, bran of cereals, green leafy veggies, tubers etc

Significance of dietary fibres

- Some of Dietary fibres are water- soluble and they form a gelatinous bulk in water that can lower cholesterol
- Others are water insoluble and they add to the to the bulk of the stool
- Some dietary fibres undergo fermentation in colon, producing flatus and organic acids. These acids includes acetic acid, butyric acid etc. these acids are absorbed and utilized as a source of energy
- Dietary fibres absorb water and softens the faeces, promote intestinal peristalsis and bowel movement, bring about comfortable defaecation, prevent constipation
- Fibres influence the functioning of the colon by affecting the bulk, weight, composition and transit time of faeces
- Pectin fibres can lower the level of serum cholesterol and thereby prevent cholesterolemia, atheroscelorosis, and other cardiovascular diseases
- Fibres accelerate digestion and egestion and thereby help to sweep out harmful wastes evev before they cause problems in body
- High fibre contents expand the colon and render defecation easier
- Fibres increase the excretion of bile acids in stool
- Fibres help to prevent colon cancer by rapid elimination of faeces and also by binding and inactivation of carcinogenic chemicals

Deficiency of dietary fibres

i. **Colonic diseases:** constipation, appendicitis, haemorrhoids (piles), irritable colon, ulcerative colitis, colon cancer

ii. **Metabolic diseases:** obesity, diabetes mellitus, ischaemic heart diseases, varicose vein, pulmonary embolism, gall stones, kidney stones, rheumatoid arthritis

iii. **Endocrine diseases:** thyrotoxicosis (graves disease), myxedema, hashimotos disease (autoimmune thyroiditis), addisons disease

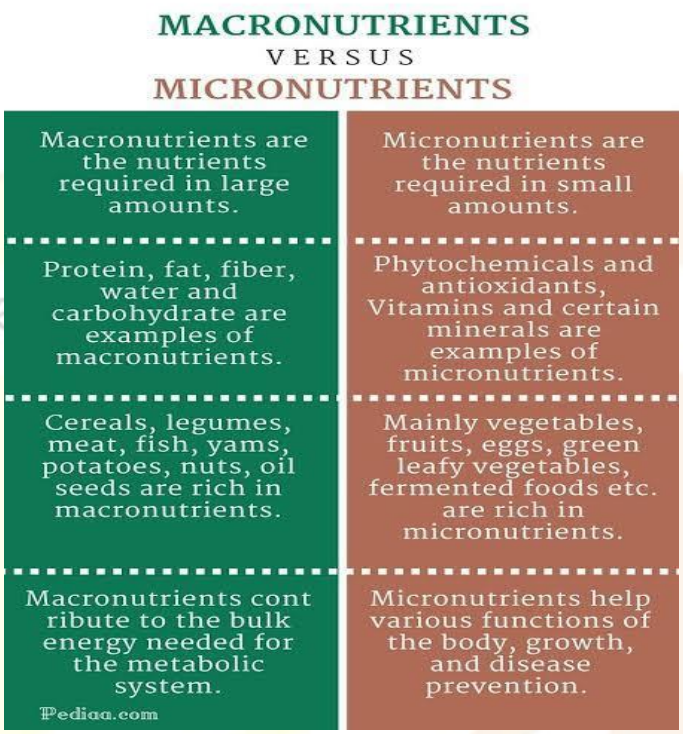
iv. **Other diseases:** dental caries (tooth decay), hiastus hernia, crohns disease

CONSTITUENTS OF A BALANCED DIET

What is a balanced diet?

- Nutrients are the substances that provides nourishment essential for the maintenance of life and for growth.
- Nutrients can be *macronutrients and micronutrients.*
- A balanced diet should offer around 60-70% of total calories from carbohydrates, 10-12% from proteins and 20-25% of total calories from fat.
- A healthy balanced diet consists of 7 components.
- Although it's important to eat the correct types of foods, it is also essential to eat the correct portions and amounts too.
- By adopting a balanced diet not only will this boot your immune system and health, but it will also help with weight loss and management.
- *Calories* are a measure of energy that foods supply.
- The number of calories you need will depend on your sex, age, and activity level.

equipping with excellence
CPA COLLEGE OF GLOBAL STUDIES



CPA COLLEGE OF GLOBAL STUDIES

1. ***CARBOHYDRATES***

Carbohydrates provide fuel to all cells, organs and tissues in the form of glucose. Some of its sources include foods such as whole grains, fruits, vegetables and legumes. You may also get good amount of carbohydrates in foods like candies, pastries, cook2ies and flavoured beverages. Carbohydrate is one of the important components of a balanced diet. On an average, an adult should get about 45 percent to 65 percent of their calories from carbohydrates.

2. ***VITAMINS***

Vitamins help with chemical reactions in the body and that is why the body needs 13 different vitamins to grow and develop. Each vitamin helps with certain functions. For example, vitamin A improves vision, vitamin C maintains healthy skin and vitamin D keeps the bones and teeth strong. You can get vitamins from fresh fruits and vegetables or from vitamin supplements.

3. ***FIBER***

Fiber, often referred to as roughage, is a type of carbohydrate found in plant foods that the body is not able to digest or absorb. Eating a balanced diet that is high in fiber can keep your body systems regular and contribute to a lowered risk of chronic disease.(30g per day)

4. ***FAT***

Fat is an important part of a balanced diet. It contributes to around 25 percent to 35 percent of the daily caloric intake, however, the content of saturated fats should be kept to no more than 10 percent of the total fat intake. The healthiest fats come from mono saturated and polyunsaturated sources such as nuts, olive oil and fish.

5. MINERALS

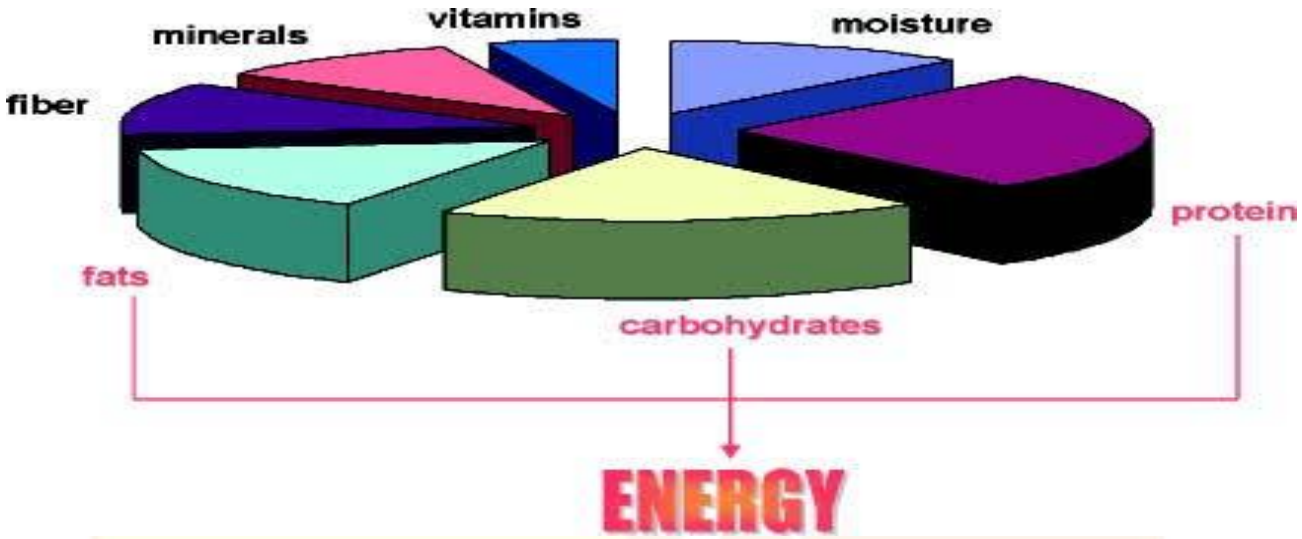
Minerals are very important for the body and they need to be delivered through food since the body can't make them. Many minerals, such as calcium, potassium and iron are vital to the proper functioning of the body and must be taken in relatively large amounts. Other trace minerals like zinc, selenium and copper are only needed in small amounts to maintain good health.

equipping with excellence
CBA COLLEGE OF GLOBAL STUDIES

6. WATER

Water is essential to our survival and should be taken in adequate amounts. It keeps the body hydrated and let the body function properly. Water accounts for 55%-65% of body weight, but because the body can't store water, we must constantly replenish it.(8 glasses per day)

with excellence
PA COLLEGE OF GLOBAL STUDIES



CPA COLLEGE OF GLOBAL STUDIES

7. PROTEIN

Proteins are nutrients that are essential to the building, maintenance and repair of body tissues such as the skin, the internal organs and muscles. Out of 22 protein types, the body can make 14, the other 8, called essential amino acids, can only be obtained from food. A balanced diet has to be rich in these 8 proteins. Fish, meat, poultry, eggs, cheese and other foods from animal sources provide all the eight essential amino acids.(50g per day)i

NUTRITIONAL DISORDERS

1. ANOREXIA NERVOSA

- It is a disorder characterized by the loss of appetite and bizarre patterns of eating
- Appetite is the craving for food, unlike hunger it is probably an acquired sensation, rather than an inborn trait.
- A new born baby experiences hunger, not appetite
- Diminished appetite is a common to almost all diseases which cause general weakness, this is because the activity of stomach and the secretion of gastric juice fall very low when the vital power is low
- Diminished appetite is a common symptom of dyspepsia (indigestion) and stomach cancer, feverish states
- In some, it is associated with stress or strain

- It is found in unmarried girls in their teens, following the onset of puberty, it may occur in older girls and women also, and very rare in males
- One view is that it represents a psychological regression in females who are ill-prepared to meet the responsibilities of adulthood
- Anorexia patients have a high fear of becoming fatty, from this fear, they develop curious habits like declination to eat in public, refusal for regular eating
- Anorexia is a serious condition with 5% mortality rate, suicide is the commonest cause of death
- Severe and progressive starvation is the physical consequence of anorexia , and cause amenorrhoea (absence of menstruation), and low BMR
- The common health risk or medical consequences of anorexia includes severe impairement of normal growth, extreme weight loss, low and irregular heart-beat, irregular menstrual cycle, low body temperature, weak bones, osteoporosis, bulimia nervosa, etc
- In women, anorexia is common in pregnancy, with high rates of premature delivery, abortion or miscarriage
- Recovery is slow and it is possible in 40% cases
- Treatment includes dietary regulations and psychotherapy, including family therapy

2. ACIDITY

- Acidity, or acid peptic disease (APD), is the condition in which the contents of the digestive tract becomes acidic due to an excessive production of HCl by gastric glands
- Emotional upsets, alcoholism, smoking, consumption of highly spicy food, non-vegetarian diet, chronic use of non-steroidal anti-inflammatory drugs (NSAID), etc are factors that cause acidity
- The major symptoms includes dyspepsia, frequent regurgitation of gastric contents, chest burn, peptic ulcers, etc.
- The gastro-intestinal wall can protect itself from the destructive actions of acids and histolytic enzymes, its mucous lining forms the first line defense against acidity
- The mucus, discharged from this lining, can dilute and neutralize acids and thereby protect the gut wall
- The bicarbonates, brought to the mucosa from the other parts of the body, can also neutralize the acids
- Prostaglandins probably promote bicarbonate production and mucus secretion and thereby indirectly protect the gut wall from acidity
- Acidity becomes harmful when one or more of these defense mechanisms become inadequate or loss effective

- Identifying and avoiding the causative factors are essential for the treatment of acidity
- Option of a suitable diet, excluding spicy, pungent and acidic foods, is very important
- Smoking and consumption of beverages must be avoided
- The use of drugs like steroids and NSAID must be avoided
- Those who are emotionally sensitive and those who are engaged in stressful jobs must try to modify their life styles to reduce mental tension
- Antacids provide immediate and temporary relief of the discomfort by neutralizing the excess acids
- Drugs called H2 receptor blockers, block histamine receptors and there by reduce gastric secretion of HCl
- Another group of drugs, called ***proton pump inhibitors,*** selectively inhibit specific acid-making mechanisms within cells
- Surgical methods such as vagotomy, are sometimes adopted to reduce acid production

3. FLATULENCE

- Flatulence is the collection of gasin the stomach or bowels
- In the former case, the gas will be frequently expelled in noisy eructations by the mouth
- In the latter case, it may produce unpleasant rumblings in the bowels,or may be expelled from the anus
- Gastric Flatulence may be due to the habitual gulping down of air when digestion is uncomfortable
- This is common in acid dyspsia
- Intestinal flatulence is usually due to bacterial fermentation
- Some carbohydrates, which cannot be digested by intestinal and pancreatic enzymes, are metabolized by the symbiotic bacteria in the colon and lower ileum
- The products of this bacterial metabolism include gases, such as H2, CH4 and CO2 and some intestinal irritants, such as some short- chain fatty acids
- Aprt from this, H2O2 and carbon disulphide are formed from eggs, peas and other sulphur containing food items
- The consequences of these includes increased fluid secretion and intestinal motility, diarrhea, cramps (gas pain), bloating and flatulence
- It can controlled by dyspepsia, by the administration of carminatives, and also by habit of gulping air
- Intestinal flatulence can be controlled by avoiding green veggies, starchy food etc which tend to decompose

4. PEPTIC ULCERS

- Ulcer is a crater like lesion in a membrane
- Peptic ulcers are open lesions or ulcers in the mucous membrane of some areas of the alimentary canal that are exposed to the action of the acidic gastric juice
- Peptic ulcers in the stomach are called ***gastric ulcers*** , and those in the duodenum are called ***duodenal ulcers***
- When the acidic gastric juice comes in direct contact with the mucous membrane, disintegration and necrosis of the tissue occur, leading to ulceration
- Discomfort and burning sensation in the stomach are the initial signs of peptic ulcer
- They are common among men than among women, and they become more common as age increases
- Low protein diet with plenty of spices may be the major reason for this
- The major causes and contributing factors for the hypersecretion of gastric juice and the formation of peptic ulcers
    - Genetic pre-disposition and familial tendency
    - Emotional turbulence and mental tendency
    - Over-excitation of vagus nerve
    - Smoking, alcoholism, irregular food habits, and skipping of timely meals
    - Excessive consumption of irritating foods, condiments, strong coffee and tea
    - Regular use of anti-inflammatory and ulcerogenic drugs
    - Chronic disorders and diseases, such as liver complaints, emphysema, rheumatoid arthritis, etc
- Ulcer is the injury to the epithelial lining and inadequacy of the mucous defence are the immediate cause of peptic ulcers
- These in turn, results from the hypersecretion of HCl and pepsin and hypersecretion of mucin
- There appears some abrasions or breaks in the mucosa which get gradually eroded and deepened by action of gastric juice
- The bacterium ***helicobacter pylori*** is believed to have active role in causing and aggravating peptic ulcers, its transmission occurs through contaminated food and water
- Pe[tic ulcers may develop in the lower part of oesophagus, lesser curvature of the stomach and the initial part of duodenum
- Thus there are 3 kinds of peptic ulcers oesophageal ulcers, gastric ulcers, duodenal ulcers
- Oesophageal ulcer is rare, other two are common
- High discomfort and burning and severely painful sensation in the abdomen are preliminary symptoms of peptic ulcers, these symptoms usually come on 2 or 3 hours after a meal and also at night

- Abdominal pain is often accompanied by vomiting, especially in advanced cases where the ulcer blocks the passage of food from stomach to duodenum

STARVATION

- Starvation is an extreme case of under nutrition in which there is totaldeprivation of food, or intake of energy and nutrients is far below the critical level
- Prolonged and extreme starvation is fatal, it may cause permanent and irreparable damages to tissues and vital organs and ultimate death
- Starvation usually causes several nutrient- deficiency diseases, such as kwashiorkor, marasmus, rickets, beriberi, scurvy, pellagra, pernicious anaemia, diarrhea, etc
- In starvating persons, there will be considerable loss of muscle mass and stored fat, since stored fat and muscle glycogen are mobilized as energy sources
- Starvating individuals are characterized by extreme loss of weight, oedema and emaciated appearance, pale and dry skin with rashes, extreme leathargy, fatigue and exhaustion

FASTING AND SIGNIFICANCES

- Fasting is the willful abstention from food and drink
- Fasting is practiced as a religious custom, and also a cure for several diseases and disorders
- Total suspension of food and drink produces 2 imminent results:
    1. Body becomes thinner and lighter since it relies on stored fat
    2. Body temperature gradually falls low
- Body weight decreases with fasting time

Physiological changes during fasting

1. Drop in the levels of fuel molecules in blood
2. Progressive decrease in basal metabolic rate
3. Mobilization of reserve nutrients with drastic drop in their store
4. Synthesis of glucose in liver from glucogenic amino acis mainly alanine
5. Synthesis of alanine from pyruvic acid
6. Steps to control protein loss
7. Formation and accumulation of ketone bodies

8. Changes in the role of renal cortex
9. Hyposecretion of insulin and hypersecretion of glucagon

Significance of fasting

1. Fasting is self=imposed control on the excessive desire, temptation or urge for over=eating
2. Fasting is the best way of coping emergency situations in which food supplies are very much limited
3. Fasting is a voluntary adaptation, which enables the body to adjust itself to a lack or shortage of food
4. Fasting and dieting are practically useful in weight reduction in obese persons
5. Fasting is medically important in controlling or curing several hard to treat disorders and diseases, such as arthritis, migraine, allergies, etc

BASAL METABOLIC RATE (BMR)

- Basal metabolism is the overall cellular metabolism , taking place under a set of empirical conditions : basal conditions (during resting , sleeping , hibernation , aestivation etc)
- Basal metabolism represents the lowest metabolism that yields only the bare minimum energy required for the immediate maintenance of normal life processes
- The rate at which basal metabolism takes place : BMR
- Thyroxine is the primary regulating agent of BMR , in vertebrates
- BMR depends on age , sex, habits , pregnancy , diet , chemicals , pathological conditions.

OBESITY

- Excessive weight gain of the body due to heavy accumulation of fat in the adipose tissues beneath skin and around certain internal organs
- Body weight goes upto 20% of the ideal weight
- Obesity is a serious health hazard and no one of the risk factor in coronary artery disease, gall bladder disease, diabetes mellitus etc
- It is associated with high mortality rate
- Women are more prone than men
- Obesity results from a combination of genetic factors and personal habits, overeating, excessive calorie consumption and large intake of fluids, especially alcohol
- Malfunctioning of some endocrine glands (thyroid, pitutory, sex glands), hormonal imbalance, hereditary factors, inert or sedentary life style are causes of obesity

- Causes:
  - Genetic factors
  - Personal habits
  - Overeating
  - Large intake of fluid
  - Malfunctioning of some endocrine glands
  - Hormonal imbalance
  - Hereditary factors
  - Inert life style
- Clinical effects :
  - Mortality
  - High BP
  - Type 2 diabetes
  - Osteoarthritis
  - Sleep apnea
  - Breathing difficulties
  - Fatigue
  - Mental illness
  - Body and joint pain
  - Cancer
  - Liver and gall bladder disease
  - Cardiovascular diseases
  - Cancers of breast and colon
  - Gout syndrome
  - Hernia
  - Back ache
  - Lethargy
  - Skin diseases such as eczema, and chafed and painful skin

equipping with excellence
CPA COLLEGE OF GLOBAL STUDIES

MODULE 2 RESPIRATION

- All biological functions require energy.
- This energy is obtained in the form of ATP from cellular respiration or biological oxidation.
- *Cellular respiration* : intracellular oxidation of nutrients and fuel molecules to release their bond energy for biological functions.
- The molecules or compounds, oxidised during respiration, : *respiratory substrates* (e.g. sugars, fatty acids, organic acids, etc.).
- The energy, released during cellular oxidation, is conserved in a biologically available form in the energy bonds of *ATP molecules.*
- The energy bonds of ATP molecules are finally broken and active kinetic energy is made available for biological process

2 types ,

- **AEROBIC**
- **ANAEROBIC**

ANAEROBIC RESPIRATION

- Also called anaerobic metabolism or *fermentation* : partial oxidation of fuel molecules in the absence of molecular oxygen.
- It releases only a small portion of the energy (In the anaerobic oxidation of glucose, only 20-30% of the energy store is released.)
- In anaerobic glucose oxidation **4 ATP** molecules will be synthesised and two will be spent per one molecule of glucose. So, there is a net gain of 2 ATP molecules.
- Example : Anaerobic respiration is common among yeasts, some bacteria (e.g., *lactic acid bacterium,* tetanus bacterium) and several endoparasites (e.g., *Taenia, Ascaris,Ancylostonma*)
- It also occurs in skeletal muscles, mature mammalian erythrocytes and the cytoplasm of all cells (through glycolysis).

- 2 TYPES ,
  - *Alcohol fermentation*
  - *Lactic acid fermentation*
- ***Alcoholic fermentation*** : fermentation of glucose to ethyl alcohol(alcoholic.fermentation),
  Example : *yeast (*baking)

- ***Lactic acid fermentation*** : fermentation of glucose and lactose to lactic acid
  Example : *Lacto Bacillus* (milk to curd :bacteria) and the skeletal muscles of vertebrates

AEROBIC RESPIRATION

- Complete cellular oxidation of organic molecules utilizing molecular oxygen and releasing CO_2
- Cellular centres : in eukaryotes *: mitochondria* ; in prokaryotes *: plasma membrane*.
- Even in some aerobic animals, anaerobic respiration Occurs in some cells and tissues.For example, lactic acid fermentation occurs in the skeletal (striated) muscles of vertebrates. Mature mammalian erythocytes are devoid of mitochondria. So, they carry out only anaerobic metabolism.

The most essential aspect of aerobic respiration is the step-by-step transfer of energised hydrogen through a chain of hydrogen acceptors within cells. Ultimately,the hydrogen combines with oxygen and forms water. Thus, oxygen is indispensable for aerobic respiration to serve as the terminal acceptor of hydrogen.Thus, the intake, transport and utilization of oxygen, and the transport and elimination of carbondioxide together constitute aerobic respiration.

- Two broad phases,
  - ***External respiration or organismic respiration*** : External respiration is the exchange of respiratory gases (O_2, and CO_2) between the organism and its external medium.
  - ***Internal respiration or cellular respiration*** : cellular uptake of O_2, and the oxidation of fuel molecules, releasing CO_2,,H_2O and energy.
- External respiration in higher animals involves two major processes,
  - **Gas Exchange**
  - **Gas Transport.**

GAS EXCHANGE

- 2 sites:

1. **Respiratory Surtace or Respiratory Organ :** takes place between the O_2 of the surrounding medium and the CO_2 of the blood or body fluid

2. **Cells / Tissues** : between the O_2 of the extracellular fluid and the CO_2 produced within the cell.

- **Mechanism :** physical process, without energy expenditure : by simple diffusion diffusion
- **Ventilation :**for high rate and maximum intake of O_2 , most organisnms continuously move air or water over their respiratory surface.

FACTORS INFLUENCING GAS EXCHANGE :

- Pressure gradient or tension gradient of the gases.
- Solubility coefficient of the gas in liquid medium.
- Diffusion coefficient and diffusion capacity of the gas in relation to the cross sectional area, distance and viscosity of the liquid.
- Molecular weight of the gas.
- Ventilation - perfusion ratio.
- Temperature.
- Thickness and surface area of the respiratory membrane.

The rate of gas exchange, in general, is directly proportional to temperature and the surface area of the respiratory membrane, and inversely proportional to the molecular weight of the gases and the thickness of the respiratory membrane.

1. **Pressure gradient or tension gradient of gases :**

   - Gas exchange takes place by *simple diffusion in a pressure gradient or tension gradient* i.e. from a region of greater to a region of lower.
   - *Partial pressure* : pressure of an individual gas in a gas mixture.
   - T*ension* : pressure of a gas in a liquid.
   - In mammals, pO_2 is always greater in the inspired alveolar air and the tension of pCO_2 is greater in the capillary blood. So, O_2 diffuses to blood from alveoli, and CO_2 diffuses from blood to alveoli.
   - In tissues, the tension of O_2 is always greater in blood, and the tension of CO_2 is greater in tissue fluid. So,O_2 diffuses to tissue fluid and CO_2 diffuses to blood.

2. **Solubility coefficient of gases in a liquid medium :**

- *Solubility coefficient is the quantity of a gas absorbed by I ml of a liquid at a temperature of 0 ℃ and a pressure of 760 mm Hg.*
- The tension of a gas in a liquid is directly proportional to the volume of the dissolved gas and inversely proportional to its solubility coefficient.
- The volume of the dissolved gas, in turn, depends on pressure and solubility constant.

Volume of dissolved gas =Pressure x solubility coefficient.

$$\text{Tension of disolved gas} = \frac{\text{Volume of gas in the liquid x 760}}{\text{Solubility coeficient at 760 mm Hg}}$$

- The tension of gases is measured by the instrument tonometer.

3. Diffusion coefficient and diffusion capacity

- *The diffusion coefficient of a gas is the volume of the gas in I ml of the liquid, diffusing over a surface area of 1 sq cm (1 cm^2) and along a distance of 0.001 mm.*
- *Diffusion capacity is the volume of the gas diffusing across the respiratory membrane every minute in a pressure gradient of 1mm Hg.*
- Diffusion capacity is directly proportional to the cross sectional area of the membrane and the solubility of the gas in the liquid medium, but inversely proportional to distance

4. Ventilation-perfusion ratio

- Gas exchange in the lungs depends markedly on a ratio between the air flow (ventilation) and blood flow (perfusion) into the lungs.
- *Ventilation-perfusion ratio* : The ratio between alveolar ventilation and alveolar vascularisation.
- Gas exchange is most efficient when each alveolus of the lungs is fully ventilated and fully

GAS TRANSPORT

- In vertebrates, cardiovascular system serves as the transport system for the delivery of O_2 to tissues and the removal of CO_2 from tissues.
- In lung-breathing vertebrates, blood is the medium of transport of respiratory gases between lungs and tissues.
- It transports O_2 from lungs to tissues, and CO_2 from tissues to lungs

1. Transport of Oxygen

Blood transports O_2 in two ways:

- in chemical combination with haemoglobin : 97%
- in physical solution in the water of plasma and corpuscles: 3%

a) Transport of 0_2 in physical solution :

- Transport of oxygen in physical solution depends on the solubility coefficient, pressure gradient and temperature.
- Normally, 1 ml of blood absorbs nearly 0.024 ml of oxygen at a temperature of 37°C and a pressure of 760 mm Hg.
- The partial pressure of oxygen inside the lungs is 100 mm Hg.
- So, at this pressure of oxygen, 1 ml of blood can carry **0.003** ml of oxygen in physical solution.

b) Transport of 0_2 by haemoglobin :

Properties of Hb to transport Oxygen :

- Can transport large quantities of O_2
- Has high solubility
- Can take up and release oxygen at appropriate partial pressures
- Can serve as a powerful ph buffer.

During oxygen transport, Hb is only oxygenated, and never oxidized. During oxygenation, its iron atom stays in the ferrous state itself. If it is oxidized to ferric state,its oxygen-carrying capacity would be lost.

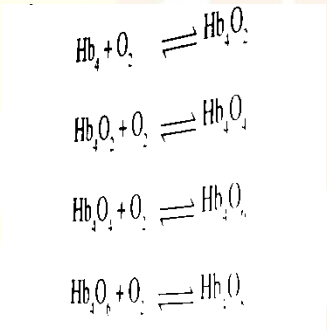
- Haemoglobin has great affinity for O, at high pO_2 and low pCO_2
- *Oxygenation of haemoglobin*: At the high pO_2 in the capillaries of respiratory surfaces or lungs, it will readily accept oxygen and its Fe^{++} ions will loosely and reversibly combine with 0_2, to form the unstable oxyhaemoglobin ($Hb_4 0_2$).
- High blood pH (low acidity) also enhances the oxygenationof haemoglobin
- The oxygenation reaction of haemoglobin is represented as ,

$$Hb_4 + O_2 \rightleftharpoons O_2$$

- *Tension of loading :* The pO_2 at which haemoglobin gets oxygenated
- *100% saturation of haemoglobin* : haemoglobin molecule contains four iron atoms, it can bind with as many as four molecules of O_2 at a time. The condition in which all the binding sites of a haemoglobin molecule are simultaneously occupied by oxygen. It occurs at high tension of loading (i.e. at high pO_2).

$$Hb_4 + 4O_2 \rightleftharpoons Hb_4O_8$$

- Haemoglobin exists in three conditions of oxygenation/ saturation:
  - *Unsaturated or unoxygenated*
  - *Partially saturated or partially oxygenated*
  - *Fully saturated or fully oxygenated.*
- The degree of the saturation of haemoglobin with O_2 is directly proportional to the level of pO_2.
- *Percentage saturation of haemoglobin* : The percentage of saturated Hb in the total haemogiobin
- Saturation of haemoglobin is a stepwise process



- 1 gm of haemoglobin can combine with as much as 1.34 ml of oxygen :*oxygen-carrying capacity of haemoglobin.*
- *Positive co-operativity* :Oxygenation of one haem group not only increases the affinity of the remaining haem groups for O_2 but also enhances their oxygen-binding capacity
- The oxygen-binding ability of Hb is directly proportional to the pO_2 level.
- *Deoxygenanon or desaturation of haemoglobin* : In the tissues, po_2 is very low and pco_2 is very high. Hence, o*xyhaemoglobin* dissociates and sets free O_2 forming *deoxyhaemoglobi*n..
- *Tension of unloading* : The po_2, at which haemoglobin gets deoxygenerated
- Dissociation of oxyhaemoglobin is influenced by :
  - acidity (low pH)
  - the presence of 2,3-diphosphoglycerate (DPG)
  - High temperature
  - High pCO 2

Bohr effect :Under acidic conditions, the equilibrium beween deoxyhaemoglobin and oxyhaemoglobin gets shifted in favour of the deoxygenation process . Conseqdently, oxygen dissociates more readily from haemoglobin.

2. Transport of Carbondioxide

Blood transports CO, from tissues to lungs in three ways:

- in physical solution as carbonic acid :5%
- as carbaminohaemoglobin :10%
- as bicarbonates. :85%

a. Transport of CO, in physical solution as carbonic acid

- CO_2 reacts with plasma water and forms the weak carbonic acid.
- This occurs in tissue sites.
- On reaching the lungs, carbonic acid dissociates and releases CO_2The remaining 95%

b. Transport of CO_2 as carbaminohaemoglobin

- CO_2 first diffuses from plasma to RBC.
- Then, it reversibly combines with the amino($-NH_2$) group of the globin part of haemoglobin and forms
- *carbaminohaemoglobin*.
- The formation of carbaminohaemoglobin is greatly influenced by the high pCO_2 in the tissue capillaries.
- On reaching the pulmonary capillaries, where pCO_2 is very low, carbaminohaemoglobin dissociates, releasing CO_2. This dissociation is catalysed by *carbonic anhydrase*.
- The CO_2 soon diffuses to pulmonary alveoli and then escapes to the outside

$CO_2 + Hb.NH_2 \longleftrightarrow Hb.NHCOOH$

c. Transport of CO_2 as bicarbonates (isohydric transport)

- This occurs with minimum change in pH and is therefore termed isohydric transport.
- In this case, most of the CO_2 at first diffuses in a tension gradient from blood plasma red blood cells, due to the high pCO_2 in the plasma.
- In the RBC, it reacts with water and forms *carbonic acid*.
- Carbonic acid soon ionizes to hydrogen ions (H^+) and bicarbonate ions ($HC0^-$)

$$CO_2 + H_2O \xrightarrow{\text{Carbonic anhydrase}} H_2CO_3$$

$H_2CO_3 \longrightarrow H^+ + HCO_3^-$

- The Hydrogen ions, formed by the ionization of H,CO, are soon buffered by
- deoxyhaemoglobin (oxygen-free haemoglobin) which acts as a proton acceptor.
- They immediately combine with *deoxyhaemoglobin a*nd form *haemoglobinicacid (H.Hb).*
- *Haldane effect :* The release of H^+ ions and their immediate buffering by deoxyhaemoglobin
- At the same time, bicarbonate ions diffuse to the plasma from red blood cells, when their concentration increases within the RBCs.
- This outward diffusion of HCO^-, from RBC to plasma momentarily upsets the ionic equilibrium and the electrical balance between plasma and red cells.
- *Chloride shift or Hamburger phenomenon :* To regain the lost balance, and also to establish electrochenmical neutrality, an equal number of chloride ions diffuse into the red cells from plasma.
- Free chloride ions are made available by the dissociation of NaCl or KCl in the plasma.
- Inside the RBC chloride ions combine with K^+ and form KCl.
- The HCO_3^- ions in the plasma combine with Na and form $NaHCO_3$
- Now, the deoxygenated blood returning to lungs, contains NaHCO, in the plasma,and *haemoglobinic acid* and KCI in the RBCs.
- When this blood reaches pulmonary capillaries, the whole series of events get reversed.

Summary of the transport of CO_2 as bicarbonate

(i) In the blood of tissue site

1. CO_2 diffuses into RBC from plasma
2. $CO_2 + H_2O \rightarrow H_2CO_3$ (in RBC)
3. $H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$ (in RBC)
4. $H^+ + Hb \rightarrow H.Hb$ (in RBC) Haldane effect
5. $NaCl \rightleftharpoons Na^+ + Cl^-$ (in plasma)
6. HCO_3^- diffuses to plasma, and Cl^- diffuses to RBC (chloride shift)
7. $HCO_3^- + Na^+ \rightarrow NaHCO_3$ (in plasma)
8. $Cl^- + K^+ \rightarrow KCl$ (in RBC)

Plasma contains $NaHCO_3$ and RBC contain KCl and HHb

(ii) In the blood of lungs

9. $NaHCO_3 \rightarrow Na^+ + HCO_3^-$ (in plasma)
10. $KCl \rightarrow K^+ + Cl^-$ (in RBC)
11. HCO_3^- diffuses to RBC, and Cl^- diffuses back to plasma (chloride shift)
12. $H.Hb \rightarrow H^+ + Hb$ (in RBC)
13. $H^+ + HCO_3^- \rightarrow H_2CO_3$ (in RBC)
14. $H_2CO_3 \rightarrow H_2O + CO_2$ (in RBC)
15. CO_2 diffuses to plasma from RBC

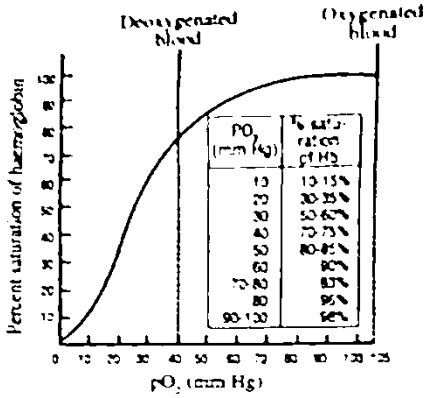
OXYGEN- HAEMOGLOBIN DISSOCIATION CURVE

- The uptake of a small amount of O2 by haemoglobin favours the relaxed (R) state of its peptide chains
- This in turn promotes the uptake of additional O2
- This can be graphically represented by a sigmoid (s shaped) curve, known as ***oxygen-haemoglobin dissociation curve***
- It is also called oxygen dissociation curve or oxygen equilibrium curve
- It is a representation of the affinity of Hb for O2 at different levels of pO2
- It represents the relation between the percentage saturation or oxygen- carrying capacity of Hb and the different levels of pO2 in the blood
- It reveals the actual relation between pO2 and formation and dissociation of oxyhaemoglobin
- Combination of the first haem molecule with O2 increases the affinity of the second haem molecule, and in the same manner it repeats,,
- The oxygen haemoglobin dissociation curve corresponds to the fact that at zero pO2 there is no HbO2 in blood
- With a rise in pO2, the curve goes up gently first and then rises more sharply

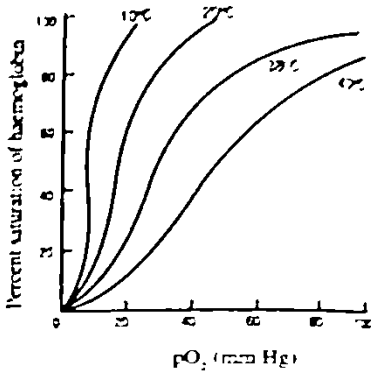
EFFECT OF VARIOUS FACTORS ON OXYGEN DISSOCIATION CURVE

- Left shift of curve is a sign of haemoglobin's increased affinity for oxygen (in lungs)
- Right shift shows decreased affinity , as appear due to increased body temperature, hydrogen ion concentration, or CO2 concentration
- Carbon monoxide has a high affinity to Hb than O2, in carbon monoxide poisoning O2 cant transported and released to body tissues thus resulting hypoxia
- With foetal haemoglobin, the shift facilitates diffusion of O2 across placenta
- The oxygen dissociation curve for myoglobin, exists even further to the left

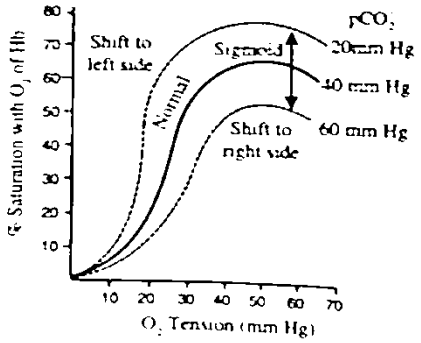
equipping with excellence
CMA COLLEGE OF GLOBAL STUDIES



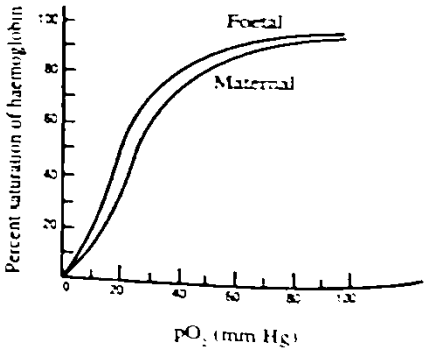
Curve at normal body temperature showing the relation between pO_2 and Hb saturation



Curve showing the relation between temperature and Hb saturation. As temperature increases less O_2 combines with Hb.



Dissociation curve showing the relation between pCO_2 and Hb saturation



RESPIRATORY PIGMENTS

- Respiratory pigments are coloured and metal-containing conjugated proteins,involved in the uptake, storage and transport of respiratory gases.
- They have very great affinity for O_2, At high pO_2, they loosely and reversibly bind with O_2, and form unstable and easily dissociable compounds.
- At low pO_2 these unstable compounds dissociate, releasing O_2. The oxygen content of the blood of most animals is greatly increased by the combination of oxygen with respiratory pigment. S0, in the absence of respiratory pigment, the oxygen content of the blood would be very low.
- The commonest respiratory pigments include *haemoglobin, haemocyanin,*

haemerythrin, chlorocruorin, echinocruorin and *echinochromne.*

HAEMOGLOBIN :

- found in both vertebrates and invertebrates
- In vertebrates, haemoglobin is a circulating respiratory pigment and myoglobin is a storage respiratory pigment.
- Haemoglobin is an iron-containing and oxygen-carrying red pigment.
- It is found in the erythrocytes of all vertebrates and in the blood plasma of some invertebrates (e.g., Ascaris).
- A modified type of haemoglobin, called *leg haemoglobin*, is found in the root nodules of leguminous plants.
- The normal haemoglobin, found in adult human beings, is called *haemoglobin A (HbA*), and that of foetus is called *foetal haemoglobin* (*HbF*
- Haemoglobin is a conjugated metalloprotein
- It is formed of a colourless and globular basic protein, called *globin,* and an iron-containing portion or prosthetic group, called *haem* (heme) or *haematin*

Globin + Heme =Haemoglobin

- Haem is the active group, taking part in O, transport.
- All the different kinds of haemoglobin have the same heme group, but different globins

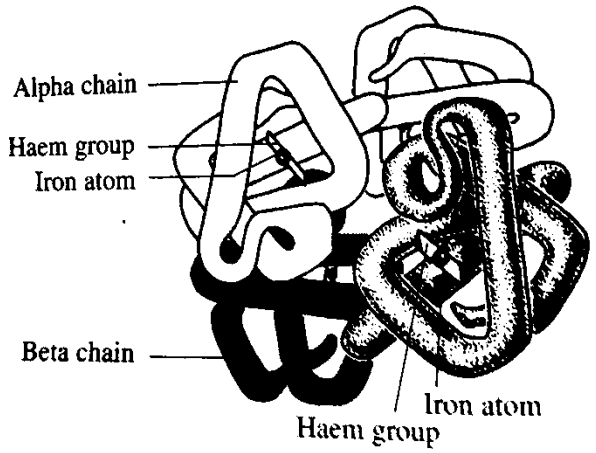
Molecular organization of haemoglobin :

- A human haemoglobin-A molecule consists of one globin molecule and four haem (heme) molecules.
- The globin molecule, in turn, is a tetramer, formed of four polypeptide chains:
  - two alpha chains (each having 141 aminoacid units)
  - two beta chains ($\alpha_2\beta_2$) in HbA (each having 146 aminoacid units)
  - two alpha chains
  - two gamma chains (α_2, γ_2) in HbF.
- Forces : weak non-covalent bonds, such as vanderWaal's forces, hydrogen bonds,salt linkages and hydrophobic interactions
- In adult. human beings, there is yet another type of haemoglobin, called haemoglobinA $_2$(HbA_2) ; globin part formed of two alpha chains and two deltachains ($\alpha_2\ \delta_2$).

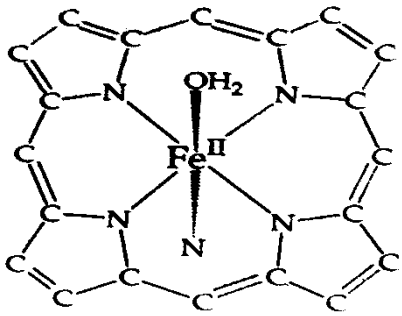
- Haem molecule is an iron-porphyrin complex, formed of aniron atom and a divalent porphyrin molecule.
- Iron occurs in the ferrous (Fe^{2+}) state.

- The porphyrin unit is a tetrapyrrole ring , formed of four pyrrole rings, with a centrally located ferrous iron. The ferrous iron is linked to the N atoms of the porphyrin ring

A haemoglobina (HbA) molecule consists of 574 amino acids, 4 polypeptide chains, 4 iron atoms, 4 porphyrin molecules and a vinyl group



Haemoglobin-A molecule



The hexa-coordinated iron atom in haemoglobin

Properties of haemoglobin :

- Haemoglobin has an active role in the transport of O_2 and CO_2

- The most important property of haemoglobin is its affinity for O_2 for its ability to reversibly bind with oxygen.
- A haemoglobin molecule can bind with as many as four oxygen molecules
- Affinity for O, depends on temperature, pH, pO_2, and pCO_2, of the blood,and the concentration of 2, 3-diphosphoglycerate (2, 3-DPG) in the blood.

The ability of Hb to bind O_2 enables it to serve as an oxygen-carrier of blood. This reaction is unique in that the iron of the haem remains in the ferrous (Fe^{2+}) state

Oxygen only loosely and reversiblycombines with the ferrous iron without actually oxidising it to ferric iron (Fe). Thus,the iron atom gets only reversibly oxygenated and not oxidised.

- The bare, oxygen-free haemoglobin is called deoxyhaemoglobin.
- The affinity of Hb for O, and its oxygen-binding capacity, depend upon the physical state of its peptide chains.
- Each chain can exist in two reversible or interchangeable states,
  - *relaxed or R-state* : favours oxygen-binding
  - *tensed or T-state* : lowers oxygen-binding

The haemoglobin content of the blood of a normal human adult consists of about 97 % HbA , 2% Hb A_2, and 1% HbF. The normal level of HbA in blood is 14 to 16g/dl in male and 13 to15g/dl in female.

MYOGLOBIN

- commonly called the muscle haemoglobin, is similar to haemoglobin
- it is a monomeric globular protein, formed of only one ferrous atom, one haem group, and a single polypeptide chain of 153 aminoacids
- its molecular weight is 16700
- myoglobin is found in skeletal and cardiac muscles
- its affinity to O2 is higher than that of haemoglobin
- Myoglobinserves as an intracellular storer and carrier of O2

- It releases oxygen when Po2 is very low

HAEMOCYANIN

- Haemocyanin is a copper containing pigment
- It is found dissolved in blood plasma of few arthropods
- Its molecular weight is 1 million to 7 million
- It is colourless when deoxygenated, and blue when oxygenated
- A molecule is formed of two copper atoms, linked to a polypeptide chin
- It takes part in O2 transport
- A haemocyanin molecule can attach to Ao2 molecule

HAEMOERYTHRIN

- It is an iron-containing respiratory pigment, found in polychaetes, sipunculids, priapulids, and branchipods
- Its molecular weight is around 100000
- It is purple colour when oxygenated, and brownish when deoxygenated
- Haemoerythrin is contained in some wandering cells, called coelomocytes, which circulate in coelomic fluid
- A molecule contains several iron atoms, without a porphyrin ring
- One O2 molecule combines with 2 or 3 iron atoms

CHLOROCRUORIN

- This is an iron-containing, green-coloured respiratory pigment found in blood plasma of marine polychaetes
- It is green in colour both in the oxygenated and deoxygenated states
- Its molecular weight is about 3 million
- The structure is similar to haemoglobin

REGULATION OF RESPIRATION

Breathing movements are controlled, ventilation rate is normalized, and the basic respiratory rhythm is established through the negative feed-back impulses from *respiratory receptors* to *respiratory centres.*

This regulation involves a rhythmic muscles.

This inherent rhythmicity arises within the *medulla oblongata*.

It may be influenced by the impulses from *pons Varolii, hypothalamus, cerebral cortex*, and the 9th and 10h *cranial nerves.*

Respiratory receptors

2types :

- ***Stretch receptors or Hering-Breuer receptors*** : located on the walls of trachea, bronchi and bronchioles.
- ***Chemoreceptors*** : medullary receptors, aortic bodies and carotid bodies ; located respectively in the medulla oblogata, wall of aorta and the wall of carotid sinus (dilated region of internal carotid artery).

- Chemoreceptors are sensitive to changes in the O_2 and CO_2 levels in blood, especially to low O_2 and high CO_2levels.
- Stretch receptors are sensitive to high 0_2 and low CO_2 levels, and also to stretches in the lungs.
- Feedback impulses from stretch receptors are concerned with the mechanics of pulmonary ventilation
- From the chemoreceptors are concerned with the rate and depth of pulmonary ventilation.

Neural control on respiration: Respiratory centres and respiratory rhythm

- Respiratory centres control the mechanics of breathing.
- During breathing, respiratory muscles contract and relax in response to the impulses from the respiratory Centres in medulla oblongata and pons Varolii
- In human beings, 2 Respiratory centres :
  - **Medullary centre**
  - **Pontine centre**
- there are 2 medullary centre :
  - Inspiratory centre
  - Expiratory centre
- Pontine centre includes :
  - *Pneumotaxic centre*
  - *Apneustic centre*

- Pneumotaxic centre is *inhibitory*
- All others are *excitatory*

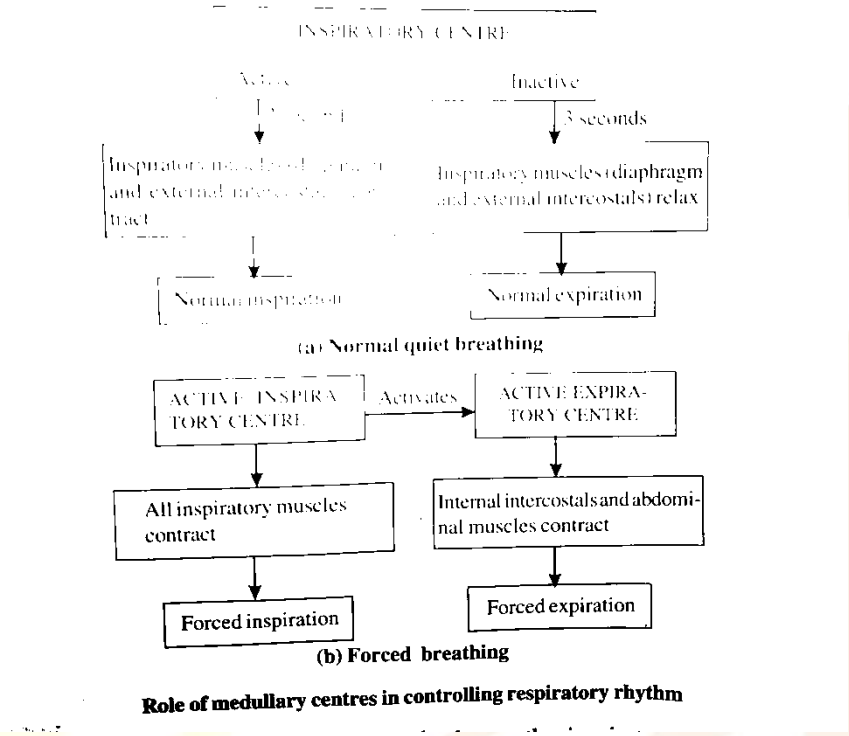
- Inspiration occurs when the O2 levels falls in blood low and CO2 level goes high
- Chaemoreceptors perceive these stimuli and transforms them as sensory impulses
- These impulses are transmitted to the inspiratorty centre via sensory neuron
- Then, inspiratory centres gets stimulated and generates motor impulses
- These impulses transmitted to the respiratory muscles
- They stimulate the inspiratory muscles and thereby set the basic respiratory rhythm
- Now, the inspiratory muscles contract, leading to the expansion of the thoracic cavity and dilation of the lungs
- This brings about inspiration
- Expiration occurs when the lungs dilated the O2 level of the blood has gone and CO2 level has come low
- Stretch receptors perceive these stimuli and transform them as sensory impulses
- These impulses are transmitted to the expiratory centres along the vagus nerve
- The expiratory centre responds to them by transmitting inhibitory impulses to theinspiratory centre
- This inhibits the inspiratory centre, leading to the relaxation of inspiratory muscles, the compression of thoracic cavity and lungs, and results in expiration
- Pneumotaxic centre exerts periodic checks on the inspiratory and apneustic centres, its signals are transmitted to the switch off points of the inspiratory centre
- These signals temporily turns off the expiratory centre, limit or suspend inspiration, so facilitates expiration
- In effect, strong pneumotaxic signals shorten inspiration and expiration and thereby increase the breathing rate
- Weak signals prolong inspiration and expiration and thereby lower breathing rate
- Apneustic centre sends impulses to the inspiratory centre, this activates the inspiratory centre and thereby prolongs inspiration and inhibits expiration
- So apneustic centre and pneumotaxic centre appear to be antagonistic in function
- In quiet breathing inspiration takes only 2 seconds and expiration takes 3 seconds, this is the basic rhythm
- At the beginning of inspiration, inspiratory centres get activated by 2 seconds this stimulates inspiratory muscles and causes inspiration
- After that it becomes inactivated 3 seconds, this causes relaxation of inspiratory muscles and results in expiration
- This turning off and on of the inspiratory centre is controlled by pneumotaxic centre

Cortical influence

- Respiratory centres have some connection with cerebral cortex,
- This enables a person to voluntarily alter the pattern of breathing, and even to stop breathing for a short while
- Voluntary control is protective in that it enables to prevent the entry of water, irritating gases etc into the lungs
- When the Pco2 goes beyond a certain level, the inspiratory centre will be activated, impulses will sent to inspiratory muscles and breathing will resume whether or not the person wishes

Chemical stimuli and control of ventilation rate

- There are certain chemical stimuli that determine how fast a person can breathe
- The main chemical stimuli, that regulates breathing rate or ventilation rate, is the CO2 level in the blood
- High CO2 level (*hypercarnia or hypercarbia*) stimulates the aortic and carotid chemoreceptors
- They generate sensory impulses and transmit them to the inspiration centre
- The inspiratory centre get highly excited, generates excitatory motor impulses and transmits them in rapid relays to inspiratory muscles
- These muscles contract and relax rapidly increasing breathing rate
- The increased breathing rate is called ***hyperventilation***
- Hyperventilation stimulates the stretch receptors on the tracheal, brancheal and branchiolar walls
- They generates sensory impulses and transmit them to the expiratory centre
- Expiratory centre gets excited and transmit inhibitory motor impulses to inspiratory muscles
- This temporarily inhibits inspiratory activity and thereby prevents sustained inspiration (***apneusis)***
- Then inspiratory muscles relax, leading to expiration
- Soon the expiratory centre becomes inactive and the inspiratory centre becomes active again
- When the blood CO2 is lower (*hypocarnia or hypocarbia*) , the chemoreceptors will not be stimulated and no impulses would be transmitted from them to inspiratory centre
- The inspiratory centre sets its own moderate pace and rhythm until CO2 accumulates and the pCO2 rises to normal this causes slow breathing rate, called ***hypoventilation***



Role of medullary centres in controlling respiratory rhythm

PROBLEMS AND ADAPTATIONS OF DIVING MAMMALS

- Many lung breating aquatic vertebrates are efficient divers and they can survive long periods of submergence without coming up of air
- This is by virtue of their auxillary respiratory mechanisms, minimal oxidation requirements, and specialized metabolic patterns.
- Such vertebrates include amphibians, turtles, crocodiles, aquatic snakes, Penguins, cormorants and aquatic mammals, such as whales, walruses, porpoises, seals, beavers,
- These animals are adapted to dive for food, or to escape from their enemies. Their ability remain under water depends on their ability for maximum storage and minimal utilization of oxygen
- While under water, they use the atmospheric oxygen already stored in myoglobin. To replenish the used oxygen, they frequently comes the surface.

- The major problems generally experienced by diving mammals are :
  - lack of oxygen availability at depths
  - difficulty for the elimination of CO_2 from tissues

- difficulty for the proper distribution of 0_2 to different parts
- depletion of the Oxygen storage
- the resulting hypoxia and anoxia
- bradycardia or low heart-rate
- slow blood circulation to organs other than brain, heart and adrenal glands
- Oxygen toxicity
- gas bubbling due to decompression sickness when the animals ascend to the surface

- At the beginning of diving, a set of physiological mechanisms get activated. The collectively serve as the ***diving reflex***.
- Now, breathing stops and the animal makes use of oxygen stored in the myoglobin. This causes a reduction in the supply of oxygen to on tissues. As a result, heart-beat becomes weak and slow.
- This adaptive adjustment minimises the utilization of oxygen. At the same time, it ensures a steady supply of oxygen to organs which are highly sensitive to hypoxia. After some time, the oxygen store in the myoglobin gets exhausted and muscles resort to anaerobic metabolism. This leads to the accumulation of lactic acid in muscles and the building up of an ***oxygen debt***.

Oxygen debt

- Oxygen debt is a physiological state in which there is an increased demand for oxygen.
- It occurs when a normally aerobic animal is forced to respire anaerobically under conditions of hypoxia, to meet the body's increased demand for energy, Pyruvate is anaerobically converted to lactic acid.
- Lactic acid is toxic and its break down requires oxygen. So, accumulation of lactic acid builds up an oxygen debt.
- The oxygen debt is repaid when oxygen is available again and lactic acid is oxidised in liver.

Decompression sickness

- Decompression sickness (*caisson disease or dysbarism*)is a serious condition of gas bubbling from blood.
- It occurs when a deep-water diver, or a caisson worker (a person who makes tunnels under rivers), suddenly returns to the surface from deep-water.

- In the deep waters pressure is very high and so large quantities of nitrogen and other gases dissolve in the blood of a diver.
- Excessive amounts of dissolved nitrogen in body fluids may cause giddiness and other symptoms, similar to alcoholic intoxication. This condition, is called nitrogen narcosis.
- The greater the depth, the more severe would be the condition.
- If a deep-water diver ascends to the surface slowly, the dissolved nitrogen may be eliminated from his blood through lungs.
- However, when he comes to the surface all of a Sudden, there occurs a rapid fall in pressure of the ambient gases in the body.
- As a result, he suffers from decompression sickness. Nitro: en and other gases bubble out from his blood.
- In human beings, it may block pulmonary circulation and may cause difficult breathing or respiratory failure, joint pain, dizziness, convulsions, seizures, cardiac arrhythmia (irregular rhythm of heart-beat), myocardial damage (anginal pain), extreme fatigue, paralysis and unconsciousness.

.

Adaptations of diving mammals

- Storage of oxygen in myoglobin and venous blood reservoirs
- Low metabolic rate and low oxygen requirement
- Low heart rate and low cardiac output
- Peripheral vasoconstriction and circulatory shunts to maintain blood flow to brain, heart, adrenal gland, etc. Large blood volume and high oxygen-carrying capacity of blood
- Low sensitivity of the respiratory and circulatory centres to increasing concentration of co_2 and lactic acid
- Tolerance to oxygen debt in muscles

The danger of hypoxia or anoxia, encountered by the under-water animals, is essentially the same as that encountered by the animals at high altitudes. However, the solution is different in the two habitats. At higher altitudes, the problem is solved by enhancing the rates of oxygen delivery to tissues, while in water the solution involves the temporary storage and judicious use of oxygen, and the capacity to deal with oxygen debt.

RESPIRATORY PROBLEMS IN NEW-BORN BABIES

1. **Infant respiratory distress syndrome**

- The lungs of RDS patients are surfactant- deficient
- Surfactant is a mixture of proteins and glycoproteins, it is produces in lung cells, called ***type 2 pneumocytes***
- In the cells, it gets packaged into lamellar bodies, which are soon extruded to the alveoli
- In the alveoli, the lamellar bodies unfold and form a complex lining of the alveoli
- This lining prevents the sticking together and collapse of alveolar walls towards the ends of expiration
- Infant RDS, formerly called ***hyaline membrane disease (HMD)*** or glassy-lung disease (GLD), is a fatal disease of new born babies
- It is found in premature infants, in the infants born by caesarian section, infants of diabetic mothers and also in the second born premature twins
- The main features of infant RDS are *developmental insufficiency of surfactant production and the structural immaturity of lungs*
- Surfactant is a surface –active agent, lining the alveoli of lungs , it plays an active role in normal respiration. It allows alveoli remain open throughout inspiration- expiration cycle
- Infant RDS begins in a few hours after birth
- It is manifested by difficult and labored breathing, tachypnea, and chest wall retraction during breathing efforts, grunting expiration, flaring nostrils, cyanosis etc are common symptoms
- As the disease progresses, the baby may suffer from ventilation failure, hypercarbia and prolonged apnea
- Complication of the disease includes acidosis, low blood sugar level, low blood pressure, chronic changes in lungs, intracranial haemorrhage etc
- Clinical course of disease may last for 2 or 3 days
- In most cases, death is occurs
- RDS affects only 1% of the new born babies with more than 50% mortality rate, It is one of the leading causes for the death of pre-term infants
- Administration of glucocorticoids to the mother at least 12 hours before delivery may sometimes prevent it or reduce its incidence. This probably speeds up the production of surfactant in the infant.
- A treatment, called positive end expiratory pressure (PEEP) is now given to RDS patients.
- It involves three principal lines, namely (i) supply of oxygen-rich air through an endotracheal breathing tube with constant positive airway pressure (up to 14 mm Hg) to offbeat apnea (ii) administration of synthetic or extracted surfactant to the lungs through a breathing tube to make up surfactant deficiency, and (iii) intravenous administration of fluids to stabilize blood sugar level, blood electrolyte level and blood pressure level.
- One of the most commonly used exogenous surfactant is Survanta, extracted from cow

Sudden infant death syndrome (SIDS)

- SIDS, also called crib death or cot death, is the unexpected sudden and silent death of an apparently healthy baby, usually during sleep.
- It kills thousands of babies every year, The unfortunate victims are aged between I week and 12 months.
- The commonest feature of the disease is the exudation of a blood-tinged froth from the nostrils.
- The actual cause is not still really known.
- Death in most cases results from laryngospasm, believed to be triggered by a viral infection of the upper respiratory tract, or from prolonged apnea due to the malfunctioning of the respiratory centre

Asphyxia neonatorum

- Asphyxia neonatorum is the infant asphyxia, characterized by imperfect breathing or difficult breathing in the new-born infant.
- It contributes to nearly 50% of infant death during the first month of life.
- It is mainly due to an interferences with the oxygenation of blood.
- Its Common causes include serious illness of the mother during the later months of pregnancy, anaesthetics or analgesics given to the mother during labour, prolonged labour, obstruction to the blood flow in umbilical cord, obstruction in air passage of infant, intracranial haemorrhage, congenital heart disease
- It can be pre-natal, intra-uterine, or post-natal and extra-uterine
- Pre-natal asphyxia could be due to proper supply of oxygen to the foetus before or during labour
- Post natal asphyxia due to prematurity or congenital diseases
- Some common causes are following
    - Prolonged and repeating uterine contraction during labour, which may interfere with gas exchange in placenta
    - Unequal pressure exerted by the uterus on placenta and umbilical cord. This may prevent the free passage of oxygen to the foetus.
    - Compression or tearing of placenta
    - Twisting or tearing of the umbilical cord.
    - Premature partial or complete separation of the placenta.
    - Maternal anaemia or asphyxia.

- Asphyxia neonatorum is of two types, namely ***asphyxia livida*** and ***asphyxia pallida.***
- Asphyxia livida of the first grade, and the asphyxia pallida is of the second grade.
- In asphyxia livida, the skin turns blue or reddish-blue, face becomes swollen, eyes protrude, heart beats strongly, and breathing effort may be absent or rather weak and infrequent.
- In asphyxia pallida, vasomotor centre gets overstimulated due to high levels of blood CO2, no attempt for respiration, or there may be feeble efforts in some cases. Heart-beat may be weak. The unfortunate baby will have a corpse-like appearance. Only the visible signs of heart-beat and a few breathing gasp show that the baby is not dead.
- The treatment of infant asphyxia involves the clearing of the respiratory passage and supplying of oxygen to tissues.
- In mild cases, the child is held in an inverted position and a finger is gently introduced into its throat. This may remove the obstruction.
- In asphyxia livida, there is usually mucus in trachea or bronchi. It must be frequently removed by inverting the child and introducing a catheter into the glottis.
- Once the air passage is cleared, external irritation must be tried for reflex stimulation of respiration. Slapping on the back and buttocks of the inverted baby, sprinkling of cold water over the body, rubbing over the body with warm cloth, etc. are some of the common measures applied in mild cases.
- In severe cases, the child is immersed in warm water for a few minutes and then in cold water. Warm bath relieves the vasoconstrictor spasm and the overloaded heart. Weak mustard bath and careful compression of the chest are also tried
- In extremely severe cases, artificial respiration is essential.

RESPIRATORY PROBLEMS IN OLD AGE

Pneumonia

- Pneumonia is the acute infection and inflammation o the alveoli of the lungs.
- Pulmonary inflammation caused by allergic reactions is called alveolitis and that caused by chemical or physical agents is called pneumonitis.
- The organisms causing pneumonia include viruses, bacteria, mycoplasmas, fungi and protozoans.
- In healthy persons, it may because of *Streptococcus pneumoniae, Mycoplasma pneumoniae,* or a virus.
- The causative organism of pneumonia, following influenza, *Staphylococcus areus.*

- The major symptoms of pneumonia are

  (i) fluid-filled alveoli, containing dead leucocytes (ii)
  (ii) low oxygen level in blood (hypoxia) due to iow rate of gas exchange in lungs
  (iii) harsh and high-pitched breathing
  (iv) cough and fever.

- In pneumonia, the alveolar sacs fill up with fluid and white blood cells, considerably reducing the air space inside the lungs.
- Oxygen has great difficulty to diffuse the inflamed alveoli and so the O2 level in the blood may fall abnormally low.
- At the same time, the blood CO2 level remains normal, since CO2 can diffuse through the inflamed alveoli more easily than O2
- . The symptoms include cough, fever. pleuritic pain, dyspnoea, cyanosis, etc.
- Formerly, pneumonia was classified into three types, namely ***lobar pneumonia, lobular or segmental pneumonia, and bronchopneumonia***
- In lobar pneumonia, all the alveoli of a lung lobe a are inflamed
- In lobular pneumonia, the alveoli of only a portion or a lobule of a lobe are inflamed
- In bronchopneumonia, alveoli and bronchial tubes are inflamed.

Obstructive lung conditions

- These are the conditions which obstruct or limit airflow through the airway in aged persons.
- Some of such conditions are the following:
  1. Build-up of naturally occurring mucus - This is quite common in chronic obstructive pulmonary diseases (COPD). This mucus accumulation is only partiall_ reversible and 80 it considerably blocks the flow of air, air, leading to respiratory problems.
  2. Disruption of the support tissue around airways: Old age wear and tear naturally disrupts the package tissue around airways. This eventually leads to the local collapse of airways, resulting in emphysema.
  3. Tightening of the ring muscles around airways : This constricts the airwa_ s, leading to severe breathin: difficulties, asthma, etc.
  4. Thickening and hardening of the walls of airways : Thickening and heardening of the walls of airways by fibrosis reduces the lumen of the airway. This also adversely affects the free flow of air.

MODULE 3 CIRCULATION

BLOOD: FUNCTIONS AN COMPOSITIONS

Composition of human blood

- Blood is the chief transporting medium in the human body.
- In a healthy male, there will be 5-6 litres of blood, and in a healthy female 4-5 litres.
- Blood constitutes nearly 8% of the total body weight.
- Human blood is a thick, red-coloured and slightly alkaline (pH7.3~7.45) viscous fluid.
- It consists of blood plasma and blood corpuscles.
- Plasma is the fluid part. Corpuscles are the blood cells, loosely suspended in the plasma.
- Plasma forms about 55% and corpuscles 45% by volume.
- Plasma weighs as much as 5% of the total body weight.
- The instrument used for the measurement of blood plasma and blood corpuscles is known as haematocrit. Its measurements are called " haematocrit readings".

1. **Blood plasma**

- Blood plasma is a slightly alkaline yellow fluid, About 90-92% of it is water.
- The rest consists of organic and inorganic compounds in solution and suspension
- Plasma water has three major functions:
  - (i) Transports substances in a dissolved or suspended condition.
  - (ii) Regulates body temperature.
  - (iii) Regulates blood pressure and blood volume.

(a) **Organic constituents of blood plasma**

- The organic compounds of blood plasma include proteins, non-protein compounds, secretion products and wastes.
- The major plasma proteins include albumins, globulins, fibrinogen thrombogen (prothrombin) and heparin.

Albumins-

- Albumins are water-soluble proteins, which readily coagulate on heating.
- They form the major fraction of plasma proteins.
- By virtue of the smaller size and large abundance of their molecules, they contribute nearly 80% of the total osmotic potential of blood plasma.
- Albumins regulate blood volume, exert considerable osmotic pressure to maintain water balance between tissues and blood, and play an active role in the transport of lipids: hormones, bilirubin, naphthoquinones, sulphonamides, barbiturates, etc.
- Liver is the major centre of albumin synthesis in the human body.
- Insufficient albumin synthesis causes a rare condition, called *analbuminaemia*, characterised by low serum albumin and low blood pressure. It has no serious clinical effects.

Globulins

- Globulins are coagulable proteins.
- They are of three major kinds, namely alpha, beta and gamma globulins.
- Alpha globulins bind and transport thyroxine, bilirubin, lipids, steroids and mucopolysaccharides.
- Beta globulin can bind cholesterol, lipids, metals like iron and copper, and the vitamins A, D and K.
- The metal-binding globulins are generally called *transferrins.* An example is the copper-binding globulin *ceruloplasmin*.
- The rate of synthesis of this protein is very low in Wilson's disease (hepato-lenticular degeneration).
- Which is characterised by excessive deposition of copper in liver and brain and neurological manifestation similar to those of Parkinsonism.
- Gamma globulins are also called immunoglobulins. They serve as antibodies and play a vital role in immune mechanism.
- They are mainly concerned with binding antigens and histamines.
- Agammaglobulinaemia is the condition in which gamma globulins are absent in blood plasma. It results in the lack of immunity against bacterial infection.

Fibrinogen and thrombogen

- Fibrinogen and thrombogen or prothrombin are the plasma :roteins involved in blood clotting.
- During blood clotting, fibrinogen is converted to bring by the enzyme thrombin.
- Fibrin undergoes polymerisation and forms the clot, with the help of the enzyme ***fibrin stabilizing factor (factor xiii)***.
- The blood plasma from which fibrinogen removed for blood clotting is called blood serum.

Heparin

- Heparin is an anticoa ulant _anti-clotting factor). It prevents thrombosis (blood clotting inside blood vessels).

Non-protein organic constituents, secretions and wastes

- Non-protein organic compounds include glucose amino acids, fattyacids, glycerol, cholesterol, vitamins, etc.
- Secretion products include hormones, enzymes, antibodies, etc. Waste products include urea, uric acid, ammoni creatinine, xanthine, hypoxanthine, etc.

(a) Inorganic constituents of blood plasma

- The inorganic constituents, or the electrolytes, of blood plasma include mineral ions, such as the chlorides, iodides, carbonates bicarbonate, phosphates and sulphates of Na, K, Ca, Mg, Fe, Cu, etc. etc.
- They are essential for the maintenance of normal acid-base balance (pH level), ionic balance, osmotic potential and the physiological balance between blood and tissues.
- They are also involved in the clotting of blood, contraction o muscles (Ca2+), transmission of nerve impulses (Na+ and K+), strengthening of bones, etc.

FUNCTIONS OF BLOOD PLASMA

(i) Transport of substances that get dissolved or suspended in plasma water, or get complexed with plasma proteins
(ii) Maintenance of the normal volume, pressure and viscosity of blood by retaining water in blood.
(iii) Maintenance of normal blood pH by neutralizing strong acids and bases.
(iv) Regulation of body temperature through uniform distribution of heat all over the body
(v) Conduction of heat to skin for dissipation.

B. Blood corpuscles

- Blood corpuscles are generally called the formed elements of blood.
- Mammalian blood corpuscles are of three main kinds, erythrocytes, leucocytes and platelets.
- Erythrocytes are the most numerous blood cells and the constitute more than 98% of the total blood cells.
- Non-mammalian corpuscles include erythrocytes, leucocytes and thrombocytes or spindle cells.

- Thrombocytes differ from mammalian platelets in that they are nucleated; platelets are non-nucleated.
- Mature corpuscles have no powers for division and multiplication:
- The total number of blood corpuscles per one millilitre or one cubic mm of blood is called total blood cell count.
- Blood cell count is taken by the instrument haemocytometer,
- Formation of blood corpuscles is called haaematopoiesis or haemopoiesis (formation of erythrocytes is called erythropoiesis that of leucocytes is called leucopoiesis and that of platelets is called thrombopoiesis).
- In mammalian embryo and foetus, they are formed mostly in yolksac, liver, spleen and red marrow. But, after the foetal life, they are formed in red marrow.

I. Erythrocytes (red corpuscles)

- Are the small and the most numerous blood cells.
- The average total count of human RBCs is 4.5 to 6 million per cubic mm of blood.
- However, it may higher in the evening, after meals, during muscular exercise, at high altitudes, high environmental temperatures, high barometric pressures, and so on. Also, it is high in infants during the first few days of life.
- Usually, it is higher in males than in females.
- The pathological condition in which RBC count goes abnormally high (10 - 15 million per cubic mm of blood) js called polycythemia.
- The opposite condition in which the RBC count or the haemoglobin content of the blood falls abnormal low is called anaemia.
- Mature mammalian erythrocytes are non-nucleated, circular, disc-like and biconcave bodies, without ER, mitochondria, Glogi bodies and centrioles.
- Non-mammalian, erythrocytes are nucleated cells. Young mammalian RBCs are nucleated. But, as they mature, they lose their nucleus and membrane-bound cell organelles.
- A mature erythrocyte consists of a spongy network, known as stroma.
- It is enveloped by a limiting plasma membrane.
- Stroma is formed of interlacing lipoprotein molecules. Its lipid constituents mainly include lecithin and cephalin.
- Stroma contains haemoglobin and carbonic anhydrase and many other enzymes (about 280 million molecules of haemoglobin in a mature red blood cell).
- Drainage of haemoglobin from RBC is known as haemolysis. Haemoglobin is a red-coloured, iron-containing respiratory pigment, involved in the transport of O2 and CO2 Carbonic anhydrase is involved in the transport of CO2
- Biochemically, erythrocytes are formed of water, haemoglobin, enzymes, organic constituents and inorganic constituents.
- Nearly 100 enzymes are believed to be present in RBCs. Carbonic anhydrase, dehydrogenases, catalases, alkaline phosphatase, etc. are the major groups of enzymes

- Organic constituents include proteins, lipids, urea, amino acids, creatinine, phosphoglycerol, etc. Lecithin, cephalin, cholesterol and cholesterol esters are the major lipid constituents.
- The average life span of erythrocytes is 120 days.
- It is estimated that nearly 3 million RBCs die every second.
- To compensate this heavy loss an equal or still greater number is Produced in the bone marrow.
- Normally, the rates of production and destruction of RBCs are mutually balancing. The rate of production of RBCs is determined by the oxygen level in the blood.
- The production is controlled by a renal hormone, called erythropoetin.
- Worn out corpuscles undergo breakdown in liver and spleen.
- During this, the globin (Protein)part of its haemoglobin gets degraded into amino acids. The porphyrin molecules and haem portion gets degraded into the bile pigment biliverdin, which eventually transforms to the yellow pigment bilirubin. Biliverdin and bilirubin serve as bile pigments.
- The tron atom of the haem part is stored in the liver in the form of an iron-containing protein, called ferritin

Functions of erythrocytes

(i) Transport of respiratory gases (O, and CO,).
(ii) Maintenance of normal blood pH and ionic equilibrium.
(iii) Formation of bile pigments by the degradation of haemoglobin. Leucocytes

2. Leucocytes (white corpuscles)

- Are the largest and the least numerous blood cells.
- Their average total count is 5000-8000 or more per cubic mm of blood.
- The average life span of leucocytes is 4-12 days.
- Leucocytes are colourless and nucleated amoeboid cells.
- They are mainly involved in the defence against infections.
- Some of them ingest and digest foreign matters and invading microorganisms. They are known as phagocytes.
- Some others produce antibodies to develop immunity against infections.
- There are two groups of leucocytes, namely granulocytes (granular leucocytes) and agranulocytes (agranular leucocytes).
- Granulocytes are formed in myeloid tissue (in red marrow), and agranulocytes in lymphoid and myeloid tissues.
- Granulocytes have granular cytoplasm and lobular nucleus.
- But, agranulocytes have non-granular and homogeneous cytoplasm.
- There are three kinds of granulocytes basophils, eosinophils, and neutrophils or polymorphs,
- Agranulocytes are of two kinds, monocytes and_lymphocytes
- Neutrophils and monocytes usually serve as phagocytes.

- There are two kinds of phagocytes. namely microphages and macrophages.
- Microphages are small neutrophils, whereas macrophages are large monocytes.
- The monocytes which can migrate to infected tissues are called wandering macrophages. they clean up cellular debris after an infection
- Some chemicals in the infected and inflammed tissues attract phagocytes to the tissues. This is called chemotaxis,
- These chemicals include toxins and the degradation products of damaged tissues.
- Most leucocytes have the ability to crawl through the minute intercellular spaces in the capillary wall and also through connective and epithelial tissues. This is called diapedesis.
- Sometimes, the total count of leucocytes falls abnormally low. This condition is called leucopenia (leucopaenia).
- Similarly, it may go abnormally high sometimes, especially in malignancies, inflammations and acute infections. This is called leucocytosis.
- In some rare instances, some parent cells of leucocytes become cancerous and they undergo uncontrolled multiplication. This leads to an abnormal overproduction of one or more kinds of leucocytes. Most of the resulting cells are immature and abnormal. This very serious condition is known as leukemia (leukaemia, leucemia, leucaemia) or blood cancer.

Basophils

- Basophils are the granular leucocytes whose cytoplasmic granules stain deeply with basic dyes (such as methylene blue).
- They comprise 0.5 to 1% of the total leucocyte count.
- They move about in an amoeboid fashion and ingest bacteria. Often, basophils leave the capillaries, enter tissues and release heparin, histamine and serotonin.
- They are also believed to be involved in allergic reactions.
- The abnormally high count of basophyls is called basophilia, and their abnormally low count is called basopenia.

Eosinophils

- Eosinophils are the granular leucocytes whose cytoplasmic granules are large and they stain brilliantly with acid dyes, such as eosin
- They comprises 1.5 3% of total leucocytes
- Eosinophils are believed to combat allergens.
- They leave the capillaries, enter tissue fluid, and produce anti-hitamines which destroy antigen-antibody complexes.
- In parasitic infection, skin diseases, and some allergic states, such as asthma and hay fever, their number goes much higher. This condition is called eosinophilia.
- Abnormal fall in the number of eosinophils is called eosinopenia. It is common under conditions of stress and strain of the body.

- Eosinophils are involved in resisting viral diseases, helminth colonization, post-pubertal mammary gland development, allograft rejection, neoplasia, etc.
- The number of eosinophils is believed to be regulated by a hormone of the adrenal cortex.

Neutrophils

- Neutrophils are the granular leucocytes whose cytoplasmic granules are very fine and they do not stain, or stain only faintly, with acidic or basic dyes.
- Their nucleus is polymorphic and many-lobed, and therefore they are also called polymorphonuclear leucocytes or Polymorphs.
- They are able to squeeze out to the intercellular spaces through the pore spaces of the capillary walls. This is called diapedesis.
- From the intercellular spaces, they move to infected areas. Neutrophils exhibit amoeboid movement and are highly phagocytic.
- They can engulf and digest foreign particles, such as bacteria, using the enzymes from their granules, Thus neutrophils provide the first line defence of the body against infectious diseases.
- They crowd together in large numbers in pyogenic (pus-forming) infections and migrate freely into the tissues during inflammation. In pyogenic tissues, they die, forming pus.
- Neutrophils are the most numerous of all leucocytes and they account for 50-70% of the leucocytes.
- Their abnormally high count in the blood is called neutrophilia, and their abnormally low count is called neutropenia.

Monocytes ;

- Monocytes are the largest of all leucocytes.
- They are agranulocytes, with a large oval or bean-shaped nucleus which stains with basic dyes.
- Monocytes are actively phagocytic and they ingest and digest foreign particles, such as bacteria.
- Just as neutrophils, they also migrate to inflammatory tissues in large numbers.
- Monocytes are believed to undergo breakdown and release substances called trephones which stimulate nutrition, cell division, growth and repair.
- Monocytes account for 4 to 7% of the leucocytes.
- Their abnormally high number is called monocytosis, and abnormally low number is called monopenia.
- Monocytosis is usually associated with typhoid fever, malaria, tuberculosis, rocky mountain spotted fever, etc.

Lymphocytes

- These are the a. anular leucocytes, with very large and DNA-rich nucleus and small amount of clear cytoplasm.
- They are the second most numerous leucocytes, next neutrophils.
- They comprise 25-35% of the leucocytes. Lymphocytes are almost rounded cells, with a small quantity of cytoplasm.
- They are found in all tissues except those of the central nervous system.
- They have a highly variable life span of 2 to 200 days.
- They exhibit only a slight degree of amoeboid movement and have little phagocytic activity. Some lymphocytes are believed to disintegrate and release trephones.
- Lymphocytes are actively involved in immune mechanisms.
- There are two major classes of immunologically active lymphocytes, namely B-lymphocytes or B-cells and T-lymphocytes or T-cells B-cells secrete antibodies which neutralise antigens. T-cells secrete powerful toxins, called lymphokines, which destroy antigens or kill pathogens.
- Abnormally high count of lymphocytes is called lymphocytosis, and abnormally low count is called lymphopenia.
- Lymphocytosis is often associated with whooping cough, severe malaria, syphilis, Hodkins disease (progressive enlargement of lymph glands), etc.

Functions of leucocytes

1. Body defence by lymphocytes, monocytes and neutrophils. Lymphocytes produce antibodies and lymphokines to fight antigens, Monocytes and neutrophils by phagocytosis or by releasing the anti-bacterial enzyme lysozyme, Sometimes, some phagocytes by diapedesis.
2. Release of trephones by the breakdown of monocytes and some lymphocytes to stimulate cell division, growth and repair in tissues.
3. Eosinophils act against allergens (substance which cause allergic responses).
4. Production of heparin by basophils in liver.
5. Scavenging of cellular debris, dead bacteria and other particles by phagocytosis (by phagocytes)
6. Wound healing and scar formation at healed wounds.

Platelets

- Blood platelets are the colourless, non-nucleated and irregular corpuscles.
- They are the smallest of all corpuscles.
- Their average total count is 200,000400,000 per cubic mm of blood.
- Platelet count usually increases during exercise, after meals, during convalescence from infections, and also in haemorrhage, allergic reactions, myeloid leukemia, Hodgkin's disease, etc.

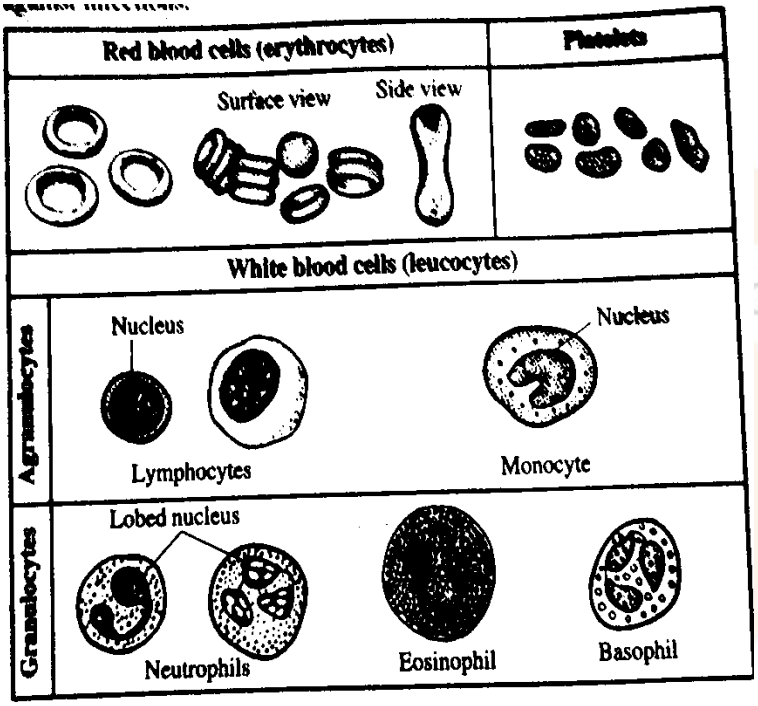
- It falls low in acute infections, irradiation, pernicious anaemia, anaemia, anaphylaxis, etc.
- Platelets are formed in red narrow by the fragmentation of the parent cells magakaryoblasts.
- Their average life span is 5 to 9 days.
- The abnormally high count of platelets is called thrombocytosis, and their abnormally low count is called thrombocytopenia,

Functions of platelets

1. **Play an active role in blood coagulation** (clotting of blood at injuries) by releasing thromboplastinogen and thromboplastinogenase which are essential for blood clotting.
2. **Bring about haemostasis** : Haemostasis is the control of bleeding. It occurs when blood vessels are punctured and slight bleeding follows. During this, the platelets physically stick to the cut edges of the vessels in large numbers. This forms a haemostatic plug or platelet plug. It seals up the cut edges of the vessels and prevents bleeding in about 3 or 5 minutes after the injury. The time required for the cessation of bleeding from a small puncture is called bleeding time.
3. **Defend the body by clumping over invading microorganisms and foreign particles in huge numbers.**
4. **Help vasodilation** (dilation of blood vessels) by releasing histamine and serotonin.

The important functions of human blood are the following:

1. Transport of nutrients from stomach, intestine and liver to tissues.
2. Transport of respiratory gases (O, and CO,) between lungs and tissues.
3. Transport of metabolic wastes and toxins from tissues to kidneys and sweat glands.
4. Transport of hormones from their sources (endocrine glands) to target sites (action sites)
5. Transport of enzymes from exocrine glands to cells.
6. Transport of metabolites among and between tissues.
7. Supply of necessary substances to secreting glands.
8. Defence against infections and toxins.
9. Regulation of body temperature (by absorbing, releasing, or distributing heat).
10. Maintenance of a proper and constant body pH (acid-base balance) through buffering actions.
11. Maintenance of water balance in cells (by transporting excess water to kidneys and sweat glands).
12. Regulation of electrolyte balance or fluid balance by removing salts from tissues to kid . "



Human blood : formed elements

COAGULATION OF BLOOD

- Coagulation or clotting of blood is the conversion of the fluid part of the blood to a thick jelly, known as clot or thrombus.
- Normally, clotting takes place when blood sheds out from injuries or wounds.
- The solid clot seals up the broken tips of blood vessels and prevents further bleeding and loss of blood.
- Thus, coagulation of blood is a major chemical defence against the loss of blood through injuries or wounds.
- The yellowish or straw-coloured liquid that oozes out-from-the-clot is-called serum.
- It is simply blood plasma without of its clotting proteins.
- Coagulation factors Blood-clotting involves a large number of biochemical agents, known as coagulation factors or clotting factors.
- They include 12 plasma coagulation factors, 4 platelet coagulation factors and a tissue coagulation factor which is a member of the plasma factors.
- Coagulation of blood is the net result of a complex series of enzymatic reactions.
- These reactions are completed in three naajor stages as follows:
- Stage I. Formation of the active enzyme thromboplastin from the inactive proenzyme thromboplastinogen with the help of activating factors.

- Stage II. Conversion of the plasma protein prothrombin or thrombogen into the active enzyme thrombin with the help of thromboplastin, several plasma coagulation factors and Ca** ions.
- Stage III. Conversion of the soluble plasma protein fibrinogen into insoluble fibrin with the help of thrombin. Fibrin forms the thread of the clot. It forms a loose tacework in which blood corpuscles get entangled forming the final clot.

equipping with excellence

BIOCHEMICAL PATHWAYS OF COAGULATION [Enzyme cascade theory] .

- Blood coagulation is the net result of a complex series ("cascade") of enzyme-catalysed biochemical reactions, called enzyme cascade system.
- Enzyme cascade mechanism involves two distinct routes, namely extrinsic .athwa and intrinsic pathways.
- In the former, thromboplastinogen is released from the damaged tissue cells, but in the latter it is released by the breakdown of blood platelets. These two pathways later on merge together.

(a) Extrinsic pathway

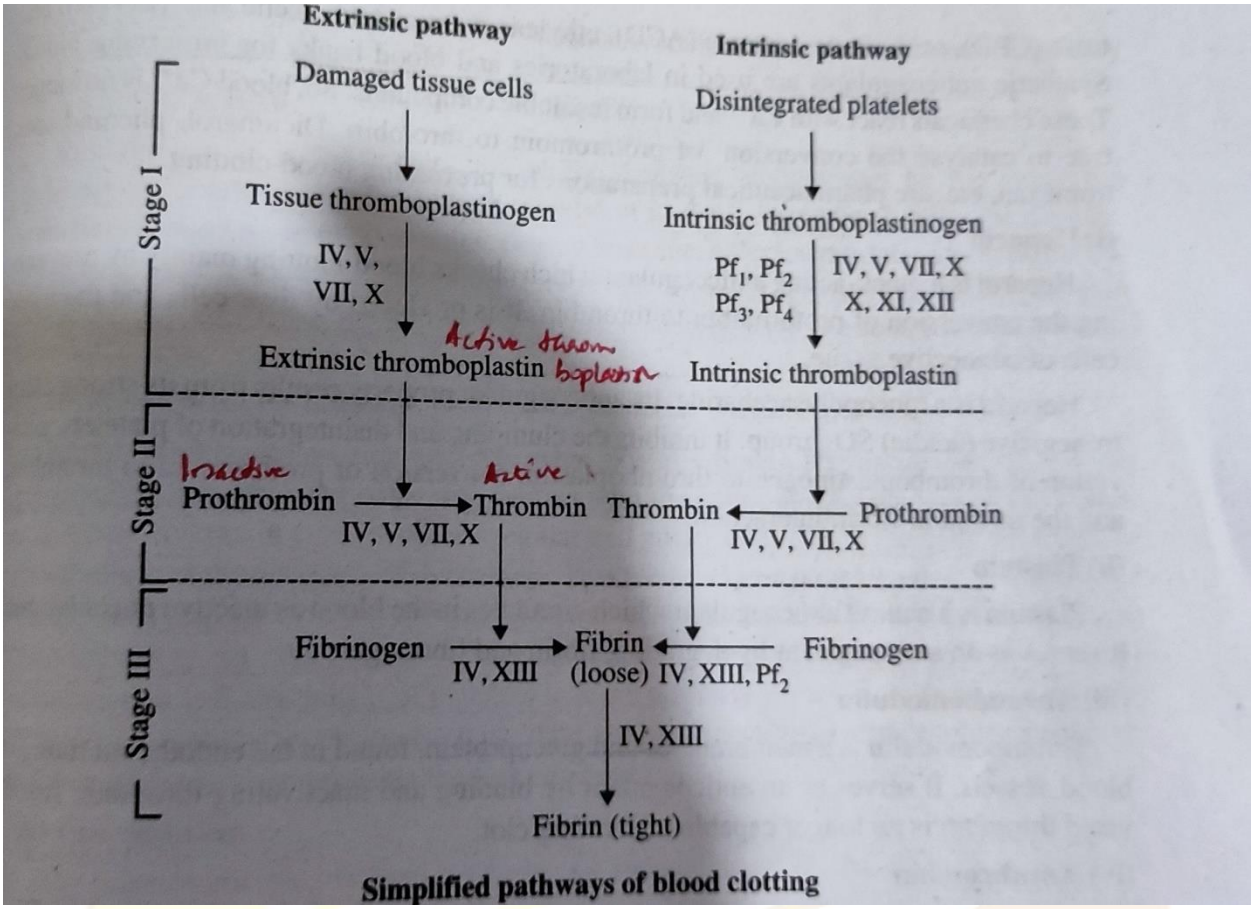
- The extrinsic pathway of blood-coagulation begins with the release of the lipoprotein extrinsic thromboplastinogen or tissue thromboplastinogen from the ruptured part of the blood vessels or from the damaged tissues around.
- Thromboplastinogen reacts with the clotting factors IV, V, VI and X and gets transformed to active thromboplastin or extrinsic thromboplastin.
- This conversion represents the first stage of coagulation.
- The second stage of extrinsic pathway involves the conversion of the plasma proenzyme prothrombin (thrombogen) into the active enzyme thrombin.
- Prothrombin is produced and released by liver. It reacts with extrinsic thromboplastin and the plasma clotting factors IV, V, VI and X.
- In the third stage of extrinsic pathway, the plasma protein fibrinogen gets transformed to insoluble fibrin by reacting with thrombin and the plasma clotting factors IV and XII.
- Initially, fibrin is a loose meshwork of interlacing strands. It is converted to a tight and dense aggregate by the formation of covalent cross-links between the strands.

- This reaction is catalised by the clotting factors IV and XIII. Intact fibrin network forms the clot. In the meshes of the fibrin network, blood corpuscles get entanged, formin a jell –like plug, Which forms the final clot.
- This plug seals up the broken blood vessel and prevents further loss of blood: From the clot, a clear yellow liquid oozes out. It is called serum. It is the blood plasma from which fibrinogen is removed for clotting.

(b) Intrinsic pathway

- The intrinsic pathway of blood clotting begins with the adherence of numerous blood .
- Platelets to the ruptured areas of blood vessels.
- This clumping together of platelets causes their disintegration, releasing the platelet clotting factors to the blood plasma.
- In small injuries, platelet clumping seals up the injury without initiating the clotting reactions.
- The first stage of the intrinsic pathway involves the conversion of inactive intrinsic thromboplastinogen to active intrinsic thromboplastin.
- In this case, thromboplastinogen reacts with the plasma clotting factors IV, V, VII, IX, X, XI and XII and the platelet clotting factors Pf1, Pf2, Pf3, and Pf4.
- In the second stage, prothrombin gets converted to thrombin by reacting with intrinsic thromboplastin and the plasma factors IV, V, VII and X.
- In the third stage, fibrinogen gets converted to fibrin by reacting with thrombin, the plasma factors IV and XIII and the platelet factor Pf2.
- Initially, fibrin forms a loose meshwork over the injured part. It is soon stabilized to a dense network by the action of plasma factors IV and XIII as in the extrinsic pathway.
- Apart from converting fibrinogen to fibrin, thrombin stimulates the clumping and disintegration of more and more platelets, releasing still more platelet factors.
- This is a kind of positive feedback and it ensures continuous platelet disintegration until the final clot is formed.

equipping with excellence
CA COLLEGE OF GLOBAL STUDIES



Simplified pathways of blood clotting

Anti-coagulants

- Anticoagulants are the chemical substances which can prevent blood-clotting.
- Naturally occurring biological anticoagulants include heparin, plasmin, thrombomodulin, anti-thrombin, protein C, hirudin, snake venom, etc.
- Synthetic anticoagulants include synthetic heparin, coumarin, the oxalates and citrates of Na and K, salicylates, citrate phosphate dextrose (CPD), acid citrate dextrose (ACD), ethylene diamine tetra acetic acid (EDTA), etc.
- Dicumarol, phenindione, tromexan, etc. are pharmaceutical preparations for preventing blood-clotting.

(i) **Heparin**

- Heparin is a quick-acting anticoagulant which checks blood-clotting mainly by preventing the conversion of prothrombin to thrombin.
- It is produced by liver cells and the mast Cells of connective tissue.
- Heparin is a mucopolysaccharide.
- Its anticoagulant property results from its strong electronegative (acidic) SO4 group.
- It inhibits the clumping and disintegration of platelets, activation of thromboplastinogen to thromboplastin, conversion of prothrombin to thrombin, and the thrombin-fibrin interaction.

(ii**) Plasmin**

- Plasmin is a natural anticoagulant which circulates in the blood as inactive plasminogen.
- It serves as an anticoagulant by degrading fibrin and fibrinogen.

(iii) **Thrombomodulin**

- Thrombomodulin is a membrane-bound glycoprotein, found in the endothelial lining of blood vessels.
- It serves as an anticoagulant by binding and inactivating thrombin.
- Inactivated thrombin is no longer capable of forming clot.

(iv) Antithrombin

- Antithrombin is a plasma globulin.
- It serves as an anticoagulant by neutralising some clotting enzymes and clotting factors and also by inactivating thrombin. In normal blood clotting,
- It binds with the excess thrombin that is left over after clot formation. This prevents clot formation in the nearby areas.

(v) **Protein - C**

- This is a plasma protein which can inactivate the clotting factors pro-accelerin and antihaemophiliac factor to control blood-clotting.
- For this role, it is activated by thrombin.

(vi) Hirudin

- Hirudin is a strong anticoagulant, found in the saliva of blood-sucking leeches.
- It is anti-thrombin in action and it interferes with the reaction between thrombin and fibrinogen.

(**vii) Snake venom**

- The venoms of cobra, some species of vipers, etc. are powerful anticoagulants by virtue of their anti-thromboplastin property.
- So, they interfere with the conversion of prothrombin to thrombin.

HAEMODYNAMICS

- Haemodynamics is the study of the 1h sical principles, mechanics and energetics of blood, pressure and blood circulation.
- It is the study of blood flow and blood pressure.
- Blood is a viscous fluid and so it flows through the blood vessels very slowly. Veins and capillaries are only passive partsof the circulatory system.
- They exert considerable peripheral resistance against blood flow so that the blood reaching the heart is practically devoid of any momentum of its own.
- Moreover, veins are valvular and so they can prevent the reverse flow of blood, if the onward flow is obstructed.
- Heart keeps on beating regularly and rhythmically, pushing the blood into the arteries.
- This provides the blood the initial pressure and momentum, essential for its circulation.
- Arteries are elastic and so they extend and relax at every hear beat.
- When blood is pumped into the ar arteries with pressure, their walls dilate momentarily.
- Very shortly afterwards, the arterial walls recoil pushing the blood further forwards.
- Before the arterial wall undergoes complete le recoiling, another spurt of blood is forced into the artery by the next heart-beat.

- This process is repeated non-stop, facilitating a continuous flow of blood through blood vessels.
- So, it becomes clear that arteries are always in a dilated state.
- This dilated condition elicits the recoiling reaction which forms the source of arterial blood pressure.
- Persistent arterial pressure causes the blood to move forward continuously.
- Arteries are progressively tapering towards capillary end.
- So, the arterial pressure never falls low till the blood reaches the capillaries, Higher arterial blood pressure is essential for several physiological processes, such as glomerular ultrafiltration.
- blood is kept in constant circulation and a proper and constant arterial blood pressure is maintained by (i) the regular and rhythmic heart beats (ii) regularly repeating distensions and recoiling of the arterial walls (iii) progressive narrowing of arteries towards the cavillary end and (iv) the passive squeezing of the veins whose valves prevent the counter-flow of blood.

The major parameters in circulatory haemodynamics are the folowing:

(i) General activity of the animal - The intensity of activity is the only force that maintains circulation in small and primitive animals. Also, it is an important factor in some regions of highly organized animals (e.g., in the lymphatics and small veins of birds and mammals).

(ii) Cardiac output - The amount of blood pumped in a unit time is related to the blood volume and the force of heart-beat.

(iii) Peripheral resistance - This is the resistance against flow in peripheral or terminal blood vessels. It is important in determining the force of circulation. Peripheral resistance is significant in vertebrates and large invertebrates with closed circulation.

iv) Velocity of blood flow - The linear velocity with which blood passes a fixed point in the circulatory area (measured in cm/second).

(V) Volume flow of blood - The amount of blood flowing through a segment of blood vessel; measured in ml/minute).

(vi) Circulation time - The time taken by blood to pass from one fixed point to another.

- The flow of blood is influenced by several factors, such as pressure gradient (driving Pressure), viscosity (the internal frictional force of blood against flow), the inertia of the mass of blood that is moved and accelerated by heart-beats, the force of gravity, the cohesive force between blood and the wall of the blood vessel, the diameter of the lumen o the blood vessel, etc.
- All Newtonian fluids exhibit a linear relation between pressure and the velocity of flow. Blood is a non-Newtonian fluid in that it does not obey the laws of viscosity and its apparent viscosity varies as a function of the flow rate.
- The viscosity of blood increases markedly as its flow rate slows down. This is called anomalous viscosity.
- It is presumably due to the aggregation of erythrocytes. The decrease in apparent viscosity when blood flows through arrow vessels (smaller than 200 in diameter) is called Fahraeus - Lindqvist effect.
- According to it, the smaller the blood vessel, the lower the viscosity, and the greater the flow rate.

HAEMOSTATIS

- Haemostasis is the control or stoppage of the bleeding from cut, damaged, or injured blood vessels.
- It involves three successive mechanisms, namely (i) vascular spasm (ii) platelet plug formation and (iii) coagulation.
- These mechanisms are useful to prevent haemorrhage only in smaller blood vessels.

Vascular spasm

- Vascular spasm is the constriction of the damaged blood vessel by the quick and spontaneous contraction of the smooth muscles of its wall, immediately after the damage.
- It reduces blood loss up to 30 minutes, During this time, other haemostatic mechanisms can go into operation.
- Vascular spasm probably results from the reflexes initiated by the pain receptors and also from the stimulation by the vasoconstrictor serotonin, released by the blood platelets.

Platelet plug formation

- Blood platelets play an important role in haemostasis. Soon after vascular spasm, they get activated by thrombin and come into contact with the cut or damaged edges of the vessel.
- Soon, they enlarge in size, become irregular and sticky and stick to the collagen fibres or endothelium if the cut edges of the Vessels.
- This forms a loose platelet patch. The activated and attached platelets release ADP and some enzymes which attract other platelets and cause them to stick to the platelet patch.
- This platelet clumping is stimulated by fibrinogen.
- The accumulation and attachment of platelets in large numbers form a tight temporary clot, in about five minutes after the injury.
- It is called haemostatic plug or platelet plug. It seals the break in the vessel and prevents the loss of blood.

Coagulation

- The haemostatic plug is soon strengthened and stabilized by the formation of a fibrin mesh over and around it.
- It is called clot or thrombus.
- If the thrombus contains platelets alone, it is called white thrombus,
- Sometimes, erythrocytes also get attached to the platelet plug. Such a thrombus is called red thrombus.
- Once bleeding has come to complete halt, the clot is dissolved by the action of an enzyme, called plasmin.
- This is called fibrinolysis. Plasmin exists in the blood as an inactive precursor or proenzyme, called plasminogen.
- It is activated by proteolytic enzymes, such as trypsin.

HAEMOLYSIS AND JAUNDICE

- Haemolysis is the breakdown or rupture of the plasma membrane of RBCs and the consequent release of haemoglobin.
- Massive haemolysis, in all probability, may cause a form of anaemia, called histolytic anaemia.

- Haemolysis can occur for various reasons, such as the Presence of haemolysin and toxic chemicals, snake poisoning, mechanical destruction, osmotic shock, incompatible blood transfusion, malaria, glucose-6-phosphate debydrogenase deficiency (a genetic disorder), etc.
- Haemolysin is an antibody that can activated Complement system to cause the lysis of RBCS.
- Haemolysis is common in pernicious anaemia and it occurs very rapidly in poisoning by haemotoxic snake venom.
- Haemolysis causes three serious disorders, namely haemolytic anaemia, erythroblastosis foetalis (haemolytic disease of the new-born) and haemolytic jaundice.
- Haemolytic anaemia results from excessive haemolysis and the consequent steep fall in RBC count and _haemoglobin content of the blood.
- If it is due to the high fragility of RBCs. is called congenital haemolytic anaemia.
- Erythroblastosis foetalis is a severe form of haemolysis that results from maternal foetal Rh incompatibility.
- In this case, maternal blood is Rh-negative and foetal blood is Rh-positivé.
- The Rh + foetal blood reaches the mother through placental circulation.
- This causes the formation of anti-Rh antibodies in the mother.
- These antibodies then reach the foetus through placental circulation.
- This causes antigen-antibody reaction in the foetus and massive haemolysis, resulting in erythroblastosis foetalis.

Haemolytic jaundice

- Jaundice or icterus is the yellow discolouration of the skin, mucous membranes, white of eyes (sclera) and body fluids due to the excessive deposition of the bile pigment bilirubin.
- During haemolysis, haemoglobin undergoes degradation in liver and spleen.
- Its haem portion is transformed into a green pigment, called biliverdin.
- Biliverdin undergoes oxidation and forms the reddish yellow pigment bilirubin.
- When liver is unable to remove bilirubin from blood because of increasingly high destruction of RBC, large amounts of bilirubin circulate through blood stream and get deposited in tissues, this causes haemolytic jaundice.
- Sometimes, liver fails to remove bilirubin from blood due to the obstruction of bile duct. This causes obstructive jaundice.

Hepatogenic jaundice

- Apart from haemolytic jaundice, there is another type of jaundice called_hepatogenic jaundice.
- It is the usual type and it results from the absorption of bile to blood and lymph, and not from haemolysis.
- Its main causes include hepatitis (inflammatory disorganization of liver due to viral infection), cirrhosis of liver, alcoholic liver diseases, obstruction to the flow of bile along bile channels and bile duct, etc.
- Obstruction to the flow of bile may be due to some causes inside the liver (e.g., gall stones) or outside the liver (e.g., pancreatic cancer, enlargement of the glands lying near the liver).
- When the bile cannot flow freely into the intestine, it is absorbed to blood and lymph and some of its constituents get deposited in various tissues all over the body.
- Certain infective diseases, such as yellow fever, malaria, typhoid fever and pyaemia (blood-poisoning in which abscesses appear in various parts of the body) may also cause hepatic jaundice.
- "Acute yellow atrophy Of liver" is a rare and serious condition accompanied by hepatic jaundice

HAEMOGLOBINOPATHIES

- Haemoglobinopathies are genetically determined and race-related hereditary human disorders due to abnormal haemoglobin.
- They are characterised by impaired formation of normal adult haemoglobin and haemolytic anaemia.
- Sickle-cell anaemia (sicklemia or sickle-cell disease - SCD) and thalassemia are two common haemoglobinopathic disorders.

(a) Sickle-cell anaemia .

- Sickle-cell anaemia is a severe type of haemolytic anaemia in which RBCs are distorted and sickle-shaped.
- The sickling of RBCs is due to the presence of an abnormal haemoglobin, ~ called sickle-cell haemoglobin or haemoglobin S (HbS).
- It partially or almost completely replaces the normal adult haemoglobin (HbA).

- HbS differs from HbA in having valine, instead of glutamic acid in the 6" position of one or both of its beta chains. Sickling of RBCs is due to the crystalization of HbS under conditions of low pO2 in veins.
- This often slows down of obstructs blood flow resulting in the infarction of the respective ussues.
- Sickled RBCs are more fragile than normal RBCs and so they rupture very castly.
- Also, they have only jow oxygen-binding powers.
- Their life span is very short and they undergo massive destruction in spleen. This causes a fatal type of haemolytic anaemia, called sickle-cell anaemia.
- The clinical symptoms of the disease include enlarged spleen, rheumatic ailments, mental disorders, severe hypoxia, and very rarely cardiac problems and renal failure.
- Sickle-cell anaemia is a congenital disease, caused by the recessive lethal mutation of an autosomal structural gene, which governs the synthesis of the beta chajn of haemoglobin.
- It js found among the populations, or the descendants of the populations, inhabiting the malaria belt around the world.
- It is common among the Negro populations of Africa and America and also among the people of Mediterranean counties.
- In Kerala, it is prevalent among the tribals of Wynad. .

(b) Thalassemia

- Thalassemia, also known as Cooley's anaemia or Mediterranean anaemia, is a serious disease of the childhood, fatal before puberty.
- It is an abnormality in the quantity and not in the chemical nature of haemoglobin
- The affected persons will have high amounts of foetal haemoglobin (HbF), but only very insufficient amounts of adult haemoglobin (HbA).
- This is due to the recessive mutation of the autosomal globin gene.
- Thalassemia has high frequency among the people of the Mediterranean countries (Greeks, Italians, Turks and Spaniards), Middle East and Far East, and it has particularly high incidence among Greeks and Italians.
- The major symptoms of thalassemia include severe anaemia, persistent jaundice, enlarged liver and spleen, retarded growth, swollen belly, etc.
- Severely affected children may die before the age of 10 years.
- Thalassemia has three major charactereristics :
    - (i) continued production of HbF, even after birth
    - (ii) much reduced production of HbA and

(iii) HbF-containing RBCs are minute and abnormal and have only very low oxygen-carrying powers.

- Thalassemia is of two types, major and minor.
- The major is the severe type, and its Victims are homozygous for the mutant gene.
- The miner is the mild form, and its victims are heterozygous for the mutant gene.
- In one type of thalassemia, there is extremely insufficient synthesis of the alpha chains, both in the foetus and in the adult. So, it is called alpha thalassemia.
- In the other type, there is extremely low production of beta Chains and so it is called Beta thalassemia.
- Both these can be major or minor, depending upoa Whether the mutant gene exists in homozygous or heterozygous conditions

TRANSFUSION OF BLOOD

- Blood transfusion is the intravenous transfer or administration of one person's blood to another's body.
- The person who receives blood is called recipient, and the person who donates blood is called donor.
- Now-a-days blood transfusion has become a common practice to make up extreme deficiency or heavy loss of blood, as a treatment for anaemia, or for giving temporary relief of haemophilia and acute leukemia.
- At the same time, it is not safe to transfuse blood from all donors indiscriminately to all recipients.
- This is because the blood of different individuals can be chemically different, and when two different types of blood are mixed together, they may react with each other. Such mutually interacting types of blood are said to be incompatible or mismatching.
- Those which do not interact are called compatible or matching types. Transfusion of incompatible blood causes the death of the recipient.
- This is because of the clumping or agglutination of donor’s red corpuscles in the recipient. The clumped RBCs crack and cause toxic reactions,
- Transfusion of mismatching blood has some more difficulties also. In it, the corpuscles of the donor blood often break up in the new circulation.
- So also, the recipient person may suffer from nettle rash, breathing difficulty, purging, etc.
- The immediate destruction of RBCs in the recipient may cause jaundice 1n some cases.
- The mandatory steps to be taken as precautions in blood transfusions include

(i) the typing of the donor blood and the recipient blood tg ascertain whether they are compatible with respect to A,B and Rh antigens

(ii) the screning of the donor blood to know whether it is infected with human immunodeficiency virus, (HIV), hepatitis B virus (HBV), malarial parasites, etc.

(iii) administration of furosamide to prevent fluid overload if the recipient is at the risk of congestive heart failure.

equipping with excellence

AGGLUTINATION OF BLOOD

- Agglutination is the clumping together of the red corpuscles of the donor blood in the recipient, when blood transfusion involves incompatible or mismatching blood
- Agglutination is the result of an antigen-antibody reaction.
- The antigen is known as agglutinogen, and the antibody, agglutinin.
- Agglutination occurs in the red corpuscles, and agglutinin in plasma.
- Most agglutinins are naturally occurring antibodies. So, they are always found in blood.
- ABO blood system In 1900, Karl Landsteiner recognized four major groups of human blood, namely A, B, AB and O groups (ABO system).
- This grouping was made on the basis of two antigens and two antibodies, namely antigens A & B and antibodies a &b anti-A antibody and anti-B antibody)
- 'A'group blood contains A BO blood system antigen A and antibody b.
- 'B'-group Group Antigen Antibody contains antigen B and antibody a.
- in the RBC in the plasma 'AB'-group has antigens A and B, but no A antibodies a,b
- O group contains antibody a, and b but no antigens
- In mismatching transfusion, antibody a of the recipient reacts with antigen A of the donor and causes agglutination.
- Similarly, antibody b of the recipient reacts only with antigen B of the donor, resulting in agglutination.
- On the other hand, the small amount of the antibody of the transfused blood is not sufficient to agglutinate the RBCs of the recipient blood.
- So, it gets dissolved and diluted in the recipient blood, soon after transfusion. This is the reason why the recipient's red cells never agglutinate. Thus, in mismatching transfusion it is always the red corpuscles of the donor blood that agglutinate, and not those of the recipient blood.

- **The possibilities of permissible blood transfusion are the following**

group	Can be donated to	Can receive
A	A & AB	A & O
B	B & AB	B & O
AB	AB	All groups
O	All groups	O

- Since A-group contains antigen A and antibody b, it can receive A & O-groups and can be donated to A & AB groups, without any danger.
- Since B-group contains antigen B and antibody a, it can receive B & O-groups, and can be donated to B & AB groups.
- AB-group contains antigens A & B and no antibodies. So, it can receive all groups, and at the same time can be donated only to AB group.
- Similarly, O-group contains antibodies a & b, but no antigens. So, it can be donated to all groups, but can receive only O-group.
- Since AB-group can receive all groups and O-group can be donated to all groups, they are known respectively as universal recipient and universal donor.

APHAERESIS

- Aphaeresis or apheresis (Gk. means to take away) is a medical technology employed for separating a particular constituent of the blood of a donor or patient.
- In it, the blood is Passed through an instrument which separates the constituent and returns the remainder of the blood to the circulation.
- Aphaeresis is thus an extracorporeal therapy.
- Blood components are separated either from the blood already collected from a person or directly from his circulation.
- Based on the components separated, the following types of aphaeresis can be recognized:
    - **(i) Plasmaphaeresis** : In this case, blood plasma is separated and collected as fresh frozen plasma (FFP) to be used as and when needed. Apart from collecting FFP, this method is also used in collecting immunoglobulin products, plasma derivatives and rare antibod ies, FFP can be stored for one year at -18°C and up to seven years at -65°C.

(ii) Platelet aphaeresis : This is the separation of platelets and the returning of the RBCs, WBCs and plasma components to circulation.

(iii) Leucopheresis : Separation of leucocytes, especially polymorphonuclear leucocytes, for transfusion into patients.

(iv) Stem cell harvesting : Separation of bone marrow stem cells to be used in marrow transplantation.

(v) LDL aphaeresis : Separation of low-density lipoproteins from patients with familial hypocholesterolemia.

(vi) Automated red cell collection : Removal of RBCs.

- Blood clotting during aphaeresis is prevented by adding an anticoagulant while the blood passes through the aphaeresis machine.
- In aphaeresis, apart from the desired constituent, small amounts of fluid would also be removed from blood.
- This fluid loss has to be made up to maintain the normal fluid volume and osmotic balance by the administration of a suitable fluid into the body.
- Aphaeresis is significant in that it can be applied either for collecting specific blood components from a donor to be transfused to a recipient, or for removing some harmful or disease-causing constituents from blood.
- In the latter case, aphaeresis has to be carried out quite often, when other means to control a particular disease are not successful.

TYPES OF HEART

- Heart is the central muscular pumping organ
- Keeps beating non-stop to maintain a constant circulation of blood all over body
- There are two classifications;
  1. Based on structure
  2. Based on stimulation of heart beat

BASED ON STRUCTURE

1. Pulsating vessels

- Contractile blood vessels
- Function as unspecialized hearts

- Rhythmic wave of pulsations, or alternate contractions and relaxations passing on their walls regulates the blood flow these peristaltic movements are not regular and co-ordinated

Example:- amphioxus
Annelids

2. Tubular hearts

- Contractile tubes without distinct chambers for separation of arterial and venous blood
- Walls are strengthened by striped muscles

Example:- ascidians
Arthropods (insects)

- Insect heart has series of compartments with valvular openings between successive compartments
- Each compartment has a pair of valvular opening ; ostia
- Blood flow is behind forwards
- In ascidians ; no compartments, no valves
Has a periodic reversal of blood flow direction

3. Chambered hearts

- Specialized hearts with distinct chambers for arterial and venous blood

Example :- cephalopod molluscs
Vertebrates

- In fishes heart is two chambered with 1 atrium and 1 ventricle (exception lung fishes)
- In amphibians heart is trilocular with 2 auricles and 1 ventricle
- In reptiles heart is incompletely 4 chambered with 2 auricles and a partially divided ventricle (exception crocodiles)
- In lung fishes, crocodiles, birds and mammals heart is tetralocular with 2 auricles and 2 ventricles

4. Accessory hearts (Auxillary or ampullary)

- Contractile sacs supplementing function of heart to boost up pressure of lymph or blood

Example :- blood pumps of crustaceans
Accessory pulsatile ampular organs of some isects
Branchial hearts of cephalopod molluscs
Bulbils of amphioxus
Lymph hearts of vertebrates

BASED ON STIMULATION OF HEART BEAT

1. Myogenic heart

- Cardiac muscles has the autonomous ability to initiate, maintain heart beat without nervous stimulation
- Rhythmicity of heart beat by cardiac muscles
- Example ; molluscs, tunicates, vertebrates

2. Neurogenic heart

- Heart beat is initiated and controlled by nervous control
- Example : all other animals

CARDIO VASCULAR PROBLEMS IN MAN

ABNORMAL VARIATIONS OF BP

1. HYPOTENSION

- Persistently low blood pressure
- Blood pressure falls below 100 mm Hg during systole 60 mm hg during diastole.
- It Cause general weakness, easy tiring, head-ache, dizziness, pain in the region of heart, etc
- Serotonin and histamine dilate blood vessels, induce hypotension.
- Low cardiac output, low viscosity, dilation of arteries cause hypotension.

2. HYPERTENSION

- State of sustained blood pressure
- Above 140 mm hg systole, 90 mm hg diastole
- Head-ache, giddiness, visual disturbances, tiredness,
- When blood volume increases and blood vessel become constricted
- Angiotensin, a protein produced by kidneys under the influence of renal enzyme renin increases BP
- High cardiac output, high viscosity of blood, less lumen space, heart disorders causes high BP
- Two kinds

Primary hypertension

- Without known reasons
- More than 90% cases
- Above age 40
- Causes hereditary indisposition, congenital kidney disorders, excessive salt intake, prolonged stress

Secondary hypertension

- Due to disorders, kidney stones, atherosclerosis,

TACHYCARDIA

- High rate of heart beat

- Heart rates greater than 100 beats per minute
- Normal physiological condition to stress

- Harmful and life threatening in 3 ways
- When heart pumps too fast for long time, it disturbances 02, and CO2 balance in hb
- When heart beats too rapidly, it pumps blood less efficiently
- Faster heart beats, more oxygen and nutrients heart requires

BRADYCARDIA

- Abnormally low rate of heart beat
- Resting heart rate below 60 beats per minute
- Relative bradycardia is a term used to denote a heart rate below 60 beats per minute

MYOCARDIAL INFARCTION (HEART ATTACK)

- Serious form of ischaemic heart disease
- Extensive tissue damage or death of heart muscles due to lack of blood supply
- Two causes, ventricular fibrillation, coronary thrombosis

HEART FAILURES

- Congestive heart failure or congestive cardiac failures
- Any structural or functional cardiac disorder that impairs the ability of heart for fillig and pumping.

CEREBRO-VASCULAR ACCIDENT

- Stroke or apoplexy
- Loss of function of one side of body due to sudden stop of blood supply to a part of body
- Common with increasing age

Common symptoms

1. Paralysis or weakness of one half of body
2. Inability to speak, write, read, and understands speech
3. Difficulty in swallowing
4. Confusion, drowsiness, depression, involuntary urination
5. Loss of consciousness

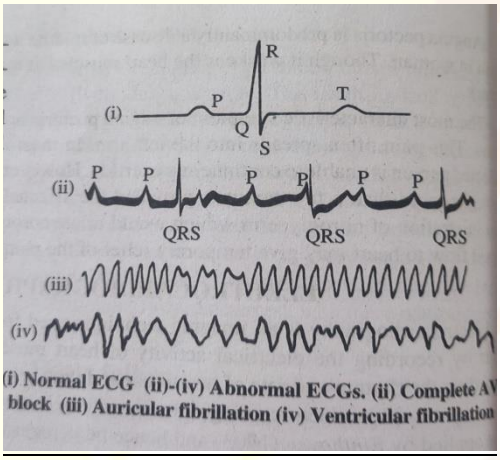
- Two types
- Complete stroke and transient stroke

CEREBRAL HAEMORRHAGE

- Bleed in to substance of cerebrum
- Lead to haemorragic strokes , they are medical emergencies

ELECTROCARDIOGRAPHY

- Imaging technique used to study the functioning of heart by recording electrical activity of heart muscles
- Gives correct information regarding rhythm and rate of heart beat
- Instrument used is electrocardiograph
- First applied by Einthoven (1903)
- Father of electrocardiography
- Heart muscles are in a state of intermittent excitations
- There is an incessant flow of impulses over heart walls, causes generation of electrical potentials over heart walls. they are called action potentials.
- They can recorded on a graph paper.
- Graphical representation of electrical activity of heart is called electrocardiogram



(i) Normal ECG (ii)-(iv) Abnormal ECGs. (ii) Complete AV block (iii) Auricular fibrillation (iv) Ventricular fibrillation

- 5 characteristic waves P,Q,R,S and T
- P,R,T are upward waves.
- Q,S downward waves
- P WAVE excitation and repolarization of atrial muscles, known as auricular complex.
- Q,R,S, and T represents initiation and spreading of excitation of base of ventricle, so ventricular complex.
- Interval between P , Q waves represents articular systole
- Interval between P, R waves represents the time required for spreading of excitation from SA node to ventricle

MODULE 4. OSMOREGULATION AND EXCRETION

OSMOREGULATION AND EXCRETION

- Osmoregulation is the active regulation of the osmotic potential through the maintenance of a proper & constant concentration of water & mineral ions in the body fluid.
- It is the energy consuming dynamic process which regulate the movement of water & salts between body fluids & external medium.
- They accomplish this by two physiological mechanisms, excretion & osmoregulation.
- It plays a vital role in homeostasis.
- Maintenance of a proper concentration of water is known as osmotic regulation.
- Maintenance of a proper concentration of mineral ions is known ionic regulation.
- Osmoregulation is carried out by different mechanisms :
    1) Regulation of the permeability of the body surfaces to salts & water.
    2) Active absorption or excretion of salts & water.
    3) Alterations in the tonicity of urine or excretory fluid.

Euryhaline & stenohaline animals

- Euryhaline animals can tolerate or withstand a wide range of salinity variations in the external medium, either by conformity or by regulation.
  Eg:- Salmon, eel
- Stenohaline animals can tolerate only slight variations, they may not survive beyond a certain limit of salinity change in the medium.

Iso-osmotic, hyposmotic & hyperosmotic animals

- The body fluids of marine invertebrates & the sea water around them have the same osmotic concentration or osmotic potential, such animals are *iso-osmotic* in relation to medium. They will not normally have any osmotic stress.
- The body fluids of fresh water animals are osmotically more concentrated than the medium. They are *hyperosmotic animals*.
- The body fluids of marine vertebrates of high salinity waters are osmotically less concentrated than the medium. They are called *hyposmotic animals*.
- Hyposmotic & hyperosmotic animals have osmotic stress.
- *Isosmotic animals are osmoconformers*.
- Hyperosmotic & hyposmotic animals are osmoregulators, known repectively as *hyperosmoregulators & hyposmoregulators*.
- Hyperosmotic regulators are subjected to gain water by endosmosis & loss of salt by diffusion.

- Hyposmotic regulators are subjected to loss water by exosmosis & gain of salts by diffusion.

OSMOCONFORMERS AND OSMOREGULATORS

- The internal osmotic and ionic concentrations remain constant, irrespective of the changes in the surrounding medium. they are called osmostable animals (homeosmotic animals).
- They are endowed with osmotic independence with respect to the external environment.
- They regulate their internal concentration through certain checks and controls to counterbalance the external changes. So they are called osmoregulators.
- All vertebrates, most of the freshwater invertebrates, and a few marine invertebrates are osmoregulators.
- Some animals are incapable of osmoregulation. So they adjust themselves not by employing regulatory mechanism, but slowly succumbing to the changes in the external environment.
- Their internal osmotic and ionic concentrations fluctuate in relation to external environment.such animals are called osmolabile (poikilosmotic) animals.
- They are characterised by osmotic dependence with respect to external environment.
- Since their internal concentration always conforms to the surrounding medium, they are osmotic conformers.
- Most marine invertebrates are osmoconfomers.

WATER CONSERVATION IN DESERT FORMS

Animals living in hot deserts or harsh conditions have to facehigh temperature and extreme water scarcity.

(a) Adaptations for getting water

1. Adaptations for drinking water from small springs.
2. Herbivores are adapted to sustain on the juice of succulent plants.
3. Carnivores are adapted to sustain on the body fluids of their prey.
4. Some desert animals are adapted to sustain on metabolic water.
5. Some animals are adapted to absorb atmospheric water by their hygroscopic skin, which act as blotting paper.(Australian lizard)

(b) Adaptations for conserving water

1. Uricotelism in insects, reptiles and birds to reduce or prevent water loss.
2. Storage of large quantities of water in large intestine. (desert lizard uromastix)
3. Great tolerance to high temperatures and extreme water scarcity in camels
4. Absence of sweat glands in desert mammals to reduce perspiration and water loss
5. Surface secretion and scaly or spiny covering to reduce evaporation

Osmoregulatory adaptations of camels

- Camels deals with severe heat & extreme loss of water by virtue of their high tolerance to fluctuations in body temperature, changes in blood concentration & loss of water.
- They can tolerate temperature fluctuation of as much as 6.5^0 C.
- Camels never sweat till their body temperature rises upto 41^0 C.
- When the water scarcity occur, camels produce concentrated urine & dry faeces & thereby considerably reduce water loss.
- When water is not available, they will not produce urine but will retain urea in tissues.
- When water is sufficiently available they may drink large quantities of water (upto 80 litres in 10 minutes).

OSMOTIC AND IONIC REGULATION IN TERRESTRIAL ANIMALS

1. A highly impermeable and water proof body surface to prevent evaporation. This is accomplished by a coating of wax, greese or keratin,or a covering of cuticle, scales, feathers, or fur
2. Internal respiratory surfaces to avoid water loss.
3. Re-absorption of water in colon or rectum to reduce the loss of water through faeces.
4. Renal re-absorption of water and the production of hypertonic (concentrated) urine to prevent the loss of water through urine.
5. Ureotelic or uricotelic excretion with little or no loss of water
6. Ability for water conservation within body
7. Ability to sustain on metabolic water, produced by the oxidation of food stuffs, mainly stored fat. kangaroo rats and hibernating mammals etc depend on metabolic water
8. Tolerance to dehydration and rise in blood concentration
9. Regulation of temperature in homeotherms to reduce evaporation and the loss of water and salts
10. Hormonal and nervous regulation on water loss

OSMOREGULATION IN FRESH WATER ANIMALS

- The salt concentration in the body fluid of fresh water animals is always higher than that of the water around. So their body is hyperosmotic and watery medium is hyposmotic.
- There is a problem, steady gain of water by endosmosis and steady loss of salts by diffusion.

General adaptations to maintain hyperosmotic state of the body

1. Presence of an impermeable cuticle or any other body covering to prevent the endosmosis of water

2. Small and much restricted areas of permissible surface
3. Production of large quantities of dilute urine, which is hyposmotic to blood and hyperosmotic to the medium. This brings about elimination of excess water.
4. Salt absorption by chloride cells to make up the loss of salt through the excretion of urine
5. Elimination of excess water form the body by contractile vacuoles, flame cells, nephridia, antennary tubule, vertebrate renal tubule, etc for maintaining water balance, rather than excretion of nitrogenous wastes.

equipping with excellence

- Contractile vacuoles –fresh water protists and amoebocytes and choanocytes of some fresh water sponges- pulsating activity of contractile vacuoles pumps excess water
- Flame cells- flat worms- collect surplus water and some salts and excrete as dilute urine
- Nephridial tubules- annelids- collect surplus water and some salts and excrete as dilute urine
- Antennary glands- prawns, cray fishes- collect and eliminate excess water and reabsorb chloride ions from urine
- Anal gills and anal papillae- aquatic larvae of some insects such as chironomus, culex, aedes- they permit the entry and exit of water and absorb salts from the medium
- In fresh water insects, reptiles, birds and mammals- body wall is impermeable to waterand salts
- Gills and buccal epithelium- fresh water fishes- wter exchange is possible
- Higher salt concentration is maintained in 3 ways
  1. By the intake of diatery salts
  2. By the absorption of salts by buccal epithelium and chloride cells of gills
  3. The tubular reabsorptionof salts from urinein the glomerular kidney

OSMOREGULATION IN MARINE ANIMALS

- The body fluids of most marine non- chordates, ascidians, and myxine are nearly isotomic to the surrounding sea water. So they have no osmotic problem and there is no need of osmotic regulation. They are stenohaline osmotic conformers
- However they want to regulate ionic concentration.
- Glomerular pronephric kidney of myxine is an ion regulating organ, concerned with elimination of calcium, magnesium, and sulphates and also reabsorption ofpottassium and chloride
- Marine vertebrates and some invertebrates are euryhaline osmotic regulators.

(a) Osmoregulation in marine bony fishes

- marine bony fishes are hyposmotic to the sea water
- there will be a tendency for an inflow of salts by diffusion and outflow of water by exosmosis. This may cause osmotic dehydration.

- To prevent osmotic dehydration marine bony fishes are capable of water conservation and salt elimination
- The water content of the body kept high in four ways
  1. By minimising exosmosis through reduction of permeable surface
  2. By the renal reabsorption and retention of water and production of hypertonic urine by aglomerular kidney
  3. By osmotic entry of water through buccal epithelium
  4. By drinking sea water to compensate water loss
- The salt concentration of body fluid kept low by elimination of salts by aglomerular kidney and chlioride cells

(a) Osmoregulation in marine cartilaginous fishes

- Marine cartilaginous fishes are either isosmotic or hyperosmotic to the sea water
- This is achieved by the retention of large quantities of nitrogenous wastes such as urea and trimethyamine oxide in their blood
- The excessive concentration of these materials causes osmotic and ionic balance between blood and surroundings.
- The lost ionic balance is soon regained by active elimination of salts by rectal glands
- Chloride cells are absent in gills and their function is taken by rectal gland
- The retention of urea is normally harmful to animals, but tissues of cartilaginous fishes have greater tolerance to urea, and optimum concentration of urea is a normal physiological condition in them.

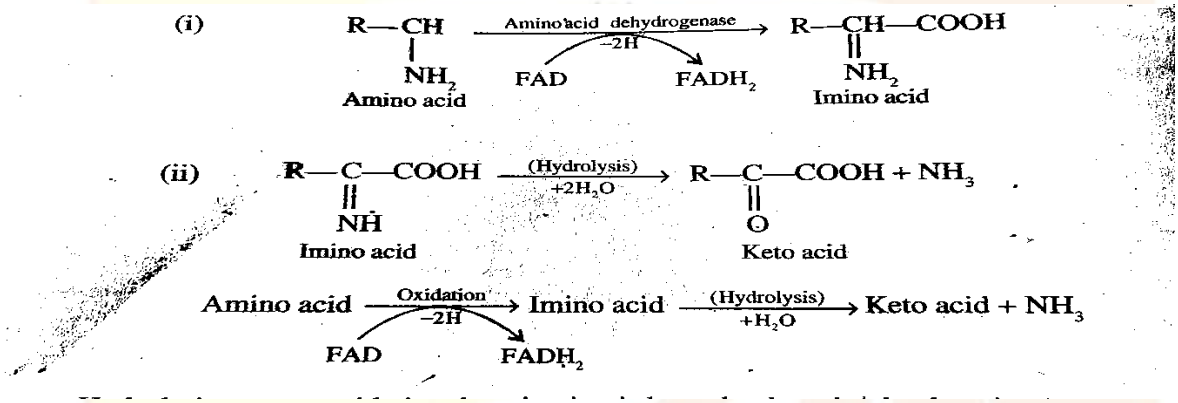
TYPES OF EXCRETION

- Excretion is the separation and elimination of metabolic wastes as well as excess of essential materials from the body to maintain homeostatis
- Based on chemical nature of excretory products, four major kinds of excretion can be recognised. They are ammonotelism, uricotelism, uroetelism, and guanotelism.

1. AMMONOTELISM

- Ammonotelism is the excretion of nitrogenous wastes as ammonia(NH3).
- Animals which excrete ammonia are called ammonotelic animals
- They include aquatic protozoans, sponges, cnidarians, flat worms, leeches, crustaceans, marine lamellibranchs, larval amphibians.
- Ammonia is produced by the deamination of aminoacid
- Deamination is the removal of amino group from an aminoacid, producing free ammonia and a corresponding keto acid or hydroxyl acid.
- It is two types, namely oxidative deamination and hydrolytic deamination.

- Oxidative deamination is the splitting of aminoacid into ammonia and α keto acid. It is catalysed by amino acid oxidases or amino acid dehydrogenases.
- It is completed in two stages, namely oxidation and hydrolysis.
- Enzymatic oxidation of an amino acid produces imino acid, which undergoes spontaneous hydrolysis and yields keto acid and ammonia



- Hydrolytic or non-oxidative deaminationis brought about by the deaminating enzymes amino acid hydrases or amino acid desulfhydrases.
- Amino acid hydrases deaminates hydroxyl amino acids (serine) and desulfhydrases deaminates sulfer-containing amino acids (cysteine).
- The action of dehydrases is completed in two stages, namely dehydration and hydrolytic deamination.
- Dehydration produces an imino acid, which undergoes hydrolysis and yields a keto acid and ammonia

Serine $\xrightarrow[+H_2O]{\text{dehydration}}$ intermediate compound $\longrightarrow$ imino acid $\xrightarrow[+H_2O]{\text{hydrolysis}}$ pyruvic acid + NH_3.

- The action of desulfhydrases is also completed in two stages, namely desulfhydration and hydrolytic deamination.
- Desulfhydration produces an imino acid, which converts into a keto acid and ammonia through hydrolysis

Cysteine $\xrightarrow[+H_2O]{\text{desulfhydration}}$ intermediate compound $\longrightarrow$ imino acid $\xrightarrow[+H_2O]{\text{hydrolysis}}$ pyruvic acid + NH_3.

- Ammonia is highly toxic and water soluble,so it has to be immediately eliminated from body,

- Ammonia dissolves in water and forms ammonim hydroxide
- Ammonia excretion involves heavy loss of water, so ammonotelic animals are aquatic forms.

2. URICOTELISM

- Uricotelism is excretion of nitrogenous wastes as uric acid
- The animals which exhibit uricotelism is known as uricotelic animals
- Uric acid is produced from ammonia in liver and also from by the metabolism of nucleic acids and purines
- Uric acid is toxic and water insoluble
- It easily precipitates as crystals from a supersaturated colloidal solution. So it is excreted as dry crystalline pellets, with little or no loss of water
- Uricotelism is an adaptation to minimise water loss
- Uricotelic animals are completely terrestrial
- They include land snails, terrestrial insects, lizards, snakes, marine turtles and birds
- The droppings of lizards and birds contain white and brownish-black materials. The white material consists of uric acid and black material is the faecal matter
- In many birds, such as comorants, pelicans etc uric acid is excreted as a phosphorus-rich faecal matter, called guano, which is used as fertilizer
- Though man is ureotelic, small amounts of uric acid is produced in the body by purine metabolism. Normally eliminated through urine. When its level is high, it precipitates in joints as crystals, causing acute pain. This is called gout

URICOTELISM MAJOR ADVANTAGES FOR TERRESTRIAL HABITATES

- Uric acid is water insoluble and so its excretion involves only negligible loss of water
- Since uric acid is non-toxic, its prolonged retention in the body is not harmful to the animal

3. UREOTELISM

- Ureotelism is the excretion of nitrogenous wastes as urea
- Animals exhibiting ureotelism are called ureotelic animals
- Urea is water-soluble and less toxic
- It is excreted through urine
- Ureotelism is an adaptation for a semi-terrestrial life
- It is more advantageous than ammonotelism in that-

1. Urea is much less toxic than ammonia and so it can be retained in the blood for long time
2. The elimination of urea requires only a small quantity of water and so ureotelism minimise water loss in excretion

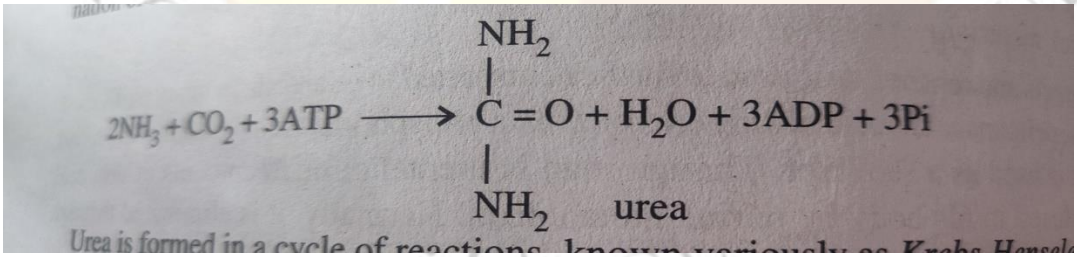
- Ureotelic animals, include earthworms, prawns, cartilaginous fishes, frogs and toads, crocodiles, turtles, mammals etc
- Cartilagenous fishes can retain large amount of urea in their blood. This makes their blood almost isosmotic to the medium & prevents osmotic loss of water from the body.
- Ureotelic animals produce hypotonic urine when there is heavy intake of water, when there is only small intake of water, they produce hypertonic urine.
- Frog is ureotelic where as tadpole is ammonotelic.
- In summer lung fishes are ureotelic, typically they are ammonotelic.
- Crocodiles are uricotelic when they are on land, but ammonotelic when they remain in water.
- Earthworms are ammonotelic in rainy season & ureotelic in dry season.

4. GUANOTELISM

- Process of excretion seen in spiders and scorpions (arachnids)
- Guanine is the excretory waste material from purine metabolism
- Guanine is non toxic and insoluble
- It is excreted as solid form
- Adaptation visible in organisms living in arid areas
- Inosinic pathway terminates in guanine formation

UREA CYCLE

- Urea is formed by the combination between two molecules of NH3 and one molecule of CO2, with elimination of one molecule of H2O
- Urea formation enables the elimination of ammonia and CO2
- 3 ATP molecules are spent to drive the process

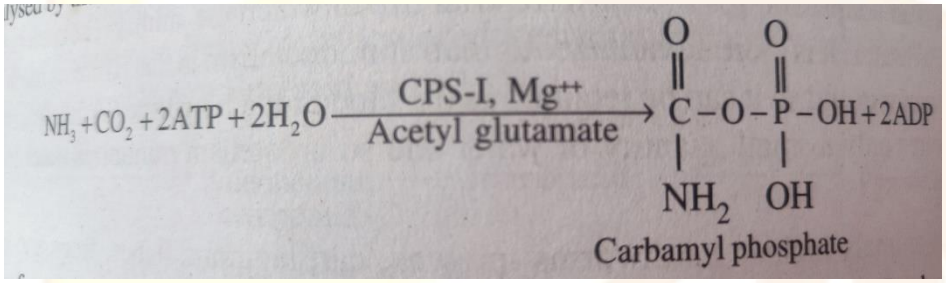


- Urea is formed in a cycle of reactions, known as krebs-henseleit cycle, urea cycle, ornithine cycle.
- Liver is the site of urea formation

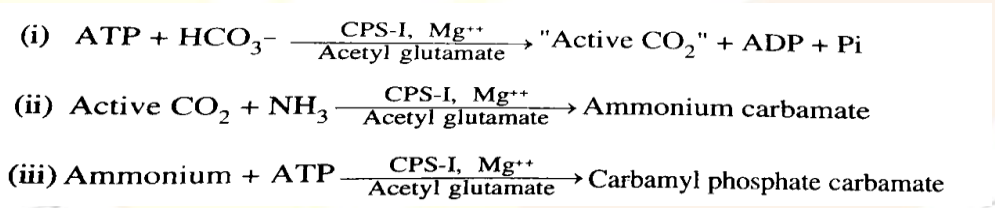
- Urea is a multistaged process, it is completed in 5 steps

1. Formation of carbamyl phosphate from NH3 and CO2

- The first step in urea synthesis is the formation of energy=rich compound carbamyl phosphate in mitochondria
- It involves the condensation of one molecule of NH3 with one molecule of CO2 at the expense of two molecules of ATP
- The reaction is irreversible

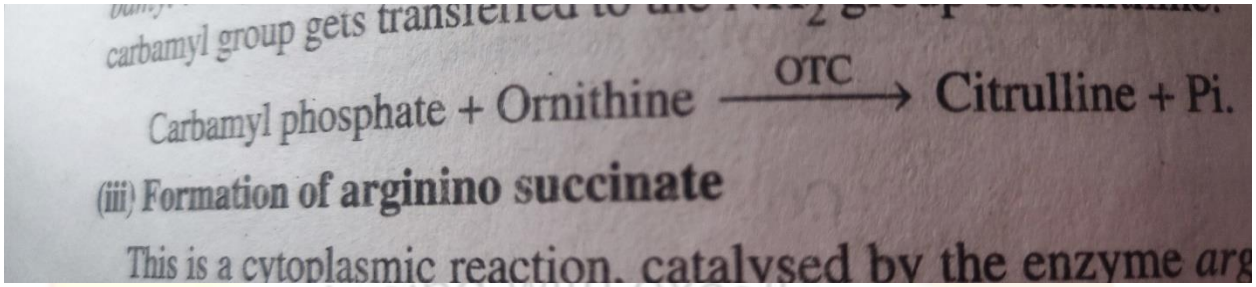


- The formation of carbamyl phosphate is a three step reaction,
  (a) Activation of CO2 by ATP forming carboxyl phosphate
  (b) Reaction of carboxyl phosphate with NH3, forming ammonium carbamate
  (c) Reaction of ammonium carbamate with another molecule of ATP, forming carbamyl phosphate



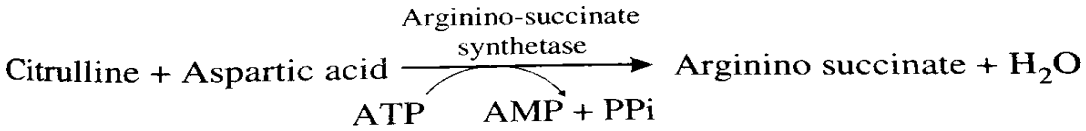
2. Formation of citrulline from carbamyl phosphate and ornithine

- The second major step is also mitochondrial
- It involves formation of citrulline, during this carbamyl phosphate enters urea cycle, combines with ornithine and forms ctrulline
- This is reversible, catalysed by the mitochondrial enzyme ornithine carbamyl transferase



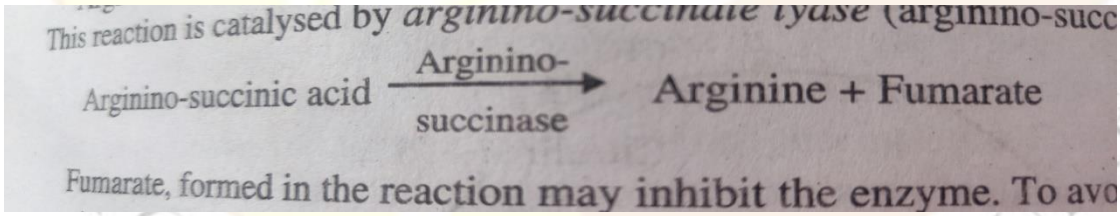
3. Formation of arginine- succinate from citrulline and aspartic acid

- This is cytoplasmic reaction, catalysed by enzyme arginine succinate synthetase
- Utilizing one molecule of ATP
- Citrulline escapes to the cytoplasm from mitochondria, combines with the α-amino group of aspartic acid and forms arginine-succinic acid



4. Formation of arginine from arginine-succinate

- Arginine succinic acid undergoes cleavage and forms arginine and fumaric acid
- This reaction is catalysed by arginine- succinate lyase



- Fumarate formed in the reaction may inhibit the enzyme
- To avoid this, fumarate soon gets into the mitochondria, enters TCA cycle and gets converted first to maleic acid ,then oxalo-acetic acid,finally aspartate

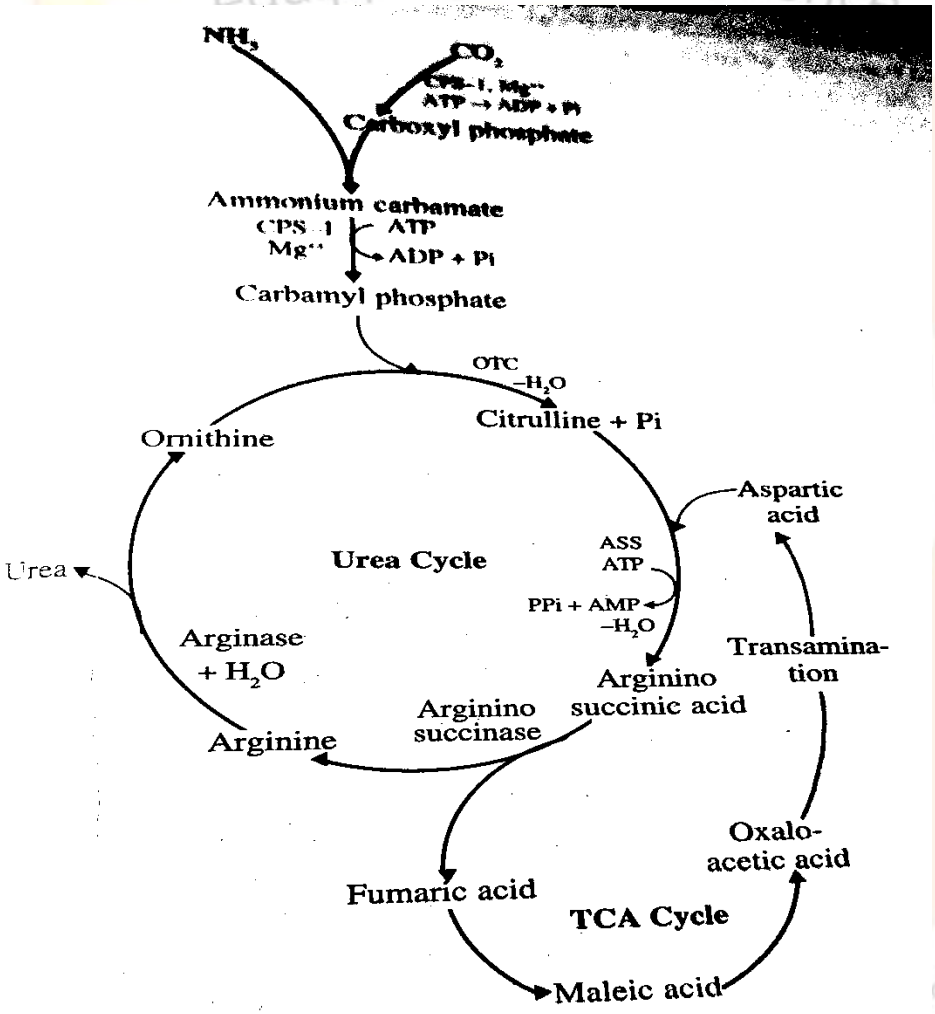
5. Formation of urea and ornithine from arginine

- The final step in urea cycle is the hydrolysis of arginine, forming urea and ornithine
- The reaction is catalysed by arginase
- Ornithine returns to mitochondria, combines with other molecule of carbamyl phosphate and repeats the cycle

reaction is catalysed by
other molecule of carbamyl phosphate and repeats the cycle.

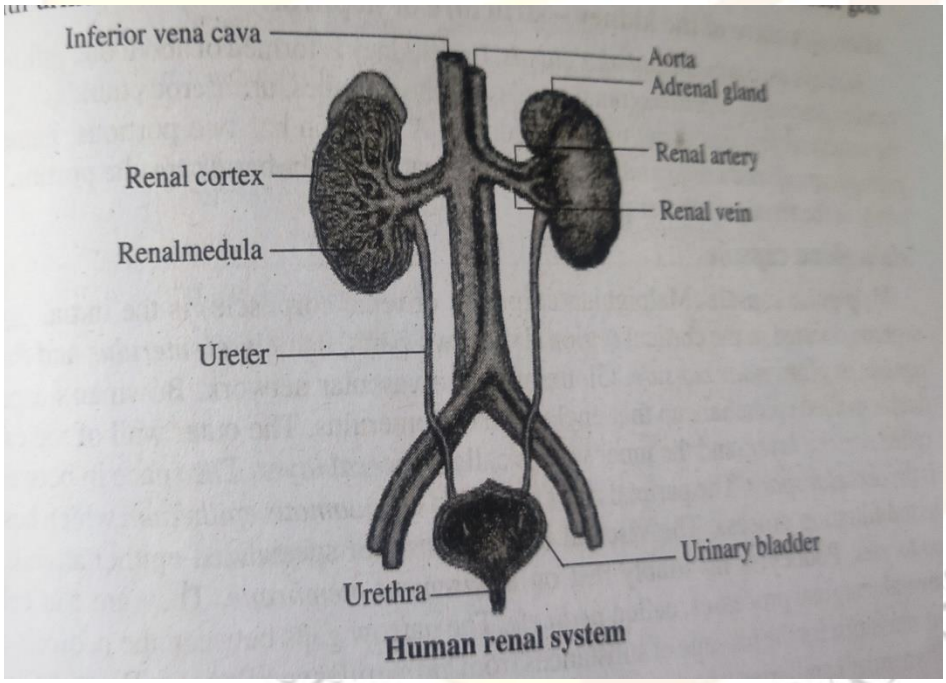
$$\text{Arginine} \xrightarrow[+\,H_2O]{\text{Arginase}} \text{Urea} + \text{Ornithine}$$

UREA CYCLE



HUMAN KIDNEY

- A pair of mesodermal kidney are the principle urinary organs of man
- Human kidneys are bean shaped, and dark red coloured lying on each side of thevertebral column
- The inner margin of each kidney is concave, and outer margin convex
- On the concave side, there is adepression, known as hilus
- Hilus leads to a duct, called ureter
- Ureter opens to the urinary bladder
- Leading from the bladder is atube, called urethra
- In male, urethra joins the sperm duct and forms the urino-genital duct, that opens out at the tip of the penis
- The opening of bladder to urethra is guarded by a pair of muscular rings, called urethral sphinctures
- Urinary is lined by transitional epithelium, which has great powers for recoil (elasticity)
- It protects the bladder from damage due to enlargement

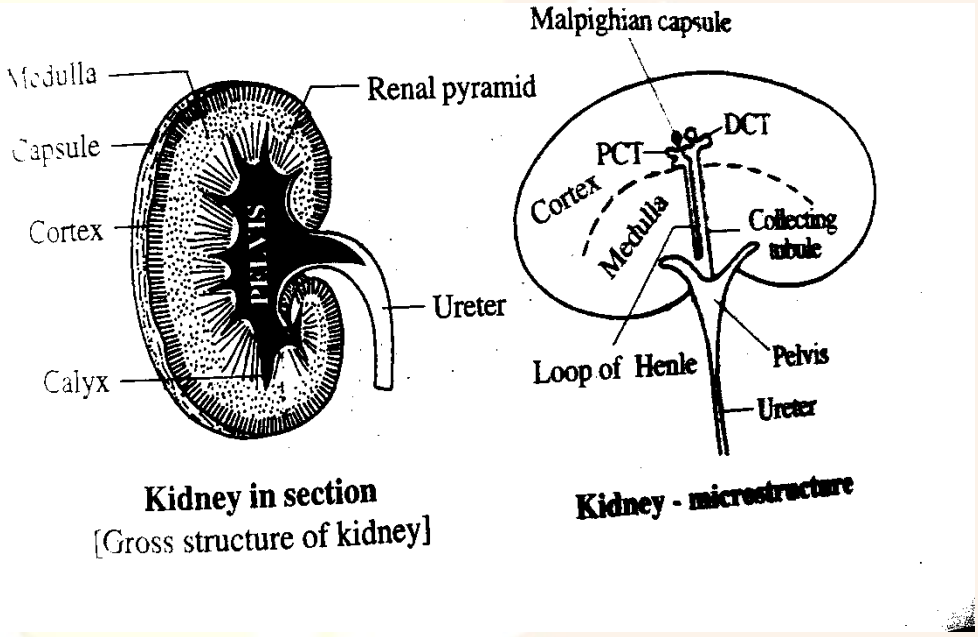


Human renal system

GROSS STRUCTURE OF THE KIDNEY

- Kidney is enclosed within a 3 layered fibrous capsule,
- 3 layers of fibrous capsule are the inner renal capsule, middle adipose capsule, and the outer renal facia
- Renal capsule is a smooth, transparent, and fibrous membrane

- Adipose capsule is a mass of fatty tissue
- Renal fascia is athin layer of fibrous connective tissue
- Structurally, kidney has two regions, outer cortex and inner medulla
- Renal cortex has two regions, namely outer cortical zone, and inner juxtamedullary zone
- Cortex has several projections in the medulla, known as renal columns, orcolumns of bertini
- Renal medulla has several conical bundles, known as medullary pyramids or renal pyramids
- Their apices are called renal papillae
- Cortex and the the renal pyramids together constitute the paranchyma of the kidney
- In the substance of the medulla, the base of the ureter expands to a cavity, called renal pelvis
- Its extensions to the spaces in between the renal pyramids are known as calyces



Kidney in section
[Gross structure of kidney]

Kidney - microstructure

Microstructure of the kidney -structure of nephron

- Kidneys are compound tubular glands.
- Each kidney is formed of about one million coiled tubules, known as nephrons (renal tubules, nephric tubules, uriniferous tubules).
- These are the structural and functional units of kidneys.
- A nephron has two portions, namely Malpighian capsule and urinary tubule.
- Malpighian capsule is the basal capsular portion.
- Urinary tubule is the terminal tubular portion.

MALPIGHIAN CAPSULE

- Malpighian capsule (Malpighian corpuscle or renal corpuscle) is the initial part of the nephron, located in the cortical region.
- It has two parts, namely glomerulus and Bowman's capsule or glomerular capsule. Glomerulus is a vascular network.
- Bowman's capsule is a double-walled epithelial cup that encloses the glomerulus.
- The outer wall of the capsule is called parietal laver, and the inner wall is called visceral layer.
- The space in between them is the capsular space.
- The parietal layer is formed of squamous epithelium which has no role in the filtration process.
- The visceral layer consists of specialized epithelial cells, called podocytes.
- Podocytes invariably rest on a basement membrane.
- They are flat cells with several marginal processes, called pedicels. The narrow gaps between the pedicels serve as filtration slits for the passage of substances from glomerular capillaries to Bowman's capsule.
- Glomerular capillaries consist of a highly porous endothelium.
- The visceral layer of the Bowman's capsule and the endothelium of the glomerulus together form an endothelial-capsular membrane or filtration membrane.
- This membrane hears extremely minute pores called filtration slits or slit pores, for the ultrafiltration of water and solutes from blood to Bowman's capsule.
- Glomerulus is a capillary network.
- It is the centre of the filtration of water and solutes from blood to Bowman's capsule.
- Blood enters it through an afferent arteriole, which is a branch of the renal artery.
- This arteriole breaks up into a capillary network.
- Terminally these capillaries join together and form an efferent arteriole, which carries blood away from the glomerulus.
- Efferent arteriole breaks up into a capillary network around the urinary tubule.It is called peri-tubular capillary network.
- It also gives rise to long loops of thin-walled capillaries, called vasa rectae.
- The capillaries terminally join together and form small venules, which in turn, join the renal vein.

URINARY TUBULE

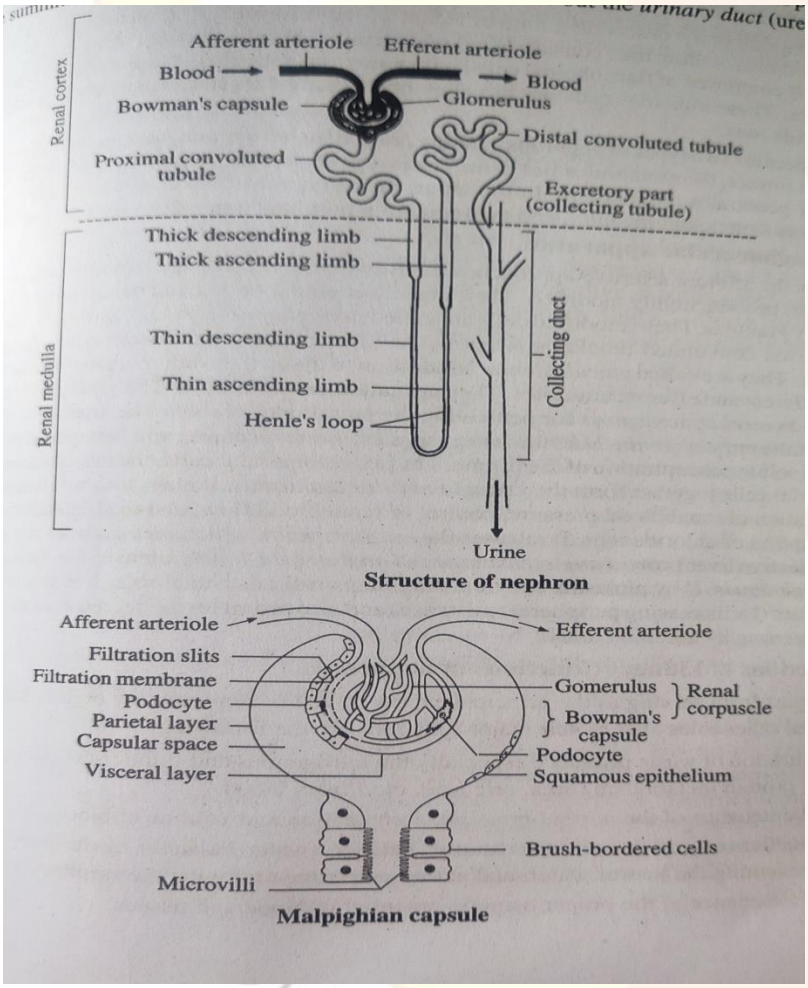
- Urinary tubule is the long and coiled part of the nephron.
- It has two portions, namely proximal secretory part and distal excretory or collecting part.
- Secretory part, in turn, has three portions, namely (i) proximal convoluted tubule (PCT) (ii) Henle's loop and (iii) convoluted fubule (DCT),

- Convoluted tubules are the highly contorted portions, lying in the cortex region.
- Henle's loop is the narrow loop-like middle portion, lying in the medulla.
- It has two limbs, namely descending limb and ascending limb.
- Terminally, the excretory portions of several tubules join to form a collecting tubule.
- Several collecting ducts join to form a discharging tubule (duct of Bellini) in the medulla.
- All the discharging ducts open to the pelvis at the summits of the renal pyramids.
- From the pelvis leads out the urinary duct (ureter).
- Each limb of Henle's loop has two regions, thick and thin. The thick descending limb is short and wide, and impermeable to ions, urea and water.
- On the other hand, the thin descending limb is freely permeable to water.
- The thin ascending limb is permeable to Nacl and urea.
- Nacl diffuses out of the limb, and urea diffuses into the limb.
- The walls of the proximal and distal convoluted tubules are formed of brush bordered cuboidal epithelium with microvilli
- The wall of the descending limb of Henle's loop is formed of squamous epithelium, that of the thin ascending Limb consists of columnar epithelial cells and that of the thick ascending limb is composed of dat cuboidal cells, with numerous mitochondria and rudimentary brush border.
- These cuboidal cells are the sites of the active outward transport of sodium and chloride ions
- There are two types of nephrons, namely cortical nephrons and juxtamedullary nephrons,
- In the former, the glomerulus lies in the cortical zone, and the remaining part of the nephron rarely penetrates the medulla.
- In the latter, the glomerulus lies at or close to the junction between cortex and medulla, and the remaining part penetrates deep into the medulla.

JUXTAGLOMERULAR APPARATUS

- As the afferent arteriole approaches the Bowman's capsule, the smooth muscle cells of its wall become highly modified.
- Their nuclei become rounded and the cytoplasm becomes highly granular.
- These modified cells are called juxtaglomerular cells. Similarly, the cells of the distal convoluted tubule, adjacent to the afferent arteriole, become considerably narrower.
- They are called macula densa.
- In addition to these, there are specialized cells between the afferent and efferent arterioles.
- They are called granular cells.
- The juxtaglomerular cells serve as mechanoreceptors for perceiving the pressure of blood in the arterioles.
- They also secret the enzyme renin.
- Macula densa serve as chemoreceptors and they perceive changes in the solute concentration of the filtrate.

- The jaxtaglomerular cells, the macula densa and the granular cells together form the juxtaglomerular apparatus.
- It plays a significant role in the regulation of renal blood pressure, control of renal blood flow, and the regulation of the re-absorption of chloride ions. It releases the enzyme renin, which mediates the conversion of the inactive liver protein angiotensinogen to angiotensin-I.
- Angiotensin-I is then converted to angiotensin-2 by a plasma enzyme.
- Angiotensin-II has a dual role. It raises renal blood pressure (by increasing peripheral resistance) and also promotes the secretion of the hormone aldosterone by adrenal cortex.



FUNCTIONS OF KIDNEYS (FUNCTIONS OF NEPHRONS)

- Kidneys play several other roles also. Their major functions are the following:
  1. Filtration of waste products, especially the nitrogenous and sulphur-containing products of protein metabolism (urea, uric acid, etc.) from blood.
  2. Maintenance of the normal pressure, composition and volume of blood

3. Maintenance of the normal osmotic balance (water balance) in the body fluids (by preventing the loss of water, and at the same time removing the surplus water).
4. Maintenance of the proper osmotic potential in blood and tissues.
5. Maintenance of a proper ionic balance (by removing the excess salts)
6. Regulation of acid-base balance and maintenance of normal pH
7. Production and release of renin, erythropoietin and prostaglandins. Renin is the renal enzyme which mediates the synthesis of angiotensin which, in turn, controls renal blood pressure and also promotes the secretion of the hormone aldosterone by adrenal cortex erythrocytes).
8. Regulation of blood sugar level under special conditions.
9. Activation and metabolism of vitamin D.
10. Synthesis of ammonia, hippuric acid and inorganic phosphates.

URINE FORMATION IN KIDNEYS

- The functioning of kidneys involves the formation and elimination of urine.
- Urine is a concentrated acidic solution of waste materials in water.
- The most widely accepted theory of urine formation is the secretion-absorption theory.
- It holds that nephrons are the ultimate biological units of urine formation and they exercise selective discrimination in the elimination or retention of the various substances of the body fluids.
- Urine formation involves three major processes, namely glomerular ultrafiltration, tubular re-absorption and active tubular secretion (or augmentation).

(A) GLOMERULAR ULTRAFILTRATION

- This is the non-selective ultrafiltration or pressure filtration of water and low molecular weight substances from glomerular blood to capsular space.
- Blood in the glomerulus flows under high hydrostatic pressure.
- This very high glomerular hydrostatic pressure forces out small molecules from glomerular blood to Bowman's capsule through the split pores (filtration slits) of the filtration membrane.
- This is known as ultrafiltration or pressure filtration.
- The fluid thus filtered out is known as glomerular ultrafiltrate (nephric filtrate or capsular filtrate).
- It forms the primary urine. Its composition is almost the same as that of blood, except that blood cells and some plasma proteins are absent in it.
- It contains water, amino acids, glucose, vitamins, urea, uric acid, creatinine, sodium, potassium, calcium, chlorides, bicarbonates and other salts (the presence of blood cells and high-molecular proteins in urine indicates kidney disorders or defective glomerular filtration),

Driving forces of glomerular filtration

- Glomerular filtration is mainly due to four driving forces, namely glomerular hydrostatic pressure (GHP), blood colloidal osmotic pressure (BCOP), capsular hydrostatic pressure(CHP) and net filtration pressure or effective filtration pressure (EFP), GHP is created when blood in the glomerulus flows under high tension from wide afferent arterioles to narrow efferent arterioles.
- BCOP is mainly due to the concentration of blood plasma proteins, particularly albumins, CHP is the pressure of the fluid in the Bowman's capsule. EFP, also called filtration pressure, is the difference between GHP and the sum of BCOP and CHP, GHP tends to drive water and dissolved substances form blood to Bowman's capsule.
- On the other hand, BCOP and CHP have an opposite effect.
- They tend to draw fluid substances to blood. In glomerulus, OHP is approximately 70 mm Hg, BCOP is 30 mm Hg, and CHP 120 mm Hg.
- So, the net filtration pressure is approximately 20 mm Hg. i.e., 70 - (30+20)=20

(B) TUBULAR RE-ABSORPTION

- This is the selective re-absorption of useful substances from the glomerular filtrate back to Wood.
- Tubular reabsorption occurs through the epithelial cells all along the renal tubule.
- Water, glucose, amino acids, vitamins and some ions, such as Na+, K+, Ca2+, Cl-, HCO3-, HPO4 are re-absorbed by this process.
- This helps the body to retain most of its chemical constituents.
- About 99% of the glomerular filtrate is re-absorbed. So, only about 1-1.5 litres per day will be excreted as urine,
- Tubular re-absorption is a selective process, because some substances are re-absorbed in large quantities, some in very small quantities, and still others are not at all re-absorbed.
- This selective re-absorption is based on body's needs.
- The maximum amount of a substance that can be absorbed under any condition is called the tubular maximum of that substance.
- There is an optimum rate of renal re-absorption for every substance. It is called renal threshold.
- It is different for different substances. Normally, glucose and amino acids are almost completely re-absorbed.
- Water, vitamin C, Nat and some salts are re-absorbed partly or completely, depending on their concentration in blood. Urea, uric acid, etc. may not be re-absorbed, or may be re-absorbed in negligible amounts. Creatinine, sulphates, hippuric acid, etc. are not at all re-absorbed.
- The substances, that are re-absorbed in large amounts, are called high threshold substances (e.g. glucose, amino acids, vitamin C, water, Nat, Ca, etc.),

- Those which are re-absorbed in very small amounts are called low threshold substances (e.g., ammonia, urea, uric acid), and those substances that are not at all re-absorbed are called non-threshold substances (e.g., sulphates, creatinine, hippuric acid).
- Tubular reabsorption involves both active and passive transport mechanisms.
- Water and some salts are re-absorbed by passive transport in a concentration gradient.
- Glucose, amino acids, Na, K, CH, Cats, etc. are re-absorbed by active transport against concentration gradient with energy expenditure.
- Re-absorption of water and dissolved constituents occurs mostly in the proximal convoluted tubule.
- The fluid left out after this is known as secondary urine. It slowly passes along the tubu;le.
- When it reaches the distal convoluted tubule, final re-absorption of water and sodium occurs.

(C) TUBULAR SECRETION (AUGMENTATION)

- This is the active secretion of some substances from blood to urinary tubule.
- It occurs in the distal convoluted tubule. H', Na, K, ammonia, sulphur compounds, hippuric acid, creatinine, steroids, organic acids, reactive drugs (such as penicillin), etc. are secreted by this process.
- Tubular secretion is relatively less significant in glomerular kidneys, but most significant in aglomerular kidneys.
- Tubular secretion serves two purposes:
  1. Removes some substances from the body, especially K and H.
  2. Conserves base composition and controls blood pH.
- After selective re-absorption and active secretion, a concentrated and acidic solution of wastes is left in the tubule. This is the final urine.

Urine concentration

- Mammals (and birds) are capable of producing highly concentrated urine, which is hyperosmotic (hypertonic) to blood. This ability depends upon the following factors
  1. Presence of loop of Henle and its relation to collecting tubule and vasa recta.
  2. Close proximity of the ascending and descending limbs of Henle's loop and the difference in their permeabilities to water and solutes; descending limb is permeable to water and impermeable to solutes, whereas the thin ascending limb is permeable to solutes.
  3. The active transport mechanism operating in the thick ascending limb.
  4. Operation of an ingenious mechanism, called counter-current mechanism in Henle's loop and vasa recta.
  5. High osmotic concentrations in the peritubular (interstitial) fluid around the Henle's loop.
  6. An osmotic gradient between peritubular fluid and intratubular fluid.

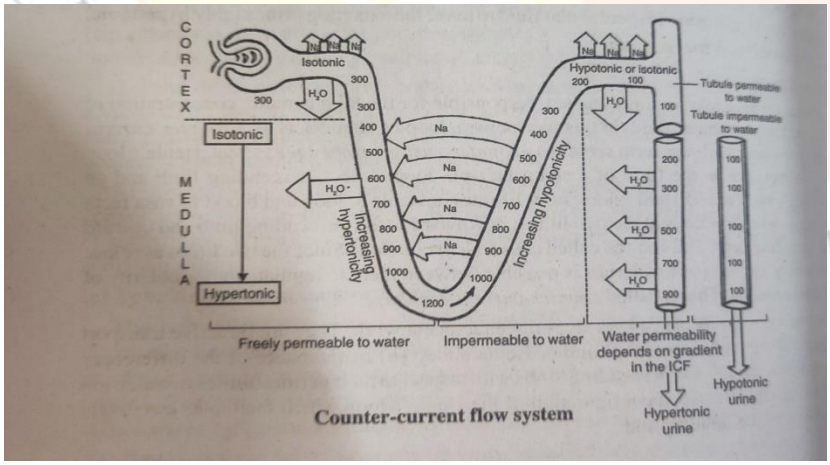
- Loop of Henle is highly specialized for urine concentration. It is long in juxtamedullary nephrons, especially in those mammals which must produce highly concentrated urine for water conservation
- In such mammals, there exists a strong osmotic gradient which causes the osmotic flow of water from the less concentrated (hyposmotic) tubular fluid to the more concentrated (hyperosmotic) peritubular fluid to make the excreting urine highly hypertonic.

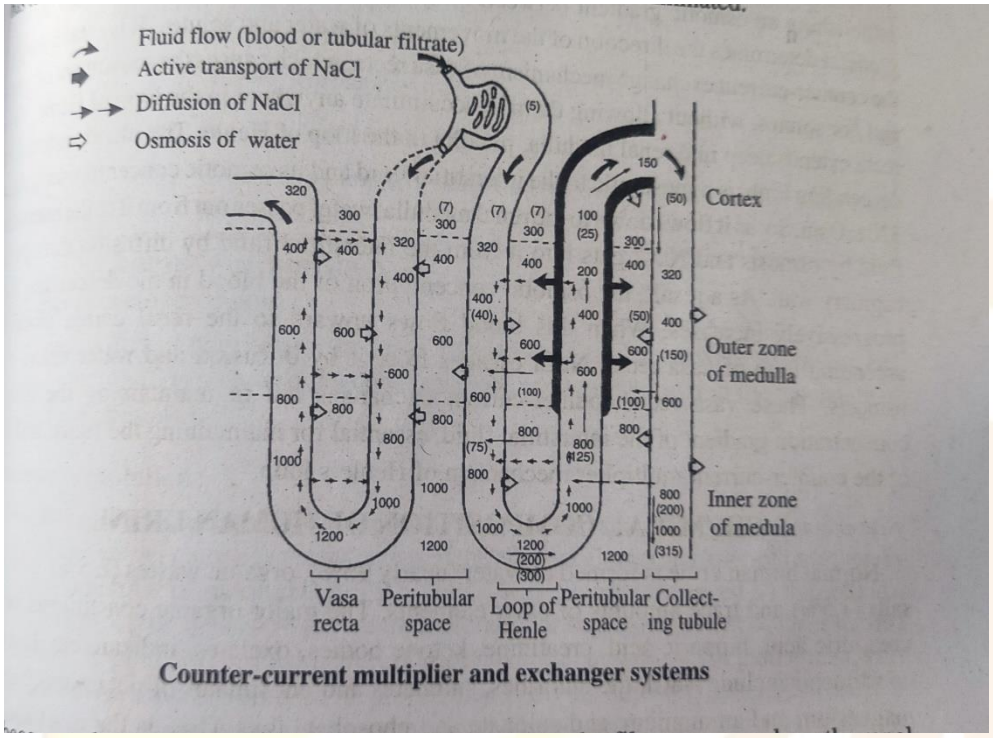
COUNTER-CURRENT MECHANISM

- Urine concentration
- This is the physiological mechanism, responsible for the high osmotic concentration of urine and the peritubular fluid.
- In this mechanism, loop of Henle acts as a counter-current multiplier system, and vasa recta serves as a counter-current exchanger system.
- Henle's loop and vasa recta are in the form of a sharp hair-pin loop, with a descending limb and an ascending limb.
- Tubular fluid (glomerular filtrate) in Henle's loop and blood in vasa recta flow in opposite directions in the two limbs, downward in the descending limb and upward in the ascending limb.
- This may be called counter-current flow. Since the two limbs are close to each other, exchange of materials is possible between them to regulate the osmolarity of their fluid contents. This is called counter-current exchange.
- Counter-current mechanism involves three factors at work. They are –
  (1) active transport of solutes by the thick ascending limb of Henle's loop
  (2) maintenance of the differences between the ascending and descending limbs with respect to their permeabilities to water and NaCl
  (3) U-shaped configuration of the Henle's loop which facilitates a counter-current flow of the tubular fluid.
- The descending limb of Henle's loop is permeable to the osmotic outflow of water and the passive inward diffusion of NaCl, although it does not actively transport NaCl.
- However, its concentration will not exceed that of the peritubular fluid around Henle's loop.
- The ascending limb of Henle's loop is impermeable to water.
- But, it serves as a site for transport results in an increase in solute concentration or osmolarity in the peritubular fluid the active outward transport of NaCl from glomerular filtrate to peritubular fluid.
- The glomerular filtrate becomes progressively less concentrated or less osmolar by losing and thereby establishes a strong osmotic gradient between the peritubular and tubular fluids.
- The flow of fluid in the descending and ascending limbs of Henle's loop in opposite directions is called counter-current flow.

- Thus, the two limbs constitute a counter-current flow system. The active and passive movements of NaCl in this system produce an osmotic gradient.
- At any one place in the Henle's loop, the concentration difference between the contents of the two limbs is only moderate.
- But, along the length of the loop, this moderate-current flow system is called counter-current multiplier system.
- The final fluid concentration in this system is determined by the length of the loop; the longer the loop, the higher the urine concentration.
- Thus, there is a direct correlation between the relative length of Henle's loop and the maximum concentration of urine.
- The collecting tubule is variably permeable to water. Its water permeability depends upon the relative concentration of the peritubular fluid.
- If the peritubular fluid is more concentrated (hyperosmotie) than the fluid in the collecting tubule, the collecting tubule becomes water- permeable and water escapes from it by osmosis.
- This results in a highly concentrated urine.
- If the peritubular fluid is isosmotic or hyposmotic to the fluid in the collecting tubule, the collecting tubule becomes impermeable to water and no water is lost from it or gained by it.
- This results in the production of dilute urine.
- Concentrated urine is produced when the fluid volume in the body is low and water has to be conserved.
- Dilute urine is produced when the fluid volume in the body is high and the excess water has to be eliminated.
- Concentrated urine is produced in very small quantities, but dilute urine is produced in large quantities.
- The glomerular ultrafiltrate that enters the proximal convoluted tubule during counter-current flow is almost isosmotic to the peritubular Muid with an osmotic concentration of approximately 300 milliosmols (mOsm) per litre.
- By the time it reaches the bend of Henles loop, it becomes increasingly more concentrated (hypentonic or hyperosmotic, with an osmotic concentration of about 1200 mOsm.
- As it moves up along the ascending limb it becomes progressively less concentrated, and by the time it reaches the distal convoluted tubule it becomes isosmotic or hyposmotic with an osmotic concentration of nearly 100 mosm.
- Again, in the collecting tubule, it becomes progressively more concentrated if water has to be conserved, or becomes hyposmotic if water has to be eliminated.
- Counter-current multiplier and exchanger systems
- It becomes clear that two major events occur as glomerular filtrate passes along the renal tubule.

- They are (1) osmotic outflow of water from the descending limb of Henle's loop andthe collecting tubule (ii) cyclic movement of sodium in which social enters the descending two processes operate simultaneously, one facilitating the other
- These progressively more concentrated in the descending Limb and collecting tube, and progressively less concentrated in the ascending limb.
- Normally the exacting is concentrate.
- However, under abnormal conditions, the collecting tubule becomes impermeable to water with the result that the excreting urine is dilute.
- The outflow of sodium from the ascending limb of Henle's loop makes me tubular fluid hyposmotic and the peritubular fluid hyperosmotic in relation to each other.
- This, in turn increases the osmotic potential of the peritubular fluid and creates an osmotic gradient that causes the osmotic outflow of water from the descending limb and the collecting tubule.
- Water cannot flow out from the ascending limb since it is impermeable to water.
- The outflow of Water makes the tubular fluid in the descending limb and collecting tubele byperosmotic to the peritubular fluid. Consequently.
- This causes the outflow of sodium from the ascending limb and the cyclic repetition of the whole series of events.
- The functional state of the counter-current multiplier mechanism is maintained by establishing an osmotic gradient between the peritubular and tubular fluids
- Vasa recta extends deep into renal medulla, parallel to the loop of Henle. The blood, entering its descending limb, is hyposmotic to the interstitial fluid.
- So, as it flows down to the renal medulla, water passes out from it to the interstitial fluid by osmosis and NaCl gets into it from the interstitial fluid by diffusion through the capillary wall.
- As a result, the osmotic concentration of the blood in the descending limb progressively increases.





Counter-current multiplier and exchanger systems

HORMONAL CONTROL OF KIDNEY FUNCTION

- The functioning of kidney in urine formation is under nervous, hormonal & enzymatic control.
- The major hormones involved in the urine production includes aldosterone, adrenaline, vasopressin, thyroxine , parathormone & atrial natriuretic hormone.

Hormonal control of urine production		
Hormone	***Gland***	***Function***
1. Diuretic hormone	Pituitary	Stimulates urine production
2. Aldosterone	Adrenal cortex	Stimulates tubular re-absorption of Na^+ & tubular secretion of K^+.
3. Epinephrine	Adrenal medulla	Inhibits glomerular filtration & thereby decreases urine production .
4. Vasopressin (anti-diuretic hormone)	Hypothalamus	Stimulates tubular re-absorption of water & thereby reduces diuresis.
5. Thyroxine	Thyroid gland	Reduces tubular re- absorption of water & thereby increases diuresis.

6. Parathormone	Parathyroid gland	Promotes tubular reabsorption of Ca^{2+} & Mg^{2+} & inhibits tubular re-absorption of phosphates.
7. Atriopeptin	Atrial wall cells	Inhibits tubular re- absorption of water & sodium & lowers the production of aldosterone.

Role of ADH in the dilution or concentration of urine

Level of body water	Solute potential of blood	ADH	DCT & Collecting duct	Urine
Loss exceeds uptake	Falls	Released	Permeable to water	Concentrated
Intake exceeds loss	Rises	Not released	Impermeable to water	Dilute

RENAL DISORDERS

Kidney functions may be impaired by infections, lesions, tumours, electrolyte imbalances, kidney stone formations, chemical poisons,..

RENAL FAILURE

- Nephrons fail to function properly resulting in *oedema, acidosis & uraemia*.
- *Oedema* – Swelling of body parts due to the retention of large amounts of sodium & fluids in tissues.
- *Acidosis* – Acidity of body fluids resulting from the excessive production of beta- hydroxyl butyric acid & acetoacetic acid in the body, low glomerular filtration of hydrogen ions, reduced production of ammonia & phosphates, marked decrease in the alkali reserve of blood,…
- *Uraemia* – Increased level of urea & other nitrogenous waste compounds in the blood that are normally eliminated by the kidney.
- Renal failure can be treated by dialysis or kidney transplantation.

RENAL HYPERTENSION

- It is the state of abnormally high blood pressure in the nephric blood vessels.
- It leads to *arteriolar nephrosclerosis*.
- It is the progressive thickening & eventual damage of renal arterioles.
- It reduces the blood supply to the kidneys, with the result in the damage of glomeruli.

NEPHRITIS

- It is the inflammatory disorder of kidney.

- Commonest & most serious forms are *pyelonephritis (pyelitis) & glomerulonephritis*.
- **Pyelonephritis** – It is the acute inflammation of the pelvis region of the kidney due to bacterial infection.
- It damages the kidney tubules.
- It is accompanied by high fever & chill, severe back pain, presence of WBC in urine, high BP,..
- It is common among children, particularly girls & pregnant women.
- **Glomerulonephritis** – Also called Bright's disease.
- It is the severe inflammation of the glomeruli.
- It results from the deposition of immune complexes in the capillary wall of glomeruli.
- Glomeruli become swollen,inflamed & engorged with blood.
- Glomerular membrane becomes highly permeable to most of the blood constituents – leads to albuminuria, haematuria,…
- *Focal or segmental glomerulonephritis* - Glomerulonephritis affects only a limited number of glomeruli.
- The disease becomes chronic & results in the progressive damage of kidney & ultimate death.

HAEMATURIA

- It is the presence of blood with numerous blood cells, especially RBC in the urine.
- It is a pathological condition
- Its common causes are glomerulonephritis, inflammatory diseases of glomeruli, kidney stones, bladder stones, high BP etc.
- Long distance runners may excrete red wine due to the damage of blood vessels in the sole

URAEMIA

- It is the excessive accumulation of urea and other toxic wastes in the blood and tissues due to kidney diseases
- Its most important causes are chronic glomerular nephritis and pyelonephritis
- Other common causes include tubular necrosis, obstruction to the outflow of urine, malignant renal hypertension, acute sugar diabetes
- Uraemia can be acute or chronic
- The symptoms of acute uraemia are rapid and those of chronic are gradual.
- Rapid symptoms include loss of appetite, weakness, leathargy, etc.
- Gradual symptoms include anaemia, vomiting, diarrhea, convulsions.

- If untreated, uraemia leads to coma and death

PROTEINURIA

- Proteinuria is increased levels of protein in the urine.
- This condition can be a sign of kidney damage.
- Proteins – which help build muscle and bone, regulate the amount of fluid in blood, combat infection and repair tissue – should remain in the blood.
- If proteins enter the urine they ultimately leave the body, which isn't healthy.
- In many cases, proteinuria is caused by relatively benign (non-cancerous) or temporary medical conditions.
- These include dehydration, inflammation and low blood pressure. Intense exercise or activity, emotional stress, aspirin therapy and exposure to cold can also trigger proteinuria.
- In addition, a kidney stone in the urinary tract can cause proteinuria.
- Occasionally, proteinuria is an early indication of chronic kidney disease, a gradual loss of kidney function that may eventually require dialysis or a kidney transplant.
- Diabetes and high-blood pressure can damage kidneys and are the number-one and number-two causes of kidney disease.
- The symptoms of proteinuria are More frequent urination, Shortness of breath, Tiredness, Nausea and vomiting, Swelling in the face, belly, feet or ankles, Lack of appetite, Muscle cramping at night, Puffiness around the eyes, especially in the morning, Foamy or bubbly urine
- Proteinuria cannot be prevented, but it can be controlled. Many of the causes of proteinuria can be treated (diabetes, high blood pressure, preeclampsia and kidney disease), allowing your healthcare provider to improve the condition.

RENAL CALCULI

- Calculi, commonly called stones are water insoluble crystalline concretions of some salts or other materials, formed within the body
- Usually they are formed in the kidneys, urinary bladder, ureters, gall bladder etc
- In urine several minerals are held in solution in supersaturated state. Sometimes they precipitates out, crystallize and get deposited over and around a small organic matter to form a kidney stone
- The central core or nucleus of the stone is called nidus
- The common constituents are calcium carbonate, calcium oxalate, calcium phosphate, uric acid
- Some stones, formed in the pelvis region of the kidney cause no pain and produce no symptoms, they are called silent stones
- Sometimes, the stone gets grow larger and highly branched, these known as staghorn calculi
- Some stones occupies only a few calyces, such stones are called dendritic stones

OEDEMA

- Formerly called dropsy or hydropsy, is thelocalised swelling of body parts
- It results from excessive or abnormal accumulation of the interstitial fluid spaces beneath the skin, or in one or more cavities of the body
- Common causes of oedema are-

1. weakening and increased permeability of capillary walls due to injury, ill health, presence of poisonous material in body
2. blockage or obstruction of blood flow through veins
3. watery condition of blood which permits seepage of fluid through capillary walls
4. obstruction to the flow of lymph in lymph channels
5. excessive lymph production
6. rise in capillary blood pressure which forces out blood plasma to intestinal space
7. increased vascular permeability to proteins
8. inadequate retention of sodium and water
9. local inflammation in which capillaries become more permeable
10. heart diseases in which impaired blood circulation and increased pressure
11. glomerulonephritis
12. snake bite, bee sting, eating poisonous shell fish
13. cirrhosis, tumours and other disease of liver
14. acute typhoid fever and pneumonia
15. starvation and poverty in which protein deficiency occurs

ACIDOSIS

- Acidosis or academia is the abnormal condition in which the body pH is below 7.35 either due to the accumulation of acids or due to the loss of bases
- In severe acidosis, total body sodium gets depleted, plasma sodium level falls low, level of total body potassium becomes low, plasma potassium remains normal.
- In acidosis, there is 2 abnormal acid production, namely acetoacetic acid and beta-hydroxy butyric acid.
- Acidosis occurs in cases of untreated diabetes mellitus, starvation, persistent vomiting and delayed anaesthetic vomiting
- The common symptoms of acidosis includes general lassitude, severe vomiting, increased thirst, restlessness, and the presence of aacetone in urine
- There are 2 major types of acidosis, namely respiratory acidosis and metabolic acidosis
- Respiratory acidosis, is characterized by abnormally high Pco2 due to hypoventilation
- Metabolic acidosis, is characterized by the accumulation non-carbonic acid in the ECF

ALKALOSIS

- Alkalosis or alkalemia is the opposite of acidosis
- It is characterized bylow hydrogen ion concentration of arterial blood

- In it, blood pH above 7.45 due to the accumulation of bases or loss of acids, in the absece of compensatory changes

Dialysis

- In acute & chronic renal failures, kidneys are unable to properly excrete nitrogenous wastes & also to regulate the pH & electrolyte concentration of the plasma.
- As a result, blood gets charged with high levels of urea, creatinine & other wastes.
- In this condition kidney transplantation or dialysis is essential as a life saving measure.
- Dialysis is the process by which cystalloid substances are removed from a solution to pure water by interposing a semipermeable membrane between the two.
- Crystalloid substances pass to water across the membrane by simple diffusion until their concentration becomes the same in water & the solution.
- There are two types of dialysis, namely *haemodialysis & peritoneal dialysis*.

a) Haemodialysis

- *Haemodialysis* is the artificial removal of nitrogenous wastes from a patients blood with the help of a semipermeable membrane.
- *Dialyzer* – The apparatus used for heamodialysis.
- Dialysing fluid – The fluid used in a dialyzer for accepting the wastes from the blood.
- *Cellulose or cellophane* – The semipermeable membrane, that seperates blood from the dialysing fluid.
- *Dialysate* – The purified blood coming out of the dialyzer after clearing of its waste.

b) Peritoneal dialysis

- It is also called *Continuous ambulatory peritoneal dialysis* (CAPD) .
- It is more convenient & time saving method of haemodialysis.
- Here peritoneum serves as semipermeable dialyzing membrane & dialyzing fluid is made to circulate through the abdominal cavity.
- Peritoneum permits the rapid bidirectional transfer of substances.

Kidney transplantation

- It is the replacement of defective, diseased or damaged kidney by a functional kidney from a donor.
- When medication & haemodialysis fails this gives a satisfactory result.
- For kidney transplantation the donor & recipient should be either identical twins or immunologically matching individuals.
- *Kidney rejection or tissue rejection* - During the transplantation, the immune system of the recipient produces antibodies against the proteins of the transplanted kidney, if the proteins are mismatching.These antibodies react with the kidney transplant & destroy it.

- *Immuno suppressive drugs* – Kidney rejection can be avoided by administering this drug. This suppress the immune power of the recipient.
- The success of kidney transplantation depends upon the genetic similarity between the donor & the recipient.
- Accepting kidney from the identical twin will be most reliable & safest & from siblings will be safer.

equipping with excellence
CPA COLLEGE OF GLOBAL STUDIES

MODULE 5. MUSCLE PHYSIOLOGY

MUSCLE PHYSIOLOGY

- Muscles are the contractile tissue concerned with the body movements, including locomotion.
- Muscle constitute 45% of body weight & 35% of body proteins, they carry out nearly 50% of total metabolic activities of a resting body.
- Fundamental properties of muscles are

Excitability – ability to perceive & respond to the stimuli.

Contractility – ability to shorten & thicken when sufficiently stimulated.

Extensibility – ability to stretch or extend

Elasticity – ability to extension & recoil.

- Muscles have three major functions :-
  1. ***Motion***
  2. ***Maintenance of posture***
  3. ***Heat production***

MUSCLE CELLS

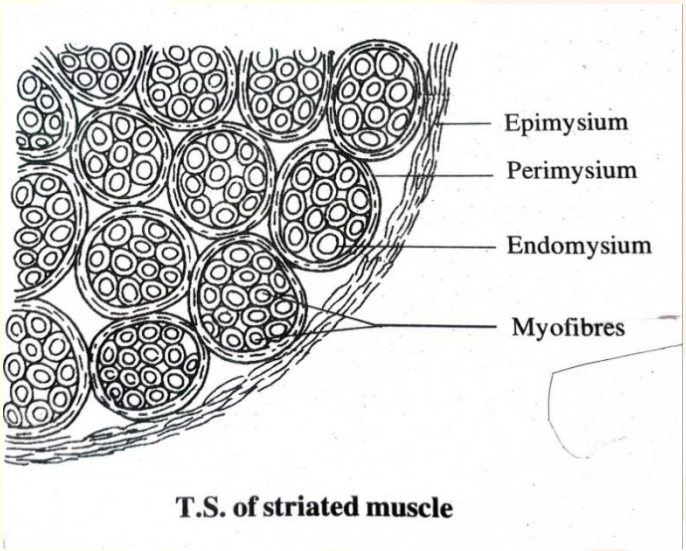
- Also called muscle fibres.
- Long, slender & fibre like.
- Plasma membrane – sarcolemma.
- Cytoplasm – sarcoplasm, it contains nucleus, mitochondria, sarcoplasmic reticulum, myofibrils,
- Myofibril is formed of myofilaments.
- Myofilaments – two types
  Thick- myosin & thin - actin.

STRUCTURE OF VERTEBRATE SKELETAL MUSCLE

EM STRUCTURE OF MYOFIBRILS AND MYOFILAMENTS

- Striated muscles are arranged in thick bundles known as ***fascicles***.

- Fasciculus.
  Swollen middle portion – ***belly.***
  Two narrow ends attaches to a bone through tendon.
- When the tendon is flat & broad, called ***aponeurosis***.
- ***Epimysium*** – The entire muscle is wrapped within a fibrous connective tissue covering.
- ***Perimysium*** – within the muscle each muscle bundle is enclosed within a connective tissue sheath.
- ***Endomysium*** – each muscle cell in a bundle is surrounded by a connective tissue packing.

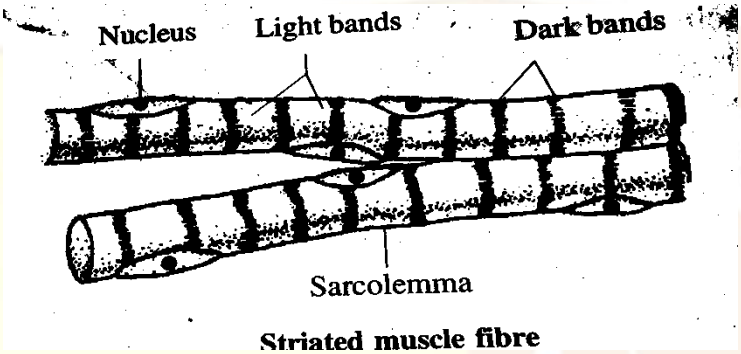


T.S. of striated muscle

ULTRA STRUCTURE OF STRIATED MUSCLES AND CONTRACTILE PROTEINS

- Muscle bundles are formed of long, cylindrical multinucleate muscle cells called ***muscle fibres.***
- Muscle fibre is formed by the fusion of uninucleate embryonic cells called ***myoblasts***.
- Sarcoplasm contains nucleus, mitochondria, sarcoplasmic reticulum, myofibrils, glycogen reserve, myoglobin, transverse tubules,….
- ***Transverse tubules (T tubules)*** are the extensions of sarcolemma & they open to the outside of the fibre. They run transversly through the fibre & perpendicular to the sarcoplasmic reticulum. It contains a fluid rich in Ca^{2+}.
- One T tubule & a pair of sarcoplasmic vesicles together form a ***triad.***
- The specialized regions of SR which are in contact with the T tubules are called ***terminal cisternae.***
- Muscle fibres have alternate dark and light bands, known as stripes or striations.
- The light bands are called ***isotropic bands or I-bands***.
- The dark bands are called ***anisotropic bands or A-bands***.
- Each I-band is bisected by an ***Z-line*** (Z-zone or Krause's membrane).
- Each A-band by an ***H-zone*** (Hensen's zone).

- In the centre of the H-zone, is the ***M-line***.
- Each muscle fibre is formed of a large number of cylindrical, unbranched and longitudinal ***myofibrils (sarcostyles).***

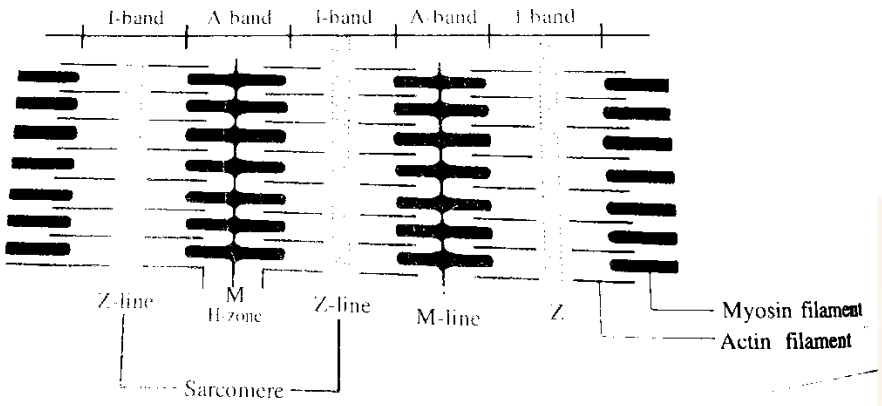


Striated muscle fibre

- Each of them, in turn, is formed of still delicate protein filaments, called ***myofilaments.*** Myofilaments are arranged in repeating bundles, called ***sarcomeres***.
- Sarcomeres are the structural units of muscle fibres.
- Adjacent sarcomeres are separated by the narrow Z-zone.
- So, repeating Z-lines divide the muscle fibre into a series of sarcomeres.

MYOFILAMENTS AND MUSCLE PROTEINS

- Myofilaments of striated muscles are of three kinds, ***thick, thin and elastic***.
- They are formed of ***contractile, globular and fibrous proteins***.
- Thick filaments are formed by the protein ***myosin***.
- Thin filaments are formed mostly by ***actin***.
- Elastic filaments are formed by a long, thin, coiled and spring-like protein, called ***titin***.
- Myosin filaments have projecting ***cross bridges*** for linking with actin filaments.
- Actin & myosin filaments are arranged separately in alternating bundles.
- Actin filaments from the two sides overlap the myosin filaments & interlock with them
- Actin filaments extend between the boundary of the H-zone & the boundary of Z line.
- Myosin filaments extend between the two boundaries of the same A-band.
- In the I-band, only actin filaments are present.
- In the H-zone of the A-band only myosin filaments are present.



Arrangement of myofilaments (diagrammatic)

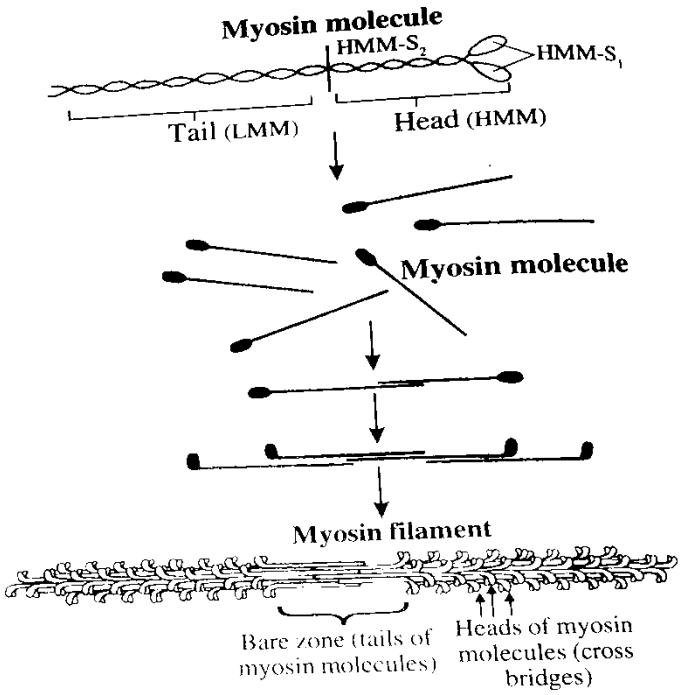
CHEMISTRY OF SKELETAL MUSCLES

- Nearly 75-80 % of skeletal muscles is formed of water.
- The remainder consists of proteins, lipids, glycogen and inorganic ions.
- Muscle proteins are of different types.
- Nearly 20% of them consist of collagen and elastin.
- Another 20% includes enzymatic proteins.
- The remaining muscle proteins include *myosin, actin, titin, troponin and tropomyosin*, which are actively involved in muscular contraction.
- Myosin has enzymatic ATP-ase activity also, while the others have no ATP-ase activity.
- In vertebrate muscles, the high-energy phosphate compound ***creatine phosphate, or phosphocratine***, is present as an energy reservoir.
- In invertebrate muscles, arginine phosphate is present, instead of creatine phosphate.
- The inorganic ions of muscles include Ca^{2+}, Mg^{2+} and K^{+}.
- In resting muscle fibres, sarcoplasmic reticulum stores large amounts of Ca^{2+}.
- When the muscle gets stimulated for contraction, sarcoplasmic reticulum releases Ca^{2+}.
- This activates the enzyme ATP-asę and thereby initiates muscle contraction.
- Mg^{2+} ions are important for muscular contraction and relaxation, though they do not initiate contraction.
- K ions are essential for the maintenance of the normal physical and physiological states of actin and myosin.

ORGANIZATION OF MYOSIN FILAMENTS

- Myosin (thick) filaments are polymers of the contractile protein myosin.
- Myosin amounts to more than 50% of the total contractile protein content of skeletal muscle.

- It exists in two forms, namely partially folded alpha form (***α -myosin***) and fully folded beta form (***β-myosin***).
- Myosin molecule is a dipeptide, formed of two spirally twisted polypeptide chains.
- It is almost rod-like, with a globular head and a filamentar "tail".
- Myosin head is called heavy ***meromyosin (HMM),*** and myosin tail is called ***light meromyosin (LMM).***
- Head has two sub-units, namely a ***globular sub-unit, called heavy meromyosin – S_1 (HMM-S_1), and a helical rod, called heavy meromyosin-S_2 (HMM-S_2).***
- S_1 is the most important part of the myosin molecule in that it forms a projecting cross bridge for binding with actin filament.
- It contains binding sites for the enzyme ATPase which hydrolyses ATP to ADP.
- Thus, HMM-S_1 has both actin-binding and ATPase activities.
- Cross bridges are arranged in pairs in a spiral pattern around the main axis of the myosin filament.
- Projecting cross bridges are absent in the middle portion of the filament, which is called ***bare zone***.

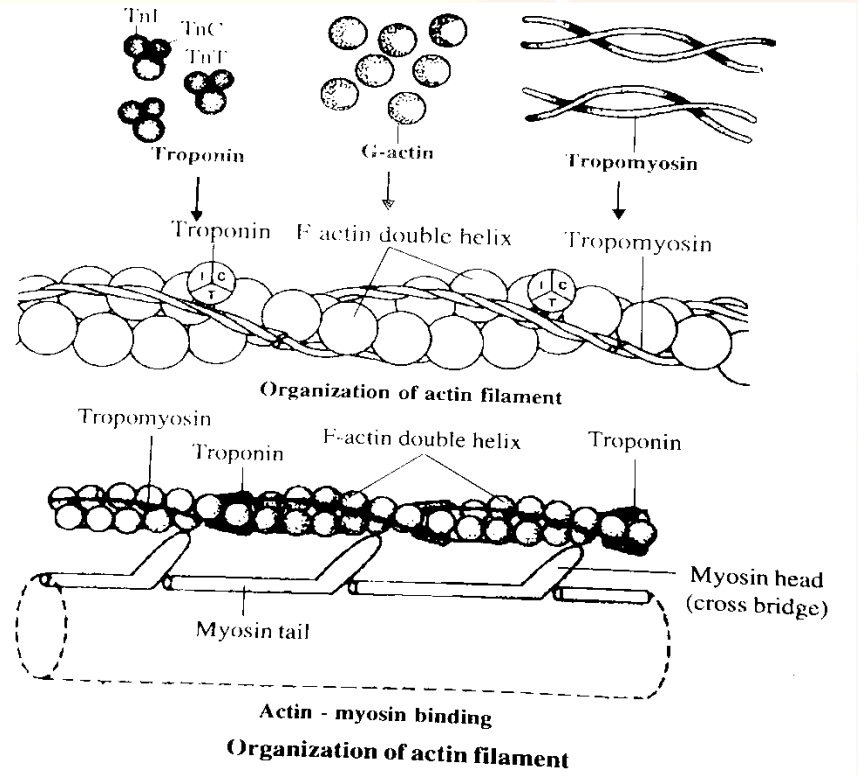


Organization of myosin filament

ORGANIZATION OF ACTIN FILAMENTS

- Thin myofilaments are formed mainly of the globular protein ***actin***.
- Actin is the second major protein of skeletal muscle.

- It is contractile, but elastic.
- Actin amounts to nearly 25% of the total proteins of skeletal muscles.
- Each actin filament is formed of two beaded strings, called ***F-actin (fibrous actin).***
- They remain helically twisted, forming an actin double helix.
- Each F-actin is a polymer, formed of several globular actin monomers, called ***G-actin (globular actin).***
- Thus, actin exists in polymeric and monomeric forms, known respectively as F-actin and G-actin.
- In skeletal muscles, actin exists mostly as F-actin.
- Polymerisation of G-actin to form F-actin requires ATP.



- Associated with the F-actin double helix are some accessory proteins also.
- The important ones among them are ***tropomyosin, troponin, alpha-actinin and beta-actinin.***
- ***Tropomyosin and troponin act as regulator proteins*** and control the movement of actin filaments during muscular contraction.
- They inhibit actin-myosin interaction in the absence of Ca^{2+} ions.
- On the other hand, ***α and β-actinins regulate the polymerisation of G- actin monomers***.

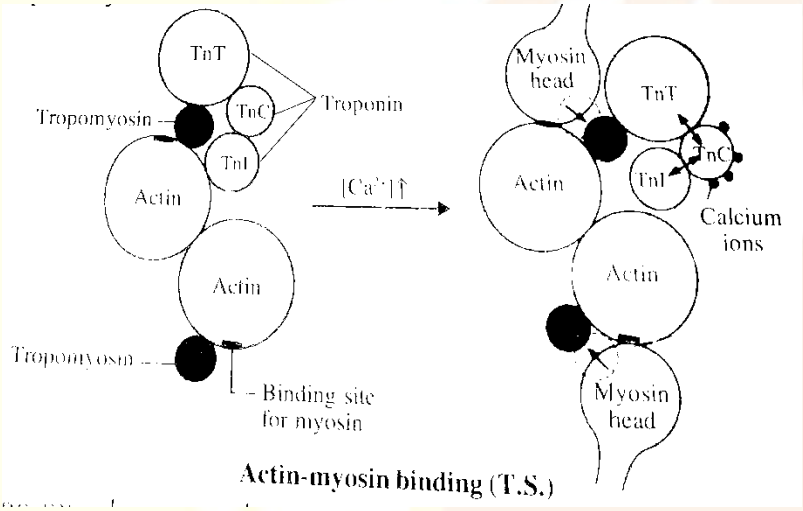
Tropomyosin

- Tropomyosin is a rod-shaped, contractile fibrous protein.
- It amounts to 5-10 % of the total contractile proteins of skeletal muscle.

- It exists as two helically twisted longitudinal filaments, ***enclosed in the groove of the F-actin double helix.***
- Tropomyosin plays an important role in sensitizing actin and myosin molecules to Ca^{2+} ions.
- The tropomyosin of vertebrate striated muscles is called ***tropomyosin-B***, and that found in the non-striated muscles of many invertebrates is called ***tropomyosin –A or paramyosin.***

Troponin

- Troponin occurs at intervals on actin filaments.
- It takes up calcium ions from sarcoplasm to initiate muscle contraction.
- Troponin is a complex globular protein with ***three sub-units, namely troponins T, C and I.***
- ***Troponin-T (TnT) binds to tropomyosin***.
- ***Troponin-C (TnC) reversibly binds to Ca^{2+} ions***.
- ***Troponin-I (Tnl) is an inhibitory component***, capable of inhibiting any interaction between actin and myosin.



Actin-myosin binding (T.S.)

Titin filaments

- Titin filaments, or elastic filaments, are remarkably long and thin.
- They are formed of a special type of exceptionally large., extremely long and thin, and excessively coiled and spring-like contractile protein, called ***titin***.
- Titin is the ***largest of all known single polypeptides***.
- Titin filaments extend between the Z line and the myosin filaments.
- Titin filarments are significant in three respects:
  - (i) They hold the actin and myosin filaments in tight alignment with each other.
  - **(ii)** Facilitate the anchorage of myosin filaments to the Z line.
  - **(iii)** Serve as a molecular spring and thereby provide passive elasticity to the muscle.

CHEMISTRY & MECHANISM OF MUSCLE CONTRACTION

- Muscular contraction is the shortening of myofibrils, in response to a nervous stimulation.
- During this, actin filaments slide over myosin filaments and link with them, forming ***acto-myosin complexes.***
- During muscular relaxation, they delink and move away from each other.
- During muscular contraction, an action potential reaching the axon endings of a motor neuron, spreads to the muscle fibres and excites them.
- As a result, a post synaptic action potential is produced in the motor end plate of each muscle fibre.
- This leads to muscular contraction.
- The triggering of muscular contraction by the excitation of nerve fibres and the generation of a post-synaptic action potential is called ***excitation-contraction coupling (ECC) or electrochemical coupling.***

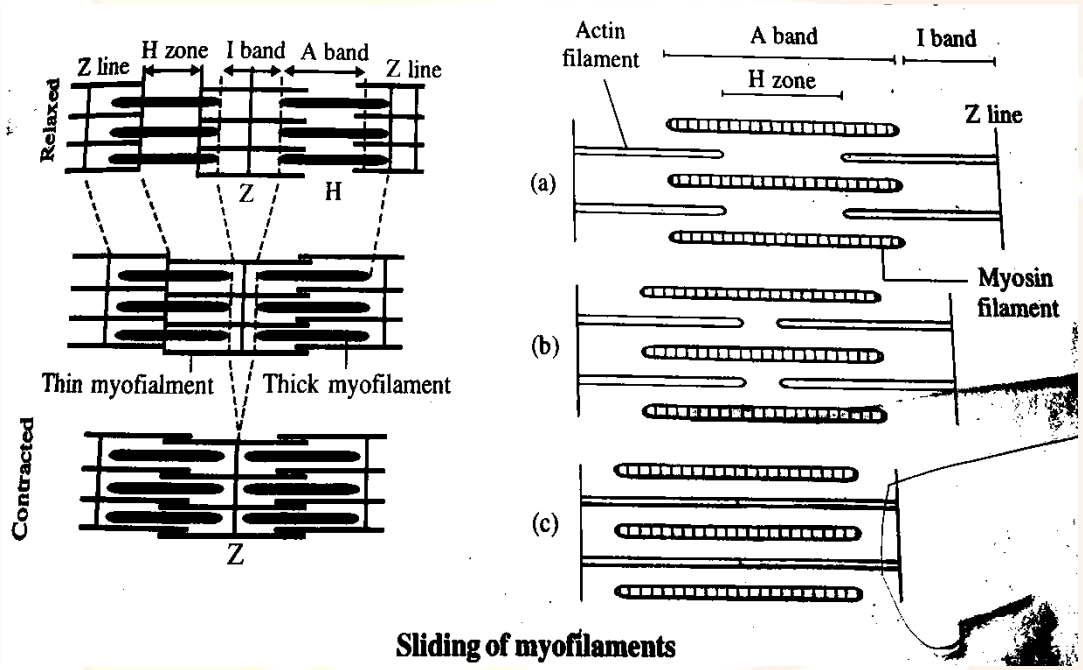
CONTRACTION OF SKELETAL MUSCLES

- The contraction of skeletal (striated) muscles involves two sets of events, namely physical or ultrastructural changes and physiological or biochemical changes.

ULTRASTRUCTURAL CHANGES

- The ultrastructural changes during muscular contraction include the regular and cyclic attachment and detachment between the myosin cross-bridges and the actin filaments.
- These changes are best explained by the "***sliding-filament theory of muscle contraction"***
- According to this theory, muscle fibres become short and thick during contraction by the shortening of their sarcomeres.
- The shortening of the sarcomeres is not due to the contraction and shortening of myofilaments, but by their sliding and overlapping.
- Actin filaments slide inward from adjacent Z-zones to the H-zone in between.
- In the H-zone, they completely overlap the myosin filaments and link with them, forming acto-myosin chains.
- This inward movement of actin filaments brings the Z-zones closer and closer together.
- So, the length of the I-band and that of the sarcomere become progressively shorter and shorter.
- Actin filaments from the two sides ultimately meet together at the H-zone.
- The H-zone also becomes shorter and finally it disappears.
- The length of the A-and remains unchanged.
- During muscular contraction, the head of the myosin filament functions as a hook.

- It attaches to a binding site on F actin filament
- It pulls the actin filament further towards the H-zone in the A-band.
- Now, the myosin head detaches from the actin, returns to its original form and shape and then re-attaches to a new site a little ahead in the actin filament.
- This shortens the sarcomere up to 30 % of its length.



Sliding of myofilaments

- The energy required for the actin-myosin interaction is obtained by ATP breakdown.
- It has been suggested that the binding of actin with myosin occurs at a site different from the ATPase site of myosin.
- The formation of actomyosin is believed to activate the ATPase site by an allosteric mechanism.
- This, in turn, results in ATP hydrolysis.
- The free energy of this hydrolysis is utilized for the detachment of myosin head.

THE SEQUENCE OF EVENTS OCCURING DURING CROSS-BRIDGE BINDING ARE THE FOLLOWING:

1. Myosin head first attaches to a stable site in the actin filament.
2. This binding produces a rocking or rotatory movement of the myosin head and causes it to exert a pull on the myosin filament.

3. Consequently, tension is transmitted to the myosin filament and this causes the sliding of the actin filament over the myosin filament.
4. Once the rotation of the myosin head is over, ATP is hydrolysed by ATPase.
5. The free energy of ATP hydrolysis is used for the detachment of the myosin head.
6. Soon, the head attaches to the next binding site in actin and the whole cycle of events is repeated until the actin filament reaches the centre of the sarcomere.

PHYSIOLOGICAL CHANGES

- The physiological mechanism involved in the contraction of skeletal muscles is known as ***electrochemical coupling or excitation-contraction coupling (ECC).***
- The contraction of skeletal muscles requires nervous stimulation.
- When a motor impulse reaches the myo-neuronal synapse, the synaptic vesicles of the axon ending get activated and they release the transmitter substance acetylcholine to the synaptic cleft.
- Acetylcholine diffuses towards the muscle fibre and binds to specific receptor sites in the sarcolemma.
- This stimulates the sarcolemma and temporarily enhances its permeability to ions, especially to Na^+ and K^+.
- As a result, sodium channels open, heavy influx of Na^+ follows, and there develops an end plate potential.
- This leads to the post-synaptic depolarization of the sarcolemma and the generation of a post synaptic action potential at the motor end-plate.
- Acetyl choline is soon hydrolysed to ***choline and ethanoic acid*** by the enzyme ***choline esterase*** to prevent overstimulation and the sustained or persistent post-synaptic depolarisation.
- The end-plate action potential soon spreads deep into the interior of the muscle fibre along the T-tubules.
- This excites the whole set of fibrils and triggers muscular contraction by releasing Ca^{2+} from sarcoplasmic reticulum and T- tubules.
- During this, there is the coupling of the electrical events of excitaton with the ultrastructural events of muscular contraction. This is called ***excitation contraction coupling.***
- During muscular contraction, free Ca^{2+} ions diffuse from the sarcoplasm in to the myofilaments and bind to troponin C (TnC).
- The TnC-Ca^{2+}complex soon interacts with Tnl.
- This causes conformational changes and also reverses the inhibitory influence of the troponin system on actin-myosin interaction
- As a result of the reversal of the inhibitory effect, actin gets 'switched on' and its myosin-binding sites are free for actin-myosin interaction and cross-bridge cycle.

- The active state of actin and the high level of free sarcoplasmic Ca^{2+} stimulate the ATPase activity of myosin.
- ATP hydrolysis follows to provide energy for muscular contraction.
- Simultaneously, myosin cross bridges attach to actin filaments and undergo interaction.
- This causes the myosin heads to rock against the actin filament, pulling the filaments away from each other.
- Actin filaments slide over myosin filaments, leading to muscular contraction.
- When the excitation of the sarcomere ceases Ca^{2+} ions are actively pumped back to the sarcoplasmic reticulum and T-tubules by an ATP-driven calcium pump.
- The free energy of ATP hydrolysis is used to detach the myosin head from the actin.
- The myosin head is now free to attach to the next site in the actin filament and thereby to repeat the attachment-detachment cycle.
- If the active transport of Ca^{2+} from sarcoplasm to sarcoplasmic reticulum is inhibited, relaxation does not occur. This results in a state of sustained contraction, called ***muscle contracture.***

MUSCULAR RELAXATION

- Relaxation of the sarcomere begins when the concentration of Ca^{2+} ions in the sarcoplasm fall below the threshold level.
- During relaxation, most of the calcium ions would be absorbed back to the SR from sarcoplasm.
- At a low calcium level, the enzyme ATPase becomes less active.
- As a result, the breakdown of ATP and the release of energy for muscular contraction come to an end.
- During relaxation, the cross-bridges between actin and myosin filaments undergo reorganization.
- As a result, the actin filaments delink from myosin filaments and slide out from the H-zone.
- This pushes the Z-lines away from each other, causing the lengthening of the muscle fibres.
- The muscle fibres return to their original physical form and physiological state.

ENERGY FOR MUSCULAR CONTRACTION

- Muscular contraction requires a sustained supply of energy.
- This energy supply is maintained by a series of biochemical reactions, known as ***Lohmann scheme of reactions***.

The major energy-related biochemical events are ,

1. Breakdown of ATP to provide immediate energy for the contraction of muscle fibres.
2. Breakdown of creatine phosphate to provide phosphate and energy for the re-synthesis of ATP.
3. Anaerobic oxidation of muscle glycogen to lactic acid to provide ATP for the re-synthesis of creatine phosphate.
4. Aerobic oxidation of a part of the lactic acid to provide energy for the re-synthesis of muscle glycogen.
5. Re-synthesis of glycogen from the remaining lactic acid.

Breakdown of ATP

- The enzyme ***ATPase breaks ATP to ADP*** and inorganic phosphate (Pi).
- A portion of its energy store is liberated as active kinetic energy.
- This free energy facilitates actin-myosin interaction.
- This leads to the sliding of myofilaments and the shortening of muscle fibres.

ATP $\xrightarrow{\text{ATPase}}$ ADP + Pi- Energy for muscular contraction

Breakdown of creatine phosphate and re-synthesis of ATP

- For continued muscular activity the spent ATP has to be quickly re-synthesised.
- For this, energy and inorganic phosphate are made available by the ***break down of creatine phosphate (phosphocreatine), with the help of the enzyme creatine phosphatase.***
- During this, the high-energy phosphate splits off from creatine and combines with ADP to ***form*** ***ATP***.

Creatine phosphate $\xrightarrow{\text{creatine phosphatase}}$ creatine + High energy phosphate for the resynthesis of ATP.

ADP + High energy phosphate $\xrightarrow[\text{phosphotransferase}]{\text{creatine}}$ ATP

Anaerobic breakdown of muscle glycogen to lactic acid

- For repeated muscular contraction creatine phosphate also has to be re-synthesized from creatine and ATP.
- Muscle glycogen is oxidized to lactic acid in a chain of reactions known as ***muscle glycolysis or lactic acid fermentation.***
- At first, ***glycogen is oxidized to pyruvic acid*** through several intermediate reactions and products.
- Pyruvic acid is soon ***transformed to lactic acid.***
- In the course of muscle glycolysis, ATP is synthesised.
- creatine combines with it and forms creatine phosphate

Muscle glycogen $\xrightarrow[\text{fermentation}]{\text{lactic acid}}$ Lactic acid + ATP for re- synthesizing creatine phosphate

Creatine + ATP $\longrightarrow$ creatine phosphate

Aerobic oxidation of lactic acid

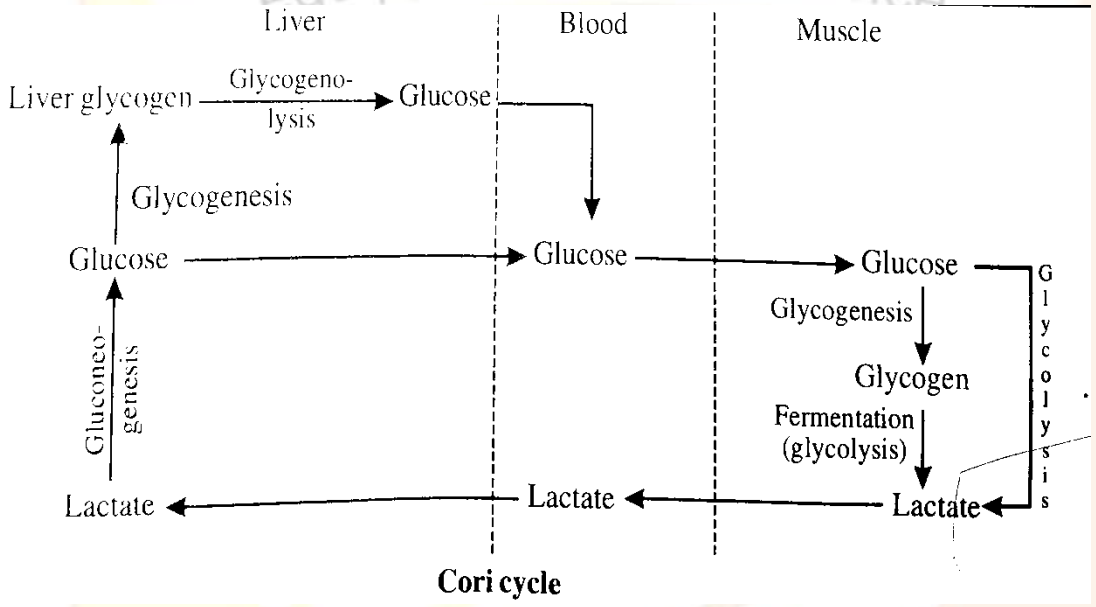
- 1/5 of the lactic acid produced is aerobically oxidized to CO_2, $H_2O$and energy through a cycle of reactions, known as ***Krebs cycle.***
- Lactic acid first gets ***converted to pyruvic acid***.
- Pyruvic acid is soon ***transformed to an energy-rich compound, called acetyl co-enzyme A (acetyl CoA).***
- Acetyl CoA enters the Krebs Cycle.
- The energy released from Krebs Cycle is utilized for re-synthesizing muscle glycogen from the remaining 4/5 of the lactic acid.

- Lactic acid $\longrightarrow$ Pyruvic acid $\longrightarrow$ Acetyl CoA $\xrightarrow{\text{Krebs Cycle}}$ $CO_2 + H_2O$ + energy for re-synthesizing Muscle glycogen

Re-synthesis of muscle glycogen from lactic acid - Cori cycle

- 4/5 of the muscle lactic acid is used for the re-synthesis of muscle glycogen.
- This ***occurs in liver***, since the enzymes necessary for it are absent in muscles, but present in liver.
- At first, muscle lactic acid passes to blood and reaches liver. Here, it gets converted to glucose through gluconeogenesis.
- A part of this liver glucose may be converted to liver glycogen. This is called ***glycogenesis***.

- The rest is released to blood and it reaches the muscle.
- A part of the liver glycogen is converted to glucose by the process of ***glycogenolysis*** and then discharged to blood.
- This blood glucose also reaches muscles.
- In the muscle, glucose gets converted to muscle glycogen (by ***glycogenesis***).The cycle of reactions by which muscle lactic acid is transformed to muscle glycogen is known as ***Cori cycle or lactate-glucose cycle.***



MUSCLE TWITCH & MUSCLE TETANUS

- ***Muscle twitch*** - The sum total of muscle events, occurring during a single contraction.
- Three stages :
  1. *Latent phase* – time interval between the initial stimulation & the beginning of actual contraction.
     - No physical changes occur, several biochemical changes takes place.
     - Transmission of action potential to the sarcoplasmic reticulum.
     - Release of Ca^{2+} from sarcoplasmic reticulum .
  2. *Contraction phase*
     Muscle shortens & its tension increases.
  3. *Relaxation phase*
     Muscle returns to its original physical state & physiological condition.
     It lasts longer than contraction phase.
- ***Myograph*** – apparatus which can measure muscle twitch.
- ***Myogram*** – the record produced by the myograph.

- *Muscle tetanus* – sustained hyper contraction of muscles due to the fusion of numerous twitches with no time for relaxation between stimuli
- Continuous stimuli results in the overlapping or fusion of successive twitches to form a large single twitch.
- Two types :

  Incomplete or unfused tetanus – stimuli are spaced so that the muscle can relax partially .

  Complete or fused tetanus – stimuli are fused so that relaxation is altogether absent in between successive stimuli.

ISOMERIC & ISOTONIC CONTRACTIONS

- ***Isomeric contraction*** – muscular contraction in which the tension on the muscle increases sharply.
    4. Only minimal muscle shortening.
    5. No movement is produced.
    6. Energy is utilized.
- ***Isotonic contraction*** – muscular contraction in which the force on the muscle remains same or constant.
    7. Muscle shortens.
    8. Pulls on another structure such as bone.
    9. Produce movement
    10. Energy is utilized.

ALL OR NONE LAW

- ***The magnitude of muscle contraction is independent of the intensity of the stimulus, & muscle contraction never be partial, but will always be complete***.
- This implies that either there will be maximal contraction, or there will be no contraction.

SUMMATION OF STIMULI

- Super positioning of one contraction over the previous one.
- Results in excessive contraction or extreme shortening of the muscle, much greater than in a single stimulus.
- Tension developed during summation would be much greater than that of a single twitch.
- If two stimuli are too close, the second one will have no effect. This is because muscle membranes will be in the refractory period, & will not able to elicit a contraction – triggering action potential.

MUSCLE FATIGUE & RIGOR MORTIS

- ***Muscle fatigue*** – muscle loses its power for contraction, fails to respond to stimuli, & becomes relaxed & flabby.
- Cardiac muscles are immune to fatigue.
- ATP, phosphocreatinine & glycogen becomes almost exhausted.
- Release of Ca^{2+} from SR is very slow & much reduced.
- Accumulation of lactic acid & other wastes.
- The neuromuscular junction gets fatigued before the muscle is fatigued.
- ***Rigor mortis*** – temporary condition in which all the muscles of a dead individual become rigid, non-elastic & permanently contracted.
- The body becomes stiff.
- ***Rigor*** is a state of muscular rigidity due to the depletion of ATP, creatine phosphate,…
- After death enzyme stops functioning, ATP synthesis become impossible.
- Energy is not available for the relaxation of muscle fibres, & they remain in the contracted state.
- Rigor mortis commences 3 hours after death, reaches maximum stiffness after 12 hours, & then gradually disappears.

TETANY

- This is a disorder characterized by enhanced neuromuscular excitability that is caused by various metabolic abnormalities
- Muscular spasm occurring in parathormone deficiency
- It is characterized by abnormal muscular contractions
- Medical sign consisting of involuntary contractions of muscles which may be caused by disorders that increase the action potential frequency of muscle cells or the nerves that innervate them
- Signs-
    1. Contractions of distal muscles of hands (carpal spasm), and feet (pedal spasm)
    2. Numbness around mouth and distally in limbs
    3. Muscle cramps
- Causes-
    1. deficiency of calcium
    2. excess of phosphate
    3. under function of parathyroid gland
    4. low levels of CO2
    5. osteomalacia and rickets due to defiency of vitamin D

6. low magnesium level

- There are two types,
  1. Manifest – due to parathormone deficiency and hypocalcemia
  2. Latent – due to hyperventilation and magnesium deficiency

equipping with excellence
CPA COLLEGE OF GLOBAL STUDIES

MODULE 6 NERVE PHYSIOLOGY

NERVE PHYSIOLOGY

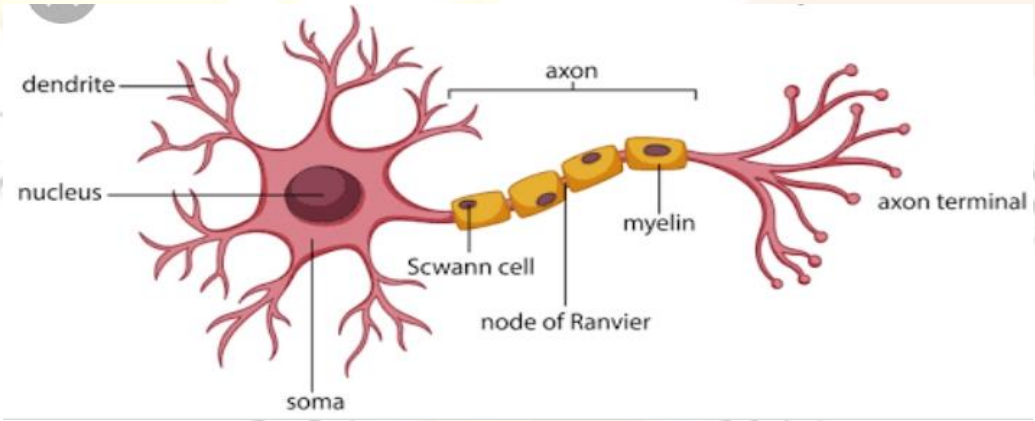
- The physiological activities of higher animals are directed, controlled & co-ordinated by two systems, namely nervous system & endocrine system.
- Nervous system act as an *electrical co-ordinator* & endocrine system act as a *chemical co-ordinator.*
- The two systems form a functional complex called *neuro endocrine system.*
- Nervous system stimulates the synthesis & release of some hormones &_nervous functions are stimulated by some hormones.

COMPONENTS OF NERVOUS SYSTEM

- Nervous system has three main components, namely nerve cells, glial cells & nerve fibres.

NERVE CELLS OR NEURONS

- They are the structural & functional units of the nervous tissue.
- They are the longest cells in the animal body, specialized for the generation & transmission of messages.
- They have no powers for mitotic multiplication.
- A neuron has three parts, namely *cyton, dendron & axon.*



Cyton

- Cyton (soma) is the cell body.
- Its cytoplasm is called neuroplasm. It contains nucleus, all cell organelles except centrioles, numerous long & thin neurofibrils & a pigment called *lipofuscin*.
- Mitochondria are numerous to meet the high energy needs for the transmission of impulses.

- *Nissl granules / chromatoid bodies* – ribosomes are seen in clusters on rough ER.
- *Lipofuscin* is a by-product of lysosomal activity & its concentration increases with ageing.

Dendrons

- They are the short processes radiating from the cyton.
- They may contain mitochondria, ribosomes & other cell organelles.
- Dendrons end in small branches called dendrites.
- Dendrons & dendrites transmit impulses towards the cyton.

Axon

- Axon is a long & axial process of cyton.
- It transmits impulses away from the cyton.
- *Axolemma or axon membrane* – plasma membrane of axon.
- *Axoplasm* – protoplasm of axon. It contains numerous neurofibrils.
- *Axon hillock* – thick & conical area in between cyton & axon.
- *Axon terminals / axonites / telodendrons* – axons ends in fine branches.
- *Synaptic knob / end bulb* – terminal knob of axonites. It contains mitochondria & membrane bound secretory bodies called synaptic vesicles.
- *Neurotransmitters* – the chemicals synthesized & stored by synaptic vesicles. It helps in impulse transmission. Eg :- Acetylcholine.
- *Collateral axons* – lateral branches of axons.

CLASSIFICATION OF NEURONS

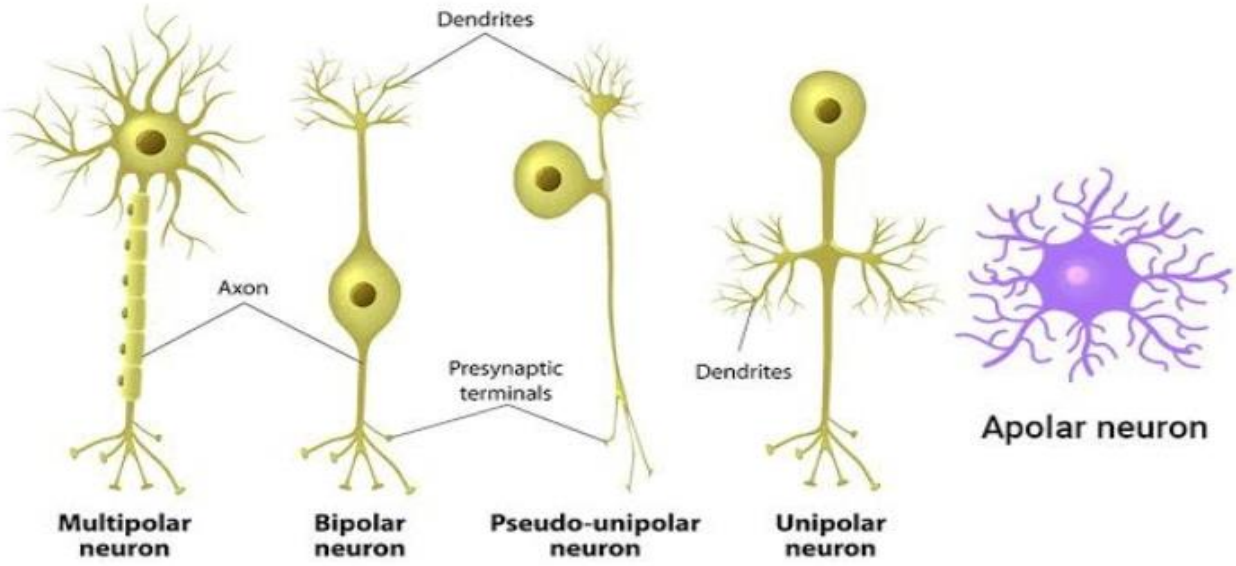
- **Based on the number of processes**
    1. ***Apolar neurons***
       Non polar neurons has no definite dendron or axon.
       Nerve impulses radiate in all directions
       Eg:- *Hydra*

    2. ***Unipolar neurons***
       Monopolar neuron has an axon, but no dendrons.
       Eg:- Invertebrates

    3. ***Bipolar neurons***
       Bipolar neuron has an axon at one end & a Dendron at the opposite end.

Eg:- Retina, inner ear & the olfactory epithelium of vertebrates

4. ***Multipolar neurons***
   It has one axon & several dendrons.
   Eg:- Brain & spinal cord.



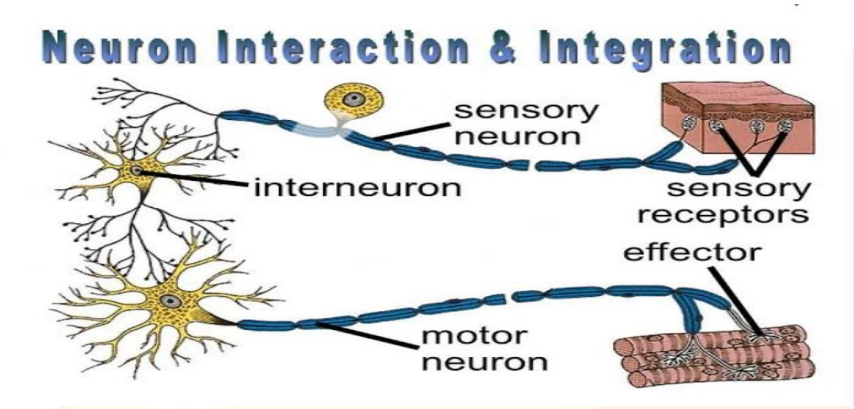
- **Based on the nature & direction of impulses**

1. ***Sensory neurons***
   Receptor or afferent neurons.
   Transmits sensory impulses from receptor organ to brain or spinal cord.

2. ***Motor neurons***
   Effector or efferent neurons
   Transmits motor impulses from brain or spinal cord to effector organs, such as muscles & glands.

3. ***Connecting neurons***
   Internuncial or association neurons.
   They serve as the link between sensory & motor neurons.
   They are located in brain & spinal cord.

- The processes of sensory & motor neurons are arranged in bundles. Such bundles are called *nerves* in PNS, & *nerve tracts* in CNS.



GLIAL CELLS

- Also called *neuroglia.*
- These are the unexcitable, non nervous, supporting & protective connective tissue cells.
- They are present in the CNS, nerve ganglia & also around nerve fibres.
- They provide mechanical & metabolic support to brain & spinal cord.
- They repair the damages of nerves & nerve fibres.
- Glial cells are of two main groups : *microglial cells & macroglial cells*.
- Microglial cells are mesodermal & macroglial cells are ectodermal in origin.

(i) Microglia

- Also called brain macrophages.
- Phagocytic glial cells.
- Protect the neurons of CNS by phagocytising cellular debris & invading microbes.

(ii) Macroglia

- Larger glial cells of the CNS.
- They include *astrocytes, oligodendrocytes, ependymal cells, radial glial cells Schwann cells & satellite cells*.

a. Astrocytes

- Largest & numerous of all glial cells with numerous processes..
- They form the supporting network around the neurons of brain & spinal cord.
- Attach neurons to blood vessels.
- Regulate external chemical environment of neurons by removing excess ions, mainly K^+.
- Play significant role in recycling the neurotransmitters.
- Two type of astrocytes :

- Protoplasmic astrocytes – found in grey matter of CNS.
- Fibrous astrocytes – found in the white matter.

b. Oligodendrocytes

- Similar to astrocytes, but with only fewer & shorter processes.
- They are involved in the formation of myelin sheath.
- Support the neurons of brain & spinal cord.

c. Radial cells.

- They are numerous in the retina of eye.

d. Schwann cells.

- They are similar to oligodendrites.

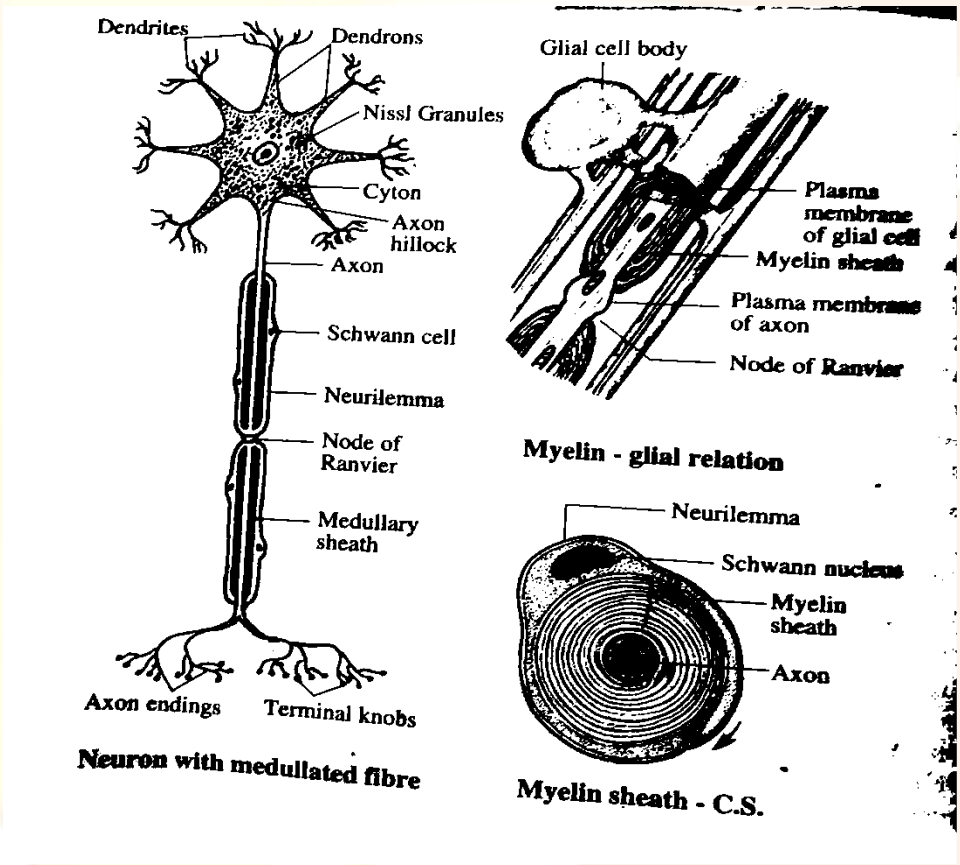
e. Ependymal cells,

- Also called *ependymocytes*.
- They are single layer of squamous or columnar or ciliated cells.
- They line the internal cavity of the CNS and helps in circulation of cerebro-spinal fluid.

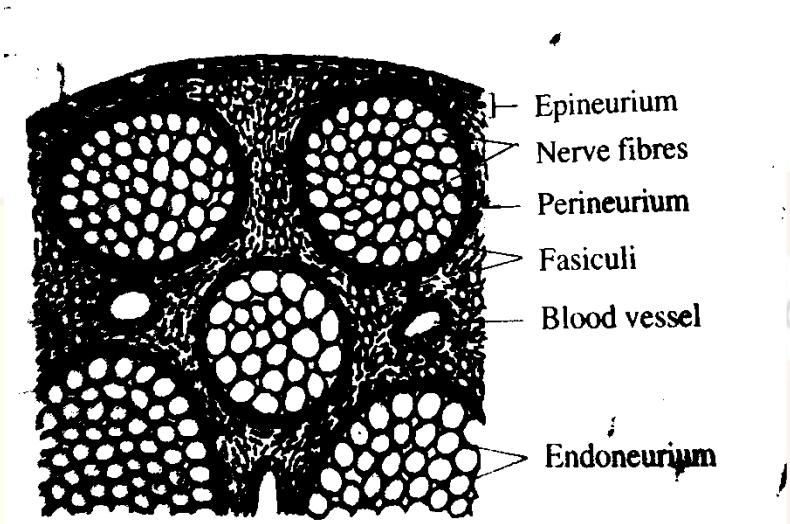
NERVE FIBRES

- Nerve fibres are axons, covered with one or more sheaths
- They are arranged in bundles to form nerves
- There is acontinuous primary sheath around the axon membrane. It is called neurilemma Or schwann sheath,
- it is formed of a single layer of flat and non-nervous glial cells, called schwann cell
- Neurilemma nourish the nerve cell and brings about regeneration and repair
- In brain and spinal cord, neurilemma is absent
- In some fibres, inner to the neurilemma, there is a secondary sheath, called medullary sheath, od myelin sheath
- Nerve fibres with myelin sheath are called myelinated or medullated fibres
- Those without it are known as non-medullated or amyelinated fibres
- In CNS of mammals, most neurons are myelinated
- Medullary sheath is formed of oligodendrocytes
- Medullary sheath is a multilayered insulating jacket around the axon
- It is formed of a protein lipid material, called myelin.
- Myelin sheath is non-continuous, but constricted. At intervals it is broken by consrictions called nodes of ranveir
- The part of the fibre in between two adjacent nodes is known as internode
- Medullary sheath has 3 important functions
    1. It covers and protects the nerve fibre
    2. Serves as an electrical insulation around the fibre to prevent spreading and distribution of impulses
    3. Speeds upimpulse transmission

- Medullated nerve fibres are found in cranial nerves, spinal nerves and also in white matter of brain and spinal cord
- Non-medullated nerve fibres are seen in autonomous nervous system and also in grey matter of brain and spinal cord



- Nerve fibres are also seen in bundles to form nerves, a bundle of nerve fibres is called fascicle
- Several fascicle together form nerve trunk
- The nerve trunk, as a whole enclosed within a thick connective tissue sheath, is called epineurium
- The fascicles enclosed in a connective tissue, called perineurium
- Each nerve fibre is wrapped in a thin envelope of connective tissue, called endoneurium



Nerve bundle – T.S.

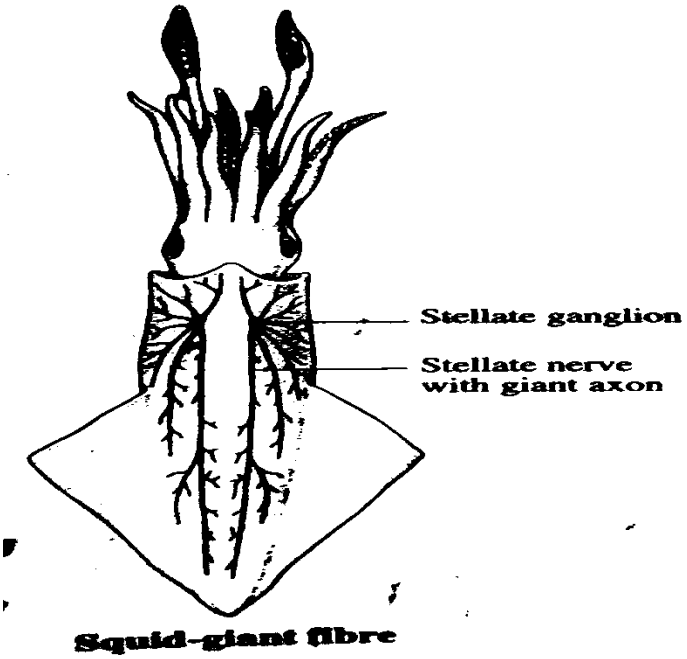
CLASSIFICATION OF NERVES AND VERVE FIBRES

1. **Medullated or myelinated nerve fibres-** Nerve fibres with medullary sheath
2. **Non-medullated or amyelinated fibres-** nerve fibres without medullary sheath
3. **Somatic fibres-** fibres between CNS and peripheral parts such as skin, skeletal muscles
4. **Visceral nerves-** fibres between CNS and visceral or internal organs
5. **Sensory (receptor or afferent) fibres-** fibres which transmit sensory impulses from receptor organs to CNS
6. **Motor (effector or efferent) fibres-** fibres which transmit motor impulses from CNS to effector organs
7. **Mixed nerves-** fibres which are sensory as well as motor in function.
8. **Cranial fibres-** fibres arising from brain
9. **Spinal fibres-** fibres arising from spinal cord
10. **Adrenergic fibres-** fibres which release adrenaline
11. **Cholinergic fibres-** fibres which releases acetyl choline

GIANT NERVE FIBRES OF CRUSTACEANS AND CEPHALOPODS

- They are exceptionally large and enormously thick nerve fibres

- characteristically found in some annelids (lumbricus- earthworm), and in crustaceans (squilla, cambarus- cray fish), and in molluscs (loligo, sepia)
- They can transmit impulses at much higher rates and maximum speed
- Squid giant axons contain large amounts of the anion isethionate, which has no known function
- The axoplasm also contains Na+, K+, Ca2+, Mg2+, and organic phosphates (ATP, ADP) , arginine phosphate, aspartate, glutamate, succinate etc
- There are two kinds of giant nerve fibres- **unicellular** and **multicellular** based on their ontogeny
- A unicellular giant fibre is simply an enlarged and extended axon of a single neuron
- A multicellular fibre develops by the fusion of several or many neurons
- The giant fibres of aquatic vertebrates are called mouthner fibres
- Giant fibres are a adaptation for quick and flashing withdrawal movements of startled animals to escape from enemies
- They are concerned with the rapid co-ordination of large groups of muscles for the quick movements of the body
- In squids, they helps the quick and powerful contraction of mantle to force out an explosive jet of water through siphon for rapid movements
- They also helps in sudden contraction of the ink glands to release ink that discolourise surroundings for escape
- Giant fibre's large size is highly advantageous in study of electro chemical changes taking place during impulse transmission



Squid-giant fibre

REGENERATION OF MEDULLARY FIBRES

• Nerve cells have no powers for multiplication.

• Nerve cells have only limited powers for regeneration.

• In human beings, most developing neurons lose their mitotic apparatus and powers for mitotic multiplication around the time of birth.

• So, in the brain and spinal cord, any damaged or destroyed neuron will not be replaced by the daughter cells of another neuron.

• Neurons are unable to repair or regenerate the degenerated, injured, or damaged parts of brain and spinal cord.

• The medullated or myelinated axons of the peripheral nerves have powers for *reparative regeneration.*

• In such nerves, the axons are myelinated by Schwann cells which initiate reparative regeneration.

• In CNS axonal damage, the affected region get converted to scar tissue by proliferation of astroglial cells. This scar tissue forms a barrier to regeneration.

• In peripheral nerves, axonal regeneration is possible before the formation of scar tissue.

• The injured peripheral nerve cell undergo initial *retrograde degeneration* called *wallerian degeneration.*

• The Schwann cells proliferate and grow out in all directions from the two sides of the injury.

• These cells establish contact with each other and thus bridge the gap of injury.

• This re-establishes the continuity of the neurolemma tube and thereby patches up the injury.

• RNA synthesis, multiplication of ribosome and the formation of ER and golgi bodies occur and cell loses its excess water.

• Neurofibrils sprout out from the cyton and basal part of the axons.

• They extend irregularly towards the distal part through the scar tissue and establish connection with neurolemma tube.

• Soon, myelin sheath is formed at injured part by activity of Schwann cells.

• The selective growth of neurofibrils toward the distal part of the neurolemma is called *neurotropism*.

- Neurofibrils may form tumor like mass called *neuroma*.

NEUROTROPHINS

- Neurotrophins are the substances, secreted by the cells in the target site of neurons
- They inhibit the programmed physiological destruction "apoptosis" of neurons
- Thereby prevents the natural damage of nervous tissue

TRANSMISSION OF NERVE IMPULSE

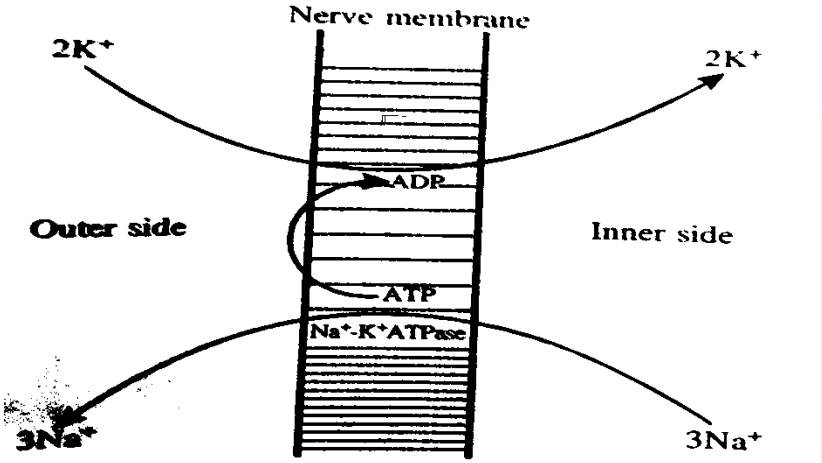
- Nerves & nerve fibres are excitable and are capable of transmitting messages as electric pulses, called nerve impulses or nerve signals.
- Excitability is the ability of nerve cells to respond to stimuli & to convert them as nerve impulses.
- Nerve impulses are electrochemical excitation waves, passing along the membranes of stimulated neurons.
- Transmission of impulses involves three fundamental processes, namely
- Maintenance of membrane potential
- Generation of action potential
- Propagation of action potential

1. MAINTENANCE OF MEMBRANE POTENTIAL

- The plasma membrane of a neuron is electrically unstable, dynamic & polarized.
- ***Membrane potential*** : the potential difference existing across a nerve membrane is known as membrane potential or bioelectric potential.
- It is established & maintained by the operation of three molecular mechanisms, namely anion trap, ion leak channels & sodium- potassium pump.
- **Anion trap**
- It is the mechanism by which the negatively charged ions & molecules remain trapped inside the cell in large abundance. Trapped ions are called *fixed ions*.

- They are too large to diffuse out & so they remain trapped within the cell, contributing – ve charge inside.
- **Ion leak channels**
- These are the transmembrane ion channels which permit the selective facilitated diffusion of ions.
- Eg:- sodium & potassium channels.
- Potassium channels are more numerous than sodium channels.
- So outward diffusion of K^+ ions will be much greater than the inward diffusion of Na^+ ions.
- This contribute inward negativity.

- **Sodium- potassium pump**
- Also called *sodium potassium transmembrane pump or transmembrane cation pump*.
- It is an ATP – dependent active transport mechanism.
- A non-stimulated neuron is called resting neuron & a stimulated one is called an active neuron.
- *Resting potential* – membrane potential of a resting neuron.
- *Action potential* – membrane potential of an active neuron.
- In resting potential, the membrane is electrically –ve inside & +ve outside.
- In action potential, the membrane is electrically +ve inside & -ve outside.



Schematic representation of sodium-potassium pump

- The cytoplasm inside the membrane has more K^+ ions than outside, & the extracellular fluid outside has more Na^+ ions than inside.
- This unequal distribution creates an electro-chemical gradient across the membrane.
- These processes are maintained by the sodium-potassium pump with the aid of *sodium-potassium ATPase.*

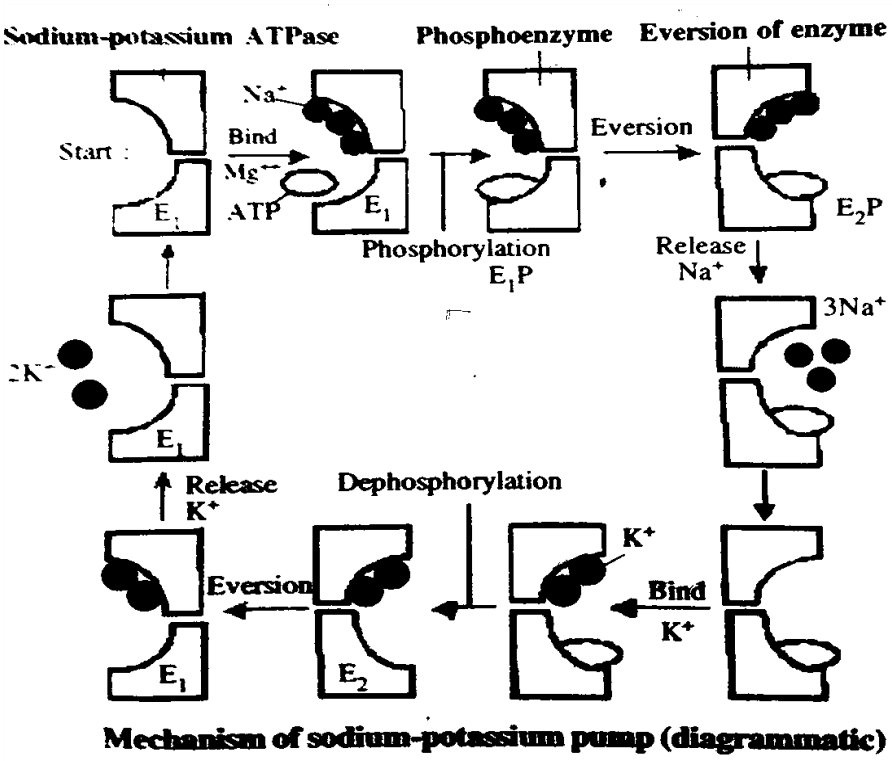
- By this Na^+ ions are actively transported outward & K^+ ions inward across the membrane against concentration gradient.
- In a resting membrane, potassium channels remain wide open, & sodium channels remain almost closed.
- The free outward diffusion of K+ ions that is mainly responsible for the inside negativity & the maintenance of the resting potential.

equipping with excellence

MECHANISM OF NA^+ - K^+ PUMP

- It operates in a step by step manner.
- One molecule of ATP & three Na^+ attach to the membrane bound enzyme *sodium-potassium ATPase* (E_1).
- The enzyme gets phosphorylated in the presence of Na^+ & Mg^{2+} ions & becomes a phosphoenzyme (E_1P).
- E_1P undergoes conformational change & transforms to E_2P by a revolving door mechanism.
- This brings the bound Na+ ions to the outer surface of the membrane.
- E_2P then undergoes dephosphorylation in a K^+ dependent process & the three Na^+ ions are replaced by two K^+ ions.
- Dephosphorylation causes a reverse conformational change in the enzyme ($E_2 – E_1$) & the enzyme transports the two K+ ions into the cell interior where they are released.
- The free E_1 is again available to repeat the cycle.
- The outer surface of the membrane becomes positively charged in relation to the inner surface because for every $3Na^+$ ions expelled, only $2K^+$ ions are taken in.

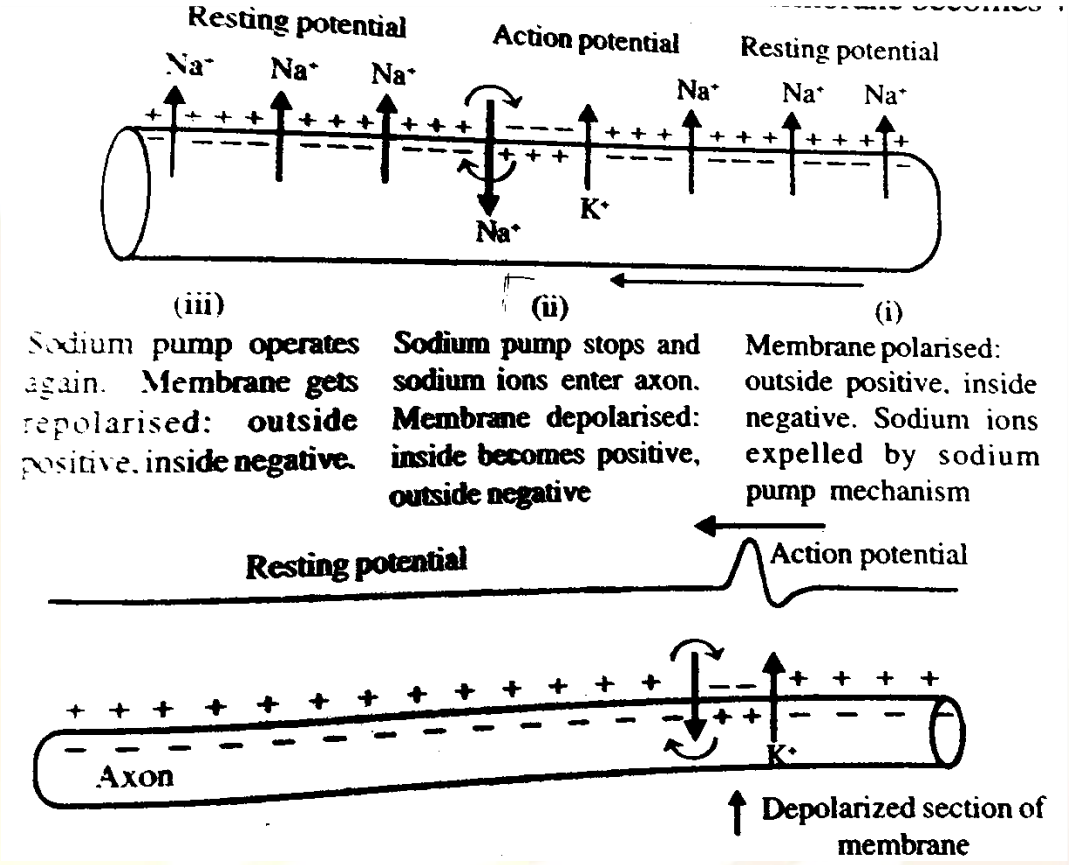
CPA COLLEGE OF GLOBAL STUDIES



Mechanism of sodium-potassium pump (diagrammatic)

2. GENERATION OF ACTION POTENTIAL

- Changes in the permeability of the nerve membrane to K^+ & Na^+ ions lead to the changes in the potential differences across the membrane. This results in the formation & propagation of nerve impulses.
- When a resting neuron gets stimulated or excited, a cyclic series of electro chemical changes takes place. This is known as ***action potential.***
- Action potential is very rapid & short living. After that resting potential is regained.
- In the stimulated point sodium-potassium pump stops functioning for a short period, sodium gates open widely & the membranes freely permeable to Na^+ also.
- Heavy influx of Na^+ occurs by diffusion. This increases sodium conductance & reverses the resting potential.
- Interior of membrane becomes +ve & the exterior becomes –ve.



- ***Depolarization*** :The reversal of resting potential.
- Depolarisation is the beginning of action potential & the generation of nerve impulses.
- Depolarisation lasts for a short period, afterwards the sodium potassium pump resumes functioning, the sodium gates get closed & the membrane becomes impermeable to Na^+.
- Na^+ conductance decreases & K^+ conductance increases. This regains the resting potential.
- ***Re-polarisation*** : restoration of resting potential.
- Depolarization & repolarization together constitute action potential.
- ***Refractory period*** : time interval between depolarization & repolarization.

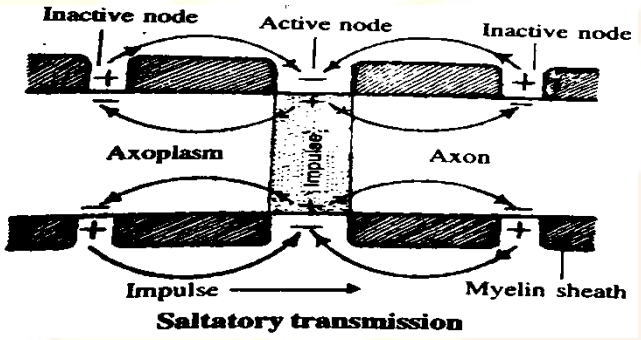
3. PROPAGATION OF ACTION POTENTIAL

- Transmission of impulses involves the propagation of a wave of depolarization or action potential.
- Action potential excites the next resting area.
- Initial depolarization is accompanied by local currents & local potentials of graded intensity.

- This establishes an electric circuit in between depolarized & resting area called *mini circuit.*
- Current flows inward from the resting area to the depolarized area & outward from the depolarized area to the resting area.
- The outward current stimulates the next resting area.
- Thus action potential gets shifted to that point.
- In this manner it moves the whole length of the neuron rapidly without any change in its amplitude.
- It can be transmitted over an infinite distance & so they are called *non decremental*.

SALTATORY TRANSMISSION

- This is the jumping of nerve impulses through axoplasm & extracellular fluid from one node to the next in medullated nerve fibres.
- In medullated nerve fibres only the uncovered nodes of Ranvier are excitable & capable of generating action potential.
- Advantages of saltatory transmission
- Enhances the transmission velocity & ensures the fastest transmission of impulses.
- It is energy efficient, in that energy requiring depolarization occurs only at nodes



Saltatory transmission

THRESHOLD STIMULUS & ALL OR NONE LAW

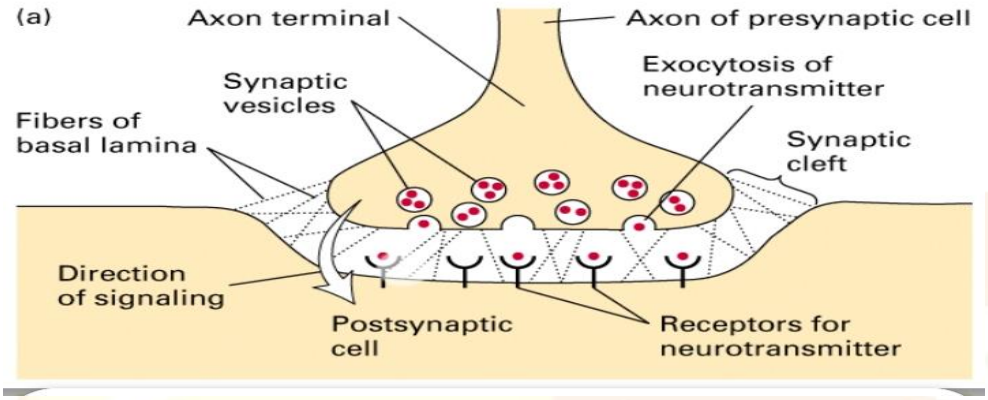
- ***All or none law*** : The magnitude of a nerve impulse is independent of the intensity of the stimulus and the action potentials are never partial or week, but are always maximal or are altogether absent.
- ***Threshold stimulus*** : The lowest intensity of a stimulus, that can generate an action potential.
- ***Sub threshold stimulus*** : A stimulus below the threshold level, that can never initiate an action potential.

- ***Hyper threshold stimulus*** : Stimulus above the threshold intensity, which can produce a full-fledged action potential.
- Any increase in the intensity of the stimulus, beyond an optimum level, will not change the character or magnitude of the action potential.
- The amplitude of the action potential is always constant.

SYNAPSE

- It is the functional junction either between two neurons (neuronal synapse), or between a neuron & a muscle cell (neuro muscular junction).
- ***Pre-synaptic neuron*** : The neuron, which transmits impulses to a neuronal synapse.
- ***Post-synaptic neuron*** : The neuron which receives impulses from the neuronal synapse.
- There are *morphologically three different types of neuronal synapses*.
- ***Axodendric synapses*** : Neuronal synapses occur between the axon endings of the pre-synaptic neuron & dendrites of the post-synaptic neuron.
- ***Axosomatic synapses*** : Neuronal synapses occur between the axon endings of the pre-synaptic neuron & cyton of the post-synaptic neuron.
- ***Axoaxonic synapses*** : Neuronal synapses occur between the axon endings of the pre-synaptic neuron & axon hillock of the post-synaptic neuron.
- Most invertebrate synapses are axodentric, whereas most vertebrate synapses are axosomatic.
- ***Synaptic knobs*** : Knob like terminals of axon endings. It is packed with mitochondria, smooth endoplasmic reticulum, microfilaments & synaptic vesicles.
- ***Synaptic vesicle*** : Membrane bound secretory bodies which synthesise & secrete neurotransmitters. Transmits neurotransmitters to the synaptic cleft, which brings about the transmission of impulses across the synapse. Mitochondria provides energy for its synthesis & release.
- ***Synaptic cleft*** : A synaptic knob is separated from the post synaptic neuron by a narrow, fluid filled gap.
- Synaptic cleft is bounded by the pre-synaptic membrane & post synaptic membrane.
- ***Sub synaptic membrane*** : The portion of the post synaptic membrane, directly under the pre synaptic membrane.
- Pre synaptic membrane is specialized for the attachment of synaptic vesicle & release of the neurotransmitter to the synaptic cleft.
- Post synaptic membrane is modified for the binding of the neurotransmitters.

equipping with excellence
PACIFIC COLLEGE OF GLOBAL STUDIES



- *Functionally there are three types of synapses.*
- ***Chemical synapses*** : Transmission of nerve impulses occurs with the help of neurotransmitters.
- ***Electrical synapses*** : : Transmission of nerve impulses across synapses is by electrical activity
- ***Conjoint synapses*** : Transmission across synapses is bot electrical & chemical.
- Functions of synapses
- Slow down the flow of impulses.
- Allow impulses to travel only from pre synaptic neuron to post synaptic neuron.
- Selectively transmits certain impulses & inhibit others.

NEUROMUSCULAR JUNCTIONS

- The skeletal muscles are neurogenic, so their contraction is under nervous control
- The axon of motor nerves come close contact with sarcolemma of muscle fibre, such functional junctions between axon endings and muscle fibres are called neuromuscular junctions, or myo- neuronal junctions or myo- neuronal synapses or end plate areas
- Sarcolemma has a flattened and specialized area, just beneath the axolemma. It is called motor end plate or motor end organ
- In between the sarcolemma and axon membrane, is afluid filled gap called synaptic cleft or sub- neuronal cleft
- Axon endings has a knobbed appearance called synaptic knob
- It contains numerous mitochondria and secretory vesicles, called synaptic vesicles
- These vesicles contain neurotransmitters, which stimulates the muscles to contract.

SYNAPTIC TRANSMISSION

- Transmission of impulses across synapses is called *synaptic transmission*.
- Some synapses are *excitatory & some are inhibitory*.
- Synaptic transmission occurs by two mechanisms, *electrical transmission & chemical transmission.*

ELECTRICAL TRANSMISSION

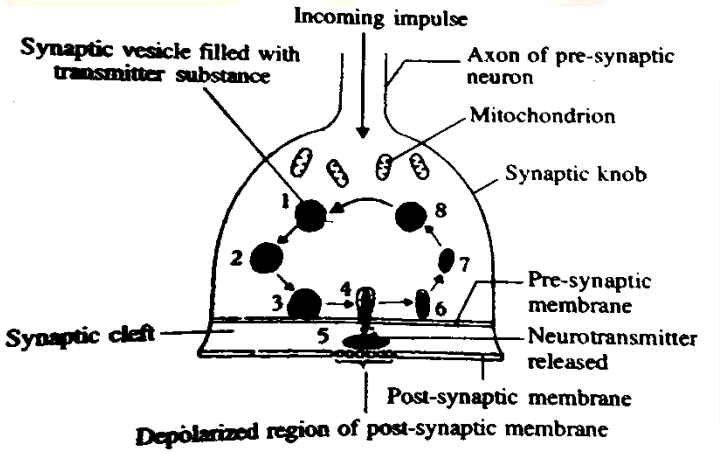
- It occur through specific points, called *tight junctions*.
- At these points pre-synaptic & post synaptic membranes are in close contact with each other.
- Tight junctions act as electrical rectifiers.
- The depolarization from the presynaptic neuron very easily spreads to the post synaptic neuron.
- Action potential from the post synaptic neuron will not travel to the pre synaptic membrane, since tight junctions offer resistance to the counter flow.
- Synaptic transmission is always unidirectional.

CHEMICAL TRANSMISSION

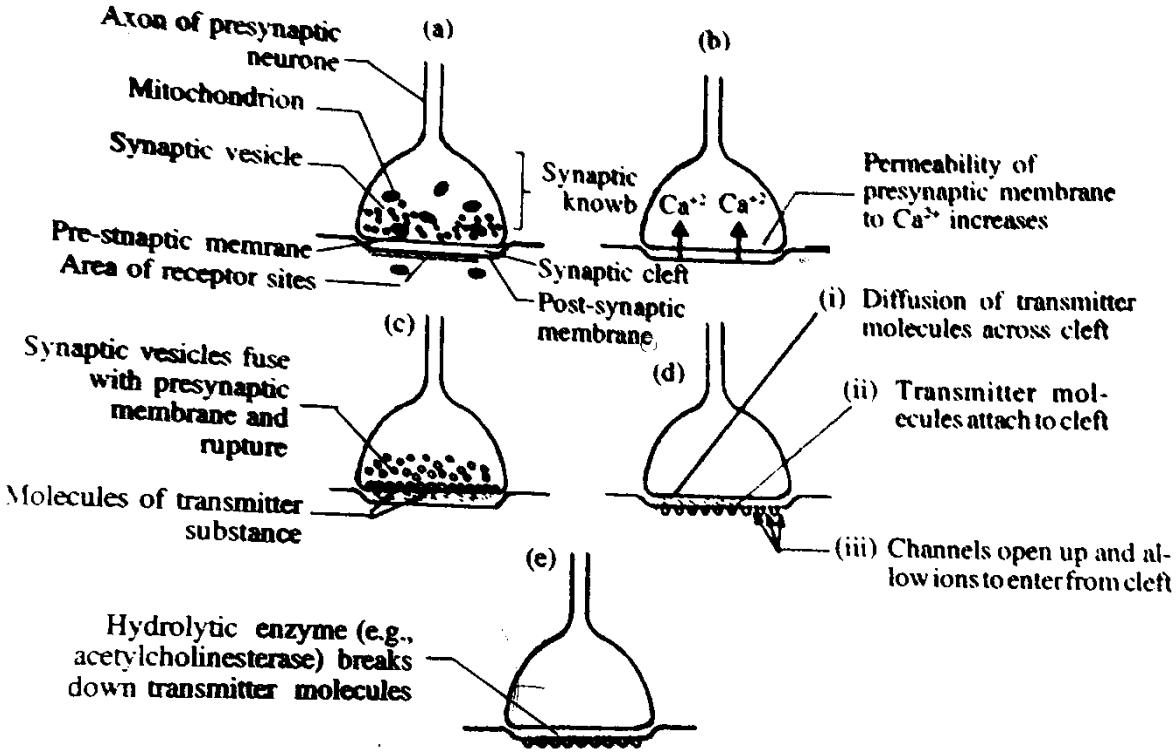
- Chemical transmission is effected by the neurotransmitter.
- When action potential reaches the synaptic knob, the pre synaptic membrane gets excited , depolarized & permeability to Ca^{2+} increases.
- ***Excitation secretion coupling*** : Ca^{2+} diffuses into the knob, this activates certain enzymes which in turn activates synaptic vesicle to secrete neurotransmitter to the synaptic cleft.
- The vesicle then return to the axoplasm to refill the neurotransmitter.
- Neurotransmitters attaches to the receptors on the post synaptic membrane. This causes post synaptic depolarization.
- Finally the neurotransmitter will be hydrolyzed by a specific enzyme.

EXCITATORY CHEMICAL TRANSMISSION

- It occurs when the neurotransmitter is excitatory in action.
- It stimulates post synaptic membrane, as a result sodium channels open widely permitting an influx of Na^+ ions.
- This lowers the post synaptic resting potential, causes depolarization & elicits a post synaptic action potential, called excitatory post synaptic potential (EPSP).
- Excitatory transmitter receptor interaction *occurs by two mechanisms*.
- Neurotransmitter binds to specific receptor proteins called neurotransmitter receptors. This causes the increase in the permeability of sodium channels. Heavy influx of Na+ leads to post synaptic depolarization & the initiation of EPSP.
- The neurotransmitter receptor binding activates an enzyme in the post synaptic membrane called *adenyl cyclase*. The activated enzyme mediates the conversion of ATP to cyclic AMP (cAMP). This in turn activates the enzyme which causes the opening of the sodium gates & thereby increases the permeability to sodium leading to the initiation of EPSP.
- Summation : *combined or cumulative effect* of neurotransmitters released simultaneously, will initiate an EPSP.



- **Excitatory chemical transmission**



Stages of excitatory chemical transmission

INHIBITORY CHEMICAL TRANSMISSION

- It occurs when the neurotransmitter is inhibitory in action.
- Inhibitory neurotransmitter binds with the receptor site & prevents post synaptic depolarization.
- ***Hyperpolarization*** : The inhibitory transmitter-receptor binding raises the post synaptic resting potential & thus prevents post-synaptic depolarization.
- In hyperpolarization, the cell interior becomes more negative than outside making the generation of an action potential rather impossible.
- Inhibitory post synaptic potential (IPSP) : The more negative post synaptic resting potential which can inhibit depolarization.

Synaptic delay

- Delay in the transmission of impulses across the synapse. It is due to the delay in releasing the neurotransmitter & also due to the time taken for its diffusion & post synaptic depolarization.

Synaptic fatigue

- Continuous transmission of impulses across a synapse eventually leads to a momentary suspension of synaptic transmission. It may due to the exhaustion of neurotransmitter.

NEUROTRANSMITTERS

- They are the chemicals involved in the synaptic transmission.
- They can amplify, modulate & transmit impulses.
- Two kinds : Excitatory & Inhibitory.
- Neurotransmitter act as both excitatory & inhibitory.
- Eg:- Acetylcholine
- Excitatory in neuronal synapses & in neuromuscular junctions of skeletal muscles.
- Inhibitory in the neuromuscular junctions of cardiac & visceral muscles.
- Excitatory neurotransmitters : Dopamine, adrenaline, serotonin, histamine,..
- Inhibitory neurotransmitters : Gamma amino butyric acid (GABA), enkephalins, beta-endorphin,..

1. Acetyl choline

- Released by many neurons outside CNS & some neurons inside the brain & spinal cord.
- ***Cholinergic synapses :*** The synapses which make use of acetyl choline for synaptic transmission.
- It binds to the receptor in the post- synaptic membrane and increases its permeability to Na2+ ions
- This depolarizes the membrane and generates excitatory post synaptic potential
- After depolarisation of post synaptic membrane, Ach is hydrolysed by *acetyl choline esterase* into choline and ethanoic acid

2. Noradrenaline

- Also called norepinephrine.
- Released from sympathetic nerve endings, brain & spinal cord.
- Soon after EPSP, it is pumped back to the synaptic knob.
- It is destroyed by the enzymes catechol methyl transferases & monoamine oxidase or recycled back to the synaptic vesicles.

3. Gamma amino butyric acid (GABA)

- An inhibitory neurotransmitter.
- It brings about hyperpolarization in the post synaptic membrane.
- Generates IPSP to prevent further transmission of impulse.

equipping with excellence
CPA COLLEGE OF GLOBAL STUDIES

MODULE 7. BIOLUMINESCENCE AND BIOELECTRICITY

BIOLUMINESCENCE

- Bioluminescence is the enzyme- controlled production and emission of light by living organisms
- It results from the oxidative transduction of chemical energy to radiant energy
- Bioluminescence is evolved independently in many unrelated groups in the different stages of evolution, probably by a by- product of tissue metabolism
- It is now found in bacteria, fungi, protists, sponges, coelenterates, ctenophores, annelids, crustaceans, insects….
- The luminescent larvae or immature adults of fireflies are called ***Glow worms***
- Insects have specialized photogenic organs. They remain scattered almost all over the body, very close to the body surface beneath a ***Translucent cuticle***.
- Each organ is formed of numerous light producing cells, called ***Photocytes***
- Behind the photocytes, is a ***Reflecting surface*** formed mainly of ***Urate granules***

CLASSIFICATION OF BIOLUMINESCENCE

- Based on the source of light emission, or the site of photogenic reactions,three kinds of bioluminescence can be recognized. Namely symbiotic, extracellular and intracellular.
- In some cases, light production is controlled by the impulses from CNS

1. SYMBIOTIC BIOLUMINESCENCE

- In this case, animals become luminous by the activity of the endosymbiotic bacteria living within them.
- Usually these bacteria live in special tissue sacs, which are provided with reflectors, lenses and pigment curtains to regulate light emission.
- The bacteria produce light continuously, but light emission is only intermittent
- This is because in some species the light is concealed intermittently by turning the light producing organ downward until its light surface is covered by a black pigmented tissue

- In some others, a fold of black tissue is drawn up and down across the light emitting organ, just like an eyelid
- It is found in decapods, squids and some deep sea bony fishes of the family Anomalopidea.

2. EXTRACELLULAR BIOLUMINESCENCE

- In this case light producing organs take the forms of unicellular or multicellular glands, which discharge their secretion to the exterior.
- These glands may sometimes contain enzyme-secreting and substrate secreting cells.
- Multicellular glands are made up of a large number of elongated, flask shaped or club shaped photocytes.
- Photocytes may be interspersed with mucus cells and provided with vertical horizontal muscles.
- Secretions of these glands take the form of a luminous slime over the body surface in balanoglossids
- In many animals, light producing reactants are first expelled to the outside where photogenic reaction takes place.
- It is common among the most marine invertebrates

3. INTRACELLULAR BIOLUMINESCENCE

- In many advanced groups, light emitting reaction take place inside the cells.
- This common among cephalopod, fishes and terrestrial arthropods.
- In higher animals with Intracellular luminance, there may be specialised photogenic cells or organs, light absorbing and light reflecting layers, light filters, refractive bodies and nerve supply.
- In many cases, the light from groups of photocytes is concentrated by a special arrangement of mirrors and lenses produce brilliant illumination
- Some photophores are very much like eyes with a photogenic light transmitting surface, instead of retina, or a light receptor surface.

PHYSIOLOGY OF LIGHT PRODUCTION

- Bioluminescence is a typical case of chemiluminescence (chemical luminescence) in which complex organic molecules, called luciferins, are oxidised by specific enzymes, called luciferases, in the presence of molecular oxygen.

- Thus, it is an oxidative, enzyme-catalysed, chemiluminescent reaction.
- The reaction requires magnesium ions and phosphate bond en ergy (ATP) and it occurs in an aqueous medium.
- In bilouminescent reaction, a substrate is oxidised with a change in free energy level and the subsequent emission of light. ▪ During this, electrons of the reactant molecules are hoisted or excited to a high-energy level.
- During their subsequent return to the ground state, the electrons give off their excess energy.
- This energy is used for the excitation of another molecule that is capable of releasing energy as photons or quanta of light.
- Bioluminescence is a non-thermal excitation of electrons.
- So, it occurs without substan tial heat production and hence is often called "cold light".
- The energy required for the excitation of electrons is obtained from a chemical reaction. revealed that an enzyme, a substrate and molecular oxygen are the biomolecules involved in bioluminescence.
- Coined the terms luciferin and luciferase to designate the substrate and the enzyme respectively.
- Luciferin is the generic name for any substrate that can be oxidised to produce light.
- Luciferase is the generic name for any enzyme that can catalyze the oxidation of luciferin for the emission of light.
- The chemical nature of luciferin and luciferase varies with species.
- So, different species of animals use different enzymes and different substrates for light production.
- The product of their reaction may be a luminescent material or an excited product.
- This product can transfer its energy to another molecule, which actually emits light.
- It has been shown that a protein - chromophore complex, called photoprotein, can react with certain ions, such as Ca++, to produce light.
- Very little is known about the exact chemical nature of luciferin and luciferase. Since they are chemically different in different species, the biochemical mechanism of bioluminescence also differs considerably in different species.
- The three groups of luminescent organisms,
- Most intensively studied, are bacteria, fireflies and the marine crustacean Cypridina.

BIOLUMINESCENCE IN FIREFLIES

- In the 1960's, McElroy and Seliger made intensive studies on the biochemical mechanism of light production in the American fire fly Photinus pyralis.

- They could show that the luciferin, secreted by photocytes (light-producing-cells), may be a low molecular weight aldehyde, polypeptide, or a protein. On the other Mechanism of light production in fireflies
- On the other hand, luciferase is a protein, or a substance with a number of properties of proteins.
- Light is produced by the oxidation of luciferin by luciferase. At first, ATP activates luciferin in the presence of luciferase and Mg to form adenyl luciferin (luciferyl adenylate).
- It is then oxidised to the excited oxyluciferin.
- During this, large amounts of energy (40-80 Kcal per mol) become available in a single step. So, the product of the reaction is in a highly excited state.
- It emits light when it returns from the excited to the non-excited ground state.
- The reaction is very efficient in that nearly 98% of the chemical energy involved is transduced to light, without heat production.
- The overall reaction of light production in fireflies may be represented as follows:

$LH_2 + ATP + 0_2$ Luciferase $Mg^{++} \rightarrow AMP + PPi + CO_2 + L(0) +$ light

- Light production in fireflies takes place in specialized abdominal organs, called lanterns.
- These are stimulated by nerve impulses.
- Nerve impulses cause the release of acetyl choline which triggers the bioluminescent reaction.
- It is also claimed that nerve impulses cause the release of a burst of air from the nearby tracheoles and the oxygen in this air initiates the light-producing reaction.

SIGNIFICATION OF BIOLUMINESCENCE

I. **Light production serves as a mating signal**

- In fireflies luminescence serves as a mating signal that attracts individuals of the same species to each other
- Females are wingless, so light production is very important to attract winged males to them.

II. Light serves as a conspecific recognition signal

- Among insects, Luminescence serves as a signal for recognizing the members of the same species for mating
- Flash patterns of light emission are species specific as well as sex specific
- Each sex of a species has a pattern and flashing rhythm of its own

III. Luminescence as an adaptation to attract the prey

- In some species, it serves as a means to attract the prey
- Some angler fishes emit light as allure for smaller prey in the darkness of ocean depths
- The cave dwelling larvae of the dipteran fly of new Zealand spin long luminous threads which serves as allure to attract the prey

IV. **Luminescence serves as an adaptation for defence**

- Some insects emit sudden flashes which frighten and scare away potential enemies and predators
- The deep sea squid *heteroteuthis* produces a luminescent material which emits a burst of light to hide the animal and also to startle the predator

BIOELECTRICITY

- Bioelectricity refers to the electric potentials and currents produced within living organisms
- The membrane potential and the electric currents that exist in nerves and muscles and the electricity generated by the electric organ of certain fishes are examples
- Living cells use bioelectricity to store metabolic energy to do work to trigger internal changes, and to signal one another

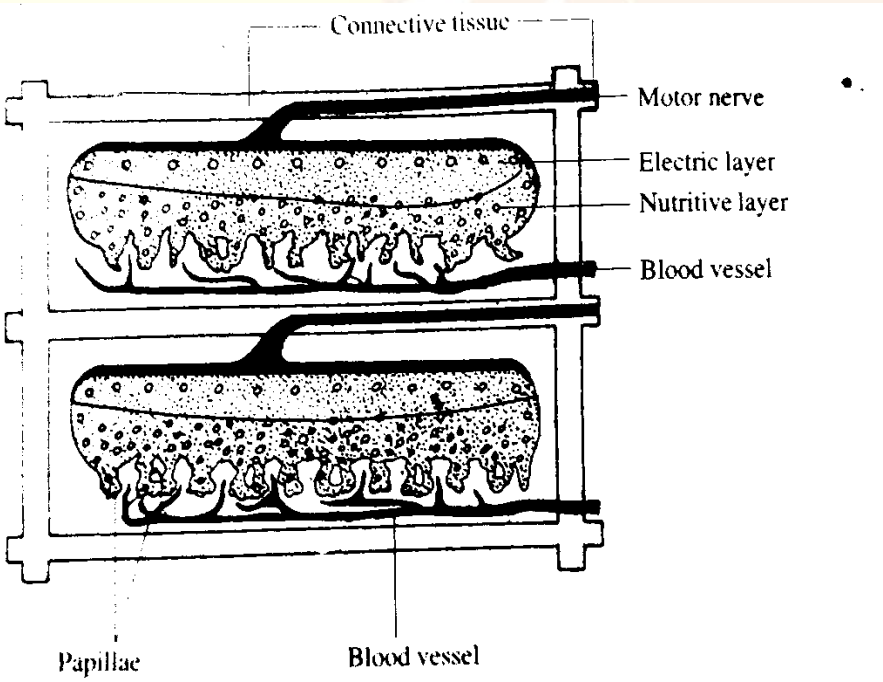
ELECTRIC ORGANS

- Electric organs are bioelectric batteries or generators, formed of specially modified muscle fibres or myoneural apparatus)
- Each organ is composed of numerous thin, flat and disc-like SI units, called electroplates (electrocytes or electroplaques).
- Discharge of electricity as an effector action occurs only in some fishes, commonly called electric fishes
- Electrogenesis (production of bioelectricity) is regarded as a pre-adaptation which became useful in the evolution of electric organs for species recognition, orientation, communication, and interaction.
- The most familiar electric fishes include *narcine, raia, torpedo, electrophorus, malapterus, etc.*

MORPHOLOGY OF ELECTRIC ORGANS

- Electric organs are bioelectric batteries or generators, formed of specially modified muscle fibres or myoneural apparatus.
- Each organ is composed of numerous thin, flat and disc-like SI units, called electroplates (electrocytes or electroplaques).
- These are embedded in a jelly- like material and each of them is housed in a connective tissue compartment.
- So, adjacent electroplates are separated from each other by connective tissue.
- Each electroplate has two layers, namely
    - (i) A smooth, nervous and non-vascular electric layer and
    - (ii) A highly folded, papilli form, vascular and non-nervous nutritive layer.
- The nervous layer has a myo-neural synapse.
- The folded vascular layer is a structural adaptation for improving the discharge capacity of the electroplate by lowering its internal resistance.
- The non-vascular nervous layer is innervated by a motor neuron, and the non-nervous vascular layer is supplied with blood vessel.
- Electroplates are orderly stacked into definite columns, similar to the piles of coins.
- In each column, they are arranged in regular rows in such a way that the smooth surfaces of all of them are facing in the same direction.
- The number and arrangement of electroplates in each column vary with species.
- For example, in electric rays, the electroplates are placed horizontally so that the columns run dorso-ventrally.
- On the other hand, in electric eel (Electrophorus), they are placed vertically so that the columns run longitudinally along the sides of the body.
- In the giant electric ray Torpedo, there are nearly 2000 columns, and each colum is composed of more than 1,000 electroplates.
- In electric eel, there are about 60 colums on each side, and each column contains 6,000 to 10,000 electroplates.
- Electric eel has much numerous electroplates in series to overcome the high resistance of the freshwater in which it liver
- Strength electric discharge from the electric organ directly depends upon the number and arrangement of the electrical columns and the number of electroplates in each column.
- The system works on the principle of serial or parallel connection of electric batteries.
- The electrocyte columns of electric organs are similar to common voltaic cells
- When stimulated, they simultaneously produce an electric discharge, large enough to stun an enemy or a prey
- Several species can discharge a powerful pulse of electricity for offensive and defensive purposes

- They can also produce weak electrical fields for peaceful purposes
- Electroplates maintain a transmembrane potential of about 85 mv
- Their membranes are selectively to K+ and impermeable to Na+
- During stimulation their nervous face gets depolarized, with a reversal of electric polarity, while the non- nervous face retains its resting potential
- The non- nervous membranes lying parallel to one another are suddenly connected in series like n electric battery
- The nervous face develops a potential difference in same direction as that of non- nervous face
- When these two become connected in series, both the faces contribute to charge of battery
- Electric organs are controlled by a command system of small groups of neurons (nuclei) in the medulla oblongata of brain and neighboring parts of spinal cord



Structure of electroplaque

FUNCTIONS OF ELECTRIC ORGANS

- Electric organs serve as useful physiological machines to meet the exigencies of the environment.
- Some of their major functions are the following:

1. Offence and defense: The electric organs of some fishes generate strong (high voltage) electric discharges to stun enemies and also to immobilize the prey.
2. Electrolocation: Some fishes generate weak (low voltage) electric discharges for electrolocation and electro-orientation, a phenomenon analogous to the echolocation of bats.
3. Detection of opposite sex in some species.
4. Navigation in murky water and also at night
5. Attraction of conspecific members to form schools.
6. Territorial defense against rivals of the same species.

equipping with excellence
CPA COLLEGE OF GLOBAL STUDIES

equipping with excellence

SECTION B VERTEBRATE ENDOCRINOLOGY

CPA COLLEGE OF GLOBAL STUDIES

MODULE 8 INVERTEBRATE AND VERTEBRATE ENDOCRINOLOGY

NEURO- ENDOCRINE ORGANS AND HORMONES IN CRUSTACEANS AND INSECTS

ENDOCRINE SYSTEM OF CRUSTACEANS

- Crustaceans have true (non-neural) endocronine glands and masses of neurosecretory cells.
- Their hormonal regulation is complex and it influences many processes, such as moulting, migration of retinal pigment, colour change, reproduction, heart rate, and metabolism.
- The neuroendocrine system of crustaceans appears to play an important role in the control of visceral activities also, which in vertebrates are regulated primarily by the autonomic nervous system.
- In decapod crustaceans, neurosecretory cells are found in the different parts of the brain, in the ganglia of the ventral nerve cord, and in the optic stalks and optic ganglia.
- The major endocrine organs of crustaceans include the sinus glands, X-organs, Y-organs, post-commissural organs, pericardial organs, androgemic glands and optic stalks (eye stalks).

1. SINUS GLANDS

- Sinus glands are not true endocrine glands, but are neurohaemal organs located in the optic stalks.
- Functionally sinus glands are analogous to the neurohypophysis (posterior pituitary) of vertebrates and the corpora cardiaca of insects
- Sinus gland is a thickened disc separated from a blood sinus by a thin membrane.
- Upon appropriate stimulation, it releases the stored hormones to blood.
- These hormones are very significant in the regulation of colour changes, even though they may serve other functions also.

2. X – ORGANS

- These are collections of neurosecretory cells, located at different regions of the optic stalk.
- They are of two types, namely ganglionic X-organs and pars distalis X-organs or sensory pore X-organs.
- In some species, these two types combine to form a complex.
- The hormone of X-organs is moult-inhibiting and is involved in the regulation of moulting, colour changes and the movement of retinal pigment.
- It inhibits the activity of Y-organs, ovary and testis.
- The hormone of X-organs is released to the sinus gland by axon transport.

4. Y ORGANS

- These are neurosecretory complexes, located behind the oesophagus.
- They serve as neurohaemal organs for the collection, storage and release of the neurohormones from brain. The hormones they release regulate colour changes.

5. POST -COMMISSURAL ORGAN

- These are neurosecretory complexes, located behind the oesophagus.
- They serve as neurohaemal organs for the collection, storage and release of the neurohormones from brain.
- The hormones they release regulate colour changes.

6. PERICARDIAL ORGANS

- These are endocrine structures. lying stretched across the pericardium
- They contain neurosecretory cells and the axon terminals of the neurosecretory cells in ventral ganglia.
- Their hormones increase the rate and force of heart - beat.

7. ANDROGENIC GLANDS

- These are the structures located on vasa deferentia in males.
- They produce a steroid hormone which stimulates the development of male secondary sexual characteristics.

8. EYE STALK

- Crustacean eye stalk produces a gonad - stimulating hormone and a gonad - inhibiting hormone.
- The former stimulates the development of testis in male and ovary in female,
- The latter inhibits the development of testis and ovary and prevents the formation of yolk in female.
- Some other eye stalk hormones prevent moulting during the time when female carries eggs

ENDOCRINE SYSTEM OF INSECTS

- Just like crustaceans, insects also have a well-developed endocrine system, composed of endocrine glands and neurosecretory cells.
- The major endocrine structures of insects include neurosecretory cells, corpora cardiaca, corpora allata and prothoracic or ecdysial gland.

1. NEUROSECRETORY CELLS

- Neurosecretory cells are lo cated in the cerebral, sub-oesoph ageal and other ganglia.
- Cerebral neurosecretory cells are arranged in two groups on each side.
- They secrete the brain hormone.
- Their axons extend to the corpora cardiaca. The cerebral neurosecretory cells and the corpora cardiaca together form the cerebral neurosecretory system.
- Cerebral neurosecretory cells produce the hormones bursicon and brain hormone.

2. CORPORA CARDIACA

- Corpora cardiaca are a pair of neurohaemal organ located close to the heart behind the brain.
- They are mainly concerned with the storage and release of the neurohormones of cerebral neuro secretory cells and the control of heart beat.
- They also contain neurosecretory cells which secrete orthodiphenol.
- This substance indirectly accelerates heart beat by stimulating the pericardial cells to release a heart-activating substance.

3. CORPORA ALLATA

- Corpora allata are a pair of non-nervous endocrine glands, lying behind the corpora cardiaca.
- In Diptera, particularly in dipteran larvae, there is only a single corpus cardiacum, ventral to the aorta, and a single corpus allatum dorsal to the aorta.
- These two are connected together by nerves, forming a ring-shaped compound structure, called Wiesmann's ring or ring gland.
- Corpora allata produce a hormone, called juvenile hormone or neotenin.

4. ECDYSIAL GLANDS

- Ecdysial glands are also non nervous endocrine glands, located in the prothorax.
- They are functional in the immature larval and pupal stages.
- They are innervated by the nerves originating from the cerebral neurosecretory cells, sub-esophageal ganglia, and thoracic ganglia

equipping with excellence
SPC COLLEGE OF GLOBAL STUDIES

CLASSIFICATION OF HORMONES

AMINEHORMONES

- Hormones derived from the modification of amino acids are referred to as amine hormones
- Amine hormones are synthesized from the amino acids tryptophan or tyrosine
- Amine hormones do not all share identical properties and have properties common to both peptide and steroid hormones
- These are secreted from the thyroid and adrenal medulla
- Some are polar (adrenaline) other must have protein bond
- Adrenaline act on membrane receptors and thyroid hormone directly act on nuclear receptors
- Adrenaline functions as peptide, thyroids functions as steroids
- Eg: adrenalin,thyroxin,triiodothyronine,T3,T4,Epinephrine,norepinephrine

PEPTIDE HORMONES

- these are hormones which contains a peptide chain
- eg: oxytosin ,vasopressin, insulin,ADH,glucagon etc
- Made up of few amino acids residues only and present in a simple linear chain
- vasopressin and oxytosin contain 9 AA residues only
- these cannot freely cross the plasma membrane due to the hydrophilic and lipophobic (fat-hating) property
- they bind to receptors ,present on the surface of the cell wall –
- the receptor complex activates a series of intracellular molecules called secondary messengers which initiate cell activity

STEROID HORMONES

- These are made up of lipids, basically derived from cholesterol
- Two classes : corticosteroids and sex steroids
- The adrenal steroids are so called because they are secreted by adrenal cortex
- Adrenal cortical hormones consists of the glucocorticoids and mineralocorticoids
- Glucocorticoids eg; cortisol (maintain normal blood pressure, treatment of rheumatoid arthritis, preventing rejection of transplanted organs etc...)
- Mineralocorticoids: aldosterone (maintains the balance between the water and salts in the body)
- Sex steroids are those produced by the overies and testes
- Two classes ; male and female sex hormones Androgens are the male sex hormone, testosterone are produced primarily from testes, adrenal cortex and overies produce lesser amounts
- Functions as development and maintenance of reproductive function and secondary sex characteristics

ENDOCRINE GLANDS IN MAN

1. HYPOTHALAMUS

- Hypothalamus is the glandular floor of the diencephalon of vertebrate brain
- It has both nervous and endocrine roles
- It governs the functioning of the pitutory gland and nervous system, controls emotional responses, regulates body temperature and water balance, and arouses the hunger drive.
- It serves as a link between nervous and endocrine systems and directly or indirectly controls most of the hormonal activities.
- It receives inputs from other parts of the brain, and also from the hormones in the blood.
- In response to these inputs, it secretes several regulating hormones which regulate the release of pituitary hormones .
- The neurosecretory cells of hypothalamus secrete three major groups of hormones, namely regulating hormones, oxytocin and vasopressin.
- Regulating hormones are then transported to the adenohypophysis by blood.
- On the other hand, oxytocin and vasopressin are transported to the neurohypophysis along the fibres of the neurosecretory cells by a transport protein called neurophysin.
- In the neurohypophysis, they are stored in the axon terminals.
- When the hypothalamus. gets excited by appropriate stimuli, the impulses would be transmitted to the axon endings of the neurosecretory cells.
- These impulses would cause the release of the stored hormones from axon terminals to blood. Blood will carry them to their target sites.

1. Regulating hormones

- The hypothalamic regulating hormones govern the production and release of pituitary tropic hormones.
- They are of two kinds, releasing hormones or releasing factors and inhibiting hormones or inhibiting factors.
- Releasing hormones stimulate the release of the pituitary tropic hormones, whereas inhibiting hormones inhibit the release of pituitary tropic hormones.
- For each pituitary tropic hormone, there will be a corresponding releasing hormone and an inhibiting hormone.
- The major releasing and inhibiting hormones of hypothalamus are the following:

(a) Releasing hormones

(i) Somatotropin-releasing hormone (STRH) –

- Also called somatostatin or growth hormone-releasing factor (GHRF).
- Stimulates the release of the pituitary growth hormone (somatropin).

(ii) Thyrotropin-releasing hormone (TTRH)

- Stimulates the release of the thyroidstimulating hormone (thyrotropin) of pituitary.
- Its production is regulated by the levels of thyroid hormones in blood.
- High levels of thyroid hormones inhibit its production and low levels stimulate its production.

(iii) Adrenocorticotropin-releasing hormone (ACTRH)

- Stimulates the release of adrenocorticotropic hormone (adrenocorticotropin) from pituitary

(iv) Gonadotropin-releasing hormones (GTRH)

- Stimulate the release of gonadotropic hormones (gonadotropins) from pituitary.

(v) Prolactin-releasing hormone (PRH)

- Stimulates the release of prolactin or lactogeni¢ hormone from pituitary.

(b) Inhibiting hormones

(i) Somatotropin-inhibiting hormone (STIH)

- Also called growth hormone - inhibiting factor (GHIF).
- Inhibits the release of pituitary somatotropin.

(ii) Thyrotropin-inhibiting hormone (TTIH)

- Inhibits the release of pituitary thyrotropin

(iii) Inhibiting hormone (ACTIH)

- Inhibits the release of adrenocorticotropin from pituitary.

(iv) Gonadotropin-inhibiting hormones (GTTH)

- Inhibit the release of pituitary gonadotropins.

(v) Prolactin-inhibiting hormone (PIH) –

- Inhibits the release of prolactin from pituitary.

2. Oxytocin

- In females, oxytocin hastens the onset of sexual cycle, stimulates the contraction of mammary glands and the ejection of milk during lactation (lactagogic effect), governs the contraction of uterus during parturition (oxytocic effect), and promotes the renal reabsorption of sodium.
- It is released in large quantities just before parturition to accelerate uterine contraction and to hasten parturition.
- It is sometimes artificially administered to induce labour and also to speed up the return of uterus to its normal size after delivery
- The role of oxytocin in male is not definitely understood.

3. Vasopressin

- Vasopressin is also called the antidiuretic hormone (ADH).
- It stimulates the constriction of arterioles and raises blood pressure (pressor effect).
- Promotes the renal reabsorption and conservation of water, decreases the volume of urine (antidiuretic effect), and controls water balance.
- The amount of the ADH normally secreted varies with body's needs.
- When the body gets dehydrated, the water level in blood falls abnormally low and the salt to-water ratio gets abnormally altered.
- An "osmostat" (osmoreceptors) in the hypothalamus detects this and stimulates the neurosecretory cells to increase the output of ADH.
- The hormone reaches the kidneys through vascular transport and stimulates the kidneys to reduce urine output.

- When the blood becomes increasingly dilute with excessive amounts of water, the thermoreceptors detect the stimulus and inhibit ADH production in the neurosecretory cells of hypothalamus.
- This lowers or stops ADH production. Kidneys then remove large quantities of urine, bringing the volume and concentration of blood back to normal.
- ADH production is altered by several factors. Pain, trauma, stress, anxiety, acetyl choline, nicotine, anaesthetics, tranquilizers, etc.stimulate its secretion.
- Alcohol inhibits its production and thereby increases urine output.
- Deficiency of ADH (due to damage or tumours in hypothalamus) causes diabetes insipidus, characterised by polyurea (increased diuresis or urine excretion) and polydipsia (excessive thirst and high fluid intake) and frequent urination.
- This is due to the inadequate water reabsorption in kidney tubules, The disease is treated by the administration of ADH

2. PINEAL GLAND

- Pineal gland or epiphysis cerebrum is the glandular dorsal outgrowth from the roof of the third ventricle of brain
- It enclosed by a capsule formed by pia mater
- The capsule consist of two kinds of cells, neurological cells and pinealocytes
- Pinealocytes are secretory parenchymal cells
- At time of puberty, pineal gland gets calcify, these calcium deposits are called brain sands
- The presence of these brain sands indicates the inactive pineal gland
- The anatomical features of pineal gland have long been known to us
- The pineal gland acts as biological clock
- In human beings, pineal is believed to be involved in the metabolism of potassium, magnesium, phosphorus, water and salts
- it secretes the hormones melatonin, serotonin, vasotocin and adrenoglomerulotropin
- Melatonin controls the onset of puberty, prevent the premature development sex organs, reduce sexual excitement, inhibit reproductive activities by inhibiting gonadotropin hormones and control the synthesis of melanin
- In human infants especially ially in boys the deficiency of melatonin mal functioning of pineal may cause macrogenitosoma
- Administration of melatonin has been found useful in the treatment of cancer and Aids
- Serotonin controls mood and behaviour, constricts blood vessels, stimulates gastro intestinal peristalsis and raises body temperature
- Adrenoglomerolotropin is believed to stimulate the adrenal cortex to secrete aldosterone

3. THYMUS GLAND

- Thymus is bilobed gland, located above the heart and in between the lungs in the superior mediastinal space
- It is an endocrine as well as a lymphatic gland
- Thymic lobes are enclosed by a connective tissue capsule
- Each lobe as still smaller globules
- Each globules has two region's outer cortex and inner medulla
- Cortex is composed almost entirely of tightly packed lymphocytes
- Which are held in position supporting testicular tissue
- Medulla is composed mostly of epithelial cells widely scattered lymphocytes and certain characteristics cells called thymic corpusceles
- Thymus gland is most conspicuous in the infant's, it maximum size in puberty, thereafter gradually undergo gradual degeneration and the thymic tissue replaced by fat and connective tissue
- Function of thymus gland related to immune system
- Maturation of T cells by producing hormone
- Important thymic hormones are homeostatic thymic hormone(HTH), thymosin, thymopoietin, thymine I, thymin II, thymic numeral factor(THF) and thymic factor(TF)

4. PITUTORY (hypophysis)

- Pituitary or hypophysis is a small gland, seen very closely associated to the brain.
- It is placed in a depression of the sphenoid bone, called sella turcica, and is connected to the hypothalamus of the brain by a stalk-like structure, called infundibular duct
- Human pituitary has two lobes, anterior and posterior, known respectively as adenohypophysis and neurohypophysis
- Both these are connected to the hypothalamus.
- In between them is a vascular zone, known as pars intermedia. Its role in human beings is rather obscure.
- Adenohypophysis is hormone producing.
- Neurohypophysis only stores and then secretes the hormones produced by the hypothalamus.
- Adenohypophysis and neurohypophysis are ectodermal in origin.
- The former is derived from an embryonic invagination of pharyngeal epithelium, whereas the latter is derived from an n Outgrowth of the hypothalamus.
- The anterior lobe is an endocrine gland, and it contains hormone secreting cells.
- The posterior lobe does not synthesise hormones and so, in the strict sense, it is not an endocrine gland.
- It contains axon endings of the secretory neurons whose cytons are located in the hypothalamus.
- These secretory neurons are called neurosecretory cells.
- Their fibres extend from the hypothalamus to the neurohypophysis and terminate on blood capillaries in the neurohypophysis. They form the hypothalamic"hypophyseal tract.

- The cell bodies of the neurosecretory cells produce a variety of hormones.
- The fibres of the neurosecretory cells, located in the neurohypophysis, are supported by specialized pituitary cells, called pituicytes.
- Hypothalamus is connected to the adenohypophysis by a system of blood vessels, and to the neurohypophysis by nerve fibres.
- The cell bodies of the neurosecretory cells in the hypothalamus produce the hormones oxytocin and vasopressin.
- They are soon transported to the neurohypophysis along nerve fibres by a carrier protein, called neurophysin.
- In the neurohypophysis, they are stored in the axon terminals. Later, when the hypophysis is properly stimulated, it sends impulses to the neurosecretory cells. These impulses cause the release of the hormones to blood from axon terminals.
- Pituitary directly or indirectly controls most of the metabolic activities and regulates the functioning of most other endocrine glands. So, it was customarily described as the "master gland" of the endocrine system or as the "band-master of the endocrine orchestra."
- But, the actual fact is that pituitary itself is under the control of the hormones of hypothalamus. So, pituitary and hypothalamus together constitute what is called the hypothalamo-hypophyseal axis, which serves as the "master control of the endocrine system."

PITUITARY HORMONES

- The anterior pituitary produces a large number of hormones which regulate the whole range of bodily activities from growth to reproduction and development.
- The release of these hormones is stimulated or inhibited by corresponding hypothalamic hormones, generally called regulating factors, These factors constitute a link between nervous system and endocrine system.
- They are of two sets, namely releasing factors and inhibiting factors. The former stimulates the release of pituitary hormones, and the latter inhibits their release.
- Pituitary hormones fall under two major groups, namely tropic hormones and metabolic hormones.
- Tropic hormones mostly regulate the functioning of other endocrine glands, whereas metabolic hormones control metabolism.
- The important tropic hormones are somatotropic hormone, thyrotropic hormone, adrenocorticotropic hormone, gonadotropic hormones and melanocyte-stimulating hormone.
- Gonadotropic hormones are of three types, namely follicle-stimulating hormone, luteinizing hormone and luteotropic hormone.
- The important metabolic hormones include diabetogenic or hyperglycaemic hormone, ketogenic hormone, glucostatic hormone, fat-mobilizing hormone or adipokinin, glycotropic hormone and pancreotropic hormone.

(i) Somatotropic hormone (STH)

- Also known as somatotropin, growth hormone (GH), or growth stimulating hormone.
- It is a protein hormone which stimulates the body cells to grow and multiply, and also to maintain their size once optimum growth is attained.
- It mainly acts on skeleton and skeletal muscles. GH causes the cells to grow and multiply by increasing the rate of protein synthesis in them.
- The major functions GH are the following
  (i). Stimulates the multiplication and growth of cells, and maintains their size after maximum growth is attained.
  (ii). Increases the rate of protein synthesis for growth.
  (iii). Promotes the breakdown of fats by causing the cells to switch from the oxidation of sugars to the oxidation of fats for energy. In this process, GH stimulates adipose cells to release fat, and stimulates the other cells to break down the released fat molecules.
  (iv). Acclerates liver glycogenolysis and the release of glucose to blood. This may cause hyperglycaemia and diabetes mellitus. So, it is called diabetogenic effect.

- The growth promoting effects of GH probably result from the conversion of certain to growth promoting substances, such as somatomedins and insulin-like growth factors (IGF).
- These are peptides, synthesised in the liver under the influence of GH.
- They are structurally and functionally similar to insulin. However, their growth promoting effects re much more potent than those of insulin.
- The physiological mechanism which controls the secretion of GH is not clearly underSood.
- Deficiency of GH in infants causes stunted growth (dwarfism) and delayed sexual maturity.
- Pituitary dwarfs are generally called midgets.
- Deficiency of GH in adults may cause Simmond's disease or pituitary cachexia, a rare condition characterised by wasting of bones and skin, loss of hair, impotence, etc.
- Overproduction of GH in infants may cause gigantism or giantism (enormous growth of the body).
- Overproduction in adults often causes acromegaly, characterised by the abnormal and disproportionate growth of the bones of head, hands, face and feet.

(ii) Thyrotropic hormone (TTH)

- Also called thyrotropin or thyroid-stimulating hormone (TSH).

- This hormone is a glycoprotein which stimulates the cellular uptake of iodine and the production and release of thyroid hormones (iodothyronines).
- It binds to specific surface receptors on the thyroid cells and stimulates them to synthesise thyroid hormones (these receptors are called G protein-coupled receptors -GPR).
- The secretion of TSH is governed by a regulating factor from hypothalamus, called thyrotropin releasing factor (TRE).
- It operates through a negative feedback mechanism depending on the blood levels of thyroxine.
- So, high thyroxine level inhibits the release of TRF. This, in turn, inhibits the release of TSH and thereby minimises thyroxine production to bring down the thyroxine level back to normal.
- Low thyroxine level stimulates the release of TRF which, in turn, promotes the release of TSH and thereby enhances thyroxine production. This raises the thyroxine level back to normal.
- Deficiency of TSH may cause hypothyroidism, and its excessiveness may cause hyperthyroidism.
- TSH deficiency has also been implicated as a cause of osteoporosis.
- Recombinant human TSH is now available to treat patients with TSH dificiency.

(iii) Adrenocorticotropic hormone (ACTH)

- Also known as adrenocorticotropin
- It is a peptide hormone which acts on the cells of adrenal cortex and stimulates them to secrete the cortical hormones.
- The secretion of ACTH is governed by a regulating hormone of the hypothalamus, called corticotropin releasing factor (CRF).
- Release of CRF results from a negative feedback mechanism, depending upon the blood levels of the corresponding cortical hormones.
- Hypersecretion of ACTH is 3 frequent cause of Cushing's disease.

(iv) Gonadotropic hormones or gonadotropins

- These are the pituitary hormones which act on the sex organs influencing their growth, maturation and functioning.
- The important gonadotropic hormones are follicle stimulating hormone, luteinizing hormone and luteotropic hormone.

(a) Follicle stimulating hormone (FSH)

- FSH is a glycoprotein which acts in the primary sex organs, namely testes and ovaries.
- In sexually mature females, it (in association with LH) controls the maturation of ovarian follicles, stimulates ovulation and promotes the production of female hormones oestrogens
- In sexvally mature males, FSH stimulates spermatogenesis
- The secretion of FSH is governed by a regulating hormone of hypothalamus, known a as gonadotropin releasing factor (GnRF),
- Release of GnRF involves a negative feedback mechanism, depending upon the levels of oestrogens and progesterone in female, and those of androgens in male.

(b) Luteinizing hormone (LH)

- LH is a glycoprotein which acts in testes and ovaries.
- In male, it is also known as interstitial cells stimulating hormone (ICSH).
- In female, together with oestrogens, it stimulates ovulation, implantation of the embryo, production of progesterone, functioning of corpus luteum, and maturation of mammary glands for milk production.
- In male, it stimulates spermatogenesis in the seminiferous tubules, and the production of the male hormones androgens in the interstitial or Leydig cells.
- The secretion of LH, like that of FSH, is governed by the GnRF from hypothalamus and placenta.
- Placental GnRF is termed placental luteotropic releasing factor (PLRF).
- Release of GnRF, in tum, is governed by a negative feedback system, involving oestrogens, progesterone and androgens.

(c) Luteotropic hormone (LTH)

- Also called prolactin (PRL), lactogenic hormone, or mammotropic hormone (MTH).
- In association with some other hormones, it initiates and maintains milk production by mammary glands and maintains functional state of corpus luteum.
- The actual ejection of milk from mammary glands is controlled by the hypothalamic hormone oxytocin.
- Secretion and ejection of milk together form lactation.
- In milk production, mammary glands are first primed by oestrogens, progesterone, thyroxine, corticosteroids, insulin, etc. Then, LTH acts on the mammary cells and stimulates milk production.

- The secretion of prolactin is governed by hypothalamic hormones, namely prolactin releasing factor (PRF) and prolactin inhibiting factor (PIF). The former stimulates and the latter inhibits the release of PRL from anterior pituitary.

(vi) Melanocyte-stimulating hormone (MSH)

equipping with excellence

- MSH controls skin pigmentation by regulating the synthesis and dispersion of melanin granules in melanocytes
- Normally, it stimulates the synthesis and dispersion of melanin and thereby increases skin pigmentation.
- In its absence, skin may become pallid.
- The secretion of MSH is governed by two hypothalamic hormones, namely melanocyte Stimulating hormone releasing factor (MRF) and melanocyte stimulating hormone inhibiting factor (MIF). The former stimulates and the latter inhibits the release of MSH.

5. THYROID

- Thyroid is a bilobed gland, lying on the ventral side of the trachea just below the larynx.
- Its right and left lateral lobes lie one on either side of the trachea.
- The two lobes are connected together by a narrow bridge, called isthmus, lying just below the cricoid cartilage.
- Sometimes, a median pyramidal lobe may also be seen, extending upward from the isthmus.
- Thyroid is an acinar gland, composed of spherical sacs called thyroid follicles or acini.
- Their walls are formed of two types of cells, namely follicular cells and: parafollicular cells.
- During the inactive state, these cells cuboid, but when they are actively secreting hormones, they become columnar.
- The lumen of the follicles contains a mass of iodinated glycoprotein, called thyroglobulin (TGB), secreted by the follicle cells.
- TGB is believed to serve as a matrix in which thyroid hormones are formed.
- Thyroid gland secretes three hormones, namely thyroxine (also called tetra iodo thyronine or T4 since it contains four iodine atoms), triiodothyronine (T3-contains three iodine atoms) and thyrocalcitonin (TCT).
- T4 and T3 are produced by the follicular cells, and TCT by the parafollicular cells.
- T4 and T3 have similar functions and so they are collectively called thyroid hormones.

- Normally, T4 is secreted in greater quantities than T3 but T3 is 3 or 4 times more potent than T4
- In peripheral tissues, particularly in liver and lungs, nearly one - third of the T3 may be converted to T4
- Chemically, thyroid hormones are iodo thyronines, formed of iodine and the amino acid tyrosine.
- The combination of these probably occurs in the TGB.
- Thyroid gland has the unique ability to store hormones and release them in a steady flow over a prolonged period.
- Thyroid hormones form an integral part of TGB, so long as they are stored in the thyroid follicles.
- TGB and the hormones together form a viscous complex, called thyroid colloid.
- Before the release of the hormones to blood, droplets of this colloid would be taken into the follicular cells by pinocytosis.
- Within these cells, hormones dissociate from TGB.
- In the blood, most of the hormones bind with certain carrier proteins of blood plasma, commonly called thyroxine - binding globulins (TBG).
- The protein-bound thyroid hormone is generally Called protein - bound iodothyronine (PBI).
- The production of thyroid hormones is regulated by an intrinsic negative feed-back mechanism, called thyroid autoregulation.
- In it, high levels of thyroid hormones in the blood inhibit the hypothalamus from stimulating the thyroid.
- As a result, further production of thyroid hormones gets inhibited.
- On the other hand, low levels of thyroid hormones in the blood stimulate the hypothalamus which, in tum, stimulates the thyroid.
- The production of TCT is not regulated by hypothalamus. Its production is stimulated directly by low blood calcium levels, and inhibited by high blood calcium levels.

Functions of thyroid hormones

- Thyroid hormones (T, and T,) have multiple roles in the various aspects of metabolism, Some of their major functions are the following:

(i) Increase the oxygen consumption in most tissues and thereby stimulate energy metabolism and control the basal metabolic rate (BMR). Thyroid hormones stimulate almost all aspects of the catabolism of carbohydrates and lipids, and also

increase the rate of protein synthesis. Rise in catabolic rate raises the BMR, increases heat production and elevates the body temperature. This is called calorigenic effect.

(ii) Promote growth, differentiation and development. In amphibian tadpoles, thyroid hormones stimulate cellular differentiation and initiate metamorphosis.

(iii) Elevate heart-rate, cardiac output and blood pressure and promote cutaneous vasodilation.

(iv) Increase pulmonary ventilation and the cellular uptake and utilization of oxygen.

(v) Reduce the tubular reabsorption of water in kidneys and increase diuresis and the excretion of Na‘, K*, nitrogenous wastes, etc.

(vi) Regulate the functioning of nervous system.

(vii) Promote the intestinal absorption and also the synthesis of glucose.

(viii) Promote the maturation of erythrocytes and the differentiation and maturation of gametes. .

(ix) (ix) Maintain or improve milk production in lactating females. (x) Promote normal bone growth and the maturation of nervous tissue, especially brain.

- Deficiency of thyroid hormones (hypothyroidism) causes the diseases cretinism in children and myxoedema (Gull’s disease) in adults.
- Cretinism is characterized by stunted growth, mental retardation, low intelligence, delayed sexual maturity, disproportionate size of different parts, etc.
- Myxoedema is characterised by physical inertia, mental dullness, low metabolic rate, low heart rate (bradycardia), dry skin, puffed face, etc.
- In women, hypothyroidism often causes hypomenorrhoea (scanty menstruation) or amenorrhoea (total absence of menstruation).
- Overproduction of thyroid hormones (hyperthyroidism or thyrotoxicosis) often interferes with the synthesis of ATP in muscles, leading to energy exhaustion and increased muscle fatigue.
- The commonest consequence of hyperthyroidism is exophthalmic goitre (Basidow’s or Grave's disease), characterised by the enlargement of thyroid gland (goitre), bulging of eyeballs (exophthalmos), abnormally high metabolic rate, high heart-rate (tachycardia), low blood pressure, tremor, nervousness, weight loss, etc.
- Deficiency of iodine in thyroid hormones (due to dietary deficiency of iodine) causes simple or endemic goitre, characterised by the morbidity and pathological enlargement of thyroid gland. Jodination of table salt is a preventive measure.

Functions of calcitonin

- Calcitonin is also called the hypocalcaemia hormone. It is primarily concerned with the homeostasis of blood calcium level.
- In this capacity, it maintains low blood calcium level (hypocalcaemia), and also promotes the deposition of calcium in bones and teeth.
- It lowers levels of calcium and phosphate in blood in two ways:
  (i) by promoting the cellular Uptake of calcium and phosphate from blood
  (ii) by inhibiting their mobilization from bones through bone resorption.
- This, in turn, prevents hypercalcaemia (high levels of blood calcium), strengthens bones and teeth and prevents osteoporosis.

6. PARATHYROID GLANDS

- Parathyroids are two pairs of small glands, embedded on the lateral lobes of the thyroid.
- They are so named because of their location along the sides of the thyroid
- Each parathyroid is formed of closely packed masses of cells, arranged around a capillary network.
- There are two types of cells, namely chief cells or principal cells and oxyphil cells.
- Chief cells are more numerous than oxyphil cells and they form the major centres of hormone production.
- Oxyphil are not a regular feature. In man and many animals (cat, dog, rat, etc.), they may be absent up to a certain age (usually up to 10 years). They are believed to serve accessory or supplementary secretory célls to synthesise and store a reserve stock of hormone.
- Parathyroids produce a polypeptide hormone, called parathyroid hormone (PTH) or Parathormone.
- It controls the homeostasis of mineral ions in the blood plasma, especially that of Ca+, Mg2+ and PO4.
- Normally, it maintains high levels of Ca2+ and Mg+ and low levels PO4 .
- The target sites of PTH include bone, kidney and gastro-intestinal tract.
- The major roles of PTH in maintaining high plasma levels of Ca2+ and Mg+ and low plasma level of PO4 are the following: ‘

(i) Enhances the mobilization of Ca2+ and PO4 from bones by stimulating bone resorption.

(ii) Promotes the proliferation and stimulates the activity of osteoclasts (bone-destroying cells) with the result that bone tissue gets broken down and calcium and phosphate are released to blood.

(iii) Enhances the tubular reabsorption of Ca2+ and Mg2+ in kidneys.
(iv) Enhances the tubular excretion of PO4 in renal tubules.
(v) Accelerates the transportation of PO4 from blood to urine for elimination.
(vi) Stimulates the gastro-intestinal absorption of Ca2+ and Mg2+.
(vii) Stimulates the physiological activation of vitamin D in kidneys. Adequate amounts of active vit. D is essential for the increased gastro-intestinal absorption of Ca and Mg**.

equipping with excellence

- The production of PTH is not under the control of pituitary, but is regulated by a negative feed back mechanism.
- A rise in blood calcium level directly lowers the production while a fall in blood calcium level enhances the production of PTH. This is called PTH autoregulation.
- Overproduction of PTH (hyperparathyroidism) causes the bone disease osteitis fibrosa cystica, characterised by the demineralization of bones, hypercalcaemia, low blood phosphate level and excessive calcium and phosphate in urine.
- The disease results from the drainage of calcium and other minerals from bones, making the bones brittle, weak, soft and porous. They may break under the slightest stress.
- Hyperparathyroidism may also abnormally increase the level of blood calcium (hypercalcaemia), causing the calcification of soft parts, such as blood vessels. Some of these calcium ions may get into urine, precipitate with phosphate ions and form kidney stones and bladder stones.
- Hyperparathyroidism is of two kinds, primary and secondary.
- Primary hyperparathyroidism results from the disorders of parathyroids, such as parathyroid adenoma, parathyroid hyperplasia and parathyroid cancer.
- Secondary hyperparathyroidism is due to disorders outside the parathyroids. It is often associated with chronic renal failure.

CPA COLLEGE OF GLOBAL STUDIES

7. ADRENAL GLANDS [Supra-renal glands}

- Adrenal or supra-renal glands are a pair of glands, one on the top of each kidney.
- Each gland is enclosed by a connective tissue capsule.
- Human adrenal glands consist of two functionally and developmentally distinct parts, namely outer cortex and inner medulla.
- Cortex is mesodermal in origin,
- Medulla is derived from neurectoderm. Both these parts act as separate glands and secrete entirely different hormones.

(a) Adrenal cortex

- Adrenal cortex has three cellular zones or layers, namely outer zona glomerulosa, middle zona fasciculata and inner zona reticularis.
- Each zone has a peculiar cellular arrangement and it secretes different groups of steroid hormones.
- The outer zone comprises nearly 15% of the total cortical volume. Its cells are columnar and arranged in arched loops or rounded balls.
- Middle zone is the widest part. Its cells are usually cuboidal and arranged in long and straight cords or columns.
- In the inner zone, cells are arranged as branching cords.

Cortical hormones

- Adrenal cortical hormones are generally called corticoids or cortical steroids.
- They are of three major groups, namely
- (i) mineralocorticoids, secreted by the outer zone
- (ii) glucocorticoids, secreted by the middle zone and
- (iii) sex corticoids (gonadocorticoids or adrenal sex hormones), secreted by the inner zone.

Mineralocorticoids

- Mineralocorticoids are the cortical hormones concerned with the homeostasis of water and electrolytes, particularly with the concentrations of Na^+, K^+ and Cl^- in the body fluids.
- Their deficiency may cause Addison's disease, a fatal disease with very low blood sugar level (hyperglycaemia), excessive renal excretion of sodium, hypertension, dizziness, muscular weakness, mental lethargy, etc.
- The patients can survive by the administration of mineralocorticoids or by the daily infusion of NaCl.
- There are two important mineralocorticoids, namely aldosterone and dehydrocorticosterone or deoxycorticosterone.
- Aldosterone is responsible for about 95% of the mineralocorticoid activity.
- In general, aldosterone has the following functions:

(i) Increases the volume of body fluids.
(ii) Enhances the renal reabsorption of Na+ and water and the renal exeretion of K+
(iii) Maintains high concentrations of Na+, HCO3- and water and low levels of K+and Cl- in blood and extracellular fluid.
(iv) Reduces the loss of Na+ through sweat, saliva and bile.

- Aldosterone mainly acts on the cells of renal tubules and enhances the tubular reabsorption of Na+ and water and increases the tubular excretion of K+.
- As a result, sodium and water are returned to blood from urine, and potassium is removed from blood to urine. This helps to maintain high concentrations of Na+ and water and low concentrations of K+ in the body.
- These two basic functions, namely conservation of sodium and water and elimination of potassium, produce several secondary effects.
- Aldosterone causes (i) sodium reabsorption and potassium excretion. (ii) elimination of H+ ions from blood and (iii) retention of Na+, Cl-, HCO3-, and water in blood.
- Aldosterone secretion is controlled by several factors, such as renin-angiotensin system, potassium ion concentration and the influence of anterior pituitary.
- Hypersecretion of aldosterone causes aldosteronism. It is characterized by the depletion of potassium and the excessive retention of sodium and water in the body.
- Potassium depletion may interfere with depolarization of neurons, leading to muscular paralysis.
- Water retention causes increase in the volume of blood and interstitial fluid. Increase in blood volume causes hypertension, and increase in the volume of interstitial fluid causes oedema.

Glucocorticoids

- Glucocorticoids are a group of cortical hormones concerned with normal metabolism and resistance to stress.
- The major glucocorticoids include cortisol (hydrocortisone), cortisone and corticosterone. Of these cortisol is the most abundant one.
- Glucocorticoids control the metabolism of carbohydrates, proteins and fats, elevate blood sugar level, provide resistance to stress, and promote anti-inflammatory responses.
- Their major roles are the following:
    (i) **Accelerate normal metabolism**: Glucocorticoids promote the catabolism of sugars, proteins and fats and provide energy. Also, they promote

gluconeogenesis (synthesis of glucose from non-carbohydrate substances, such as amino acids and fatty acids), facilitate the transport of amino acids from muscles and fatty acids from adipose tissues to liver for the synthesis of glucose.

(ii) **Provide resistance to stress**: Glucocorticoids work in many ways to provide resistance to stress. They elevate blood glucose level and thereby make the body alert and give the body enough energy for combating stresses.

(iii) **Promote anti-inflammatory responses**: Glucocorticoids stabilize lysosomal membranes and thereby inhibits the release of inflammatory substances. Also, they decrease the permeability of blood capillaries and depress phagocytosis.

- The production of glucocorticoids is controlled by a negative feedback mechanism with the involvement of hypothalamus and pituitary.
- The two principal stimuli for their synthesis are stresses and their low concentration in blood.
- Either condition stimulates the hypothalamus to secrete the corticotropin releasing factor (CRF). CRF stimulates the anterior pituitary to release adrenocorticotropin which, in turn, stimulates the adrenal cortex to synthesise glucocorticoids.
- Hyposecretion of glucocorticoids may cause Addison's disease and Cushing's syndrome (Addison's disease may be caused by the hyposecretion-of mineralocorticoids also). Cushing's syndrome is characterised by spindle legs, 'buffalo hump" on the back, pendulous abdomen with stretch marks, "moon face" with flushed facial skin, poor wound-healing, etc.

Sexcorticoids or gonadocorticoids

- These are the adrenal sex hormones.
- They include both male and female sex hormones.
- Male hormones include androgens, and female hormones include oestrogens and progesterone.
- They are secreted so slowly that their effects are insignificant in the adult. Also, their effects may be masked by the gonadal sex hormones.
- The overproduction of androgens in females may lead to adrenal virilism or masculinization, and that of oestrogens in males may cause gynaecomastia.
- Adrenal virilism is the development of male features in females, such as deeper voice, beard, moustache, occasional baldness, masculine distribution of pubic hairs and body hairs, penis-like clitoris, etc.
- Adrenal virilism may also result from adrenal tumours, called virilizing adenomas.
- Gynaecomastia in males is characterised by enlarged feminine breast. It may also result from adrenal tumours, called feminizing adenomas,

(b) Adrenal medulla

- Adrenal medulla essentially represents an enlarged and specialized sympathetic ganglion, derived from embryonic neurectoderm.
- It serves as a neuraendocrine transducer since nerve signal to it can evoke hormone secretion.
- Adrenal medulla is formed of hormone-producing chromaffin cells, (pheochromocytes) arranged around large blood-filled sinuses.
- Hormone production by these cells is directly controlled by the autonomous nervous system.
- Adrenal medulla is regarded as an "emergency gland", since its hormones are concerned with responding to stresses, emergencies and exigencies.
- It secretes two principal hormones, namely epinephrine or adrenaline and norepinephrine or noradrenaline.
- Chemically, these are catecholamines (dihydroxylated phenolic amines).
- Epinephrine constitutes nearly 80% of the total medullary secretion.
- In action, it is more potent than nor epinephrine.
- Epinephrine increases the rate and force of heart-beat, elevates blood sugar level, enhances the ventilation rate, promotes the cellular uptake and utilization of oxygen, stimulates oxidative metabolism, and raises body temperature. Norepinephrine influences the constriction of arteries and elevates blood pressure.
- Epinephrine acts as an "emergency hormone", responsible for "fight-or-flight responses". Like the glucocorticoids of adrenal cortex, it initiates quick actions to help the body to deal with stressful situations and emergencies. The extra-ordinary courage and strength, and emotions like fear, grief, anger and excitement are partly due to its effects.

8. ENDOCRINE PANCREAS [Islets of Langerhans}

- Pancreas is a heterocrine gland with enzyme-secreting exocrine and hormone-secreting endocrine portions.
- Its endocrine part is only less than 2% of the pancreatic tissue.
- It consists of numerous scattered groups or clusters of hormone secreting cells, called pancreatic islets or islets of Langerhans.
- Each cluster is formed of four kinds of cells.
- They are beta cells (B. cells), alpha cells (A. cells), delta ceils (D. cells) and gamma cells (G. cells).
- Unmyelinated, post ganglionic, sympathetic and parasympathetic nerve fibres terminate close to these cells.

- They modulate hormone secretion through the Secretion of neurotransmitters.
- Beta cells secrete insulin and amylin,
- Alpha cells secrete - glucagon,
- Delta cells secrete somatostatin,
- Gamma cells secrete pancreatic polypeptide of unknown function.
- The balanced production of insulin, glucagon and somatostatin is regulated by a homeostatic mechanism which involves the mutual regulation of these hormones.
- Thus, insulin inhibits the Production of glucagon. Glucagon stimulates the production of both insulin and somatostatin.
- Somatostatin inhibits the production of both .
- Insulin and glucagon. Insulin and glucagon control car. - bohydrate metabolism and maintain a normal blood sugar level.
- Their secretion is directly controlled by blood sugar levels through negative feedback system.
- Beta cells secrete insulin in response to rising levels of blood sugar, whereas alpha cells secrete glucagon in response to falling levels of blood sugar.
- When the blood sugar level goes much beyond the normal, the chemical sensors in the beta cells stimulate the cells to secrete insulin.
- When the blood sugar level falls low, the cells are no longer stimulated and insulin production considerably slows down.
- Similarly, when the blood sugar level falls below normal, the chemical sensors in the alpha cells stimulate them to secrete glucagon.
- When the blood sugar level goes high, the cells are not stimulated and glucagon production considerably slackens.

Insulin

- Insulin is a small protein hormone, formed of two peptide chains, namely an alpha chain and a beta chain.
- It is primarily an “anabolic hormone,” mainly concerned with the lowering of blood sugar level.
- Its major functions are the following:
    (i) Accelerates the transport or uptake of glucose from blood into cells, especially skeletal muscle cells.
    (ii) Stimulates the cellular oxidation of glucose.
    (iii) Promotes glycogenesis, lipogenesis and the storage of glycogen in liver.
    (iv) Inhibits glycogenolysis and gluconeogenesis.

(v) Promotes protein synthesis, inhibits the catabolism of proteins and fats, and promotes fat storage.

- Deficiency of insulin (Aypoinsulinism) causes diabetes mellitus (sugar diabets). It is characterised by hypercalcaemia, glycosuria, ketonemia (presence of ketone bodies in blood), ketonuria (presence of ketone bodies in urine) and hypercholesterolemia.
- In addition to these, diabetes is characterised by three "polys", namely polyuria (increased urine production and frequent urination), polydipsia (excessive thirst and high fluid intake) and polyphagia (overeating).
- In diabetes mellitus, there is increased oxidation of fats and proteins.
- Increased oxidation of fats causes the excessive production of ketone bodies, such as acetone, acetoacetate, etc. This may result in ketonemia and ketonuria.
- Overproduction of insulin (hyperinsulinism) accelerates glycolysis and glycogenesis.
- This causes abnormal fall in blood sugar level (hypoglycaemia), often resulting in a dangerous condition, known as hypoglycaemic shock or insulin shock.
- It is characterised by sudden drop in body temperature, excessive sweating, extreme fatigue, tremors, loss of consciousness, etc. Intravenous administration of glucose may give temporary relief.

Amylin

- Amylin is a peptide hormone of 37 amino acid residues.
- It tends to supplement insulin in lowering the blood sugar level.
- It is believed to act on the gastrointestinal system and produce satiety after eating.
- Its major functions are the following:
  (i) Inhibits the secretion of glucagon.
  (ii) Slows down the emptying of stomach.
  (iii) Sends a satiety signal to the brain.

Glucagon

- Glucagon is a peptide hormone of 29 amino acid residues.
- It is anti-insulin in action, and its principal role is to raise the blood sugar level.
- Its major functions are the following:

(i) Promotes glycogenolysis and gluconeogenesis to raise blood sugar level and metabolic rate.
(ii) Stimulates the hormone-sensitive lipase and increases fat breakdown in adipose tissue.
(iii) Helps the mobilization of fatty acids, amino acids and glucose.
(iv) Promotes the secretion of growth hormone, insulin and pancreatic somatostatin.

equipping with excellence

- The insulin-glucagon system is a delicately balanced, extremely effective and quick acting mechanism for keeping the blood sugar level well within the desirable range.
- This, in turn, provides brain with a regular supply of glucose.
- Brain cells are especially dependent on a continuous supply of glucose, since they cannot normally utilize other fuel molecules.
- Thus, insulin-glucagon system is very vital to meet the energetic requirement of brain.
- The action of the insulin-glucagon system is in dynamic balance by virtue of the antagonistic roles of insulin and glucagon.
- Insulin is glycogenic, antigluconeogenic, antiketogenic and antilipolytic and it lowers the blood sugar level.
- Glucagon is antiglycogenic, gluconeogenic, ketogenic and lipolytic and it mobilizes glucose and raises the blood sugar level.

Somatostatin

- Somatostatin is a peptide hormone.
- It is produced in different locations, such as pancreatic islets, hypothalamus, nervous system and the mucosa of the gastrointestinal tract.
- Pancreatic somatostatin serves as parahormone or local hormone, hypothalamic somatostatin functions as a growth hormone-inhibiting factor, neural somatostatin acts a spinal transmitter, and gastrointestinal somatostatin acts as a regulatory hormone.
- Since pancreatic somatostatin is a local hormone, it would not get into the peripheral circulation. So, its activity is restricted to the pancreatic islets alone. It inhibits the secretion of insulin, glucagon, amylin and pancreatic polypeptide

SCHOOL OF GLOBAL STUDIES

9. GASTROINTESTINAL TRACT

- More than a dozen gastroinstestinal hormones have been isolated so far.
- All of them are invariably peptides.
- Most of them are parahormones, and some are true hormones carried away to target tissues by blood.
- The deficiency of any of them is not known to cause any disorder.
- The important gastrointestinal hormones are somatostatin, gastrin, secretin, enterogastrone, cholecystokinin (pancreozymin), duocrinin, villikinin, enterocrinin, motilin, chymodenin, gastric inhibitory peptide and vasoactive intestinal peptide.

Gastrin

- Gastrin is not, in fact, a single hormone, but is a family of at least six structurally similar polypeptides.
- They fall into two chemical groups, namely little gastrin (G-17) and big-gastrin (G-34).
- The former has 17 amino acid residues, and the latter has 34 amino acid residues.
- Gastrin is secreted by the pyloric and duodenal mucosa. *There are two kinds of gastrin, stomach gastrin and intestinal gastrin.
- Gastrin produces excitatory effects and governs the balanced production of HCl.
- It stimulates the secretion of pepsin and HCI,promotes the secretion of HCO, by pancreas and liver, constricts the lower oesophageal sphincter, increases the frequency and velocity of BER, enhances the motility of the gastro intestinal tract, and relaxes pyloric and ileo-caecal sphincters.
- High concentrations of HCI inhibit and low concentrations stimulate gastrin production

equipping with excellence
CPA COLLEGE OF GLOBAL STUDIES

Secretin

- Secretin is produced by the duodenal and jejunal mucosa. *It counters the effects of gastrin, relaxes the lower oesophageal sphincter, inhibits the secretion of gastric juice, decreases the motility of the GI tract, and stimulates the secretion of primary pancreatic juice, intestinal juice and bile.
- Primary pancreatic juice has low enzyme content, but has high levels of sodium bicarbonate ions.
- This is significant in the neutralisation of chyme.

Enterogastrone

- Enterogastrone is secreted by the duodenal and jejunal mucosa.
- It is carried to the stomach by blood stream.
- It inhibits the production of gastric juice and HCl.

Cholecystokinin

- Cholecystokinin (CCK), also called pancreozymin (PZ).
- It is secreted by the duodenal and jejunal mucosa.
- It inhibits the secretion of gastric juice, stimulates the secretion of the intestinal juice and the enzyme-rich secondary pancreatic juice, decreases the motility of the GI tract, stimulates the contraction of gall bladder and the discharge of bile, and stimulates the relaxation of the hepatopancreatic sphincter

Duocrinin and villikinin

- These are secreted by the duodenal mucosa.
- Duocrinin stimulates the activity of Brunner's glands.
- Villikinin stimulates the movement of villi.

Enterocrinin

- Enterocrinin is secreted by the mucosa of jejunum and ileum.
- It stimulates the activity of intestinal digestive glands and thereby increases the production of succus entericus (intestinal digestive juice).

Gastric inhibitory peptide (GIP)

- GIP is a peptide hormone.
- It is secreted by the duodenal and jejunal mucosa.
- The presence of glucose and fat in the duodenum induces its production.
- GIP inhibits the secretion of gastricjuice, decreases the motility of the GI tract and stimulates the production of insulin.

Vasoactive intestinal peptide (VIP)

- VIP is a polypeptide neurohormone, produced by the vasomotor nerve fibres in the Gl tract.
- It stimulates the secretion of the electrolytes-rich intestinal juice, the gastric secretion of HCI, stimulates the relaxation of the smooth muscles of the intestine, and serves as a peripheral vasodilator.

Motilin

- Motilin is a polypeptide hormone.
- It is secreted by the duodenal mucosa.
- It stimulates gas tric secretion and induces the contraction of the smooth muscles of the intestine.

Chymodenin

- Chymodenin is a peptide hormone.
- It is secreted by the duodenal mucosa.
- It stimulates the selective secretion of chymotrypsinogen by pancreas.
- Some other hormones are also believed to regulate digestive activity.
- They include bombesin, nearotensin, somatostatin, etc.
- The source of **bombesin** is not known
- It promotes gastric secretion, contraction and emptying of gall bladder and the motility of small intestine.
- **Neurotensin** is secreted by the motor neurons of the enteric nervous system.
- It inhibits the motility of the GI tract.
- **Somatostatin** is a hypo thalamic hormone, which inhibits the pituitary growth hormone.

- It may be brought to the GI tract also where it inhibits the secretion of gastric and pancreatic juices and some gastro intestinal hormones (secretin, motilin, GIP and VIP), decreases intestinal motility, and increases the contractility of gall bladder.

HORMONAL DISORDERS

1. Cushing's syndrome

- Cushing's syndrome is an endocrine disease due to hypersecretion of adrenocorticoids specially glucocorticoids.
- It was first discovered by American neurologist Harvey cushing in 1932.
- It is characterised by obesity and weight gain ,"moon face" ,spindle legs, buffalo hump, bulky buttocks, flushed facial skin, excessive hair loss, cutaneous striae in abdominal skin, high blood sugar, blood pressure, poor wound healing etc...
- Other symptoms include disturbed sexual functions and loss of libido, menstrual irregularities or amenorrhea in women and impotency in men, increased susceptibility to infection, atherosclerotic changes, emotional instability with frequent maniac outbursts.
- Common causes are malignant or benign pituitary tumours which increase ACTH production, adrenal tumours which enhance production of corticoids and ectopic production of ACTH from tumours in lungs and pancreas.

2. **ADDISON' S DISEASE**

- Also known as adrenal insufficiency, hypocortisolism and hypocrotism.
- It is a rare fatal endocrine disease due to extreme deficiency of adrenal glucocorticoids and mineralocorticoids.
- Its common cause is damage or destruction of adrenal cortex.
- It was first discovered by British physician Dr Thomas Addison in 1855.
- The symptoms include weight loss, hypoglycemia , hypertension, dizziness, muscular weakness, low BMR, low body temperature, mental lethargy, depression, restlessness , insomnia, nausea, anorexia, excessive renal excretion of Na + , low extracellular fluid volume, bronzing of skin, poor response to stress , delayed wound healing.
- Usually patients suffering this disease may continue to live well .but, sometimes, they may collapse due to shock from even a minor stress .this is called **addisonian crisis.**

3. Diabetes mellitus

- It is commonly called sugar diabetes, it is an metabolic disorder
- It is charactirised by *hyperglycaemia, glycosuria, ketonuria* and *ketonemia*
- Its major symptoms include *polyuria* (excessive urine production), *polydipsia* (increased thirst and high fluid intake) *polyphagia* (excessive hunger and overeating), weight loss, eczema etc.
- Three main forms of diabetes mellitus, type 1. Type II and *gestational*
- Gestational diabetes occurs in women only during pregnancy.
- The ultimate cause of all of them is the inability of the pancreatic beta cells to produce sufficient insulin to prevent hyperglycaemia
- Type 1 diabetes is insulin-dependent diabetes and it mostly occurs in young people.
- The peak of its onset is the age between 12 and 14 years. So, it is often called juvenile – onset diabetes or juvenile diabetes.
- Its onset is usually rapid It mostly results from the autoimmune destruction of beta cells with little or no endogenous insulin
- Type Il diabetes is insulin-independent diabetes. It tends to affect older people.
- It is commonly called maturity-onset diabetes or senile diabetes.
- It usually results from tissuewide insulin resistance. In this case, insulin production is normal, or even increased.
- Gestatational diabetes occurs only in pregnant women and it resolves with delivery.
- In some cases, diabetes mellitus appears as a secondary effect of certain other disorders.
- For example, chronic pancreatitis often destroys the islet cells resulting in insulin insufficiency. Cushing's syndrome enhances gluconeogenesis and thereby causes hyperglycaemia

4. Diabetes insipidus

- Diabetes insipidus is a disorder of water metabolism, characterised by polyuria (increased diuresis or excessive excretion of dilute urine) and polydipsia (increased thirst and heavy fluid intake) and frequent urination.
- It results from the inadequate renal reabsorption of water mainly due to the hyposecretion of the antidiuretic hormone (ADH) of hypothalamus or doc to the insensitivity of renal tubules to ADH.
- Hyposecretion of ADH may be caused by damage to hypothalamus or neurohypophysis.
- Some of the symptoms of diabetes similar to those of untreated diabetes mellitus, except that hyperglycaemia and glycosuria are absent.
- In children, diabetes insipidus may be often accompanied by fever, vomiting, diarrhoea, etc.

- It may also reduce their appetite and food intake and adversely affect their growth and weight gain. Both in child and adults, there is the persistent threat of dehydration.

5. Pituitary dwarfism

- Dwarfism is the condition of short stature or underdevelopment of the body.
- Causes are developmental, deficiency of pituitary growth hormone, achondro which is an autosomal genetic disorder), cretinism, rickets, etc.
- Pituitary dwarfism is characteristic in that the body is extremely small with normally proportional parts. But in achondroplastic dwarfism, body parts are disproportion ate with large and globular head, short and thick limbs, and short and blunt digits.

6. Gigantism

- Giantism is the enormous size of the body due to the hypersecretion of pituitary growth hormone in children.
- Gigantism in characterised by abnormal height, with generalized overgrowth of bones and soft tissues. Limbs are exceptionally long.

7. Acromegaly

- Acromegaly is the disproportionate growth of bones in different parts.
- Acromegaly is characterised by the abnormal thickening of the bones of hands, feet, face and jaws, and protrusion of lower jaw (prognathism).
- Often, eyelids, lips, tongue and nose enlarge and skin thickens with loss of elasticity and furrows on forehead and soles of feet.
- Other symptoms of acromegaly include broad hands and thick fingers, kyphosis or forward bending of the spine, thickening of the sub-cutaneous tissues, atrophy of gonads and gradual loss of sexual functions.
- Hypersecretion of pituitary growth hormone often results from benign tumours (ad enomas) in the adenohypophysis.
- The common local effects of these tumours are headache and impairment of vision due to pressure on eyes.
- Sometimes, the tumours may damage other pituitary cells, leading to gonadal, thyroid or adrenocortical hyposecretions.

8. CRETINISM

- It is an endocrine disorder due to defective thyroid functioning and extreme hypothyroidism in the foetal life or early infancy.
- Two clinical features of cretins are dwarfism and mental retardation.
- Dwarfism results from the failure of skeleton to grow and mature.
- Mental retardation is due to the failure of the brain to develop fully and properly.
- Other features of disease include slow heart rate ,low body temperature, muscular weakness,general lethargy, yellow, thick,coarse,dry and wrinkled skin,round face,thick nose,large thick and protruding tongue,pot belly,abnormal faint,speech problem,poor co-ordination and slow reflexes,retarded sexual development(sexual infantilism) etc.
  Cretinism some times result from iodine deficient diet.
- Iodine is essential for the synthesis of thyroid hormones.
- Iodine deficiency may cause the impairment of physical and mental development,and the enlargement of thyroid.

9. MYXOEDEMA

- Myxoedema is an endocrine disease of adult individuals.
- It is primarily due to the underactivity of thyroid gland or extreme hypothyroidism,and secondarily due to the underactivity of pituitary.
- It may also be caused by Hashimoto's disease (auto immune thyroiditis), surgical removal of thyroid, etc.
- It is more common among adult females below the age of 35 years than among men.
- The hallmark of this disease is facial oedma with swallen and puffy face.
- Other clinical features include enlarged heart,slow heart rate,low body temperature,muscular weakness and pains ,generally lethargy, sluggish movement,lack of concentration,mental alertness and initiative loss of memory,slow intellectual functions,hoarse voice,slurred speech,dry and swollen skin, accumulation of hyaluronic acid and chondroitin sulphate in the dermis,thin and brittle hairs,constipation,hearing impairment, intolerance to cold, etc.

10. Goitre

- Goitre is the partial or total swelling and enlargement of the thyroid gland.
- There are four major varieties of goitre namely simple goitre, exophthalmic goitre, nodular goitre, lymphadenoid goitre and toxic goitre.

(i) Simple goitre

- Simple or endemic goitre is the benign enlargement of the thyroid with normal production of hormones.

- It results from the deficiency or absence of iodine; iodine is essential for the synthesis of thyroid hormones.
- Simple goitre is a physiological response to maintain the synthesis of thyroid hormones.
- It may occur when the gland does not get enough iodine to produce sufficient hormones for body's needs.
- In such a situation, the anterior pituitary releases large amounts of TTH.
- In response to TTH, the follicular cells of the thyroid enlarge and produce large amounts of thyroglobulin.
- This enlargement leads to hyperplasia and simple goitre. Simple goitre commonly occurs at puberty, during pregnancy, and at menopause which are times of high thyroxine demand.
- It may also result from the defective utilization of iodine in the synthesis of thyroid hormones.

(ii) Exophthalmic goitre

- Exophthalmic goitre is the goitrous condition due to hyperthyroidism.
- Just like myxoedema, it is also more common among females than among males.
- The disease is characterised by the excessive enlargement of the thyroid (goitre), oedema behind the eyes, bulging of the eyeballs (exophthalmos), abnormally high metabolic rate, high heart rate and pulse rate, nervousness, tremor, etc.

(iii) Nodular goitre

- This is the permanent thyroid enlargement due to alternating episodes of hyperplasia and involution in the thyroid
- It may cause pressure symptoms, and rarely may it lead to malignancy.

(iv) Lymphadenoid goitre

- This is an auto-immune disease due to the production of antibodies against antigens in the thyroid.
- In this case, the gland is much firmer than the soft gland of simple goitre.

(v) Toxic goitre

- This type of goitre is with nodular outgrowths of the thyroid. It is less frequent and is responpible for toxic hyperthyroidism.

HORMONES OF REPRODUCTION

2. TESTES

- Testes contain groups of endocrine cells in between the seminiferous tubules. They are called interstitial cells or Leydig's cells.
- They secrete the male hormones *inhibin* and *androgens*, under the stimulation of ICSH of pituitary.
- The chief androgen is *testosterone*.
- In addition to it, a few minor androgens are also present. They include *androsterone, epiandrosterone, alpha-hydroxytestosterone and ß – hydroxytestosterone.*
- Inhibin inhibits the release of FSH by adenohypophysis and thereby inhibits spermatogenesis.
- Androgens trigger virilization or male pubertal changes (enlargement of primary sex organs and development of male secondary sexual characteristics and sexual behaviour), accelerate muscular development, increase the rate of protein synthesis, enhance basic metabolic rate, raise red cell count and blood volume, and promote spermatogenesis.
- Extreme deficiency of testosterone often results in *eunuchoidism*.
- Eunuchs or neuters are impotent males with non-functional testis and underdeveloped penis, prostate gland and seminal vesicles.
- Earlier and excessive secretion of testosterone may induce precocious puberty (premature sexual maturation).

2. OVARY

- Ovaries secreting the female hormones Oestrogen, Progesterone, Relaxin.
- These are under the influence of the FSH of pituitary
- Oestrogen and Progesterone are steroid hormones
- Relaxin is a water soluble proteinous hormones

Oestrogen

- The commonest Oestrogen are Oestradiol, Oestriol, Oestrone
- Oestrogen are synthesised in adrenal and cortex, placenta and testis

Roles:-

- Oestriol is the main oestrogen produced during pregnancy, mostly in the placenta.

- Govern the growth of both external and internal genitalia, including the growth and maturation of ovarian follicles, enlargement of uterus, cyclic changes in vagina, growth and rhythmic contraction of the fallopian tubes etc
- Stimulate the development of female secondary sexual characteristics, sexual behaviour and sexual drive. These include the enlargement of mammary glands, pattern of hair line and fat distribution, changes in pelvis, increased libido, etc
- Stimulate the onset of pubertal changes and sexual cycle
- Initiate uterine changes for the preparation and maintenance of pregnancy
- Increases water retention in the body. This is mainly responsible for the pre menstrual tention, irritability and discomfiture.
- Cause the thickening, softening and smoothening of skin.
- Raise the blood levels of calcium and phosphates
- Stimulate the increased deposition of fat in the subcutaneous tissue in buttocks, thigh, breast etc
- Lower the plasma cholesterol level and prevent atherogenesis
- Promote the production of angiotensinogen, thyroid binding proteins, and corticosteroid binding proteins

Progesterone

- Secret by functional corpus luteum of the ovary only during the first three or four months of pregnancy
- Other sources adrenal cortex and testes
- Generally called hormone of gestation

Roles :-

- Makes the endometrium vascular, glandular and secretory as a preparation for implantation of pregnancy. These changes are possible only when the endometrium is previously Stimulated by Oestrogen
- Reduce the force and frequency of the contraction of myometrium
- Stimulate the development of breast, and make the mammary glands sensitive to the action of the lactogenic hormone of pituitary for milk production
- Suppress sexual cycle and ovulation during pregnancy
- Increases the body temperature soon and ovulation. This thermal shift gives a clue to know whether ovulation has taken place or not
- Promotes the reabsorption of water, Cl-, and Na+ in renal tubules. This in turn, increases the extra cellular fluid volume and electrolyte concentration
- Stimulates sebaceous glands to increase sebum production, this makes skin and hairs glossy and also cause acne
- Causes the relaxation of the smooth muscles of uterus, blood vessels, and gastro intestinal tract

RELAXIN

- Just as Progesterone, Relaxin also is a hormone of pregnancy, mostly concerned with parturition
- It is secreted by corpus leuteum first, then by placenta during late pregnancy
- Its production usually within 24 hours after parturition
- It Stimulate the relaxation of pelvic ligament softening of pubic symphysis, expansion of the pelvic girdle, dilation of cervix and enlargement of the birth canal during parturition
- This facilitates the expulsion of the baby during delivery.
- Soon after parturition it falls zero

3. PLACENTA

- Placenta has a dual function. Primarily, it serves as an organic connection between the mother and the developing foetus in her uterus for the exchange of materials.
- Equally important is its role as an endocrine organ.
- It secretes several hormones and cytokines which have a major influence on ovarian, uterine, mammary and foetal physiology.
- All placental hormones are related to pregnancy.
- Placental hormones are of two major groups, steroid hormones and protein hormones.
- Steroid hormones include the oestrogens and progesterone.
- Protein hormones include the chorionic gonadotropins and relaxin. Placental oestrogens, progesterone and relaxin supplement the action of their ovarian counterparts.
- Chorionic gonadotropins supplement the pituitary gonadotropins FSH and LH.

(a) Placental Progesterone

- Placental progesterone has the following three major roles during pregnancy.
  - (i) Modifies and supports the endometrium to provide a most favourable environment for the implantation of the embryo and the survival and development of the foetus.
  - (ii) Suppresses the contraction of the smooth muscles of uterine myometrium. This is often called “progesterone block”. It avoids premature parturition. Towards the end of gestation, this effect will be countered by the rising levels of oestrogens to facilitate parturition.

(iii) Inhibits the secretion of pituitary gonadotropins (FSH and LH) to prevent ovulation during pregnancy.
(iv) Promotes the development of mammary glands and initiates milk production.

(b) Placental oestrogens

- Different species of mammals produce different types of placental oestrogens.
- They may be derived from foetal androgens, placental progesterone, or other steroid precursors, depending upon the species
- In general, their concentration in maternal blood rises to the peak towards the end of gestation. Oestriol, oestradiol and oestrone are the commonest placental estrogens.
- The principal effects of placental oestrogens are the following:

(i) Stimulate the growth of uterine myometrium.
(ii) Counterbalance the myometrium-suppressing activity of progesterone. (iii) Stimulate the growth and development of mammary glands.
(iii) Suppress gonadotropin secretion by pituitary.

(c) Chorionic gonadotropins

- Chorionic gonadotropins are similar to pituitary gonadotropins in that they also stimulate the growth and functioning of gonads.
- The important chorionic gonadotropins of human females are human chorionic gonadotropin (HCG), human chorionic somatomammotropin {HCS) and placenta luteotropin releasing actor (PLRF).

(i) Human chorionic gonadotropin (HCG)

- HCG is a glycoprotein, secreted by the chorionic villi of placenta.
- In action, it is almost Similar to the pituitary LH.
- Its major functions are the following:

(i) Prevents the regression of corpus luteum and maintains its functional state for the continued production of ovarian progesterone.
(ii) Ensures the continued attachment of the developing embryo to the endometrium and thus maintains pregnancy.
(iii) Stimulates the conversion of androgens to oestrogens.

- HCG appears in the urine of a pregnant woman from about the 8" day of pregnancy.
- It reaches its peak of excretion by about the 8" week of pregnancy.
- Its level falls sharply during the 4^{th} and 5^{th} months and then levels off until parturition.
- Excretion of HCG through urine serves as the basis for pregnancy tests.

(ii) Human chorionic somatomammotropin (HCS)

- HCS (formerly known as human placental lactogen - HPL) is a protein hormone, syothesised by the chorionic villi and discharged exclusely to the maternal circulation.
- In chemical nature, it is similar to prolactin and growth hormone.
- Neither the functions of HCS nor the factors controlling its production are not definitely known.
- It is believed to have the following functions.
  (i) Modulates foetal and maternal metabolism, probably by causing changes in carbohydrate and protein metabolism and also by mobilizing energy fuels for foetal metabolism.
  (ii) Maintains the functional state of corpus luteum.
  (iii) Stimulates the development of mammary glands for milk production prior to parturition.
  (iv) Enhances bodily growth by causing the deposition of proteins in tissues.
  (v) Reduces glucose utilization by the mother, making more glucose available for f metabolism.
  (vi) Promotes the release of fatty acids from fat depots as an alternative source of € for maternal metabolism.

(iii)Placental leuteotropin releasing factor (PLRF)

- PLRF is a placental hormone which is believed to stimulate the secretion of placental (chorionic) gonadotropin.

(d)Placental relaxin

- Placental relaxin is exactly similar to the ovarian relaxin in chemical nature of physiological function.
- Just as ovarian relaxin, it is also concerned with the ree pelvic ligaments, dilation of the pelvic girdle, expansion of cervix and enlargement of bir th canal during parturition. .

HORMONAL CONTROL OF FEMALE SEXUAL CYCLE

- The reproductive behavior of mammalian females is cyclic processes leading to ovulation.
- These cycles include repeating cycles of ovarian and uterine changes, commonly called *sexual cycles*
- Sexual cycles are two kinds, *menstrous cycle* and *oestrous cycle*

Menstrous cycle in human females

- In primates, sexual cycle ends in menstruation. So, it is called menstrous cycle.
- In human females it is regularly repeated from puberty to menopause.
- It would not occur during pregnancy, would be suppressed during lactation, and would stop for ever after menopause
- Normally, a cycle lasts for about 28 days (one lunar month). At the end of it menstrual flow occurs for about 3-5 days. This period is known as the menstrual period.
- Menstrual cycle includes two separate cycles, namely *ovarian cycle* and *uterine cycle*
- Ovarian cycle involves the maturation of ovarian follicle, collapse of the Graafian follicle, release of ovum (ovulation) and the development of corpus luteum.
- Uterine cycle involves the preparation of the uterine wall and endometrium to receive and retain the embryo.

(a) Ovarian cycle

- Ovarian cycle is the cycle of changes occurring in the ovary.
- It is completed in three stages, namely pre-ovulatory, ovulatory and post-ovulatory periods.
- Pre-ovulatory and ovulatory periods are marked by profound changes in the ovarian follicle. Consequently, they together constitute the follicular phase.
- Post-ovulatory period is marked by the development and functioning of corpus luteum. Hence, it is often known as luteal phase.
- Pre-ovulatory period includes the first 12 or 13 days of the cycle.
- During this period, there is increased production of the follicle stimulating hormone (FSH) and luteinising hormone (LH) of pituitary.
- Under the influence of FSH, a primary follicle matures to a Graafian follicle. Graafian follicle soon secretes oestrogens, which inhibit the secretion of FSH and promote the production of LH.
- Shortly afterwards, Graafian follicle collapses, leading to ovulation. This represents the ovulatory period.
- Ovulation occurs between the 13th and 15th days of the cycle.
- Soon after ovulation, LH stimulates the formation of corpus luteum, which in turn, secretes progesterone.
- This is the post-ovulatory or luteal phase. It includes the last 13 or 14 days. Progesterone inhibits the secretion of FSH and thus prevents the maturation of additional follicles.
- If fertilization and pregnancy follow, corpus luteum continues its functional existence.
- If fertilization does not occur, corpus luteum atrophies. The entire Series of changes, taking place during the ovarian cycle, can be summarised as follows:

(i) Pre-ovulatory period (increased FSH and LH)

1. Primary follicle —FSH—» Graafian follicle

2. Graafian follicle secretes oestrogens.

3. Ocstrogens stimulate the production of LH and inhibit the production of FSH. .

(ii) Ovulatory period (increased LH)

4. Graafian follicle→FSH & LH→ Follicular collapse and ovulation

(iii) Post ovulatory (increased LH)

5. Collapsed follicle →LH→Corpus luteum.

6. Corpus luteum secretes progesterone.

7. Progesterone inhibits FSH production and prevents further follicular maturation, if pregnancy occurs.

8. In the absence of pregnancy corpus luteum degenerates.

(b) Uterine cycle

- Uterine cycle is the cycle of changes taking place in the uterus.
- It consists of three stages, namely proliferation phase, secretory phase and menstrual phase.
- The last stage is present only in the absence of pregnancy.
- Proliferation phase coincides with the follicular phase of the ovarian cycle, and secretory phase coincides with the luteal phase.
- During the proliferation stage, there is high secretion of oestrogens.
- With their action endometrium (uterine lining) becomes thick, vascular and glandular.
- During the secretory period, under the influence of oestrogens and progesterone, endometrium attains maximum thickness, vascularity and glandularity and gets ready to receive and retain the embryo for implantation.
- If pregnancy occurs, corpus luteum continues to secrete progesterone, and endometrium continues to be thick, vascular and glandular. In the absence of pregnancy, corpus luteum degenerates, progesterone secretion stops, and endometrium regresses and finally collapses, this results in menstrual flow.
- The period of menstrual flow represents the menstrual phase.
- The changes, taking place during the uterine cycle, can be summarised as follows:

A. Proliferation phase (increased oestrogens)

1. Thin endometrium →Oestrogen→Thick, vascular and glandular endometnum.

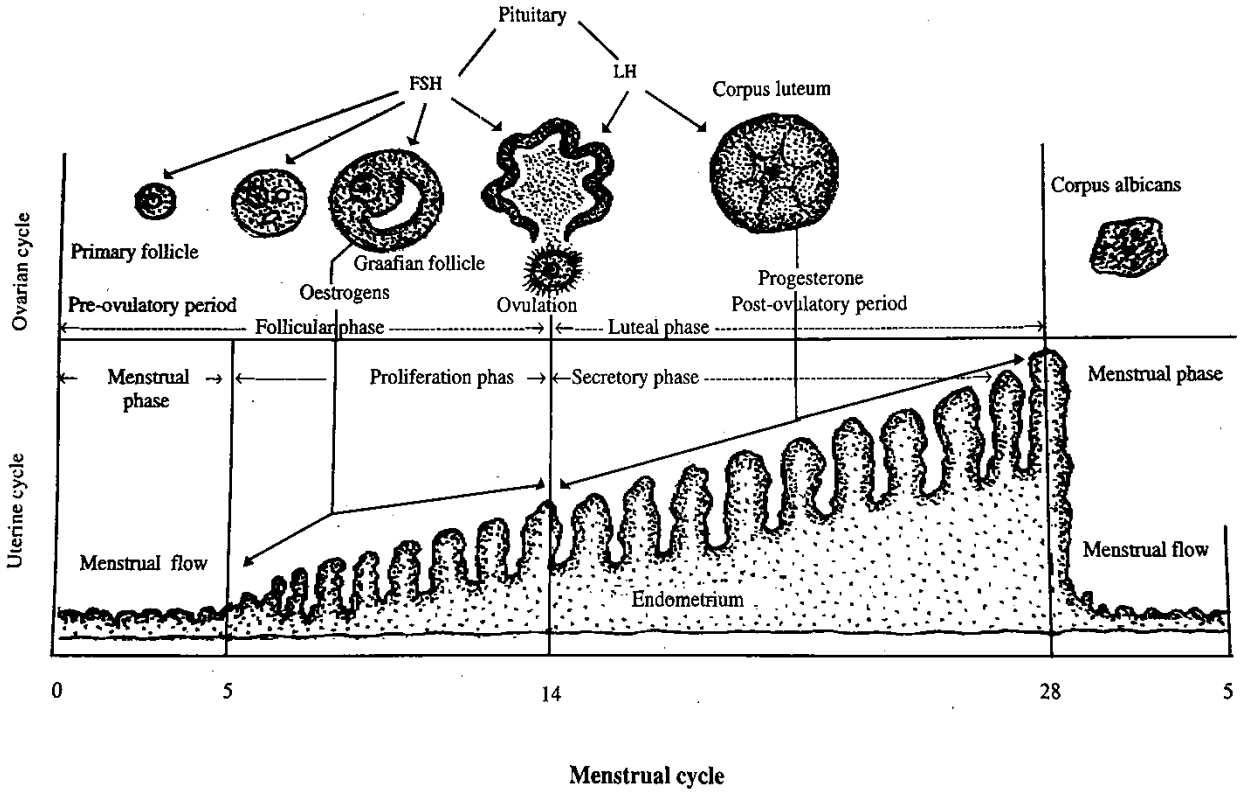
B. Secretion phase (increased progesterone)

2. Glandular endometrium →oestrogen & progesterone→ Endometrium ready to receive & retain embryo

C. Menstrual phase (no pregnancy, no progesterone)

3. Corpus luteum disappears, progesterone secretion stops, endometrium collapses, menstruation follows.

equipping with excellence
CPA COLLEGE OF GLOBAL STUDIES



REPRODUCTIVE HORMONE DISORDERS

- Reproductive hormone disorders can affect fertility and may have long-term effects on metabolic, cardiovascular and bone health.
- The reproductive hormones include estrogen and progesterone in women and testosterone in men.
- They originate from the primary reproductive glands (ovaries in women and testes in men) and are regulated by hormone signals from the pituitary gland; luteinizing hormone (LH) and follicle stimulating hormone (FSH).

1. Ovarian insufficiency

- Ovarian insufficiency (sometimes called premature menopause) occurs when the ovaries either do not develop or are damaged and no longer function normally.
- Ovaries can be surgically removed, or damaged by the immune system, or from chemotherapy, or radiation treatments for certain types of cancer
- The premature loss of ovarian function (before the age of 40) can result in infertility and the loss of the beneficial effects of estrogen and progesterone, including benefits to bone and heart health, which are usually not lost until the natural age of menopause (approximately age
- Symptoms of low estrogen can develop in many, but not all, women with ovarian dysfunction.
- These can include hot flashes, night sweats, poor sleep, and vaginal dryness.

2. Menopausal symptoms

- Menopause (the normal loss of the menstrual cycle) is a natural part of female aging and occurs at about the age of 50 years in most women.
- In some women, menopause can be associated with symptoms of low estrogen including hot flashes, night sweats, poor sleep, and vaginal dryness.
- The post-menopausal period may also be associated with a gradual loss of bone density, which can result in osteoporosis in some women.

3. Polycystic ovary syndrome

- Polycystic ovary syndrome (PCOS) is a metabolic condition that occurs in some women of reproductive age.
- Symptoms can include irregular menstrual periods, loss of fertility, increased hair growth on the face, chest, or abdomen, acne, and a tendency toward weight gain and insulin resistance (diabetes).
- One of the primary features of PCOS is the appearance of small cysts in the ovaries that can be seen on a pelvic ultrasound.
- Most women with PCOS benefit from diet, exercise and weight loss, which tends to improve metabolism and underlying hormone balance.
- Other treatments are directed toward specific symptoms.

4. Low testosterone in man

- Testosterone, the male hormone (produced in the testes), has an important role in maintaining fertility, energy, strength and metabolism
- Men with low testosterone can have symptoms of low energy and mood as well as reduced strength and libido (sex drive).

- In the long term, they are also at risk for low bone density (osteoporosis).
- Men with testosterone levels that are clearly below the normal range may benefit from testosterone supplementation.
- The benefits can include improved energy, mood, strength and libido.
- Testosterone can be given by injection, or by patch or gel that is applied to the skin.

equipping with excellence
CPA COLLEGE OF GLOBAL STUDIES

MODULE 9. CONCEPT OF NEUROSECRETION AND HORMONAL ACTION

HYPOTHALAMUS- HYPOPHYSEAL INTERACTION

- Hypothalamus is the glandular floor of the diencephalon of vertebrate brain
- It has both nervous and endocrine roles
- It governs the functioning of the pitutory gland and nervous system, controls emotional responses, regulates body temperature and water balance, and arouses the hunger drive.
- It serves as a link between nervous and endocrine systems and directly or indirectly controls most of the hormonal activities.
- It receives inputs from other parts of the brain, and also from the hormones in the blood.
- In response to these inputs, it secretes several regulating hormones which regulate the release of pituitary hormones .
- The neurosecretory cells of hypothalamus secrete three major groups of hormones, namely regulating hormones, oxytocin and vasopressin.
- Regulating hormones are then transported to the adenohypophysis by blood.
- On the other hand, oxytocin and vasopressin are transported to the neurohypophysis along the fibres of the neurosecretory cells by a transport protein called neurophysin.
- In the neurohypophysis, they are stored in the axon terminals.
- When the hypothalamus. gets excited by appropriate stimuli, the impulses would be transmitted to the axon endings of the neurosecretory cells.
- These impulses would cause the release of the stored hormones from axon terminals to blood. Blood will carry them to their target sites.
- Pituitary or hypophysis is a small gland, seen very closely associated to the brain.
- It is placed in a depression of the sphenoid bone, called sella turcica, and is connected to the hypothalamus of the brain by a stalk-like structure, called infundibular duct
- Human pituitary has two lobes, anterior and posterior, known respectively as adenohypophysis and neurohypophysis
- Both these are connected to the hypothalamus.
- In between them is a vascular zone, known as pars intermedia. Its role in human beings is rather obscure.
- Adenohypophysis is hormone producing.
- Neurohypophysis only stores and then secretes the hormones produced by the hypothalamus.
- Adenohypophysis and neurohypophysis are ectodermal in origin.
- The former is derived from an embryonic invagination of pharyngeal epithelium, whereas the latter is derived from an n Outgrowth of the hypothalamus.
- The anterior lobe is an endocrine gland, and it contains hormone secreting cells.

- The posterior lobe does not synthesise hormones and so, in the strict sense, it is not an endocrine gland.
- It contains axon endings of the secretory neurons whose cytons are located in the hypothalamus.
- These secretory neurons are called neurosecretory cells.
- Their fibres extend from the hypothalamus to the neurohypophysis and terminate on blood capillaries in the neurohypophysis. They form the hypothalamic"hypophyseal tract.
- The cell bodies of the neurosecretory cells produce a variety of hormones.
- The fibres of the neurosecretory cells, located in the neurohypophysis, are supported by specialized pituitary cells, called pituicytes.
- Hypothalamus is connected to the adenohypophysis by a system of blood vessels, and to the neurohypophysis by nerve fibres.
- The cell bodies of the neurosecretory cells in the hypothalamus produce the hormones oxytocin and vasopressin.
- They are soon transported to the neurohypophysis along nerve fibres by a carrier protein, called neurophysin.
- In the neurohypophysis, they are stored in the axon terminals. Later, when the hypophysis is properly stimulated, it sends impulses to the neurosecretory cells. These impulses cause the release of the hormones to blood from axon terminals.
- Pituitary directly or indirectly controls most of the metabolic activities and regulates the functioning of most other endocrine glands. So, it was customarily described as the “master gland” of the endocrine system or as the “band-master of the endocrine orchestra.”
- But, the actual fact is that pituitary itself is under the control of the hormones of hypothalamus. So, pituitary and hypothalamus together constitute what is called the hypothalamo-hypophyseal axis, which serves as the “master control of the endocrine system.”

HYPOTHALAMUS RELEASING AND INHIBITING HORMONES AND THEIR ROLE

1. Regulating hormones

- The hypothalamic regulating hormones govern the production and release of pituitary tropic hormones.
- They are of two kinds, releasing hormones or releasing factors and inhibiting hormones or inhibiting factors.
- Releasing hormones stimulate the release of the pituitary tropic hormones, whereas inhibiting hormones inhibit the release of pituitary tropic hormones.

- For each pituitary tropic hormone, there will be a corresponding releasing hormone and an inhibiting hormone.
- The major releasing and inhibiting hormones of hypothalamus are the following:

(a) Releasing hormones

(vi) Somatotropin-releasing hormone (STRH) –

- Also called somatostatin or growth hormone-releasing factor (GHRF).
- Stimulates the release of the pituitary growth hormone (somatropin).

(vii) Thyrotropin-releasing hormone (TTRH)

- Stimulates the release of the thyroidstimulating hormone (thyrotropin) of pituitary.
- Its production is regulated by the levels of thyroid hormones in blood.
- High levels of thyroid hormones inhibit its production and low levels stimulate its production.

(viii) Adrenocorticotropin-releasing hormone (ACTRH)

- Stimulates the release of adrenocorticotropic hormone (adrenocorticotropin) from pituitary

(ix) Gonadotropin-releasing hormones (GTRH)

- Stimulate the release of gonadotropic hormones (gonadotropins) from pituitary.

(x) Prolactin-releasing hormone (PRH)

- Stimulates the release of prolactin or lactogeni¢ hormone from pituitary.

(b) Inhibiting hormones

(vii) Somatotropin-inhibiting hormone (STIH)

- Also called growth hormone - inhibiting factor (GHIF).
- Inhibits the release of pituitary somatotropin.

(viii) Thyrotropin-inhibiting hormone (TTIH)

- Inhibits the release of pituitary thyrotropin

(ix) Inhibiting hormone (ACTIH)

- Inhibits the release of adrenocorticotropin from pituitary.

(x) Gonadotropin-inhibiting hormones (GTTH)

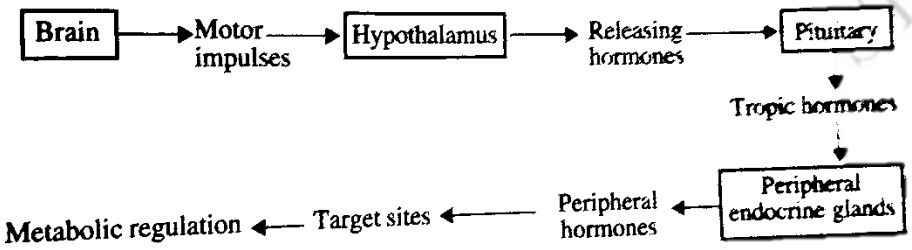
- Inhibit the release of pituitary gonadotropins.

(xi) Prolactin-inhibiting hormone (PIH) –

- Inhibits the release of prolactin from pituitary.

NEURO- HORMONAL INTEGRATION

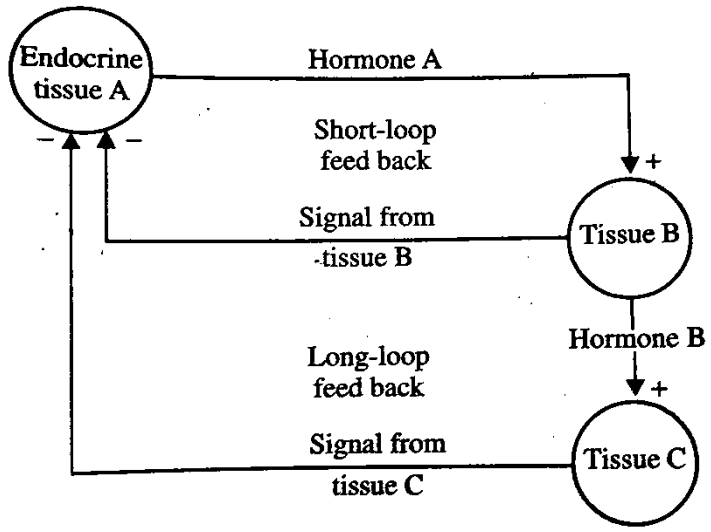
- Metabolism and effector functions (muscular contraction and glandular secretion) are regulated directly and indirectly.
- Direct regulation involves the transmission of motor impulses from CNS to peripheral organ or tissue.
- Indirect regulation involves hormonal action.
- Both these information channels meet at the level of hypothalamus.
- The motor impulses, transmitted from brain, stimulate the secretion of hypothalamic hormones
- These hormones stimulate the secretion of the pituitary tropic hormones which in turn, regulate the secretion of hormones by peripheral endocrine glands (glands other than hypothalamus, pituitary and pineal)



Flow chart of neurohormonal integration

NEURO- ENDOCRINE PATHWAYS

- Based on the complexity of pathways, neuro-endocrine systems may be grouped under three categories, first-order, second-order and third-order.
- In the first order system, neuro hormones are first liberated from secretory cells to blood, and then they directly reach the target cells.
- This is the case with the hypothalamic hormones oxytocin and vasopressin, and also with the peripheral hormones.
- In the second-order system, two different secretions are liberated from two different sources before a final physiological change is brought in. For example, gonadotropin releasing hormone is first secreted by hypothalamus.
- It reaches the anterior pituitary and stimulates the secretion of gonadotropin. Gonadotropin in turn reaches the gonad and stimulates the growth and functioning of the gonad.
- In third-order system, three hormonal secretions are involved. For example, thyrotropin releasing hormone is first secreted by the hypothalamus.
- It reaches anterior pituitary and stimulates the secretion of thyroropin.
- Thyrotropin, in turn, reaches the thyroid glands and stimulates the secretion of thyroid hormones.
- Thyroid hormones reach their target sites and fulfil their physiological function.



Regulation of hormone production through negative feed-back

REGULATION OF HORMONE ACTION

- Hormones of the peripheral glands are liable to fast inactivation and destruction.
- So, their synthesis and secretion take place incessantly to readily compensate their loss and to maintain their appropriate levels in blood.
- This controlled production of peripheral hor mones is effected by a self-regulating mechanism, which involves a mutually exclusive interhormonal relationship, often called "plus-minus interaction"
- With very few exceptions (e.g., the cells which produce growth hormone), the secretory activities of endocrine tissues are modulated by negative feedback in this case, the exces sive concentration of a particular hormone, or the response of a target tissue to such a high concentration, indirectly inhibits the further production of that hormone, This checks a further increase in its concentration.
- The rate of hormone production is usually determined by the body's need for the hormone.
- So hormone production is regulated in such a way that under normal conditions there is neither hyposecretion nor hypersecretion.
- Negative feed back mechanism two kind
  1. short loop feedback
  2. long loop feedback

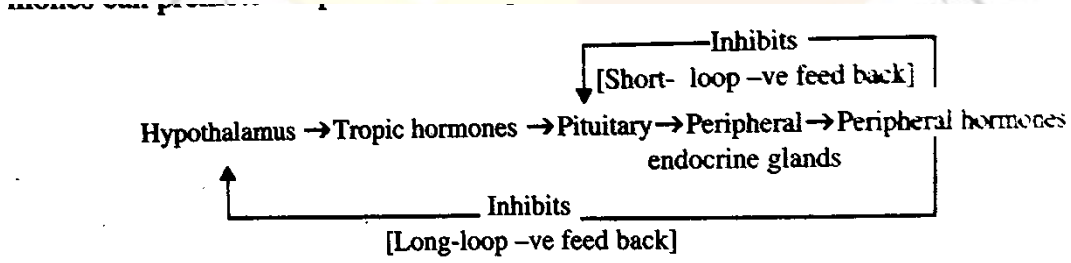
1. Short loop feedback

- A product of the target tissue, or an effect produced by it, acts directly back upon the endocrine tissue and keeps the hormone secretion under check.

2. Long loop feedback

- Long loop feedback also operates on the same principle, but it includes more elements.
- Eg:-

  Some hypothalamic hormones promote the release of pituitary tropic hormones which, in turn, stimulate the production and secretion of peripheral hormones



Feed-back control of hormone secretion

- Overproduction or high concentration of the peripheral hormones normally inhibits the further production of the pituitary tropic hormones by negative feed-back.
- This is accomplished by inhibiting either the pituitary cells (short-loop feed-back) or the neuro-secretory cells of the hypo thalamus (long-loop feedback).
- In the same manner, the hyposecretion of peripheral hor mones can promote the production of pituitary or hypothalmic hormones.
- Production of thyroxine is a typical example of long-loop feedback control. Thyroxine production is stimulated by the pituitary hormone thyrotropin (TTH).
- The production and release of thyrotropin is stimulated by the thyrotropin releasing hormone (TRH) of hypothalamus. (The production and action of this hormone, in turn, is controlled by the thyroxine level in blood.
- High thyroxine level inhibits the production and action of TRH. Low TRH level leads to low thyrotropin production which, in turn, causes low thyroxine Synthesis.
- On the other hand, (low thyroxine level stimulates the production and action of TRH High TRH level promotes the production of TTH which, in turn, leads to high thyroxine synthesis.
- High thyroxine level leads to low thyroxine production. This is called negative feedback. On the other hand low thyroxine level enhances thyroxine production.
- The production of parathormone (PTH) is an example of short-loop feedback mechanism.
- PTH controls blood calcium level in the body.
- Its over-production abnormally raises blood calcium level.
- This high blood calcium level, in turn, serves as a stimulus to inhibit PTH production.
- Similarly, (under- production of PTH abnormally lowers blood calcium level.
- This low blood calcium level acts as a stimulus to promote PTH production
- Thus, low concentration of PTH stimulates its further production, and its high concentration inhibits its further production

Synergism and antagonism among hormones

- Synergism is the collective or co-operative action of two or more factors to produce a combined effect, which would be much higher than the sum of their separate effects.
- Antagonism is the mutually opposing action of two factors. Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) are synergistic hormones.
- Insulin and glucagon as well as thyrocalcitonin and parathormone are antagonistic.
- In females FSH and LH can individually stimulate follicular maturation and ovulation in the ovary, but neither of them can by itself cause ovulation without the involvement of the other.
- So, ovulation results from the combined action of FSH and LH. Similarly, lactation (production and ejection of milk) is stimulated by oestrogens, progesterone, prolactin and oxytocin. At the same time, none of them can cause lactation all by itself. ,
- Insulin and glucagon are antagonistic in that insulin lowers blood sugar level and glucagon elevates blood sugar level. In the same manner, calcitonin lowers blood calcium level, and parathormone raises blood calcium level

HORMONAL ACTION

- Hormonal action is triggered mostly by changes in the internal environment, rather than by external changes.
- Different hormones act in different ways in different cells and produce - different effects.
- These effects fall under four categories, namely kinetic, metabolic, morPhogenetic and corrective. Kinetic or triggering effects cause the effectors to act in a specific manner.
- They include pigment migration, muscular contraction, glandular secretion, etc.
- Metabolic effects include changes in the rate and equilibrium of biochemical reactions, changes in the concentrations of tissue constituents, etc.
- Morphogenetic or formative effects are related to the stimulation of growth and differentiation. Corrective effects alter the intensity of the functions of the entire organism or its organs.
- Many hormones may have multiple effects, and they often cut across the limits of this classification. For example, thyroid hormones have metabolic effects on some cells and morphogenetic effects on some other tissues.
- This means that hormones do not produce net effects all by themselves directly; they only activate certain intermediate processes, which are different in different cell types.
- Hormones influence the target cells in different ways as follows:
  (I) By altering the catalytic activity of critical enzymes.
  (II) By activating the transcription and translation of the genes which code for enzymes.
  (III) By altering the membrane permeability of the target cells.
  (IV) By stimulating the activity of target enzymes.
  (V) By directly or indirectly influencing the physical state of multiunit enzymes (for example, they may cause an active multiunit enzyme to dissociate into catalytically inactive monomers).

MECHANISM OF HORMONE ACTION

- Hormones produce their effects by binding first with specific hormone receptors of the target cell.
- Only those cells with receptors for a specific hormone respond, and those without receptors are unaffected.
- In general, hormones and receptors interact in the following ways to influence intracellular metabolism:

(i) Peptide hormones and catecholamine hormones bind to a fixed receptor on the outer cell surface.
(ii) Steroid hormones bind to a specific mobile receptor in the cytoplasm.
(iii) Thyroid hormones bind with a nuclear receptor.

HORMONE RECEPTORS

- Hormones are highly specific to their target tissues.
- This specificity of hormone action depends upon the receptor molecules of the target cells.
- A target cell can recognize its specific hormone with the help of its receptors.
- A receptor can detect a specific hormone and bind with it forming a hormone - receptor complex.
- Once this complex is formed, the hormone exerts its influence on the target cell.
- Hormone receptors Hormonal action is tissue specific. So, a hormone acts only on a specific type of cells or tissues.
- A target cell or tissue recognizes its specific hormone with the help of a receptor.
- A receptor is a macromolecule which selectively binds a particular hormone and then medi ates its effects on the target site.
- It has two major functions:
  (i) It distinguishes or detects the chemical signal of a specific hormone from among a jumble of hormones and other molecules
  (ii) It relays a signal to the cell that can produce an appropriate response.
- Some receptors are located on the cell surface, some others within the plasma membrane, and still others within cytoplasmic organelles or nucleus.
- Surface receptors are characteristic of some protein hormones (e.g., insulin), membrane receptors are characteristic of peptide hormones, protein hormones and catecholamines,
- Cytoplasmic receptors are characteristic of steroid hormones, and intranuclear receptors are characteristic of thyroid hormones.

Hormone-receptor interaction

- The binding interaction between a hormone and its receptor molecule is similar to enzyme-substrate complexing or antigen-antibody binding.
- There are four groups of hormone receptors, namely

(i) Cell surface receptors, located on the surface of the plasma membrane
(ii) Intramembrane receptors, located within the plasma membrane
(iii) Cytoplasmic receptors, located in cytoplasmic organelles and
(iv) Nuclear or chromosomal receptors, located inside chromosomes.

- This suggests that there are four levels of hormone action as follows:
  (i) Surface level or membrane type action.
  (ii) Intramembrane and intracellular level of action, or intracellular membrane type action.
  (iii) Cytosolic level of action (action of hormones having cytosolic receptors).
  (iv) Chromosomal or nuclear level of action or action at the level of genes (action of hotmones having cytosolic and nuclear receptors).

(a) Action of hormones having surface receptors (Surface level or membrane-type hormone action) -

- The hormones having their receptors on the surface of the plasma membrane of target cells do not enter into the cell interior.
- Instead, they bind to the surface receptors and make the membrane permeable to glucose, amino acids, and certain ions.
- In this case, the hormone acts as an allosteric effector for membrane transport system.
- The influx of glucose and amino acids into the cell influences its biochemical processes.
- The influx or efflux of ions alters the membrane potential of the cell and affects its function.
- Surface level, or membrane type, hormone action is very rare.
- Example :- insulin

Mode of action of insulin

- A typical example is the action of insulin, which exhibits intramembrane-intracellular type of action also.
- Insulin receptor is a protein composed of two alpha chains and two beta chains, linked together by disulfide bonds.
- Its alpha chains are entirely extracellular, and they contain insulin-binding domains. On the other hand, beta chains penetrate the plasma membrane.

- Insulin receptor functions as a tyrosine kinase, an enzyme which transfers phosphate group from ATP to the tyrosine residues of target cell proteins.
- It mediates the phosphorylation of tyrosine. Binding of insulin to the alpha sub-units causes the beta subunits to undergo phosphorylation. This may be called autophosphorylation.
- This activates the catalytic powers of the receptor. The activated (phosphorylated) receptor now phosphorylates several membrane proteins.
- This, in turn, elicits local changes and makes the membrane permeable to certain ions, glucose, and probably to amino acids also.

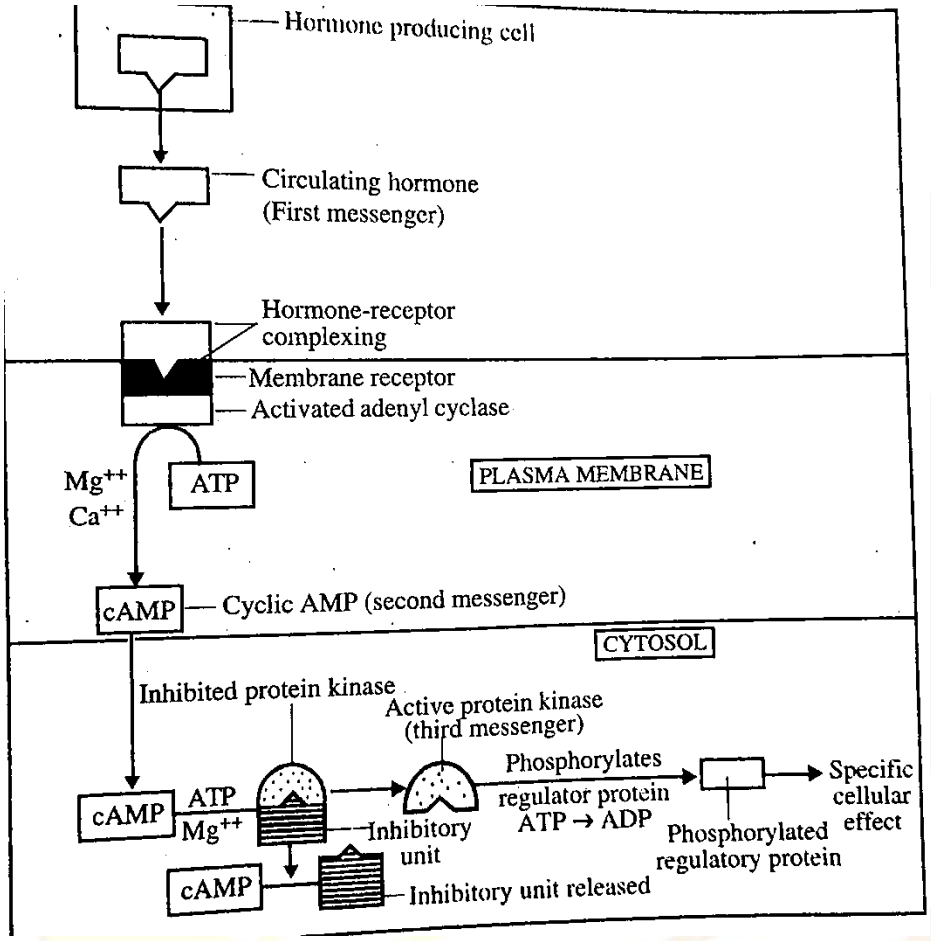
(b) Action of hormones having intramembrane receptors {Membrane-intracellular level of action}

- The hormones whose receptors are located in the plasma membrane have the intramembrane-intracellular type of action.
- The circulating hormone, already released from an endocrine gland, is called the extracellular first messenger
- In order to pass on its message to a target cell, it binds to a specific receptor molecule (an integral protein) located within the plasma membrane.
- This hormone-receptor complexing in the plasma membrane elicits three possible changes, namely
  (i) alters the permeability of the plasma membrane
  (ii) activates a second messenger system within the cell and
  (iii) activates a third messenger System to mediate the functioning of the second one.
- Changes in the permeability of plasma membrane cause an influx or efflux of ions or molecules.

Mode of action of peptide hormones

- For example, binding of insulin causes the influx of glucose into the cell; binding of thyrotropin causes the inflow of amino acids; binding of epinephrine causes the Outflow of potassium ions.
- The receptor-bound hormone in most cases may trigger off the production of a second messen ger system within the target cell.
- This second messenger, in turn, will enhance the ion Permeability or substrate permeability of all kinds of cell membranes. The most wide spread messenger, which signals the action of hormones is *cyclic adenosine 3,5- monophosphate (cyclic AMP or cAMP)*
- Other second messengers include cyclic GMP, Mg2+, Ca2+, etc

- It is believed that hormone-receptor interaction causes a conformational change in the receptor.
- This, in turn, leads to an allosteric activation of the enzyme adenyl cyclase, which remains associated with the cytoplasmic end of the receptor.
- It is also held that the hormone-receptor complexing activates a membrane protein, which serves as a membrane transducer.
- It transmits the signal to adenyl cyclase and activates it.
- The activated adenyl cyclase Serves as a biochemical amplifier and catalyses the hydrolysis of ATP to cAMP, in the presence of Ca2+ and Mg2+.
- Cyclic AMP binds to an intracellular receptor and acts as a the second messenger.
- It alters the cell function according to the message conveyed by the hormone.
- It soon binds with the intracellular enzyme protein kinase and activates it in the presence of ATP and Mg2+, this results in a specific cellular response.
- Protein kinase is in an inactive state, since it remains bound to an inhibitor unit. Its binding with cAMP removes the inhibitory unit from it.
- This activates it, and also protects CAMP from hydrolysis.
- The active protein kinase forms the third messenger or the internal effector
- It alters or Calcium ions may sometimes serve as second messengers along with cAMP.
- They bind to the intracellular protein calmodulin and activates its. Activated calmodulin, in tum, activates certain enzymes to produce specific hormonal effects.
- The action of cAMP is indirect with several intermediate steps.
- These steps greatly amplify the response of a cell to a hormone. For example, a single hormone-receptor complex can cause the production of many cAMP molecules, each of which can activate a protein kinase.
- A protein kinase, in turn, can phosphorylate many protein molecules.
- When the level of hormones in the blood falls low, the intracellular level of cAMP also falls low. In such a condition, protein kinase reverts back to its inactive form.
- Consequently, the proteins phosphorylated by it get dephosphorylated.
- Within the cell, high levels of cAMP persist only for a brief period.
- This is because the enzyme cAMP phosphodiesterase rapidly inactivates CAMP by converting it to S'-AMP.
- This inactivation may be reversed or inhibited by inactivating phosphodiesterase by methyl xanthine (caffeine), which can thus increase the level of cellular cAMP.



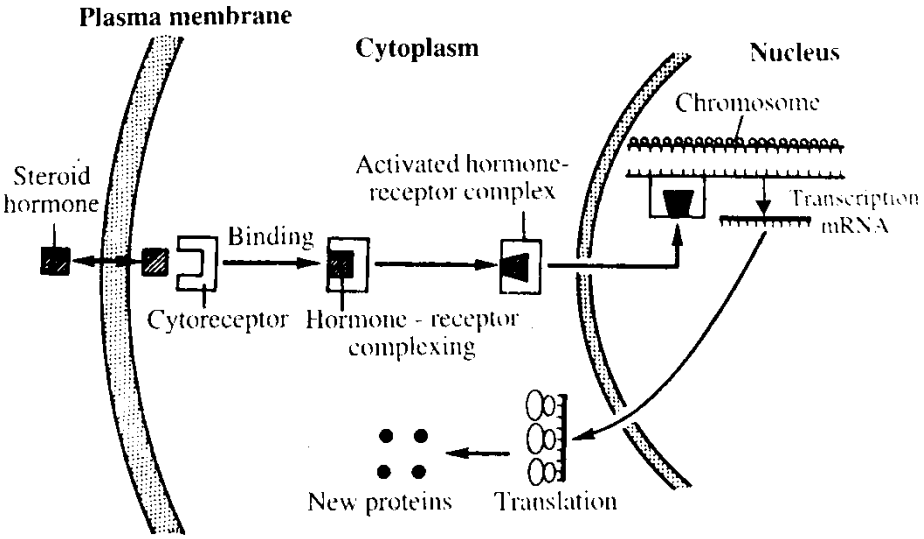
(c) Action of hormones having nuclear receptors [Hormone action at the level of chromosomes or genes]

- The lipophilic steroid and thyroid hormones have cytosolic-nuclear mechanism of action.
- Both of them alter cell function by activating genes but by somewhat different mechanisms. :

(i) Action of steroid hormones

- Steroid hormones directly penetrate the plasma membrane of their target cells and bind with specific cytoplasmic receptors. This activates the receptors.
- The activated hormonereceptor complex now serves as a gene inducer.
- It selectively stimulates the synthesis and activation of specific enzyme systems.

- During this, it penetrates the nuclear envelope and selectively activates specific chromosomal genes.
- The genes undergo transcription and translation and produce specific enzymes. These enzymes influence metabolism, control cell function and bring about specific effects.
- Steroid hormone-receptor complexing apparently regulates the transcription and translation of only a limited number of genes in the target cell. This is known as primary response.
- Some gene products of the primary response may activate other genes, producing delayed secondary effects. This is called secondary response



Chromosome-bound mechanism of hormone action

(ii) Action of thyroid hormones (thyroxine)

- Thyroid hormones enter the cytoplasm and bind with cytoplasmic receptors.
- This thyroid hormone - recepter complex enters the nucleus and makes use of specific binding sites in chromosomes.
- This binding selectively activates specific genes to undergo transcription and translation to produce specific cellular effects.

(d) Action of hormones having cytosolic receptors [Cytosolic level of hormone action]

- Thyroid hormones resort to cytosolic type of action also.
- In this case, they penetrate the plasma membrane, enter the cytoplasm and bind to specific cytoplasmic protein receptors of cell organelles, such as mitochondria.
- This complexing may activate the enzymes of the mitochondrial electron transport system (ETS).
- As aresult, more ATP wouid be synthesised. Increased production of ATP would provide enough energy for anabolic (synthetic) function.
- Thus, thyroid hormones accelerate cellular metabolism by their action at the cytosolic level.
- It becomes clear that the action of cell-invading lipophilic hormones is direct, without the involvement of a second messenger, whereas the membrane-bound action of the lipophobic hormones is indirect, with the help of a second messenger system.

Inactivation and the excretion of hormones

- Most hormones are enzymatically inactivated and degraded in the body, once their action is over.
- Their degradation products are excreted in urine or bile.
- The tropic hormones of the pituitary are inactivated and degraded in the target tissues. Steroid hormones are degraded in liver.

POSITIVE AND NEGATIVE FEEDBACH REGULATION

- Their synthesis and secretion take place incessantly to readily compensate their loss and to maintain their appropriate levels in blood.
- This controlled production of peripheral hor mones is effected by a self-regulating mechanism, which involves a mutually exclusive interhormonal relationship, often called “plus-minus interaction”

Negative Feedback

- With very few exceptions (e.g., the cells which produce growth hormone), the secretory activities of endocrine tissues are modulated by negative feedback in this case, the excessive concentration of a particular hormone, or the response of a target tissue to such a high

concentration, indirectly inhibits the further production of that hormone, This checks a further increase in its concentration.

- The rate of hormone production is usually determined by the body's need for the hormone.
- So hormone production is regulated in such a way that under normal conditions there is neither hyposecretion nor hypersecretion.
- Negative feedback mechanism two kind
  3. short loop feedback
  4. long loop feedback

equipping with excellence

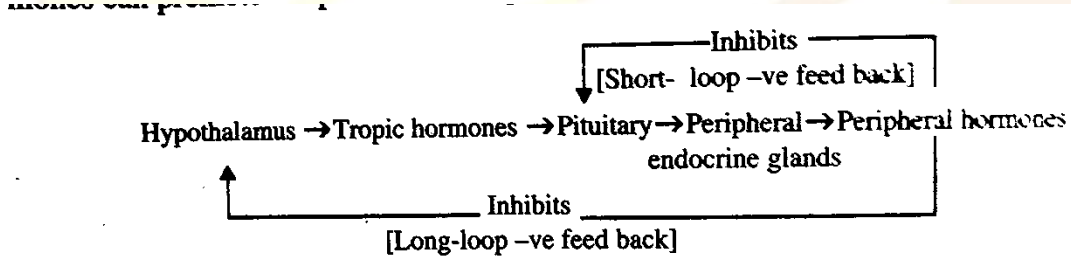
1. Short loop feedback

- A product of the target tissue, or an effect produced by it, acts directly back upon the endocrine tissue and keeps the hormone secretion under check.

2. Long loop feedback

- Long loop feedback also operates on the same principle, but it includes more elements.
- Eg:-

  Some hypothalamic hormones promote the release of pituitary tropic hormones which, in turn, stimulate the production and secretion of peripheral hormones



Feed-back control of hormone secretion

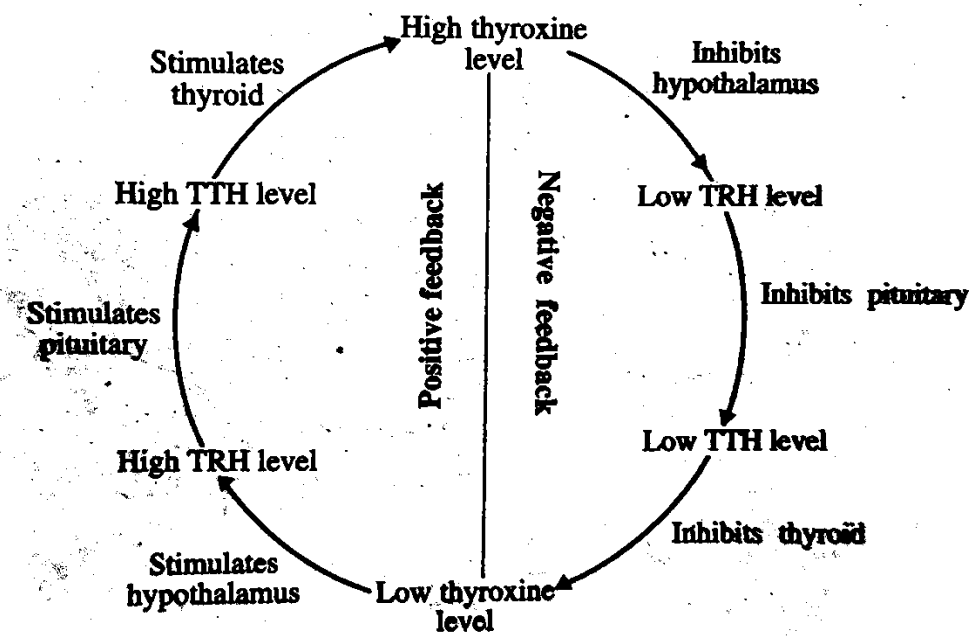
- Overproduction or high concentration of the peripheral hormones normally inhibits the further production of the pituitary tropic hormones by negative feed-back.
- This is accomplished by inhibiting either the pituitary cells (short-loop feed-back) or the neuro-secretory cells of the hypo thalamus (long-loop feedback).
- In the same manner, the hyposecretion of peripheral hor mones can promote the production of pituitary or hypothalmic hormones.
- Production of thyroxine is a typical example of long-loop feedback control. Thyroxine production is stimulated by the pituitary hormone thyrotropin (TTH).
- The production and release of thyrotropin is stimulated by the thyrotropin releasing hormone (TRH) of hypothalamus. (The production and action of this hormone, in turn, is controlled by the thyroxine level in blood.
- High thyroxine level inhibits the production and action of TRH. Low TRH level leads to low thyrotropin production which, in turn, causes low thyroxine Synthesis.

- On the other hand, (low thyroxine level stimulates the production and action of TRH High TRH level promotes the production of TTH which, in turn, leads to high thyroxine synthesis.
- High thyroxine level leads to low thyroxine production. This is called negative feedback. On the other hand low thyroxine level enhances thyroxine production.
- The production of parathormone (PTH) is an example of short-loop feedback mechanism.
- PTH controls blood calcium level in the body.
- Its over-production abnormally raises blood calcium level.
- This high blood calcium level, in turn, serves as a stimulus to inhibit PTH production.
- Similarly, (under- production of PTH abnormally lowers blood calcium level.
- This low blood calcium level acts as a stimulus to promote PTH production
- Thus, low concentration of PTH stimulates its further production, and its high concentration inhibits its further production

Positive Feedback

- Positive feedback produces a response that continues to increase in order to produce the desired effect
- In this mechanism, the activity of a hormone signals the system to produce and release more of the hormone
- An example of a positive feedback mechanism is the release and response of oxytocin during childbirth
- The first contractions of the uterus signal the body to release oxytocin
- Oxytocin travels to the uterus, where it stimulates more contractions
- The contractions signal back to the body to release more oxytocin, which stimulates more contractions, and so on
- The feedback loop continues until the child is born- the contractions stop, signaling the body to stop releasing oxytocin

CPA COLLEGE OF GLOBAL STUDIES



Flow chart of the feedback regulation of thyroxine production

CPA COLLEGE OF GLOBAL STUDIES

equipping with excellence
CPA COLLEGE OF GLOBAL STUDIES

equipping with excellence
CPA COLLEGE OF GLOBAL STUDIES

equipping with excellence
CPA COLLEGE OF GLOBAL STUDIES

equipping with excellence
CPA COLLEGE OF GLOBAL STUDIES

equipping with excellence
CPA COLLEGE OF GLOBAL STUDIES

equipping with excellence
CPA COLLEGE OF GLOBAL STUDIES

equipping with excellence
CPA COLLEGE OF GLOBAL STUDIES

equipping with excellence
CPA COLLEGE OF GLOBAL STUDIES

equipping with excellence
CPA COLLEGE OF GLOBAL STUDIES

equipping with excellence
CPA COLLEGE OF GLOBAL STUDIES

equipping with excellence
CPA COLLEGE OF GLOBAL STUDIES

equipping with excellence
CPA COLLEGE OF GLOBAL STUDIES

equipping with excellence
CPA COLLEGE OF GLOBAL STUDIES