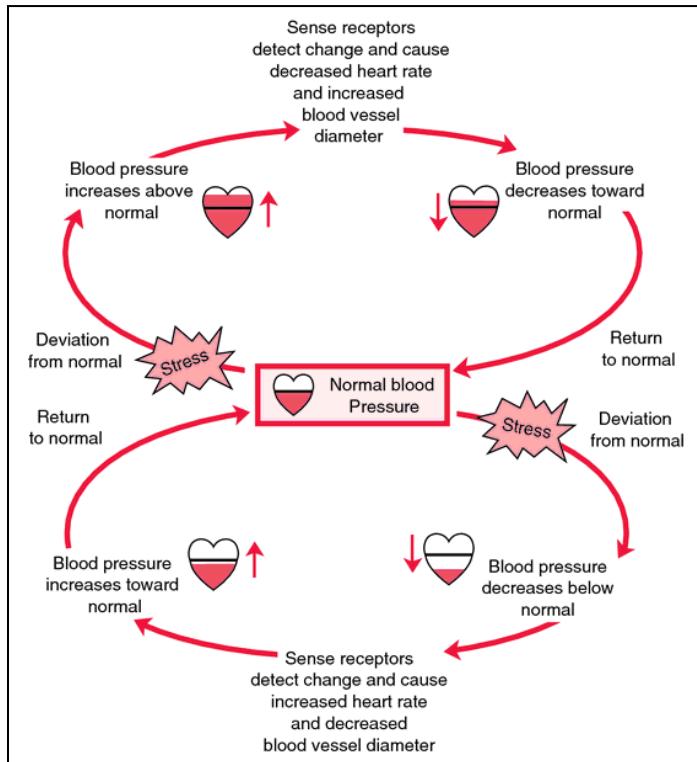




NATIONAL OPEN UNIVERSITY OF NIGERIA

SCHOOL OF HEALTH SCIENCES



COURSE CODE: NSC 104

COURSE TITLE: HUMAN PHYSIOLOGY I
COURSE UNITS: 4 (3-1-2)



COURSE GUIDE NSC 104 – HUMAN PHYSIOLOGY I

COURSE INFORMATION

COURSE CODE: NSC 104

COURSE TITLE: Human Physiology I

COURSE UNITS: 4 Credit units (36 hours of instruction online; 12 hours of Discussion forum online/tutorial; 48 hours of laboratory practical)

YEAR: 1 SEMESTER: 2nd Semester

PRE-REQUISITE COURSES: All courses in the BNSC degree programme in the first year

CON-CURRENT COURSES: NSc 102, 106 and 108

SESSION: 2015/2016

COURSE WEBSITE: www.noun.edu.ng/

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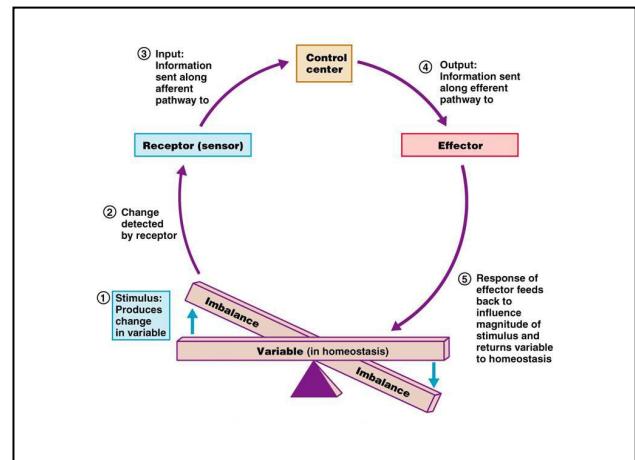
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PROGRAMME LEADER: Prof Mba Okoronkwo OON



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COURSE GUIDE

GENERAL INTRODUCTION

Welcome to the first level course in Human Physiology, NSC 104 – Human Physiology I. This is a first year foundation life science course that you need to be knowledgeable in as a nurse because it provides the foundation about how the body functions. It lays the foundation for a thorough understanding of the physiology and pathophysiology of body organs, hence this course is fundamental to nursing interventions that are evidence based.

COURSE AIM

The aim of this course is to build a solid foundation in understanding of body functions with the purpose of helping you as professionals that will develop care to meet variations in meeting normal and abnormal body physiology.

COURSE OBJECTIVES

At the completion of this course, you should be able to:

- i. Discuss the context of the cell as the functional unit of the body.
- ii. Apply the understanding of the mechanisms of dynamics of body fluids, homeostasis and the immune process in understanding changes and the control of the physiological body process of clients.

COURSE IMPLEMENTATION – WORKING THROUGH THIS COURSE

The course will be delivered adopting the blended learning mode, 70% of online but interactive sessions and 30% of face-to-face during laboratory sessions. You are expected to register for this course online before you can have access to all the materials and have access to the class sessions online. You will have hard and soft copies of course materials, you will also have online interactive sessions, face-to-face sessions with instructors during practical sessions in the laboratory. The interactive online activities will be available to you on the course link on the Website of NOUN. There are activities and assignments online for every unit every week. It is important that you visit the course sites weekly and do all assignments to meet deadlines and to contribute to the topical issues that would be raised for everyone's contribution.

You will be expected to read every module along with all assigned readings to prepare you to have meaningful contributions to all sessions and to complete all activities. It is important that you attempt all the Self Assessment Questions (SAQ) at the end of every unit to help your understanding of the contents and to help you prepare for the in-course tests and the final examination. You will also be expected to keep a portfolio where you keep all your completed assignments.

COURSE MATERIALS

Course Guide

Course Text in Study Units

Textbooks (Hard and electronic)

Book of Laboratory Practical

Assignment File/Portfolio

STUDY UNITS

This course comprises 3 modules of 14 units.

Module 1 - Cell Physiology

Unit 1: The Cell

Unit 2: Transport Across Cell membrane

Unit 3: Biologically important molecules and their functions

Unit 4: Homeostasis

Unit 5: Nerve and Muscle Physiology

Module 2- Blood Physiology

Unit 1: Body Fluids

Unit 2: Haemostasis.

Unit 3: Immune System.

MODULE 3 - Cardiovascular System

Unit 1 Circulatory System

Unit 2 Cardiac Functioning

Unit 3 Electrocardiography

Unit 4 Cardiac Output and Control of Cardiac Output

Unit 5 Arterial Blood Pressure

Unit 6 Circulatory Shock

REFERENCE TEXTBOOKS

- (i) Fox SI. (2012). Human Physiology. 12th edition, Mc Graw Hill, New York.
- (ii) Ganong WF. (2010). Review of Medical Physiology. 23rd edition, Mc Graw Hill, New York.
- (iii) Guyton AC, Hall JE. (2001). Textbook of Medical Physiology. Harcourt International Edition , 10th edition, W.B. Saunders, Philadelphia.
- (iv) Oyebola DO. (2002). Essential Physiology, Vol 1, Nihort Press.

COURSE REQUIREMENTS AND EXPECTATIONS OF YOU

Attendance of 95% of all interactive sessions, submission of all assignments to meet deadlines; participation in all CMA, attendance of all laboratory sessions with evidence as provided in the log book, submission of reports from all laboratory practical sessions and attendance of the final course examination. You are also expected to:

1. Be versatile in basic computer skills
2. Participate in all laboratory practical up to 90% of the time
3. Submit personal reports from laboratory practical sessions on schedule
4. Log in to the class online discussion board at least once a week and contribute to ongoing discussions.
5. Contribute actively to group seminar presentations.

EQUIPMENT AND SOFTWARE NEEDED TO ACCESS COURSE

You will be expected to have the following tools:

1. A computer (laptop or desktop or a tablet)
2. Internet access, preferably broadband rather than dial-up access

3. MS Office software – Word PROCESSOR, Powerpoint, Spreadsheet
4. Browser – Preferably Internet Explorer, Moxilla Firefox
5. Adobe Acrobat Reader

NUMBER AND PLACES OF MEETING (ONLINE, FACE-TO-FACE, LABORATORY PRACTICALS)

The details of these will be provided to you at the time of commencement of this course

DISCUSSION FORUM

There will be an online discussion forum and topics for discussion will be available for your contributions. It is mandatory that you participate in every discussion every week. Your participation links you, your face, your ideas and views to that of every member of the class and earns you some mark.

COURSE EVALUATION

There are two forms of evaluation of the progress you are making in this course. The first are the series of activities, assignments and end of unit, computer or tutor marked assignments, and laboratory practical sessions and report that constitute the continuous assessment that all carry 30% of the total mark. The second is a written examination with multiple choice, short answers and essay questions that take 70% of the total mark that you will do on completion of the course. Students evaluation: The students will be assessed and evaluated based on the following criteria.

- **In-Course Examination:** In-course examination will come up in the middle of the semester. This would come in form of Computer Marked Assignment. There would also be one compulsory Tutor Marked Assignment (TMA's) and Computer Marked Assignment that come after every module.
- **Laboratory practical:** Attendance, record of participation and other assignments will be graded and added to the other scores from other forms of examinations.
- **Final Examination:** The final written examination will come up at the end of the semester comprising essay and objective questions covering all the contents covered in the course. The final examination will amount to 60% of the total grade for the course.

Learner-Facilitator evaluation of the course

This will be done through group review, written assessment of learning (theory and laboratory practical) by you and the facilitators.

GRADING CRITERIA

Grades will be based on the following Percentages

Tutor Marked Individual Assignments	10%	30%
Computer marked Assignment	10%	
Group assignment	5%	
Discussion Topic participation	5%	
Laboratory practical	10%	

End of Course examination 70%

GRADING SCALE

A = 70-100

B = 60 - 69

C= 50 - 59

F = \leq 49

SCHEDULE OF ASSIGNMENTS WITH DATES

To be provided for each module by the facilitator in addition to the ones already spelt out in the course materials.

SPECIFIC READING ASSIGNMENTS

To be provided for each module

COURSE OVERVIEW

Human Physiology (I)

Physiology is the scientific study of how the body works under normal conditions or in a state of good health. It describes how cells operate, how they combine their functions in specific organs, and how these organs work together to maintain a stable environment inside the body. Physiology is the functional basis of the health sciences, because most disease states are the result of disturbances of physiological processes. A basic knowledge of physiology is therefore essential for all students whose professional careers will involve aspects of health and patient care. Physiology is also one of the key subjects in biomedical science and continues to be at the forefront of biomedical research. Human Physiology (I) is the first of two courses that runs in the second year of your programme. This course covers the cell physiology, the maintenance of homeostasis, muscle functioning and the immune processes.

HOW TO GET THE MOST FROM THIS COURSE

1. Read and understand the context of this course by reading through this course guide. paying attention to details. You must know the requirements before you will do well.
2. Develop a study plan for yourself.
3. Follow instructions about registration and master expectations in terms of reading, participation in discussion forum, end of unit and module assignments, laboratory practical and other directives given by the course coordinator, facilitators and tutors.
4. Read your course texts and other reference textbooks.
5. Listen to audio files, watch the video clips and consult websites when given.
6. Participate actively in online discussion forum and make sure you are in touch with your study group and your course coordinator.
7. Submit your assignments as at when due.
8. Work ahead of the interactive sessions.

- 9.** Work through your assignments when returned to you and do not wait until when examination is approaching before resolving any challenge you have with any unit or any topic.
- 10.** Keep in touch with your study centre, the NOUN, School of Health Sciences websites as information will be provided continuously on these sites.
- 11.** Be optimistic about doing well.

COURSE MATERIAL

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MODULE 1- Cell Physiology

Introduction

The human body is made of several cells that perform basic functions that sustain life. Different types of cells aggregate to form organs that ultimately perform different functions. While different organs perform different functions, the body must function in harmony. This module covers cell functioning and body's methods of achieving harmony through homeostasis.

Module Objectives

At the end of this module, you should be able to:

- i. Discuss how the cell performs the various functions.
- ii. Discuss how the plasma membrane performs its functions
- iii. Discuss how the body sustain homeostasis with contribution from the different body systems

Contents

- Unit 1:** The Cell
Unit 2: Transport across cell membrane
Unit 3: Biologically important molecules and their functions
Unit 4: Homeostasis
Unit 5: Nerve and Muscle Physiology

UNIT ONE - THE CELL

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- 1.0** Introduction
- 2.0** Objectives
- 3.0** Main Content
 - 3.1** Organization of the cell
 - 3.2** Cell Structure
 - 3.3** Cell or Plasma Membrane
- 4.0** Conclusion
- 5.0** Summary
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- 6.1** Activity
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1.0 Introduction

The basic living unit of the body is the cell. Each organ is an aggregate of many different cells held together by intercellular supporting structures. Each type of cell is specially adapted to perform one or a few particular functions. For instance, the red blood cells, numbering 25 trillion in each human being, transport oxygen from the lungs to the tissues.

2.0 Objectives

At the end of this unit, you should be able to:

- i. Explain the Organization of the cell
- ii. Explain 3 different substances that make up the cell
- iii. Give detailed explanation of the Cell Structure
- iv. Draw a typical cell showing the organelles in the cytoplasm and the nucleus.
- v. Explain the functions following concepts- (a) Nucleus (b) Cytoplasm (c) Endoplasmic reticulum and ribosomes (d) Golgi apparatus (e) Mitochondria (f) Centrosome (g) Lysosomes
- vi. Describe the Cell or Plasma Membrane

3.0 Main Content

3.1 Organization of the cell

The cell has two major parts namely the nucleus and the cytoplasm. The nucleus is separated from the cytoplasm by a nuclear membrane, and the cytoplasm is separated from the surrounding fluids by a cell membrane, also called the plasma membrane. The different substances that make up the cell are collectively called protoplasm. Protoplasm is composed mainly of five basic substances: water, electrolytes, proteins, lipids, and carbohydrates.

The Protoplasm

Water

The principal fluid medium of the cell is water, which is present in most cells, except for fat cells, in a concentration of 70% to 85%. Many cellular chemicals are dissolved in the water. Others are suspended in the water as solid particulates. Chemical reactions take place among the dissolved chemicals or at the surfaces of the suspended particles or membranes.

Electrolytes (Ions)

The most important ions in the cell are potassium, magnesium, phosphate, sulfate, bicarbonate, and smaller quantities of sodium, chloride, and calcium. The ions provide inorganic chemicals for cellular reactions. Also, they are necessary for operation of some of the cellular control mechanisms. For instance, ions acting at the cell membrane are required for transmission of electrochemical impulses in nerve and muscle fibers.

Proteins

After water, the most abundant substances in most cells are proteins, which normally constitute 10% to 20% of the cell mass. These can be divided into two types: structural proteins and functional proteins.

Lipids

The biologically important lipids are the fatty acids, triglycerides, phospholipids and sterols. Fatty acids can be saturated or unsaturated while phospholipids are found in cell membranes where they act as a structural component. Fatty acids also serve as an important source of energy in the body.

Carbohydrates

Carbohydrates are organic molecules made up of equal amounts carbon and water. They perform both structural and functional roles. They also help in cell signaling. They are a very important source of energy in the body.

3.2 Cell structure

The cell is not merely a bag of fluid, enzymes, and chemicals; it also contains highly organized living structures, called intracellular organelles. The physical nature of each organelle is as important as the cell's chemical constituents for cell function. For instance, without one of the organelles, the mitochondria, more than 95% of the cell's energy release from nutrients would cease immediately. The most important organelles and other structures of the cell are shown in Figure 1.1.

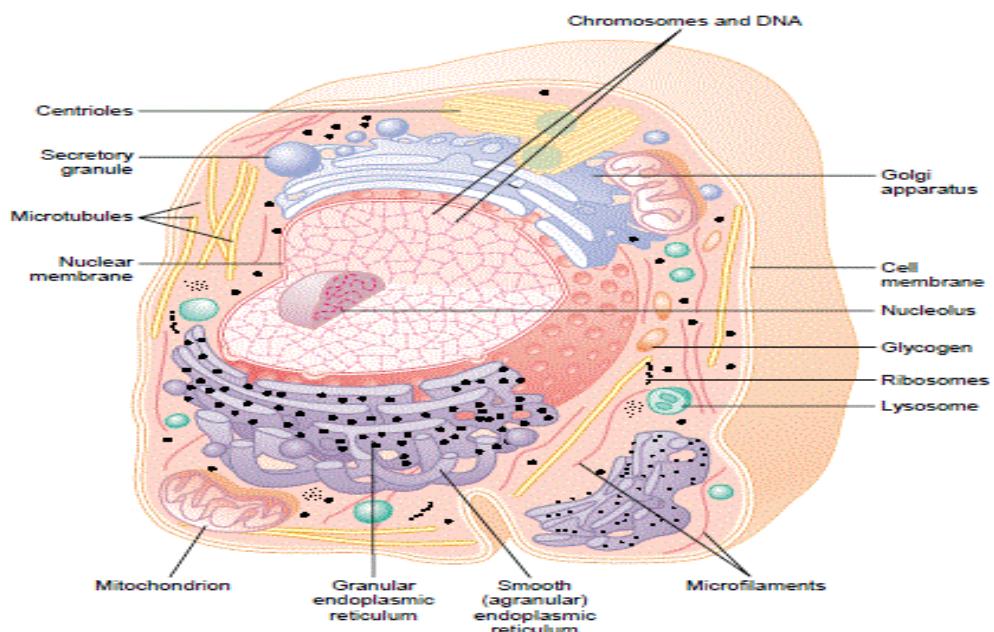


Figure 1.1: A typical cell, showing the organelles in the cytoplasm and the nucleus.

Nucleus

The nucleus, shown in Figure 1-2, is usually a spherical organelle, though its shape may vary in some cells. It is surrounded by a membrane called nuclear membrane. The nuclear membrane has double layer and the two layers are fused at some points to produce nuclear pores which are thought to allow molecules pass between the nucleus and cytoplasm. There is a smaller spherical structure within the nucleus, the nucleolus. The fluid contained within the nucleus is called nucleoplasm to differentiate it from the fluid in the rest of the cell which is referred to as cytoplasm. The nucleus is best seen in a cell that has been stained because the chromatin within the nucleus stains vividly. In the unstained state, chromatin is colourless. Chromatin gives rise to the chromosomes when a cell divides. Chromosomes are primarily composed of deoxyribonucleic acid (DNA). DNA is the basic substance for inheritance. The second basic

substance of inheritance is ribonucleic acid (RNA) which is generally contained within the nucleolus.

During cell division, genetic information contained in DNA is transferred to RNA, which carries the genetic information out of the nucleus into the cytoplasm where it directs the formation of protein. Thus, the nucleus is the repository of genetic information for the whole body.

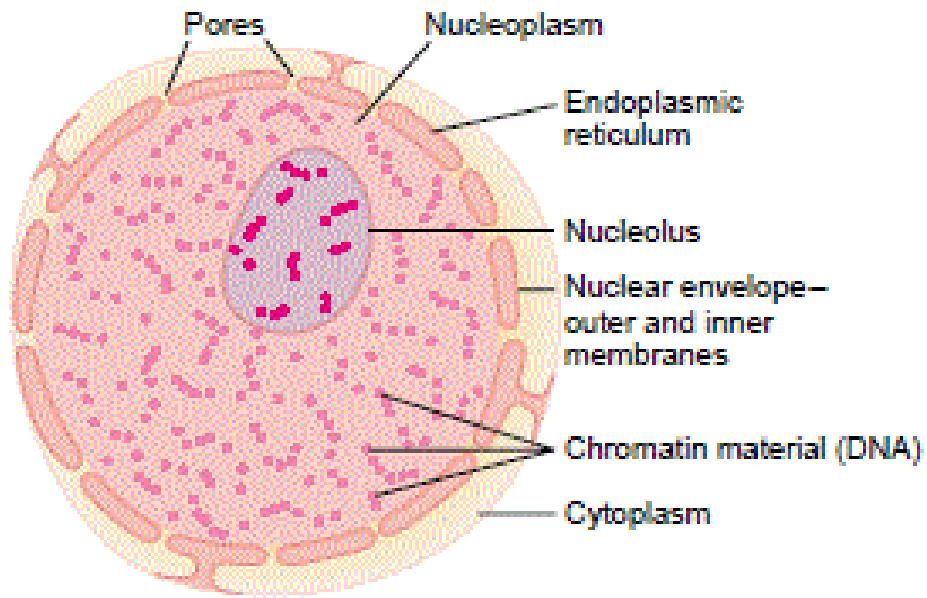


Figure 1.2: Structure of the nucleus

Cytoplasm

This is the jelly-like fluid between the nuclear membrane and the cell membrane inside which the cell organelles are suspended. The clear liquid portion in which the particles are suspended is called the cytosol. Cytoplasm is mostly water but it contains electrolyte and about 15% protein plus fat and carbohydrate. The cytoplasm comprises about 80% of the total weight of the cell.

Endoplasmic reticulum and ribosomes

There are small cytoplasmic tubules collectively called the endoplasmic reticulum. Some tubules of the endoplasmic reticulum have small, spherical structures called ribosomes attached to their membranes. Where these are present, the reticulum is called the granular or rough endoplasmic reticulum. Other tubules are free of ribosomes. This part is called the agranular, or smooth, endoplasmic reticulum, as shown in Figure 1.3.

The tubules of the granular, ribosome-containing endoplasmic reticulum are involved in the vital processes of protein synthesis and secretion in the cell. A molecule of RNA is formed from the DNA in the nucleus. This RNA is known as messenger RNA (mRNA) because it carries the genetic message from DNA in the nucleus and passes through the pores in the nuclear membrane to enter the cytoplasm. The mRNA then becomes attached to ribosomes, where it directs the formation of proteins. Once synthesized, protein enters the tubules of the endoplasmic reticulum. After the protein accumulates in the tubules, parts of the tubules break off to become spherical vesicles containing quantities of protein. These vesicles then become part of the golgi apparatus and the protein is eventually secreted from the cell.

The agranular endoplasmic reticulum does seem to be involved in protein synthesis; yet many hormones are found stored in these tubules. In the cells of glands that secrete hormones, such as the thyroid gland, the agranular endoplasmic reticular tubules contain large quantities of the hormone. Smooth endoplasmic reticulum is involved in the synthesis of lipid steroid hormones and, in liver cells, contains the enzymes which catalyze glycogen breakdown.

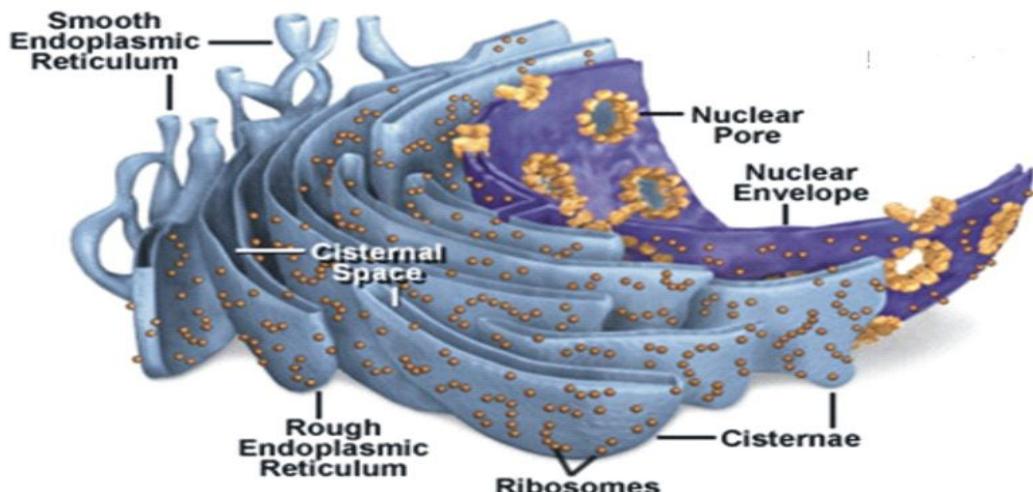


Figure 1.3: Structure of the endoplasmic reticulum

Golgi apparatus

The Golgi apparatus, also referred to as the Golgi complex or golgi body, shown in Figure 1–4, appears as a collection of tubules and vesicles. Secretory granules are formed in the Golgi apparatus. These granules are packages of highly concentrated protein. Once protein has been formed by the ribosomes, it accumulates in the Golgi apparatus where it is concentrated and may be modified and then packaged into vesicles of secretory granules. These vesicles fuse with the membrane and then open up to release the protein from the cell. Carbohydrate may be added to the protein within the Golgi body to form glycoproteins. Mucus is also formed in this area.

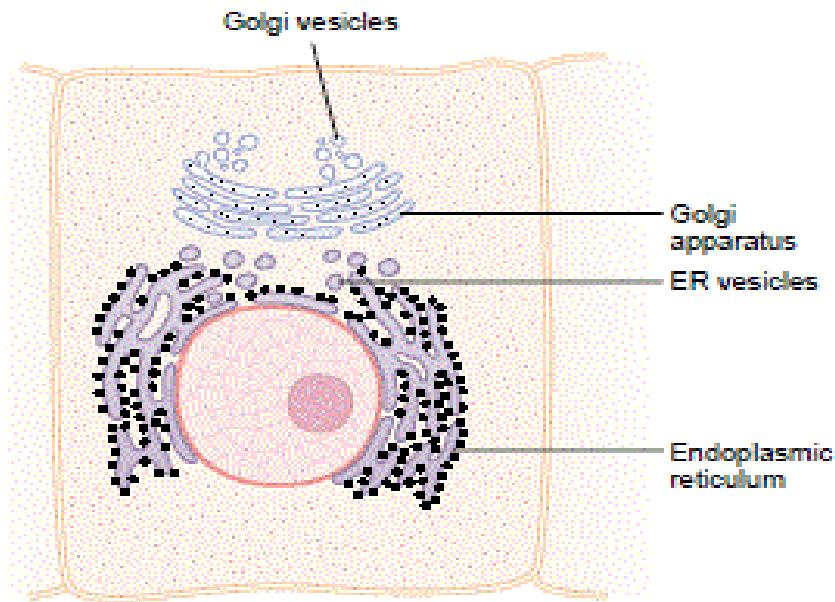


Figure 1.4: A typical golgi apparatus and its relationship to the endoplasmic reticulum (ER) and the nucleus.

Mitochondria

The mitochondrion, shown in Figure 1.5, is called the “powerhouse” of the cell. Without the mitochondria, cells would be unable to extract enough energy from the nutrients, and essentially all cellular functions would cease. In the mitochondria, the very important compound adenosine triphosphate (ATP) is formed. ATP is said to be a high-energy phosphate compound because, when it splits off a phosphate molecule to become adenosine diphosphate (ADP), energy is made available to the cell. This energy is used for the various cellular processes, such as the contraction of a muscle cell.

Mitochondria are found in varying numbers in all nucleated cells. They may be distributed evenly throughout the cytoplasm or concentrated in areas of high energy requirement; for example they lie between the fibrils of muscle fibres where they produce energy for contraction. Each mitochondria is bounded by a smooth outer membrane which is separated by a small space of about 8nm from a folded inner membrane. These folds are called cristae and they are studded with minute particles. The inner and outer membranes, the space between them, the membrane bound particles and the inner matrix contains enzymes. All of the enzymes which break down nutrient substances into carbon dioxide and water, together with the enzymes which enable the transfer of released energy to stable high-energy compounds are present within the mitochondrial structure. Virtually all of the cell’s high-energy compounds are synthesized within the mitochondria.

Mitochondria can increase its own number by repeated self-replication. This occurs when there is need for increased amounts of ATP in the cell. Mitochondria contain deoxyribonucleic acid (DNA) similar to that found in the nucleus. The DNA of the mitochondrion, like that in the nucleus, controls its replication.

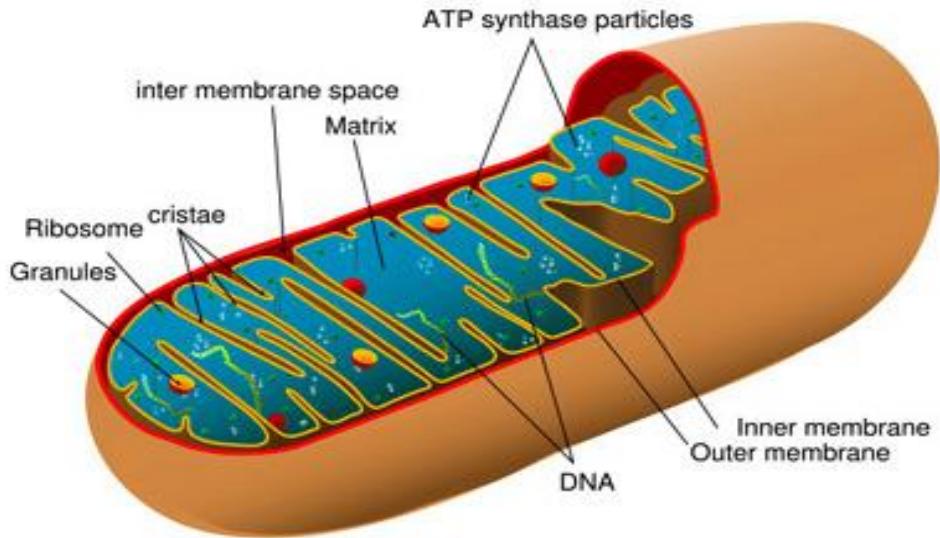


Figure 1.5: Structure of a mitochondria

Centrosome

The centrosome contains two centrioles. They lie close to the nucleus. At the beginning of cell division, the two centrioles divide, thus forming four centrioles, one pair goes to one end of the cell and the other pair to the opposite end. The centrioles function to pull the chromosome pairs apart. In this way, one set of chromosomes goes to one side of the cell and the other set to the other. When the cell divides, each new cell has a complete set of chromosomes.

Lysosomes

Lysosomes are vesicular organelles that form by breaking off from the Golgi apparatus and then dispersing throughout the cytoplasm. When a cell engulfs bacteria, the bacteria come in contact with the lysosomal enzymes, which then destroy them. When a cell dies, the lysosomal membrane disintegrates and the enzymes are freed to act on the cellular debris to digest it. Hence, lysosomes are often referred to as suicide bags. Hence, lysosome functions as a form of digestive system for the cell. Each lysosome is filled with large numbers of small granules which are protein aggregates of hydrolytic (digestive) enzymes. The main substances lysosome digest are proteins, carbohydrates, lipids.

Peroxisomes

Peroxisomes are also small membrane-bound bodies which are similar in appearance to lysosomes. They contain catalase which causes the breakdown of hydrogen peroxide. The peroxisomes membrane contains some peroxisome – specific proteins that are concerned with the transport of substances into and out of the matrix of the peroxisome. The matrix contains more than 40 enzymes and these enzymes operate in concert with other enzymes outside the peroxidase to catalyze reactions, including the catabolism of very long chain fatty acids.

3.3 Cell or Plasma Membrane

The membrane that surrounds the cell is called the cell membrane. It is also referred to as the plasma membrane. Figure 6 shows the structure of the cell membrane. The cell membrane is composed primarily of membrane protein and lipid and is about 7.5 nm (75 Angstrom units) thick. They are semipermeable allowing some substances to pass through and excluding others. The major lipids are phospholipids and the approximate composition of the cell membrane is proteins, 55 per cent; phospholipids, 25 per cent; cholesterol, 13 per cent; other lipids, 4 per cent; and carbohydrates, 3 per cent. The accepted model concept of the structure of the cell membrane is that of a fluid mosaic model. According to this concept, the lipid bilayer is in form of a fluid and membrane protein mostly lipoprotein and glycoprotein, which are loosely attached and embedded in a bilayer matrix.

Figure 6 also shows globular masses floating in the lipid bilayer. These are membrane proteins, most of which are glycoproteins. The protein components of the cell membrane are of two main types- integral proteins and peripheral proteins. Integral protein pass all the way through the cell membrane, whereas, peripheral protein are attached to the outside or inside of the cell membrane. The integral protein provide pathway through which the water soluble substance diffuses through the extra and intracellular fluid. The peripheral protein functions almost entirely as enzyme. The membrane lipid makes up the matrix that give the shape and structure to the cell membrane and embedded in this matrix are the membrane proteins. All membrane contain phospholipid and glycolipid which are amphipathic in nature (possess two coat).

The lipids are characterized by having hydrophobic and hydrophilic ends. The hydrophilic end of the bi-lipid molecule are repel by water but attracted to each other, as shown in Figure 6. Membrane lipids are almost impermeable to water and water soluble substances such as ions, glucose, urea, etc. while lipid soluble substances such as oxygen, carbon dioxide, alcohol can penetrate easily.

The proteins in the cell membrane carry out many functions. They serve as:

- (1) Pumps which are actively involved in transporting ions across the membrane e.g. Na^+ - K^+ pump.
- (2) Carriers transporting substances down the electrochemical gradient by a process called facilitated diffusion.
- (3) Ion channels which when activated permit the passage of ions into or out of the cell.
- (4) Receptors that bind neurotransmitter and hormone initiating physiological changes inside the cell.
- (5) Enzyme catalyzing reaction at the surface of the membrane
- (6) Antigen and antibodies, the antigenic properties of the cell depend on the protein outside.

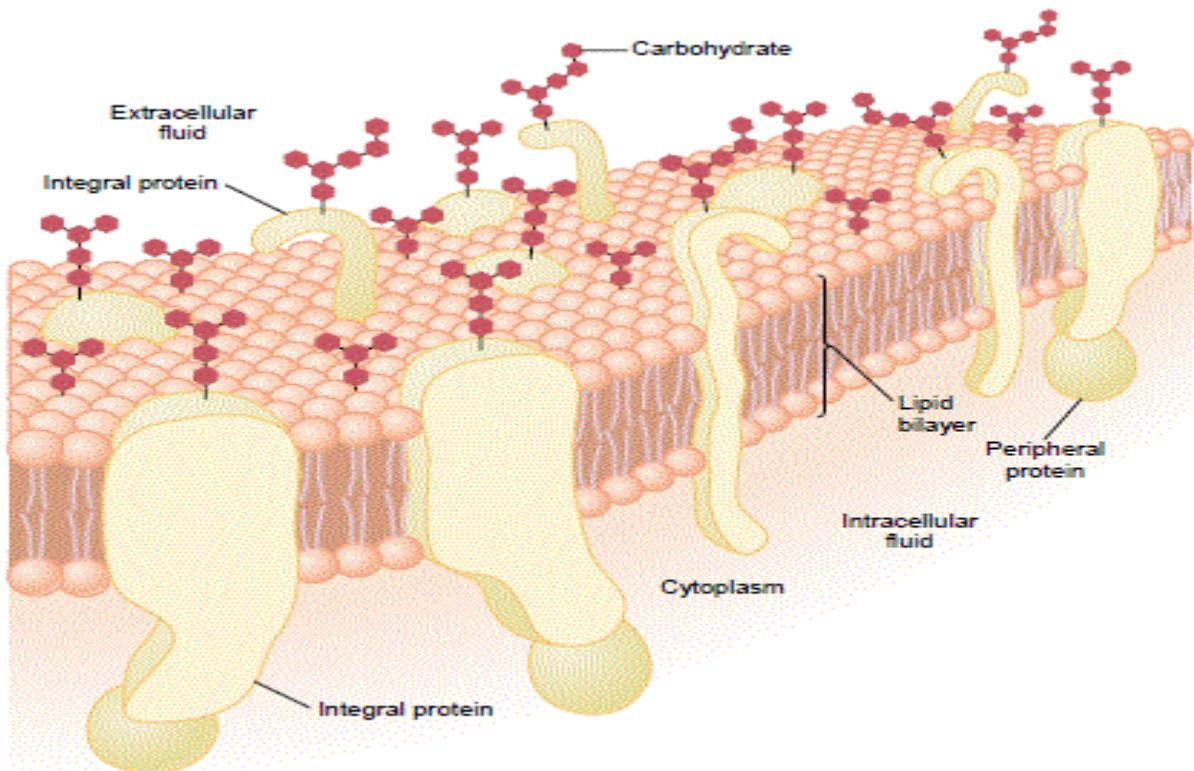


Figure 1.6: Structure of the cell membrane

4.0 Conclusion

The cell is the basic unit of life with many structures organized to perform different functions that keep the cell alive.

5.0 Summary

In this unit, you have learnt that:

The cell has two major parts, the nucleus and the cytoplasm with different substances all called protoplasm. The cell is made up of many structures and substances that perform diverse functions. The important parts of the cell that perform different functions include the Nucleus, the Cytoplasm, the Endoplasmic reticulum and ribosomes, the Golgi apparatus, the Mitochondria, Centrosome, the Lysosomes to mention a few. You have also learnt that the cell or plasma membrane made up of protein and lipid perform about six listed functions.

6.0 Tutor Marked Assignments

6.1 Activity

Check this <https://www.youtube.com/watch?v=kV1r2oVIHLI>

Checking Youtube, pick the video that best helps you learn about the cell and its functions and share the information with your colleagues in the discussion forum online

6.2 Answer the following questions:

- Explain the Organization of the cell

- ii. Explain 3 different substances that make up the cell
- iii. Give detailed explanation of the Cell Structure
- iv. Draw a typical cell showing the organelles in the cytoplasm and the nucleus.
- v. Explain the following concepts- (a) Nucleus (b) Cytoplasm (c) Endoplasmic reticulum and ribosomes (d) Golgi apparatus (e) Mitochondria (f) Centrosome (g) Lysosomes
- vi. Describe the Cell or Plasma Membrane

7.0 References and other resources

- Fox SI. (2012). Human Physiology. 12th edition, Mc Graw Hill, New York.
 Ganong, W.F. (2010). Review of Medical Physiology. 23rd edition, Mc Graw Hill, New York.
 Guyton, A.C, Hall J.E. (2001). Textbook of Medical Physiology. Harcourt International Edition , 10th edition, W.B. Saunders, Philadelphia.
 Oyebola DO. (2002). Essential Physiology, Vol 1, Nihort Press.

UNIT TWO - TRANSPORT ACROSS CELL MEMBRANE

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- 2.0** Objectives
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 - 3.1** Simple diffusion
 - 3.2** Facilitated diffusion
 - 3.3** Active transport
 - 3.4** Secondary active transport
 - 3.5** Osmosis
 - 3.6** Endocytosis
 - 3.7** Exocytosis
 - 3.8** Solvent drag
- 4.0** Conclusion
- 5.0** Summary
- 6.0** Tutor Marked Assignments
- 6.1** Activity
- 6.2** Tutor Marked Tests
- 7.0** References and other resources

1.0 Introduction

No cell is an island and life is only possible because several cells that make up the various organs of the body communicate. There is movement of substances across the cells and this is facilitated through various media. In this unit, you are going to learn about how solutes and solvents are transported across the cells.

2.0 Objectives

At the end of this unit, you should be able to explain the following concepts in details.

- i. Simple diffusion
- ii. Facilitated diffusion
- iii. Active transport
- iv. Secondary active transport
- v. Osmosis
- vi. Endocytosis
- vii. Exocytosis
- viii. Solvent drag

3.0 Main Content

3.1 Simple diffusion

This is the movement of the molecules of a substance from a region of higher concentration to that of lower concentration. This movement continues until the molecules are evenly distributed in the two regions, as demonstrated in Figure 1-9. It involves the movement of substances down their concentration gradient, it is a passive process that is it does not require energy. It is not carrier mediated. It does not display inhibition, either competitive or not. It is not saturable.

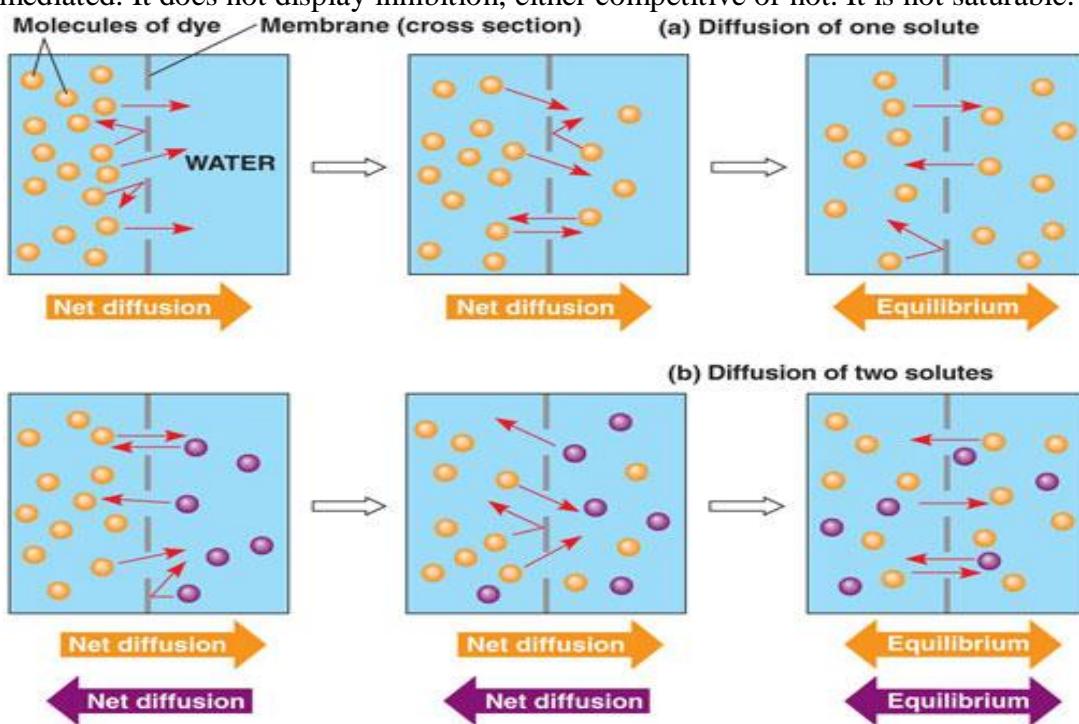


Figure 2.1: Movement of molecules by simple diffusion

3.2 Facilitated diffusion

This is a carrier mediated transport and it involves some transport proteins that transport substances of larger molecules across the cell membrane. (Figure 1-10). It transports substances down their concentration gradients, thus it also is a passive process. It is saturable and exhibits the characteristics of inhibition either competitive or non-competitive. A typical example of

facilitated diffusion is the glucose transport by glucose transporters which move glucose down the concentration gradient from extracellular fluid into cytoplasm of the cell.

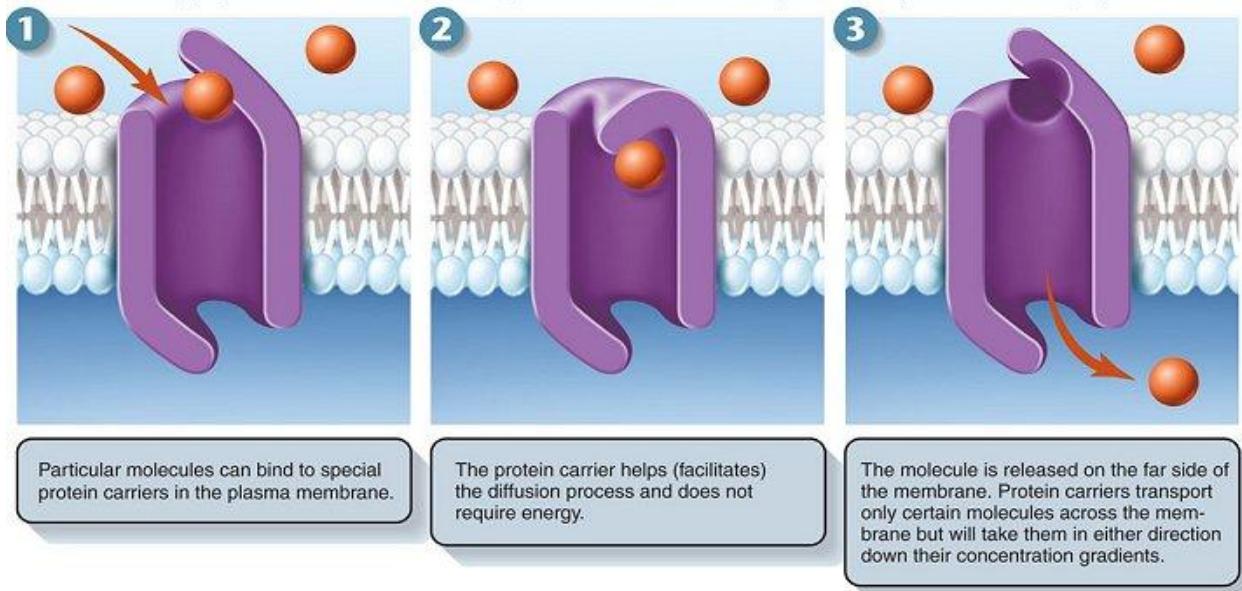


Figure 2.2: Movement of molecules by facilitated diffusion using carrier protein

3.3 Active transport

As the name implies it is an active process that requires energy. It transports substances against the concentration gradient. It is also carrier mediated and saturable. It exhibits the characteristics of inhibition either competitive or non-competitive. Energy that is utilized for this transport is obtained from adenosine triphosphate (ATP) hydrolysis. A typical example of active transport is the transport of sodium ion out of the cell against its concentration gradient and the active transport of potassium ion into the cell against its own concentration gradient by the $\text{Na}^+ - \text{K}^+$ pump ($\text{Na}^+ - \text{K}^+$ ATPase). For every, Na^+ pumped out by this pump, 2K^+ is pumped in.

Figure 1–11 shows the basic physical components of the $\text{Na}^+ - \text{K}^+$ pump. The pump consists of a carrier protein which is a complex of two separate globular proteins, a larger one having a molecular weight of 100,000 and the small one has molecular weight of 45,000. Though, the function of the smaller one is not known. The larger protein has specific features that are very important for the pump.

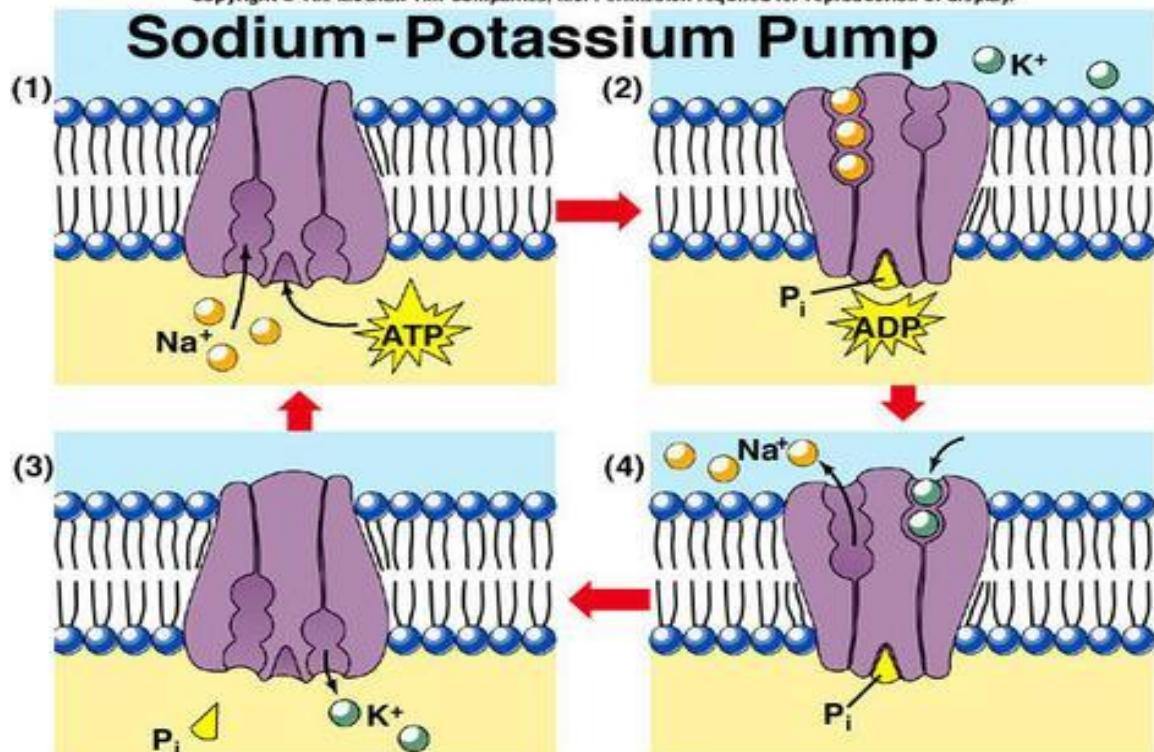


Figure 2.3: Mechanism of the sodium-potassium pump. ADP, adenosine diphosphate; ATP, adenosine triphosphate; P_i , phosphate ion.

3.4 Secondary active transport

Classes of transport protein

Some transport protein are uniport because they transport only one substance, others are called symport because the transport requires the binding of more than one substance to the transport protein and then the substances are transported across the membrane, example of symport, is a carrier protein in the intestinal mucosa that is responsible for the co-transport of sodium ion and glucose from the intestinal mucosa into the mucosa cells, other transporter are called antiport because they exchange one substance for the other. The $Na^+ - K^+$ ATPase is a typical example of an antiport. It moves three Na^+ out of the cell in exchange for each two K^+ that is moved into the cell.

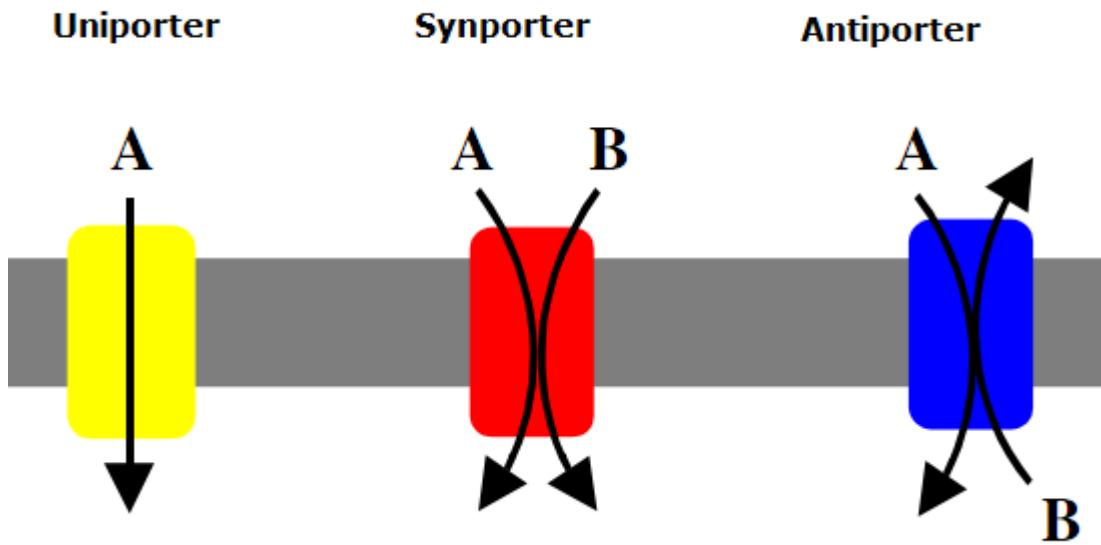


Figure 2.4: Classes of transport protein

Secondary active transport is a carrier mediated transport that involves the binding of two types of substance to the binding site of the carrier. The carrier then transports both substances in or out of the cell as the case maybe. One of these substances is transported down its concentration gradient, while the other is transported against its concentration gradient. The latter substance is being dragged along by the former substance as it moves down its concentration gradient. The driving force for this type of transport is supplied by the concentration gradient of one of the substances but not by ATP. This type of transport is also called Na co-transport.

Glucose and many amino acids are transported into most cells against large concentration gradients; the mechanism of this is entirely by co-transport, as shown in Figure 1–13. Sodium co-transport of glucose and amino acid occur especially in the epithelial cell of the intestinal tract and renal tubule to aid in the absorption of these substances into the blood. A typical example of sodium co-transport is demonstrated in the transport of glucose into the epithelial cells lining the small intestine by a synport. Present in the luminal brush border membrane of the small intestine is a synport that transports glucose into the cell following the binding of Na^+ to that carrier. The Na^+ is transported down its electrochemical gradient while the glucose is transported against its concentration gradient. The electrochemical gradient of sodium provides the driving force for the transport of glucose molecules. Thus, the sodium drag the glucose to transport across the brush border membrane. The electrochemical gradient of sodium is maintained by the $\text{Na}^+ - \text{K}^+$ pump.

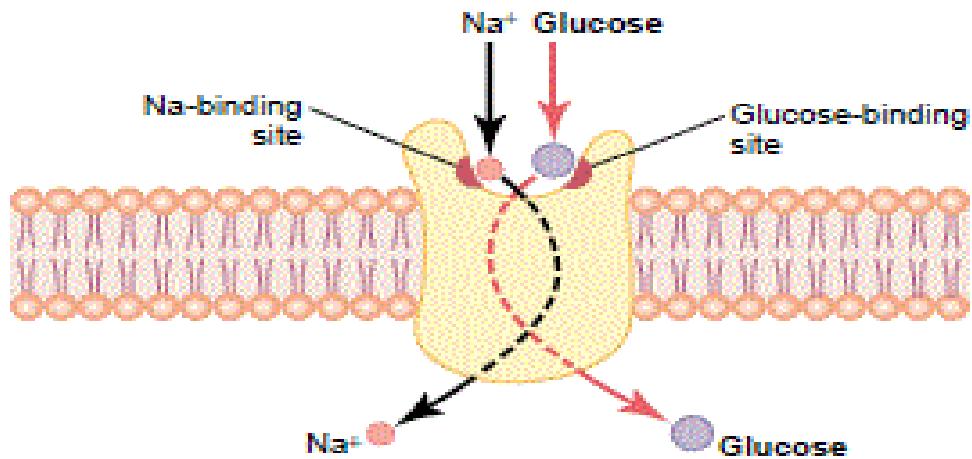


Figure 2.5: Postulated mechanism for sodium co-transport of glucose.

3.5 Osmosis

This is process of diffusion of solvent molecule from a region where there is higher concentration (low solute concentration) to a region where there is lower concentration (higher solute concentration) across a semi-permeable or selectively permeable membrane. To give an example of osmosis, let us assume the conditions shown in Figures 1-14 & 1-15, with pure water on one side of the cell membrane and a solution of sugar and sodium chloride on the other side. When a substance is dissolve in water the concentration of water molecule in the solution is less than that of pure water of equal volume. If the solution is placed on one side of the membrane that is permeable to water and not to solute and an equal volume of water is placed on the other side, water molecule diffuse down their concentration gradient into the solution. This process of diffusion of solvent molecule to a region in which there is a higher concentration of solute to which the membrane is impermeable is called osmosis.

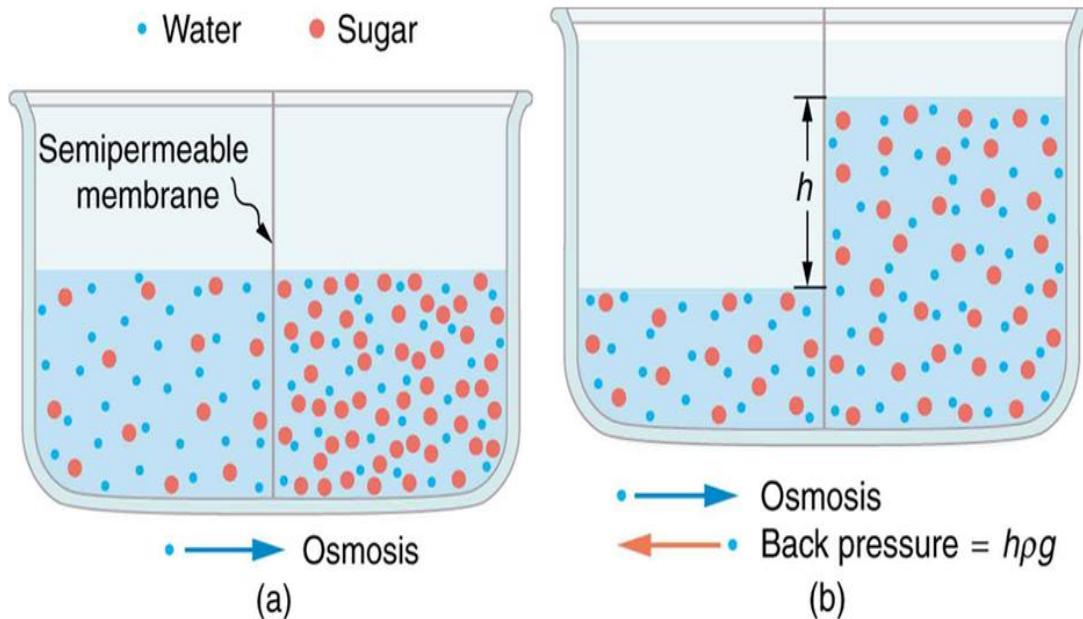


Figure 2.6: Demonstration of osmotic pressure caused by osmosis at a semipermeable membrane

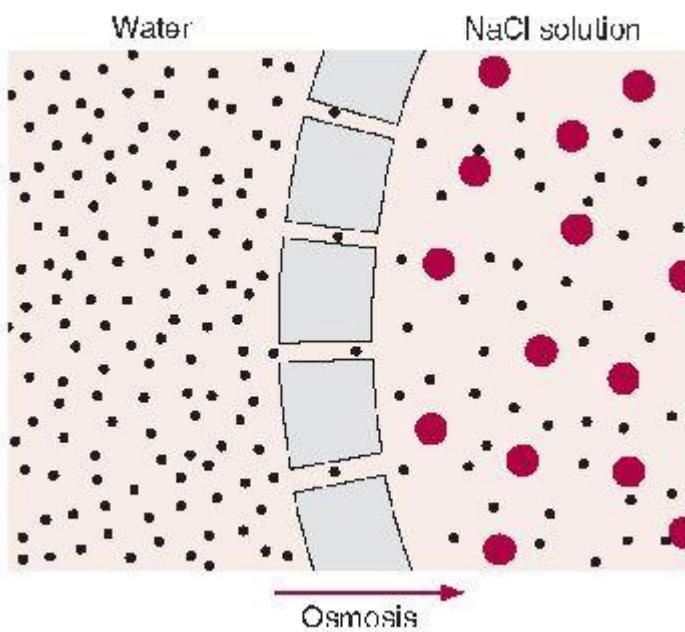


Figure 2.7: Osmosis at a cell membrane when a sodium chloride solution is placed on one side of the membrane and water is placed on the other side.

The tendency for movement of solvent molecule to a region of a greater solute concentration can be prevented by applying a pressure to the mole concentration solution. The pressure necessary to prevent solvent migration is the osmotic pressure of the solution. The osmotic pressure depends upon the number rather than the type of particle in solution.

The term tonicity is used to describe the osmolality of solution relating to plasma, solutions that have the same osmolality as plasma are said to be isotonic, those with higher osmolality are called hypertonic, while those with lesser osmolality are said to be hypotonic. (Figure 1-16).

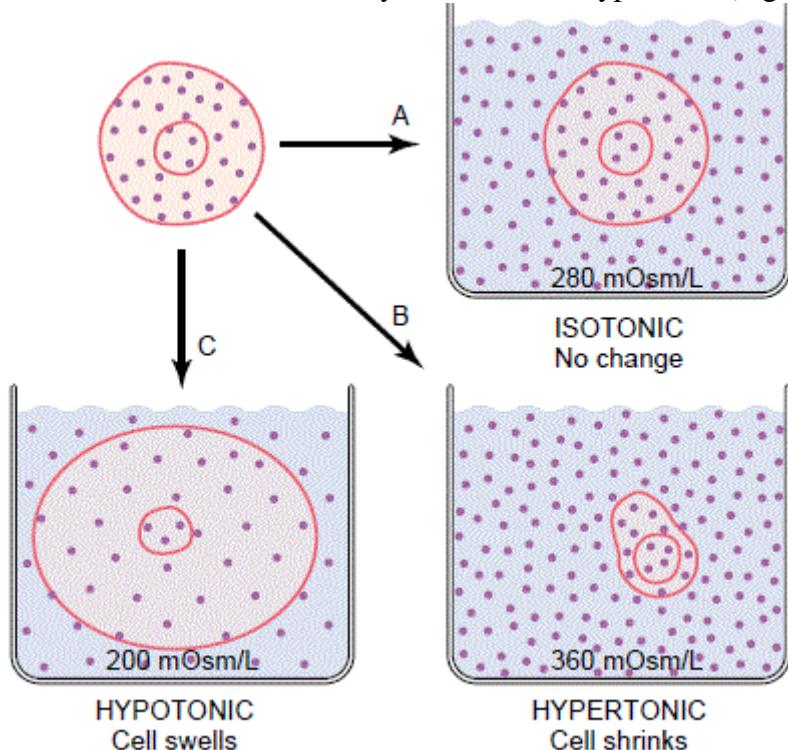


Figure 2.8: Effects of isotonic, hypertonic, and hypotonic solutions on cell volume.

3.6 Exocytosis

This is the process of extrusion of substances out of the cell. Proteins that are secreted by the cell moves from the endoplasmic reticulum to the golgi apparatus, and from the trans-golgi they are extrude into secretory granules or vesicles. These granules move into cell membrane. Their membrane then fuses with the cell membrane and the area of fusion then breaks down. This leaves the content of the granules or vesicle outside the cell while the cell membrane remains intact. This extrusion process required calcium ion and energy.

3.7 Endocytosis

It is the process of ingestion of substances by the cell. It is the reverse of exocytosis. There are two types of endocytosis, these include phagocytosis and pinocytosis. Phagocytosis (cell eating) is the process by which bacteria, dead tissue or other particles visible under the microscope are engulfed by cells such as the polymorphonuclear leukocytes. The material makes contact with the cell membrane which then invaginate leaving the engulf material in the membrane enclosed vacuole while cell membrane remains intact.

Phagocytosis occurs in the following steps:

- i. The cell membrane receptors attach to the surface ligands of the particle.

- ii. The edges of the membrane around the points of attachment evaginate outward within a fraction of a second to surround the entire particle; then, progressively more and more membrane receptors attach to the particle ligands.
- iii. Actin and other contractile fibrils in the cytoplasm surround the phagocytic vesicle and contract around its outer edge, pushing the vesicle to the interior.
- iv. The contractile proteins then pinch the stem of the vesicle so completely that the vesicle separates from the cell membrane, leaving the vesicle in the cell interior in the same way that pinocytotic vesicles are formed.

Pinocytosis means ingestion of minute particles that form vesicles of extracellular fluid and particulate constituents inside the cell cytoplasm. Pinocytosis is essentially the same process like phagocytosis, the only difference begin that the substances ingested are in solution and hence not visible under the microscope. Pinocytosis is the only means by which most large macromolecules, such as most protein molecules, can enter cells.

Figure 1–17 demonstrates the successive steps of pinocytosis, showing three molecules of protein attaching to the membrane. These molecules usually attach to specialized protein receptors on the surface of the membrane that are specific for the type of protein that is to be absorbed. The receptors generally are concentrated in small pits on the outer surface of the cell membrane, called coated pits. On the inside of the cell membrane beneath these pits is a latticework of fibrillar protein called clathrin, as well as other proteins, perhaps including contractile filaments of actin and myosin. Once the protein molecules have bound with the receptors, the surface properties of the local membrane change in such a way that the entire pit invaginates inward, and the fibrillar proteins surrounding the invaginating pit cause its borders to close over the attached proteins as well as over a small amount of extracellular fluid. Immediately thereafter, the invaginated portion of the membrane breaks away from the surface of the cell, forming a pinocytotic vesicle inside the cytoplasm of the cell.

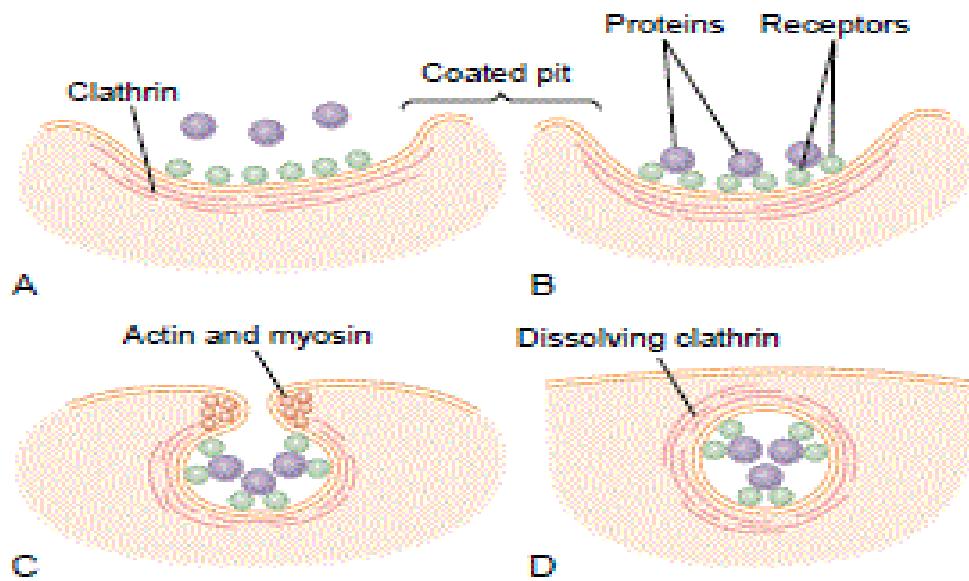


Figure 2.9: Mechanism of pinocytosis

Solvent drag

When solvent is moving in one direction (bulk flow), the solvent tends to drag along some molecules or solutes in that direction, this force is called solvent drag. In most situations in the body, its effects are very small.

4.0 Conclusion

Transportation of materials across cells are made possible through diffusion, osmosis and active transport using different media.

5.0 Summary

In this unit you have learnt that the various mechanisms utilized by the body include simple diffusion, facilitated diffusion, active transport, secondary active transport, osmosis, endocytosis, exocytosis and solvent drag. The various mechanisms allow for exchange of fluid, minerals and molecules across cells.

- i. Solvent drag

6.0 Tutor Marked Assignments

6.1 Activity – check these:

https://www.youtube.com/watch?v=w3_8FSrqc-I

<https://www.youtube.com/watch?v=U9ZfowGuLfk>

<https://www.youtube.com/watch?v=zuNMVzTeCtw>

https://www.youtube.com/watch?v=mzo_B5F7pk4

<http://www.differencebetween.net/science/difference-between-exocytosis-and-endocytosis/>

<http://www.differencebetween.net/science/difference-between-pinocytosis-and-phagocytosis/>

<https://www.youtube.com/watch?v=SSS3EtKAzYc>

Do a summary of what you have learnt from each of the listed sites and submit along with your assignments at the end of this course.

6.2 Tutor Marked Tests

- i. Distinguish between simple and facilitated diffusion
- ii. Explain the Sodium-potassium pump
- iii. Explain the relevance of the knowledge of osmosis to the nurse.

7.0 References and other resources

Fox SI. (2012). Human Physiology. 12th edition, Mc Graw Hill, New York.

Ganong, W.F. (2010). Review of Medical Physiology. 23rd edition, Mc Graw Hill, New York.

Guyton, A.C, Hall J.E. (2001). Textbook of Medical Physiology. Harcourt International Edition , 10th edition, W.B. Saunders, Philadelphia.

Oyebola DO. (2002). Essential Physiology, Vol 1, Nihort Press.

UNIT THREE- BIOLOGICALLY IMPORTANT MOLECULES AND THEIR FUNCTIONS

CONTENT

- 1.0** Introduction
- 2.0** Objectives
- 3.0** Main Content
- 3.1** Carbohydrates
- 3.2** Proteins
- 3.3** Lipids
- 3.4** Nucleic acids
- 4.0** Conclusion
- 5.0** Summary
- 6.0** Tutor Marked Assignments
- 6.1** Activity
- 6.2** Tutor Marked Tests
- 7.0** References and other resources

1.0 Introduction

The body needs digested nutrients to provide energy needed to perform functions and amino acids for body building and repairs. The nutrients in various forms are transported as small molecules of complex organic chemicals either as broken down carbohydrates, proteins, lipids and other forms. In this unit you will be introduced to the small molecules of these nutrients in the forms that they are absorbed.

2.0 Objectives

At the end of this unit, you should be able to

- i. Describe carbohydrates
- ii. Explain the three main classes of carbohydrates
- iii. Discuss the major types of Proteins
- iv. Describe lipids
- v. Describe Nucleic acids

3.0 Main Content

3.1 Carbohydrates

Carbohydrates are organic compounds made of carbon, hydrogen, and oxygen atoms. Carbohydrate are made of monosaccharide (simple sugars molecules) linked together. Their function is to provide a key source of energy for cells. An example is starch, made of many linked glucose molecules. Carbohydrates are divided into three main classes: (i) monosaccharides (ii) disaccharides (iii) polysaccharides.

Monosaccharides

Monosaccharides are simple sugar unit with a general formula $(CH_2O)_n$. The 'n' ranges between 3 and 9. Monosaccharides are all sweet, small crystalline molecules. They are readily soluble in

water and are all reducing sugars. They are classified on the basis of the number of carbon atoms: trioses (3 carbons), tetroses (4 carbon), pentoses (5 carbons). The most common are pentoses and hexoses. Most monosaccharide are metabolic energy sources and serve as building blocks for the synthesis of other macromolecules.

Disaccharides

They are formed when two monosaccharides combine by condensation. The bonds formed between the two monosaccharides units as a result of condensation is called a glycosidic bond. There are several examples of disaccharide, but the most common are maltose, lactose and sucrose.

Polysaccharides

These are made by joining several monosaccharide units. They function mainly as food and energy stores e.g. starch and glycogen or as structural material e.g. cellulose. They are not sweet, non-crystalline, either slightly or insoluble in water.

3.2 Proteins

Proteins are macromolecules with molecular weight of several thousands. They are compounds containing carbon, hydrogen, oxygen, nitrogen, sulphur. There are two distinct types of protein: (1) Fibrous proteins (2) Globular proteins.

Fibrous proteins

Fibrous proteins are insoluble in water and are physically tough. This property enables them to play a structural role in a cell. Major examples of fibrous proteins are:

- (a) Collagen: This is found in bones, skin, tendon and cartilage. This is the most abundant protein in invertebrates and it usually contains three very long polypeptide chains, each with about 1,000 amino acids.
- (b) Keratin: This is found in the outermost layer of the skin and hair, scales, hooves, nails and the feathers of animals. The main function is to protect the body against the environment.
- (c) Fibrinogen: This is blood plasma protein, responsible for blood clotting. With the action of thrombin, fibrinogen is converted into molecules of insoluble protein called fibrin, which forms a network on the surface of wounds to trap blood cells and form clots.

Globular proteins

These are proteins that are soluble in water. They have tertiary and sometimes quaternary structures. They are folded into spherical or globular shapes. They include immunoglobulins or antibodies in the blood, enzymes and some hormones, which are important in maintaining the structure of the cytoplasm.

3.3 Lipids

Lipids are non-polar molecules that are not soluble in water. They include fats, phospholipids, steroids, and waxes. Lipids functions are to provide energy and serve an important part in the structure and functioning of cell membranes. Some examples of lipids include butter (saturated fat), cholesterol (steroid) and ear wax (wax).

3.4 Nucleic acids

Nucleic acids are long chains of smaller molecules called nucleotides. Nucleic acids mainly serve the purpose of providing the organism with its genetic blueprint and coding. Deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) are two types of nucleic acids.

4.0 Conclusion

In this unit, we have learnt that carbohydrates, made of carbon, hydrogen and oxygen atoms are metabolic energy sources and serve as building blocks for the synthesis of other macromolecules. Proteins on the other hand are made up of carbon, hydrogen, oxygen, nitrogen, sulphur while lipids are non-polar molecules that include fats, phospholipids, steroids, and waxes. Nucleic acid provides basis for the genetic blueprint and coding of the DNA and RNA.

5.0 Summary

In this unit, you have learnt that:

- i. Carbohydrates are made up of three classes of monosaccharides, disaccharides and polysaccharides depending
- ii. Proteins are mainly two types, fibrous and globular proteins
- iii. Lipids are non-polar molecules, insoluble in water and include fats, phospholipids, steroids and waxes and examples include saturated fats and cholesterol.
- iv. Nucleic acids

6.0 Tutor Marked Assignments

6.1 Activity – None, see NSC 106 – Medical Biochemistry

6.2 Please answer the following questions:

- i. Differentiate between the three main classes of carbohydrates
- ii. How is fibrous protein different from globular protein
- iii. List two forms of lipids

7.0 References and other resources

Fox SI. (2012). Human Physiology. 12th edition, Mc Graw Hill, New York.

Ganong, W.F. (2010). Review of Medical Physiology. 23rd edition, Mc Graw Hill, New York.

Guyton, A.C, Hall J.E. (2001). Textbook of Medical Physiology. Harcourt International Edition , 10th edition, W.B. Saunders, Philadelphia.

Oyebola DO. (2002). Essential Physiology, Vol 1, Nihort Press.

UNIT FOUR - HOMEOSTASIS

CONTENT

- 1.0** Introduction
- 2.0** Objectives
- 3.0** Main Content
- 3.1** Homeostasis
- 3.2** The body systems
- 3.3** Feedback control systems
- 4.0** Conclusion
- 5.0** Summary
- 6.0** Tutor Marked Assignments
- 6.1** Activity
- 6.2** Tutor Marked Tests
- 7.0** References and other resources

1.0 Introduction

The human body has a remarkable capacity for self-restoration. The Greek physician Hippocrates (father of naturalism and rationalism) commented that human body usually returns to a state of equilibrium by itself and people recover from most illnesses even without the help of a physician. This tendency results from the body's ability to detect change and activate mechanisms that oppose it. In this unit, you will learn about the concept of homeostasis, how the body systems achieves physiological body maintenance through feedback mechanisms.

2.0 Objectives

At the end of this unit, you should be able to:

- i. Define Homeostasis
- ii. Explain the different types of body systems that contribute to homeostasis
- iii. Explain the different types of feedback control systems that the body uses to maintain stability.

3.0 Main Content

3.1 HOMEOSTASIS

Homeostasis is the maintenance of a constant internal environment in an ever changing external environment. It comes from the word *homeo*, which means the sameness, and *stasis*, that is, standing still. This is the maintenance of the constancy of the composition of the internal environment. The mechanisms which work towards its achievement are called homeostatic mechanisms. Essentially all the organs and tissues of the body perform functions that help to maintain these constant conditions. For instance, the lungs provide oxygen to the extracellular fluid to continually replenish the oxygen that is being used by the cells, the kidneys maintain constant ion concentrations, and the gastrointestinal system provides nutrients. Each body system contributes to the homeostasis of other systems and of the entire being. No system of the body works in isolation, and the well-being of the person depends upon the well-being of all the interacting body systems. A disruption within one system generally has consequences for several

additional body systems. Here are some brief explanations of how various body systems contribute to the maintenance of homeostasis.

3.2 The body systems and their contributions to homeostasis

Nervous system

This system is made of the brain, spinal cord, nerves and receptors. The nervous system, along with the endocrine system, serves as the primary control center of the body. It operates at a subconscious level and controls many functions of the internal organs, including the level of pumping activity by the heart, movements of the gastrointestinal tract, and secretion by many of the body's glands. For example, the hypothalamus of the brain is where the body's "thermostat" is found. The hypothalamus also stimulates the pituitary gland to release various hormones that control metabolism and development of the body. The sympathetic and parasympathetic divisions of the nervous system alternatively stimulate or inhibit various bodily responses (such as heart rate, breathing rate, etc.) to help maintain them at optimum levels. It also controls contraction of muscles like the erector pili muscles (involved in thermoregulation) and skeletal muscles. The nervous system also regulates various systems such as respiratory (controls rate and depth of breathing), cardiovascular system (controls heart rate and blood pressure), endocrine organs (causes secretion of ADH and oxytocin), the digestive system (regulates the digestive tract movement and secretion), and the urinary system (helps adjust renal blood flow and also controls voiding the bladder). The nervous system is also involved in sexual behaviours and functions.

Endocrine system

The endocrine system consists of glands hypothalamus, pituitary, thyroid, adrenal testes and ovaries which secrete hormones into the bloodstream. Each hormone has an effect on one or more target tissues. In this way the endocrine system regulates the metabolism and development of most body cells and body systems. Bone growth is regulated by several hormones, and the endocrine system helps with the mobilization of calcium and phosphate into and out of the bones. In the muscular system hormones adjust muscle metabolism, energy production, and growth. In the nervous system, hormones affect neural metabolism, regulate fluid/electrolyte balance and help with reproductive hormones that influence central nervous system (CNS) development and behaviours. In the cardiovascular system hormones are needed in the regulation of RBC's production, and blood pressure. Hormones also have anti-inflammatory effects as well as stimulate the lymphatic system. In summary, the endocrine system has a regulatory effect on basically every other body systems.

Skeletal system

It consists of all bones in the body, cartilages and ligaments. The skeletal system serves as an important mineral reserve. For example, if blood levels of calcium or magnesium are low and the minerals are not available in the diet, they will be taken from the bones. On the other hand the skeletal system provides calcium needed for all muscle contractions. Lymphocytes and other cells relating to the immune response are produced and stored in the bone marrow. The skeletal system aids in protection of the nervous system, endocrine organs, chest and pelvic regions in which vital organs are housed.

Integumentary system

This system is composed of the skin that is the epidermis, dermis and adipose tissue, nails, hair, receptors, oil glands and sweat glands. The integumentary system is involved in protecting the body from invading microbes, regulating body temperature through sweating and vasodilation, or shivering and piloerection, and regulating ions balance in the blood. Stimulation of mast cells also produces changes in diameter of blood vessels and capillary permeability which can affect the blood flow in the body and how it is regulated. It also helps synthesize vitamin D which interacts with calcium and phosphorus absorption, a factor that is very important for bone growth and maintenance. Hair on the skin guards entrance into the nasal cavity or other orifices preventing invaders from getting further into the body. The skin also helps maintain balance by excretion of water and other solutes. The keratinized epidermis limits fluid loss through skin, thus providing mechanical protection against environmental hazards.

Lymphatic system

The lymphatic system is composed mainly of the lymphatic vessels, lymph nodes, thymus, spleen and the bone marrow. It has three principal roles. First is the maintenance of blood and other body fluid volumes. Excess fluid that leaves the capillaries when under pressure would build up and cause edema, but for the role of the lymphatic system. Secondly, the lymphatic system absorbs fatty acids and triglycerides from fat digestion so that these components of digestion do not enter directly into the blood stream. Thirdly, the lymphatic system is involved in defending the body against invading microbes, and also in the immune response. This system assists in body maintenance such as bone and muscle repair after injuries. It also assists in maintaining the acid pH of urine required to fight infections in the urinary system. The tonsils are the body helpers that defend against infections and toxins absorbed from the digestive tract. The tonsils also protect against infections entering into the lungs.

Respiratory system

The components of the respiratory system are the nasal cavity, pharynx, larynx, glottis, epiglottis, bronchi, bronchioles, alveoli and the lungs. The respiratory system works in conjunction with the cardiovascular system to provide oxygen to cells within every body system for cellular metabolism. The respiratory system also removes carbon dioxide. Since CO₂ is mainly transported in the plasma as bicarbonate ions, which act as a chemical buffer, the respiratory system also helps maintain proper blood pH levels a fact that is very important for homeostasis. As a result of hyperventilation, the level of CO₂ is reduced. This causes the pH of body fluids to increase. If pH rises above 7.45, the results are respiratory alkalosis. On the other hand, too much CO₂ causes pH to fall below 7.35 which results in respiratory acidosis. The respiratory system also helps the lymphatic system by trapping pathogens and protecting deeper tissues from invading microorganisms.

Urinary system

Its main components are the kidneys, ureter, bladder and urethra. Toxic nitrogenous wastes accumulate as urea, uric acid and creatinine. The urinary system rids the body of these wastes. It is also involved in the maintenance of blood volume, blood pressure and electrolyte concentrations within the blood. The kidneys produce a hormone (erythropoietin) that stimulates

red blood cell production. They also play an important role in maintaining the water content of the body and the level of salts in the extracellular fluid.

Cardiovascular system

It consists of the heart, blood vessels and the blood. The cardiovascular system ensures the normal functioning of other body systems by transporting hormones, oxygen and nutrients to them and taking away waste products from them thereby providing all living body cells with a fresh supply of oxygen and nutrients and also removing carbon dioxide and other toxic wastes from their surroundings. Homeostasis is disturbed if the cardiovascular or lymphatic systems are not functioning properly. The cardiovascular system also contains sensors to monitor blood pressure. They are called baroreceptors. They detect the amount of stretch of the blood vessels and relay information via the nerves to the CNS which brings about the appropriate responses that regulate the blood pressure.

Muscular system

This system is made of skeletal muscles such as biceps, quadriceps, and gastrocnemius muscles and smooth or involuntary muscles such as cardiac muscle, intestinal muscles and muscles of the blood vessels. The muscular system is largely responsible for movement, posture, balance, gait, secretion by glands and maintenance of body temperature through heat production. It also contributes to blood glucose balance by storing glucose in form of glycogen. Muscles also aid in moving blood through veins, protect deep blood vessels and help the lymphatic system move lymph.

Digestive system

Its components include oral cavity, esophagus, stomach, intestines, liver and pancreas. The nutrients needed by the body are derived from the diet. Food is taken in by the mouth and broken down into its component parts by enzymes in the gastrointestinal tract (or gut). The digestive products are then absorbed into the blood across the wall of the intestine and pass to the liver via the portal vein. The digestive system absorbs organic substances, vitamins, ions, and water that are needed all over the body. The liver makes nutrients available to the tissues both for their growth and repair and for the production of energy.

Reproductive system

The main components of this system are the ovaries, testes, prostate, uterine tubes, uterus, vagina and penis. The reproductive system is responsible for the production of sperm cells and oval for the production of new offspring. The sex hormones do have various effects on other body systems, and an imbalance can lead to various disorders.

4.3 Feedback control systems

Negative feedback control

Negative feedback is the mechanism by which the body maintains conditions within particular limits. It is a control system that acts to maintain the level of some variable within a given range following a disturbance. Once equilibrium conditions are restored, the stimulus that activated the feedback loop is removed, so that the system ceases to function until an appropriate stimulus initiates the feedback process again; that is, negative feedback systems in the body normally are

reversible and they come into play on demand. The component of a simple negative feedback loop include (i) a regulated variable, (ii) sensor (or detector), (iii) controller (comparator), and (iv) effector. Each component controls the next component to it (Figure 1.1).

Various disturbances may arise within or outside the internal environment and caused undesirable changes in the regulated variable. The regulated variable is sensed by sensor, information about its level is fed back to a controller (comparator), which compares it to a desired value (set point). If there is a difference, signal is generated, which drives the effector to oppose the changes and bring the regulated variable closer to the desire

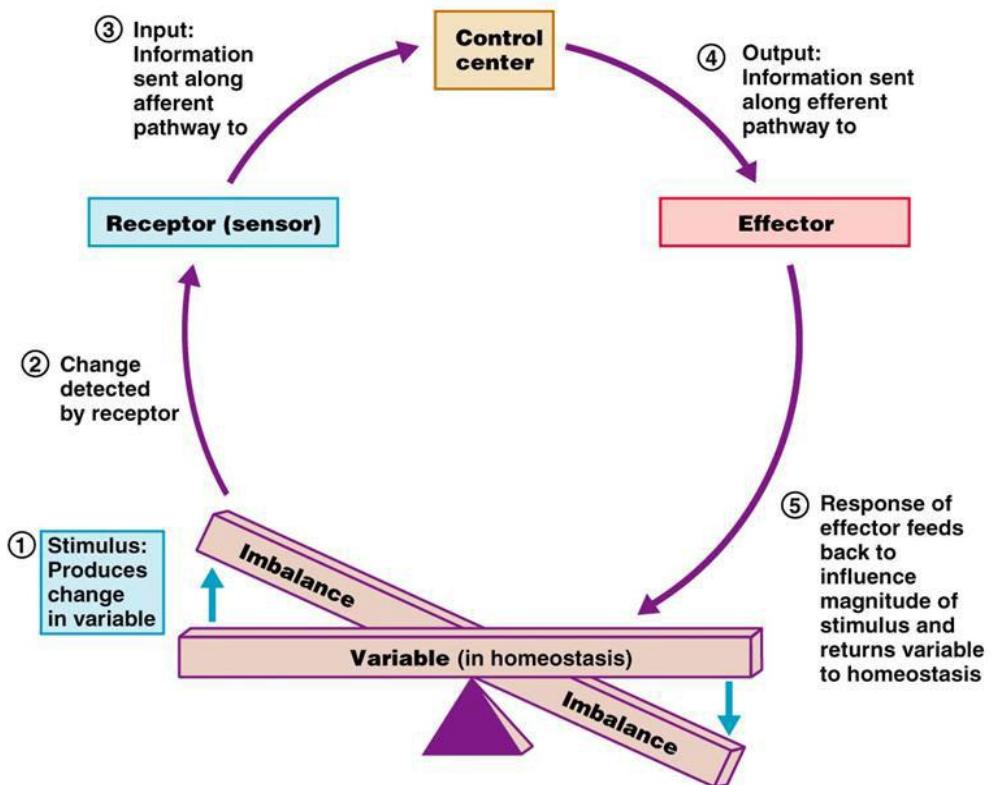


Figure 4.1: Component of a simple negative feedback loop

A familiar example of a negative feedback control is the thermostatic control of room temperature. Room temperature (regulated variable) is subject to disturbance; on a cold day, room temperature falls. The room temperature is detected by a thermometer (sensor) in the thermostat (controller). The thermostat is set for a certain temperature (set point). The controller compares the actual temperature (feedback signal) to the set point temperature and signal is generated if the former falls below the latter. The signal activates the furnace (effector). The resulting change in temperature is monitored by the controller, and when temperature rises sufficiently the furnace is turned off. Such a negative feedback system allows some fluctuation in room temperature. Effective communication between the sensor and effector is important in keeping these oscillations to a minimum.

Similar negative feedback systems maintain homeostasis in the body. One example is in arterial blood pressure regulation illustrated in Figure 1.2. These system sensors (arterial baroreceptors) are located in the carotid sinuses and aortic arch. Changes in stretch of the walls of the carotid sinus and aorta, which follow from changes in blood pressure, stimulate these sensors. Afferent nerve fibers transmit impulses to control centers in the medulla oblongata. Efferent nerve fibers send impulses from the medullar centre to the systems effectors, the heart and blood vessels. The output of blood by the heart and resistance to blood flow are altered in an appropriate direction to maintain blood pressure, as measured at the sensors within a given range values.

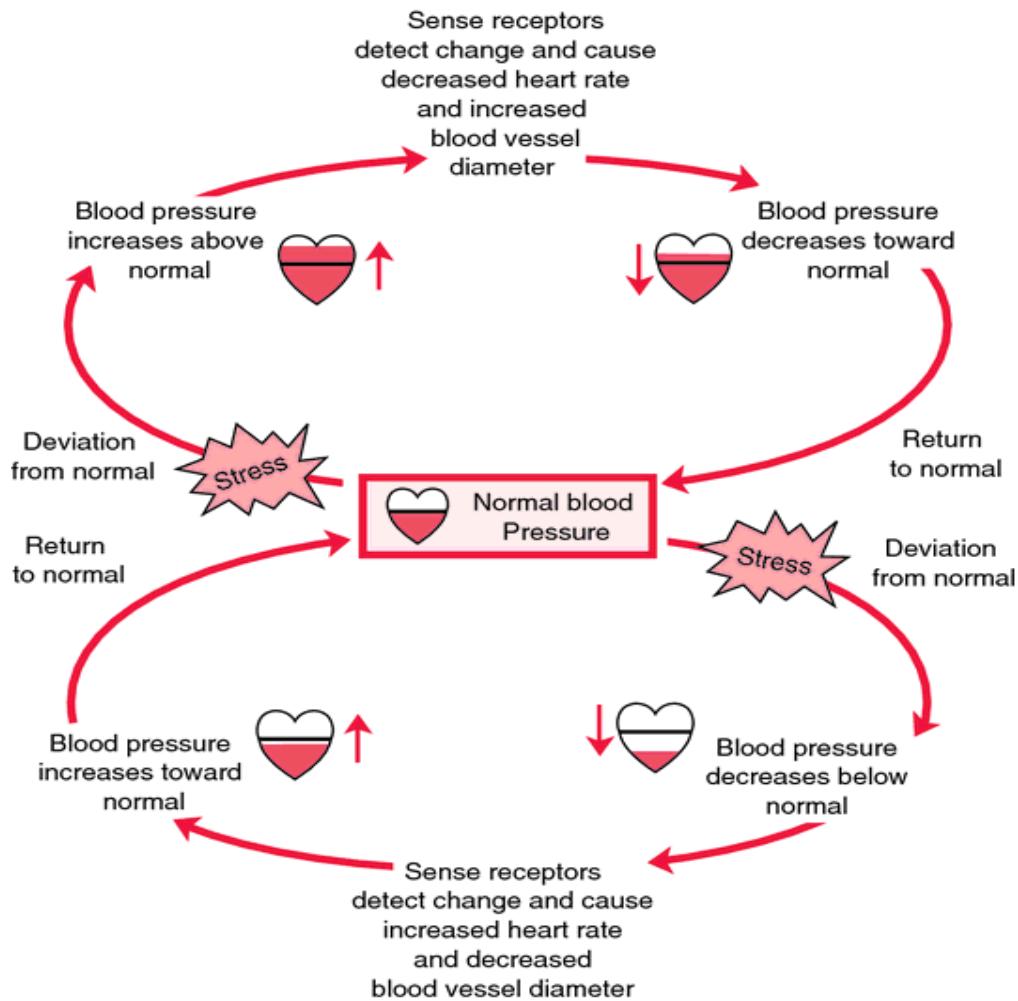


Figure 4.2: Regulation of arterial blood pressure

The control of testosterone secretion, control of calcium ions level in the blood, control of blood glucose by insulin and glucagon, control of cortisol secretion by the adrenal cortex are other examples of the operation of such mechanisms.

Positive feedback control

Positive feedback is a self-amplifying cycle in which a physiological change leads to even greater changes in the same direction, rather than producing the corrective effects of negative feedback. Positive feedback promotes rapid change and it is often a normal way of producing rapid progressive change in one direction. For example, when a woman is giving birth, the head of the baby pushes against her cervix and stimulates nerve endings there. Nerve signals are sent to the brain, which, in turn, stimulates the pituitary gland to secrete the hormone oxytocin. Oxytocin travels in the blood and stimulates the uterus to contract. This pushes the baby downward, stimulating the cervix the more and causing the positive feedback loop to be repeated. Labor contractions therefore become more and more intense until the baby is expelled.

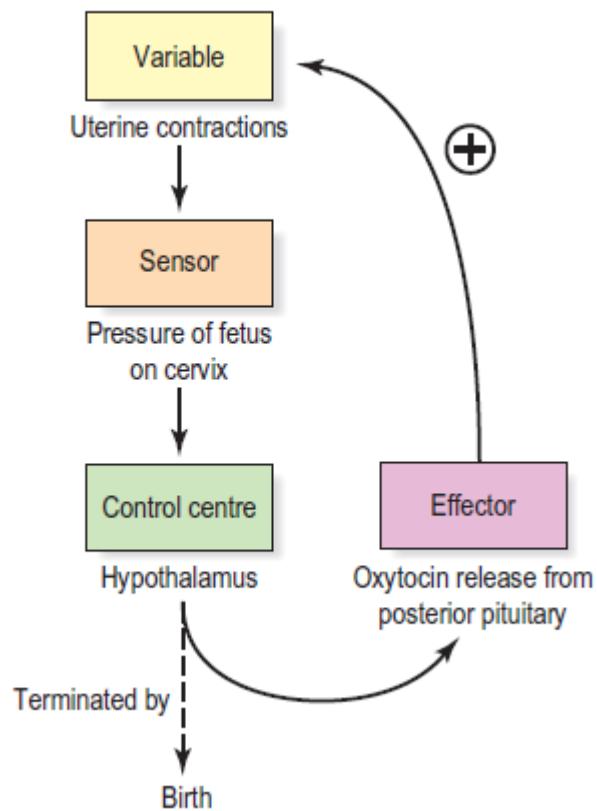


Figure 4.3: Control of childbirth by positive feedback mechanism

It should be noted however that the overall process of childbirth is a negative feedback loop- it is a response to pregnancy that terminates the pregnancy. But within this negative feedback loop, there is a smaller positive feedback loop that has just been described. Beneficial positive feedback loops are often part of larger negative feedback loops. Other examples of beneficial positive feedback includes: generation of nerve signals, blood clotting and the stomach digestion of protein. Frequently, however, positive feedback is a harmful and even life- threatening process. This is because its self-amplifying nature can quickly change the internal state of the body to something far from its homeostatic set point. Consider a high fever, for example. A fever triggered by infection is beneficial up to a point, but if the body temperature rises much above

42°C, it may create a dangerous positive feedback loop. This high temperature raises the metabolic rate, which makes the body to produce heat faster than it gets rid of it. Thus temperature rises still further, increasing the metabolic rate and heat production still more. This “vicious circle” becomes fatal at approximately 45°C such temperature are so high that they destroy the proteins that cells need to function. Convulsion and coma are some outward signs of this damage. Thus positive feedback loops often create dangerously out of control situations that require emergency medical treatment.

Feed forward control

Feed forward control is another strategy used to control systems in the body, particularly when a change with time is desired. It is anticipatory in nature. A feed forward controller generates commands without directly sensing the regulated variable. These commands specify the target or goals. Feed forward control often senses a disturbance and can therefore take corrective action that anticipates change. It often operates through the feedback controllers. The moment-to-moment operation of the feed forward controller is “open loop” (unlike closed loop in negative feedback) because the regulated variable itself is not sensed by sensor. Examples include increased heart rate and breathing rate even before a person has begun to exercise, flight reactions and others.

4.0 Conclusion

The principle of homeostasis allows the body to maintain a state of balance. All the systems are involved in the complicated process of maintaining constancy. Homeostatic control is achieved within a complex process involving the receptor, the control centre and the effector. Homeostatic imbalance results to diseases.

5.0 Summary

In this unit, you have learnt that:

- i. Homeostasis as the ability of the body to maintain relatively stable internal conditions even when the outside environment changes on a continuous basis.
- ii. All the body systems are involved in the process of attainment of homeostasis.
- iii. The body uses negative and positive feedbacks and the feed forward control of regulating homeostatic processes in the body.

6.0 Tutor Marked Assignments

6.1 Activity

Watch this video clips:

<https://www.youtube.com/watch?v=XZxuQo3ylII>

<https://www.youtube.com/watch?v=IoU3lKrOYMY>

Explore the use of thirst and sweat in achieving body's homeostasis, Explore other 5 other actions of the body that contribute to the maintenance of the body and how you can use them as guides in providing nursing care. Submit your findings to the tutor 2 weeks after the completion of this unit.

6.2 Answer the following questions

- i. Define homeostasis, and identify the components of negative feedback loops.

- ii. How do negative and positive feedbacks help to maintain the body homeostasis? Illustrate these with drawing and labeling of examples of negative and positive feedback?
- iii. What is homeostatic imbalance? Write on two examples of how this contribute to illness?

7.0 References and other resources

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John Campbell Homeostasis 2 <https://www.youtube.com/watch?v=IoU3lKrOYMY> accessed on June 30, 2015

UNIT FIVE - NERVE AND MUSCLE PHYSIOLOGY

CONTENT

- 1.0** Introduction
- 2.0** Objectives
- 3.0** Main Content
- 3.1** Nerves
- 3.2** Muscle Contraction
- 4.0** Conclusion
- 5.0** Summary
- 6.0** Tutor Marked Assignments
- 6.1** Activity
- 6.2** Tutor Marked Tests
- 7.0** References and other resources

1.0 Introduction

We respond to our living environment through our senses. We are only able to do this because we have a master controlling and communicating systems, the nervous system. In this unit, you are going to learn more about the typical nerve cell and how the nerve cells perform their functions. You are also going to learn about how the nerve cells enables the body to engage in coordinated movement as it facilitates muscle contractions.

2.0 Objectives

At the end of this unit, you should be able to:

- i. Discuss the structure and functions of a typical nerve cell.

- ii. Explain the functional unit of the muscle
- iii. Discuss the mechanisms involved in muscle contraction.

3.0 Main Content

3.1 Nerves and the functions

Nerves/Neurons are the basic structural and functional units of the nervous system. They are specialized to respond to physical and chemical stimuli, conduct electrochemical impulses, and release chemical regulators. Through these activities, neurons enable the perception of sensory stimuli, learning, memory, and the control of muscles and glands. Neurons have three principal regions: cell body, dendrites, and axon. They vary considerably in size and shape.

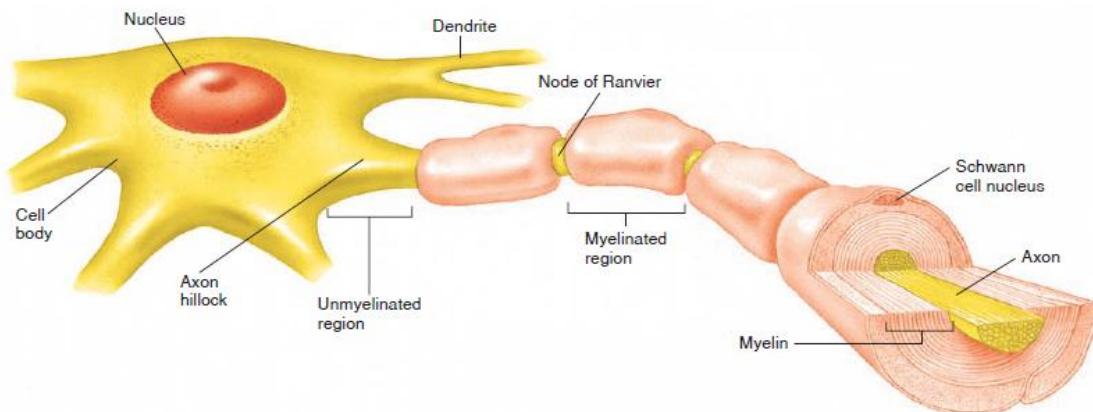


Figure 5.1: Parts of a neuron (myelinated)

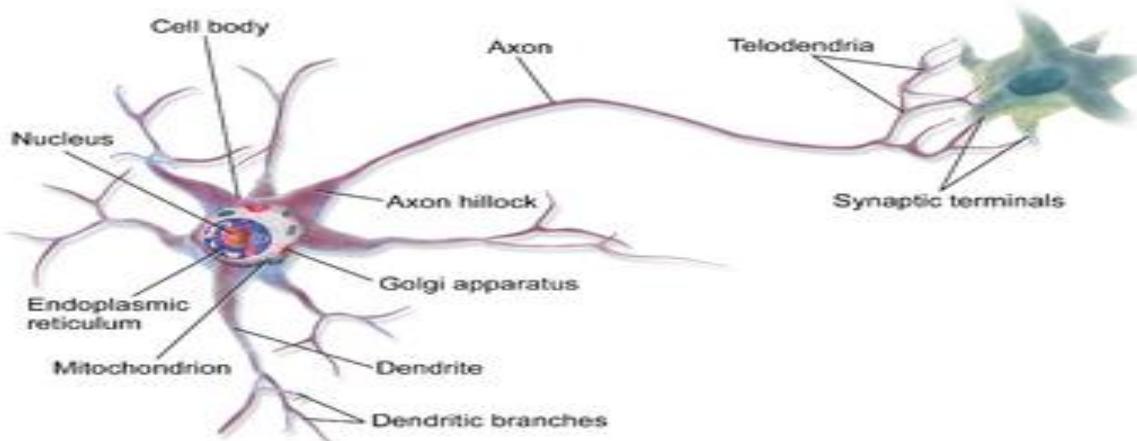


Figure 5.2: Parts of a neuron (unmyelinated)

The cell body (Soma) is the enlarged portion of the neuron that contains the nucleus. Dendrites are thin, branched processes that extend from the cytoplasm of the cell body. Dendrites provide a receptive area that transmits graded electrochemical impulses to the cell body. The axon is a longer process that conducts impulses, called action potentials, away from the cell body. The origin of the axon near the cell body is an expanded region called the axon hillock; it is here that action potentials originate. Side branches called axon collaterals may extend from the axon.

The axon at its end is divided into terminal branches. Each terminal branch ends in synaptic knobs or terminal buttons. The axon of a neuron can either be myelinated or unmyelinated. The myelinated neuron is wrapped by Schwann cells, which form a myelin sheath (Figs 2-1 and 2-2). The myelin sheath envelops the axon except at the terminal endings and at the Nodes of Ranvier.

3.1.1 Resting and Action Membrane Potential

Resting membrane potential

When the cell is not transmitting an impulse, the trans-membrane potential is called the resting membrane potential (RMP). Also the RMP can be defined as the inside negative potential across the membrane of cells. A resting membrane potential is due to uneven distribution of ions between the inside and the outside of the membrane.

The following phenomena are involved in establishing the cell potential.

- i. By means of active transport: sodium is actively pumped out of the cell and potassium is pumped into it. So the K^+ concentration in the cell is twenty times the concentration in the extracellular fluid.
- ii. The membrane at rest is far more permeable to K^+ than Na^+ . K^+ ions diffuse out of the cell with far greater ease than Na^+ diffuse into the cell.
- iii. The interior of the cell contains a high concentration of non-diffusible ions. Of particular importance in this regard are proteins, organic phosphates and organic sulphate anions. Since the resting membrane is much more permeable to K^+ than to Na^+ , the RMP is much closer to the K equilibrium potential than that of Na^+ .

The chief determinants of the movement of substances across the cell membrane are the membrane permeability, electrical as well as chemical gradients of the ions. When the chemical and electrical forces acting on ions are equal and opposite there is no net flux and the system is in equilibrium.

Action potential

This is the voltage of the cell membrane when the cell membrane is stimulated or activated. It can also be defined as the potential generated when excitable tissue (nerve and muscle) are stimulated resulting in the propagation of an impulse. The components of the action potential are: latent period, depolarization, repolarization and hyperpolarization. (Figure 2-3).

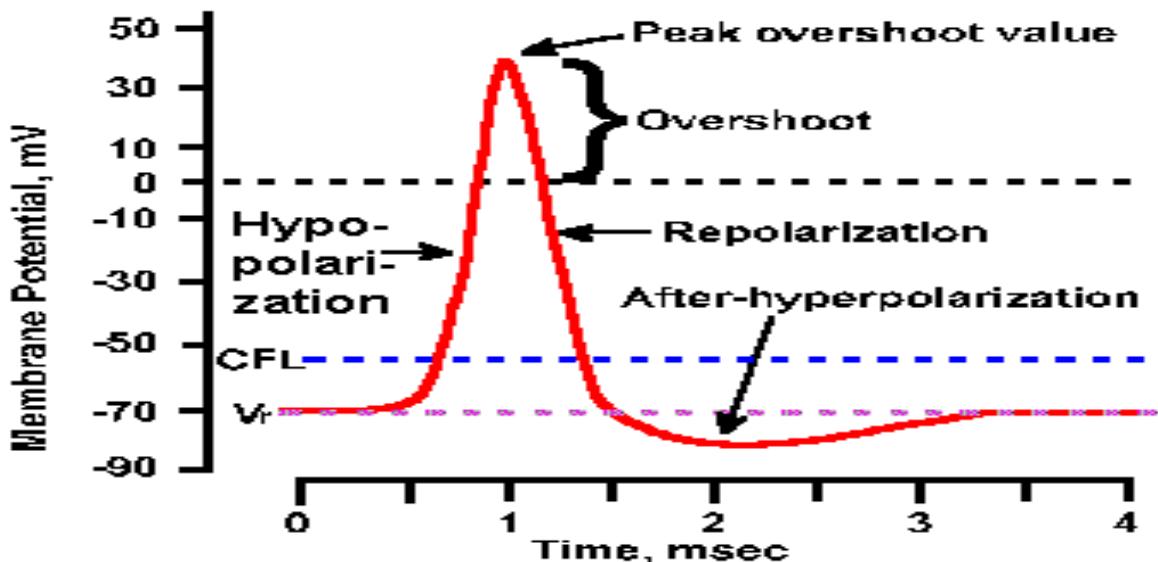


Figure 5.3: Phases of action potential

When a stimulus is applied to an axon, there is a brief irregular deflection of the baseline, called stimulus artifact. The stimulus artifact is followed by isopotential interval (latent period) that ends with the start of action potential and corresponds to the time it takes the impulse to travel along the axon from the site of stimulation to the recording electrodes.

Depolarization stage

At this time, the membrane suddenly becomes very permeable to sodium ions, allowing tremendous numbers of positively charged sodium ions to diffuse to the interior of the axon. The normal “polarized” state of -90 millivolts is immediately neutralized by the inflowing positively charged sodium ions, with the potential rising rapidly in the positive direction. This is called depolarization. In large nerve fibers, the great excess of positive sodium ions moving to the inside causes the membrane potential to actually “overshoot” beyond the zero level and to become somewhat positive. In some smaller fibers, as well as in many central nervous system neurons, the potential merely approaches the zero level and does not overshoot to the positive state.

Repolarization stage

Within a few milliseconds after the membrane becomes highly permeable to sodium ions, the sodium channels begin to close and the potassium channels open more than normal. Then, rapid diffusion of potassium ions to the exterior re-establishes the normal negative resting membrane potential. This is called repolarization of the membrane.

The sharp rise and the rapid fall are the spike potential of the axon, and the slower fall at the end of the process is the after-depolarization.

After the action potential, during the recovery period, Na^+ that came in during depolarization and the K^+ that went out during repolarization are brought back to their original positions. Since this means moving sodium against its concentration gradient (i.e. from in to out) and vice-versa for K^+ , the process involves active transport requiring energy.

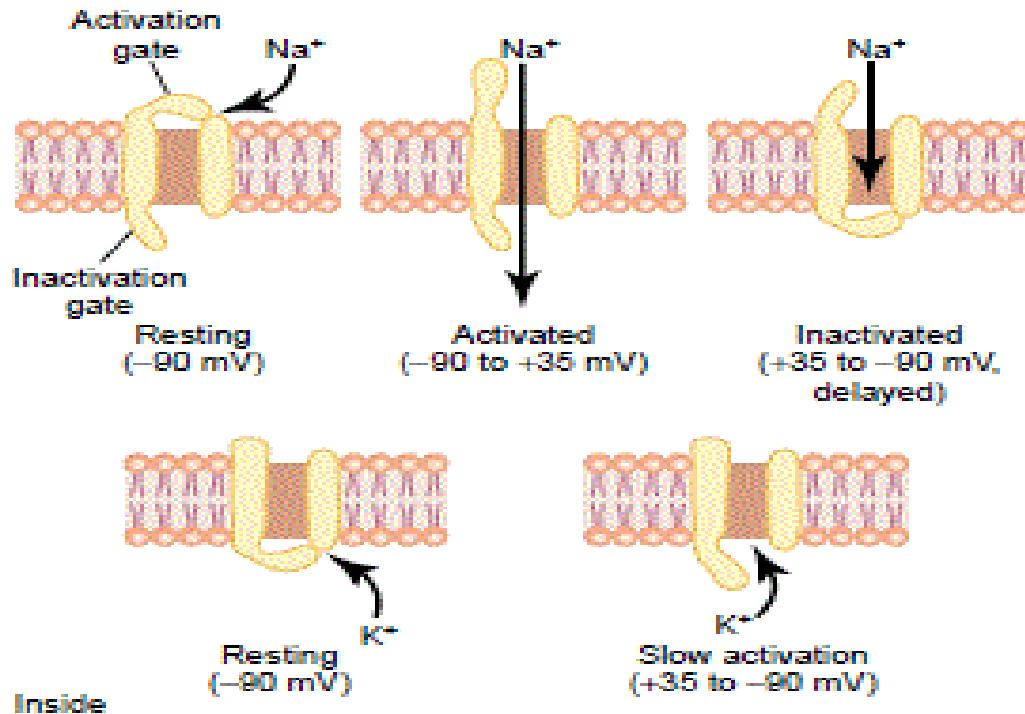


Figure 5.4: Characteristics of the voltage-gated sodium and potassium channels

Changes in excitability during action potential

The refractory period is divided into an absolute refractory period, which corresponds to the period from the time the firing level is reached until repolarization is about 1/3 complete, and a relative refractory period, lasting from this point to the start of after-depolarization. During the absolute refractory period, no stimulus, no matter how strong will excite the nerve, but during the relative refractive period, stronger than normal stimuli can cause excitation. During after-depolarization, the threshold is again decreased and during after-hyperpolarization it is increased.

All-or-nothing principle

Once an action potential has been elicited at any point on the membrane of a normal fiber, the depolarization process travels over the entire membrane if conditions are right, or it does not travel at all if conditions are not right. This is called the *all-or-nothing principle*, and it applies to all normal excitable tissues.

3.1.2. Conduction of impulse along nerve fibers

Non-myelinated nerve

The nerve cell membrane is polarized at rest, positive charges lined up along the outside of the membrane and negative charges along the inside of the membrane. During the action potential (AP), this polarity is abolished and for a period is actually reversed. Positive charges from the membrane ahead of and behind the AP flowing into the area of negativity represented by the AP (current sink). By drawing off positive charges, this flow decreases the polarity of the membrane ahead of the AP. This type of electrotonic depolarization initiates a local response, and when the

firing level is reached, a propagated response occurs that in turn electrotonically depolarizes the membrane in front of it. This sequence of event moves regularly along an unmyelinated axon to its end. Thus, the self-propagating nature of the nerve impulse is due to circular current flow and successive electrotonic depolarization to the firing level of the membrane ahead of the action potential.

Myelinated nerve

Conduction in myelinated axons depends upon a similar pattern of circular current flow. However, myelin is an effective insulator and current flow through it is negligible. Instead, depolarization in myelinated axons jumps from one node of Ranvier to the next, the “current sink” at the active node serving to electrotonically depolarize to the firing level the node ahead of the AP. This jumping of depolarization from node to node is called saltatory conduction, as shown in Figure 2-5. It is a rapid process, and myelinated axon conducts up to 50 times faster than the fastest unmyelinated fibers.

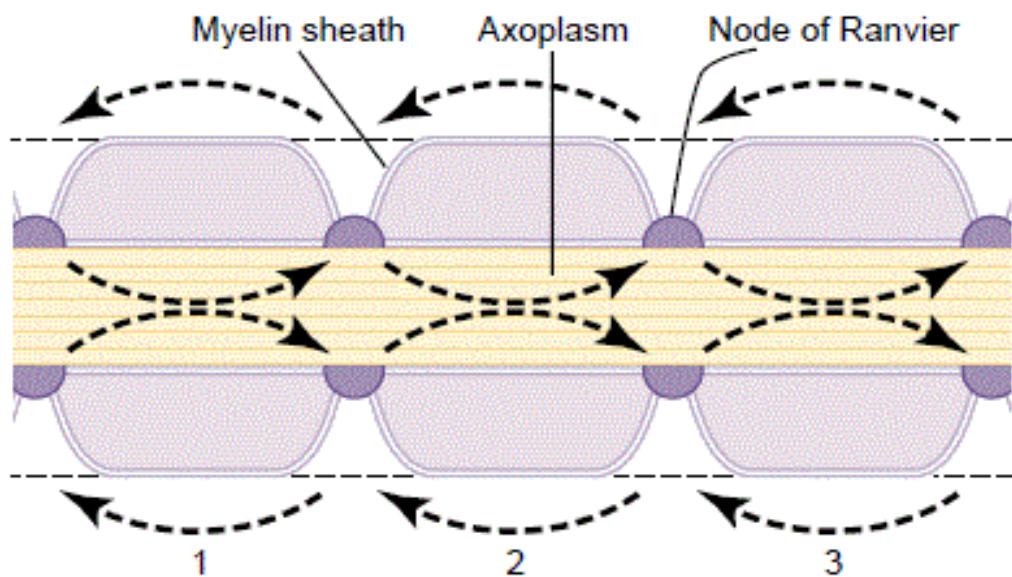


Figure 5.5: Saltatory conduction along a myelinated axon. Flow of electrical current from node to node is illustrated by the arrows.

Neuromuscular Transmission

As the axon supplying the skeletal muscle fiber approaches its termination, it loses its myelin sheath and divides into a number of terminal buttons or end-feet. The end-feet contain many small, clear vesicles that contain acetylcholine, which is the transmitter at this junction. The endings fit into depressions in the motor end plate – which is the thickened portion of the muscle membrane of the junctions. The depression is called the synaptic gutter or synaptic trough, and the space between the terminal and the end plate is called the synaptic cleft or space.

At the bottom of the gutter are numerous smaller folds of the muscle membrane of the end plate called sub-neural clefts or functional folds, which greatly increase the surface area which the synaptic transmitter can act. The whole structure is known as the neuromuscular or myoneural junction (Figure 2.6).

In the axon terminal are many mitochondria that supply ATP, the energy source that is used mainly for synthesis of the excitatory transmitter called acetylcholine. The acetylcholine in turn excites muscle fiber membrane. Acetylcholine is synthesized in the cytoplasm of the terminal button, but it is absorbed rapidly into many small synaptic vesicles. In the synaptic space, a large quantity of the enzyme acetyl cholinesterase, which is capable of destroying acetylcholine after it has been released from the synaptic vesicles are present.

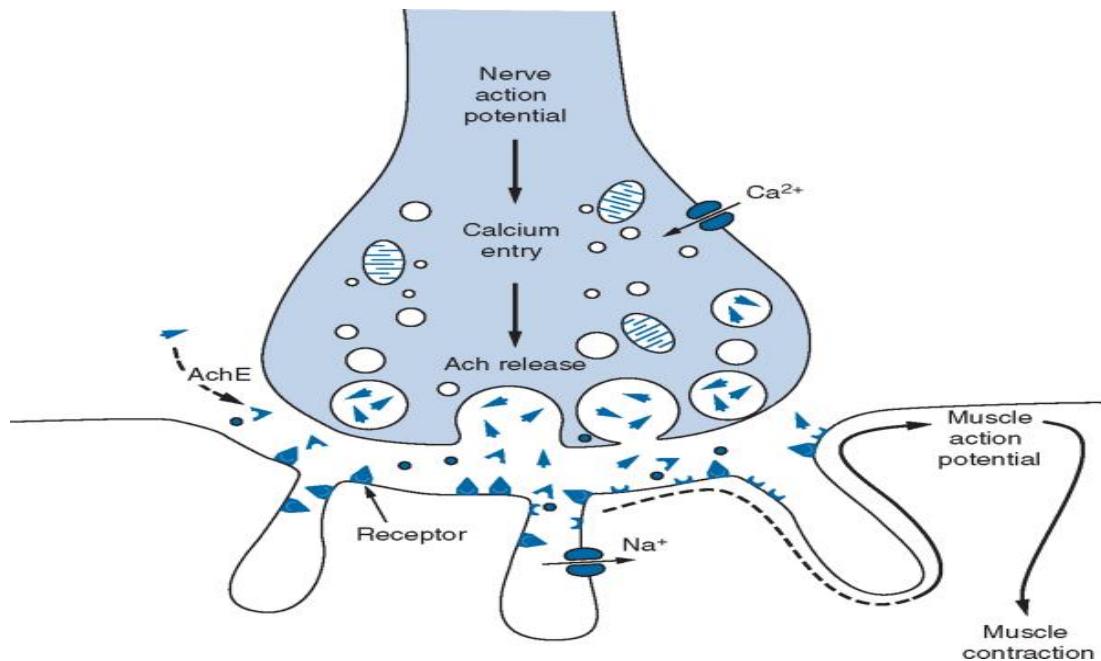


Figure 5.6: Shows neurotransmission at neuromuscular junction

3.2 Muscle Contraction

Three types of muscle cells can be identified on the basis of structure and contractile properties:
 (i) Skeletal muscle (ii) Smooth muscle (iii) Cardiac muscle

Most skeletal muscles as the name implies are attached to bones and their contraction is responsible for the movement of parts of the skeleton. Contraction of the skeletal muscle is controlled by the somatic nervous system and hence is under voluntary control. The movements produced by skeletal muscles are primarily involved with interactions between the body and external environment. Smooth muscles surround hollow organs and tubes-like stomach, intestinal tract, urinary bladder, uterus, blood vessels and air passages to the lungs. It is also found as single cells distributed throughout the organs (spleen) and the small group of cells attached to the hairs in the skin. The contraction of the smooth muscle may either propel the luminal content out of or through the hollow organs or it may regulate the flow of the contents through tubes by changing their diameters without itself initiating propulsion. Smooth muscle contraction is controlled by factors intrinsic to the muscle itself by the autonomic nervous system (ANS) and by hormones. Therefore, it is not normally under direct conscious control.

The third type of muscle; cardiac muscle is the muscle of the heart and its contraction propels blood through the circulatory system. Like smooth muscle, it is regulated by intrinsic factors and by ANS and hormones.

Skeletal muscle

Figure 2-7 shows the organization of skeletal muscle. Each skeletal muscle fiber is a cylinder with diameter of 10-100 μm and length which may extend up to 300,000 μm (1 foot). The term skeletal muscle refers to a number of muscle fibers bond together by connective tissue. From the light microscope, the most striking picture is series of transverse light and dark bands forming a regular pattern along each fiber. Most skeletal and cardiac muscle fibers have these characteristics banding and are known as striated muscles. Smooth muscle cells show no binding patterns. Although the pattern appears to be continuous across the entire cytoplasm of a single fiber, the bands are actually confined to a number of independent cylindrical elements, known as myofibrils. Each myofibril is about 1 to 2 micron (μm) in diameter and continues throughout the length of the muscle fiber. Myofibrils occupy about 80% of the fiber volume and vary in number from several hundred to several thousand per single fiber, depending on the fiber diameter.

The myofibrils consist of smaller filaments which are arranged in a repeating pattern along the length of the fibril. One unit of this repeating pattern is known as a sarcomere (little muscle), which is the functional unit of the contractile system in striated muscles. Each sarcomere contains two types of filaments: Thick filament composed of the contractile protein called myosin and thin filaments containing the contractile protein components; (i) Actin (ii) Tropomyosin (iii) Troponin.

Troponin is made up of three subunits: (i) Troponin I (ii) Troponin T (iii) Troponin C. The thick filaments, 12-18nm in diameter are located in the central region of the sarcomere, where their orderly parallel arrangements gives rise to the dark bands known as A-bands, because they are anisotropic to polarized light. Thin filaments, 5-8nm in diameter are attached at either end of a sarcomere to a structure known as Z-line. Two successive Z-lines define the limits of the sarcomere. Z-lines are short fibrous structures, which interconnect the thin filaments from two adjoining sarcomeres thus, provide an anchoring point for the thin filaments, which extends from the Z-lines towards the centre of the sarcomere where they overlap with the thick filament.

Between the ends of the dark A-bands of two adjacent sarcomeres is the I-band (because it is isotropic to polarized light) forming the lighter region of the striated pattern.

One additional band called the H-zone appears as a thin lighter band in the centre of the A-band. It corresponds to the space between the ends of the thin filament. Thus, only thick filaments are found in the H-zone. Finally, a thin dark band can be seen in the center of the H-zone. This is known as the M-line and is produced by linkages between the thick filaments. The M-line by cross linking the thick-filaments keeps all these in a single sarcomere in parallel alignments. Thus, neither the thin nor thick filaments are free floating, each is linked either to Z-lines in the case of the thin filaments or to M-lines in the case of the thick filaments.

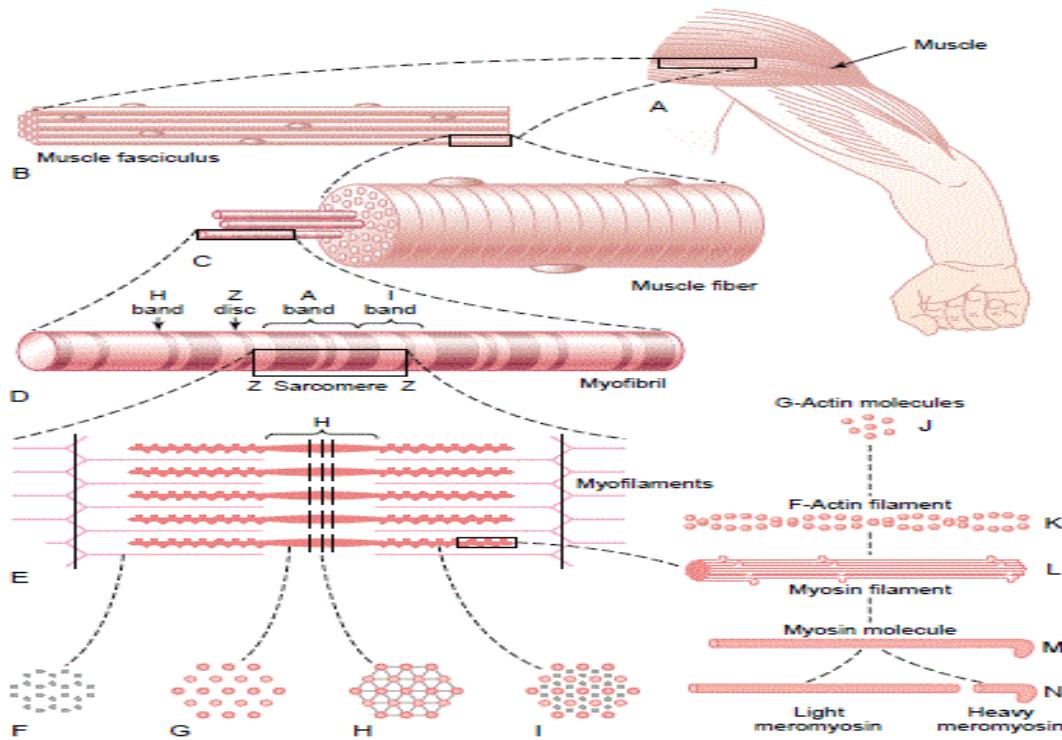


Figure 5.7: Organization of skeletal muscle from the gross to the molecular level.

Smooth muscle

Smooth muscles are distinguished anatomically from skeletal and cardiac muscles, because they lack physical cross striations. Actin and myosin are present and they slide on each other to produce contraction. However, they are not arranged in regular arrays as in skeletal muscle and cardiac muscles, and so the striations are absent. Instead of Z-lines, there are dense bodies in the cytoplasm attached to the cell membrane and these are bound by α – actinin to actin filament. Smooth muscles also contain tropomyosin, but troponin appears to be absent.

Smooth muscles can be generally divided into two major types, which are shown in Figure 2-8: multiunit smooth muscle and single unit or visceral muscle.

Multiunit smooth muscle

This type of smooth muscle is composed of discrete smooth muscle fibers. Each fiber operates entirely independently of the other fibers and is often innervated by a single nerve ending as occurred for skeletal muscle. Furthermore, the outer surfaces of these fibers, like those of skeletal muscle fibers are covered by a thin layer of glycoprotein that helps to insulate the separate fibers from each other. The most important characteristics of multi-unit smooth muscle fibers is that their control is exerted almost entirely by nerve fibers and very little by other stimuli, like local tissue factors. This is in contrast to a major share of the control of visceral smooth muscle by non-nervous stimuli. Some examples of multi-unit smooth muscle found in the body are smooth muscle fiber of the ciliary muscle of the eye, the iris of the eye, the nictitating membrane that covers the eye of some lower animals, the pilo-erector muscles that cause erection of the hairs when stimulated by the sympathetic nervous system and the smooth muscle of many of the larger blood vessels.

Visceral smooth muscle (Single unit)

Their fibers are similar to multi-unit fibers except that they are regularly or usually arranged in sheet or bundles and the cell membrane contact each other at multiple points to form many gap junctions. Thus, the fibers form a functional syncytium that usually contract large area at once. For this reason, this type of smooth muscle is also known as single unit or unitary smooth muscle. This type of muscle is found in most of the organs in the body, especially in the walls of the gut, the bile duct, ureters, uterus, etc.

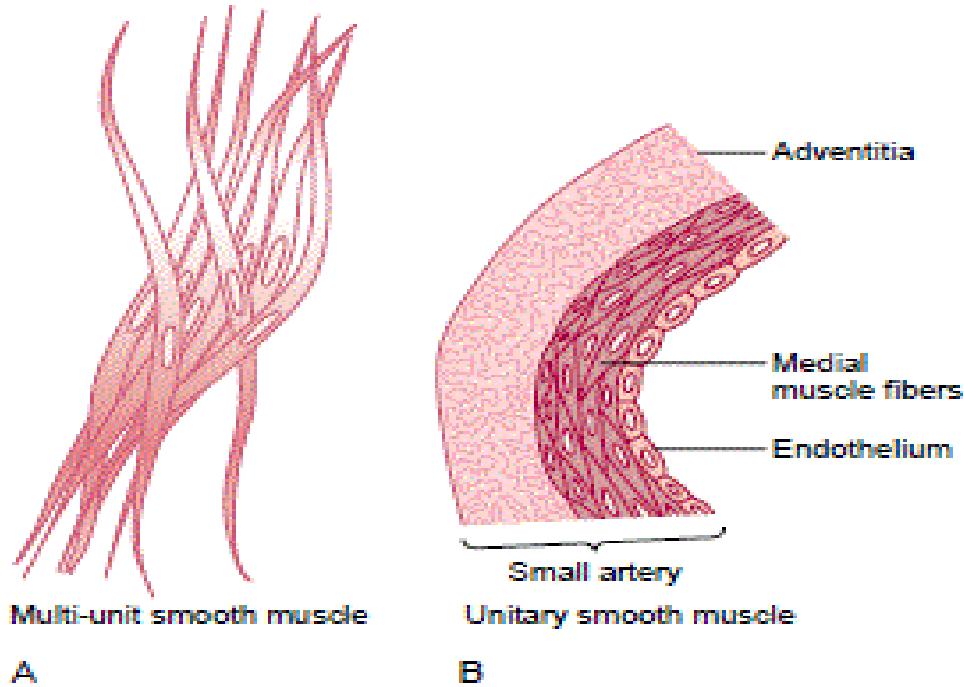


Figure 5.8: Multi-unit (A) and Unitary (B) smooth muscle.

Cardiac muscle

Striations in cardiac muscle are similar to those in skeletal muscle. There are large numbers of elongated mitochondria in close contacts to the muscle myofibrils and the muscle fibers branch and interdigitate. But each is a complete unit surrounded by a cell membrane. When the end of one muscle fiber joins on another, the membranes of both fibers parallel each other through an extensive series of folds. These areas which always occur as Z-lines and are called intercalated discs. They provide a strong union between fibers, maintaining cell-cell cohesion, so that the pull of one contractile unit can be transmitted along its axis to the next. Along the site of the muscle fibers next to the disks, the cell membranes of adjacent fibers fuse for considerable distances forming gap junctions. These junctions provide low-resistance bridges for the spread of excitation from one fiber to another.

Contractile proteins

These are proteins which participate in the contractile processes. They include muscle proteins as well as those found in other cells and tissues. In the cells and tissues, these proteins participate in localized contractile events in the cytoplasm, in motile activity, and in cell aggregation phenomena. The two types of contractile proteins that are found within muscles are actin and

myosin. Both proteins are responsible for muscle movement. The heads and necks of the myosin molecules forms cross-links to actin.

Excitation-contraction coupling

These are the events occurring between the excitation of a muscle fiber and the resulting contraction. The skeletal muscle fiber is so large that action potential (AP) spreads in along the surface membrane and causes almost no current flow deep within the fiber. However, to cause muscle contraction, this electrical current must penetrate deeply into the muscle fiber to the vicinity of all the separate myofibrils. This is achieved by transmission of APs along transverse tubules (T-tubules) that penetrate all the way through the muscle fiber from one side to the other. T-tubules action potential in turn causes release of Ca^{2+} in the immediate vicinity of all the myofibrils. This Ca^{2+} then causes contraction. This overall process is called excitation contraction- coupling (Figure 2-9).

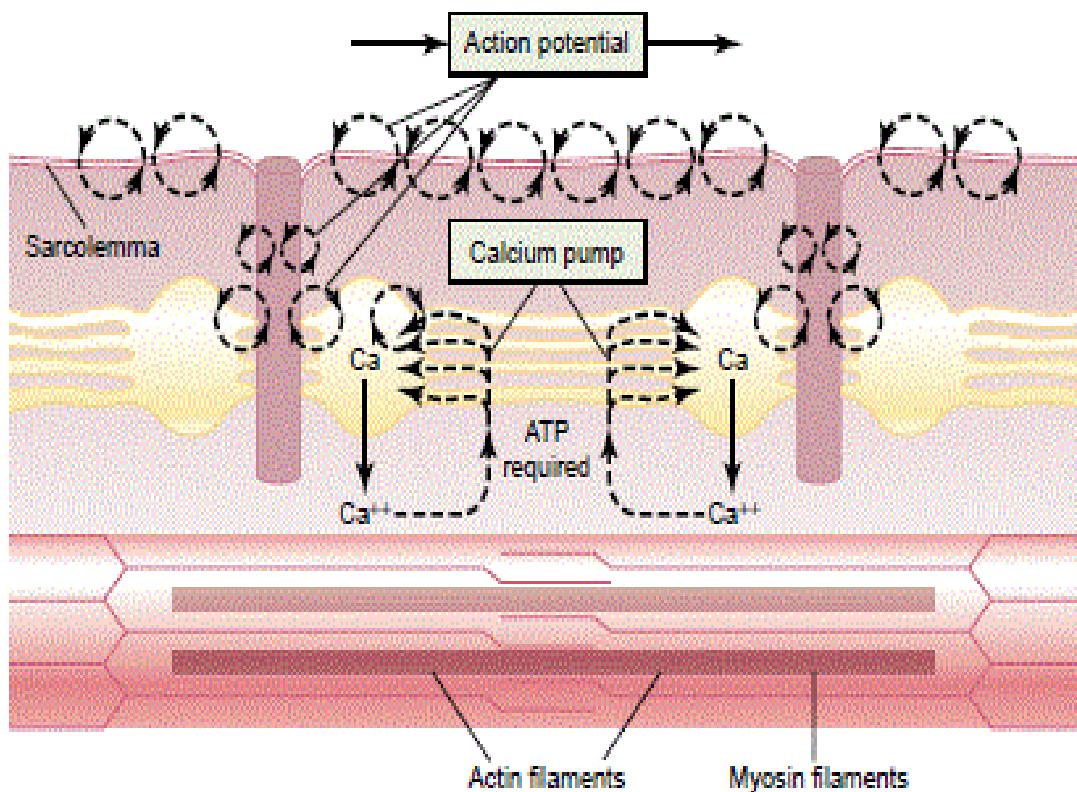


Figure 5.9: Excitation-contraction coupling in the muscle.

Molecular basis of contraction

Figure 2.10 demonstrates the basic mechanism of muscle contraction. This is the process by which the shortening of the contractile elements in muscle is brought about by sliding of the thin filaments over the thick filaments. The width of the A-bands is constant, whereas the Z-lines move closer when muscle contracts and far apart when it is stretched (Sliding filament mechanism).

Sliding during muscle contraction occurs when the myosin heads bind firmly to actin, bend at the junction of the head with the neck and then detach. “This power stroke” depends on the simultaneous hydrolysis of ATP.

Calcium ions initiate contraction by binding troponin C. In resting muscle, troponin I is tightly bound to actin and the tropomyosin covers the site, where myosin heads bind to actin. Thus, the troponin-tropomyosin complex constitutes a relaxing protein that inhibits the interaction between actin and myosin. When the Ca^{2+} is released from the terminal cisterna by the AP, it binds to troponin C, the binding of troponin I to actin is presumably weakened and this permits the tropomyosin to move laterally. This movement uncovers the active site of myosin heads. Adenosine triphosphate (ATP) is then split and contractions occur.

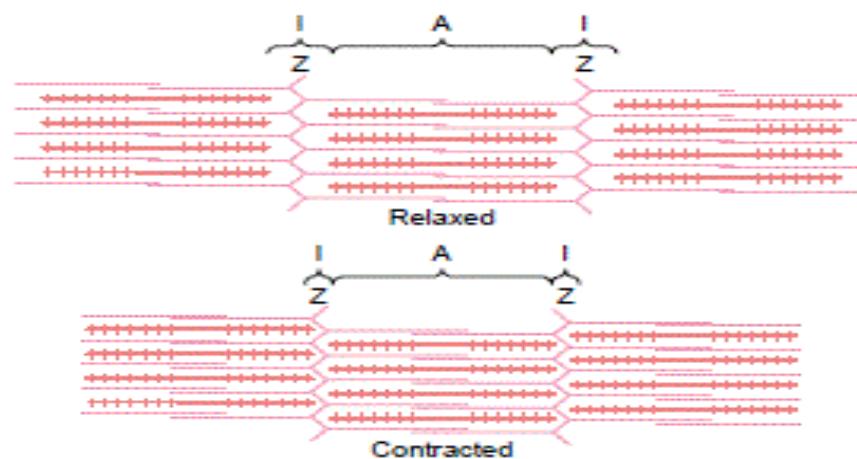


Figure 5.10: Relaxed and contracted states of a myofibril showing (top) sliding of the actin filaments (pink) into the spaces between the myosin filaments (red), and (bottom) pulling of the Z membranes toward each other.

4.0 Conclusion

Nerve cells help the body to respond to various stimuli through the mediating effect of sodium, potassium and calcium ions. The three main muscle types are distinguishable by their structure and mode of contractions.

5.0 Summary

In this unit, you have learnt about the following:

- i. The structure and functions of a typical nerve cell.
- ii. The functional unit of the muscle
- iii. The various mechanisms involved in muscle contraction.

6.0 Tutor Marked Assignments

6.1 Activity

As prescribed in the laboratory practical to be conducted by the Facilitator

- 6.2** Answer the following questions:
- i. Discuss the structure and functions of a typical nerve cell.
 - ii. Explain the functional unit of the muscle
 - iii. Discuss the mechanisms involved in muscle contraction.

7.0 References and other resources

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MODULE TWO - BLOOD PHYSIOLOGY (I)- HAEMODYNAMICS AND IMMUNOLOGY

Introduction

The body is able to perform its function because of the fluid dynamics and the organelles in body fluids. In this module, you are going to learn more about the body fluids, (intra and intercellular), the blood and the body's protective dynamics, the immune system.

Module Objectives

At the end of this module, you should be able to:

- i. Discuss the body fluids in the diverse compartments
- ii. Discuss the blood and the haemostatic process
- iii. Discuss the body's process of maintaining immunity

Contents

Unit 1:Body Fluids

Unit 2: Haemostasis.

Unit 3: Immune System.

UNIT 1- BODY FLUIDS

CONTENT

- 1.0** Introduction
- 2.0** Objectives
- 3.0** Main Content
 - 3.1** Body fluid compartment
 - 3.2** Intracellular fluid (ICF)
 - 3.3** Extracellular Fluid (ECF)
 - 3.4** Measurement of Body Fluid Compartment
 - 3.5** Blood
- 4.0** Conclusion
- 5.0** Summary
- 6.0** Tutor Marked Assignments
 - 6.1** Activity
 - 6.2** Tutor Marked Tests
- 7.0** References and other resources

1.0 Introduction

The body is made of more fluids in different locations and the nurse must be appropriate informed about the location, constituents and functions of the body fluids. In this unit, you are going to study the body fluids in the various compartments.

2.0 Objectives

At the end of this unit, you should be able to:

- i. Describe the different types of body fluids and where they are located
- ii. Explain the method of measurement of Body Fluid in the different compartments
- iii. Discuss the constituents and functions of blood
- iv. Explain the concept blood grouping and the implications in nursing practice

3.0 Main Content

3.1 Body fluid compartment

General considerations and inter-relationships of body fluid spaces.

Water is an important component of the human body. It constitutes approximately 60% of body weight. In terms of volume, total body water in adult man is about 42 liters. Body fluids can be divided into two main compartments: intracellular fluid (ICF) and extracellular fluid (ECF) (Figure 3-1).

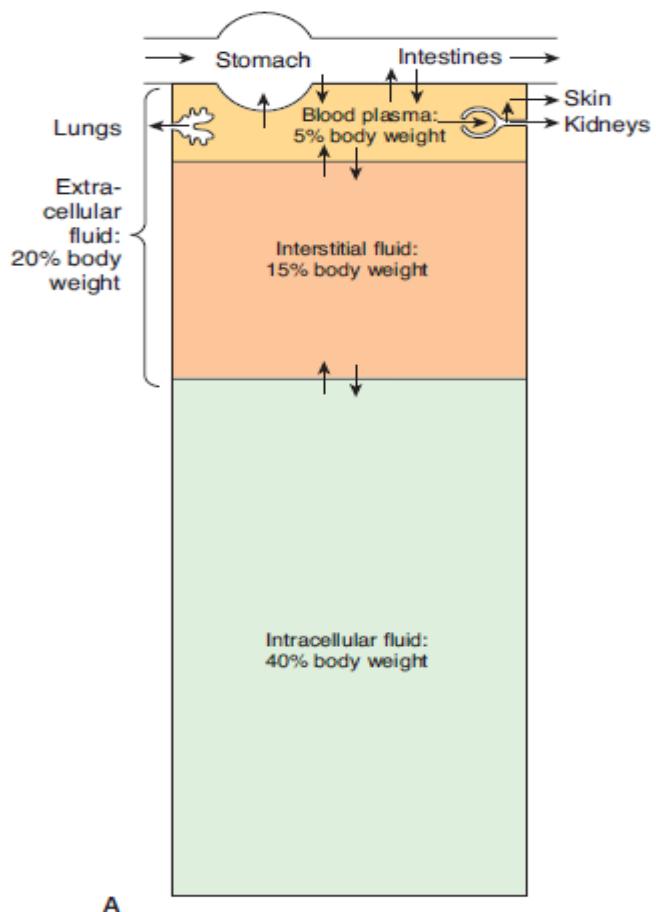


Figure 1.1: Organization of body fluids and electrolytes into compartments.

3.2 Intracellular fluid (ICF)

ICF consists of all fluid within the cell membranes of the body and is the largest fluid compartment, accounting for 40% of the body weight. Its volume is about 28 liters. Much of the ICF compartment is found within muscle cells. The primary electrolytes of the ICF compartment are potassium and phosphate. The ICF compartment contains only small quantities of sodium and chloride ions and almost no calcium ions. The cells contain 4 times as much protein as the plasma. Intracellular fluid provides body cells their turgor as well as a medium within which biochemical reactions can take place.

3.3 Extracellular fluid (ECF)

All the fluids outside the cells are collectively called the extracellular fluid. Together these fluids account for about 20% of the body weight, or about 14 liters. The ECF supports the cells and allows transport of nutrients and waste products. The extracellular fluid is divided into the interstitial fluid and the blood plasma. There is another small compartment of fluid that is referred to as transcellular fluid.

Interstitial fluid (IF)

It is the fluid that surrounds the cells in the various tissues of the body. It is about three-quarter of the ECF volume. It includes the water contained within bone and dense connective tissue. The remaining one quarter of the ECF is fluid inside the blood vessels, that is, plasma.

Transcellular fluid (TCF)

This is the fluid located in special compartments of the body. It is usually considered to be a specialized type of extracellular fluid. Their total volume is about 0.3 liter and they serve important functions. This compartment includes fluid in the synovial, peritoneal, pericardial, and intraocular spaces, as well as the cerebrospinal fluid.

1.4 Measurement of body fluid compartment

This is usually done using dilution technique. The plasma volume, ECF volume and the total body water (TBW) can also be measured using dilution technique. The interstitial and intracellular fluid volumes can then be derived as follows:

$$ICF = TBW - ECF$$

$$IF = ECF - \text{plasma volume}$$

Plasma volume can be measured using dyes that bind to plasma protein e.g. Evans blue (T1824). Plasma volume can also be measured by injecting serum albumin labeled with radioactive iodine. Total body water can be measured using the dilution technique involving a substance that will mix evenly with all the body fluid compartments. Radioactive water (tritium, $^3\text{H}_2\text{O}$) or heavy water (deuterium, $^2\text{H}_2\text{O}$) can be used for this measurement. Another substance that has been used to measure total body water is antipyrine.

The ECF volume can be measured using any of the many substances that mix freely in the plasma and interstitial fluid but do not readily pass through the cell membrane. Such substances include radioactive sodium, radioactive chloride, and inulin. Also mannitol and sucrose have been used to measure ECF volume.

Interstitial fluid volume cannot be measured directly but it can be calculated as the difference between the ECF volume and plasma volume.

$$\text{Interstitial fluid volume} = ECF - \text{plasma volume}$$

The ICF volume also cannot be measured directly but it can be determined as the difference of TBW and ECF.

$$ICF \text{ volume} = TBW - ECF \text{ volume.}$$

Blood volume can be calculated if the hematocrit (the fraction of the total blood volume composed of cells) is known, using the following equation:

$$\text{Total Blood Volume} = \frac{\text{Plasma Volume}}{1 - \text{Hematocrit}}$$

For example, if plasma volume is 3 liters and hematocrit is 0.40, total blood volume would be calculated as;

$$3 \text{ liters}$$

$$1 - 0.4 = 5 \text{ liters.}$$

Another way to measure blood volume is to inject into the circulation red blood cells that have been labeled with radioactive material. After this has mixed in the circulation, the radioactivity

of a mixed blood sample can be measured, and the total blood volume can be calculated using the dilution principle. A substance frequently used to label the red blood cells is radioactive chromium (^{51}Cr), which binds tightly with the red blood cells.

3.5 Blood

Blood is the fluid that circulates through the heart, arteries, capillaries and veins, carrying nutrients and oxygen to the body cells. It also carries waste products of metabolism, the most important of which is carbon dioxide, from the tissues to the organs where such waste products are expelled from the body. Blood is made up of yellow liquid called plasma and the cellular component. The cellular component of blood is made up of three types of cells, the red blood cells (erythrocytes), the white blood cells (leucocytes) and the platelets (thrombocytes). The “cells” in the blood are also called corpuscles.

Functions of blood

- i. It transports oxygen from air in the lungs to the tissues and carbon dioxide from the tissues to the lungs where it is expelled.
- ii. It transports food materials such as glucose, fatty acids, amino acids, vitamins and electrolytes from the gastrointestinal tract to body tissues where they are utilized for body building and energy production.
- iii. It helps in the exchange of water, electrolytes and hydrogen ions between the various body compartments.
- iv. It also plays important role in the homeostasis of other body constituents such as glucose, hormones etc.
- v. It helps in transporting heat from one part of the body to the other.
- vi. It transports humoral, antibodies, chemical agents, enzymes, and cellular elements that are important in the defense of the body against infection or invasion by non-infective foreign tissues of organisms.

Blood can be divided into two main parts namely cells or formed elements and plasma. Cells consist of red corpuscles, white corpuscles, and platelets. Plasma is a mixture of water, amino acids, proteins, carbohydrates, lipids, vitamins, hormones, electrolytes, and cellular wastes.

Haemopoiesis/Hematopoiesis

This is the formation of blood cells. In the bone marrow are cells called Pluripotent hemopoietic stem cells (PHSC) from which all circulating cells are derived. The PHSC undergoes successive divisions to form different blood cells. Growth and reproduction of the stem cell is controlled by multiple proteins called growth inducers. e.g. Interleukin – 3 (IL – 3). Another set of proteins called the differentiation inducers causes one type of stem cell to differentiate towards a final type of adult blood cell. e.g. erythropoietin (Fig. 4.1).

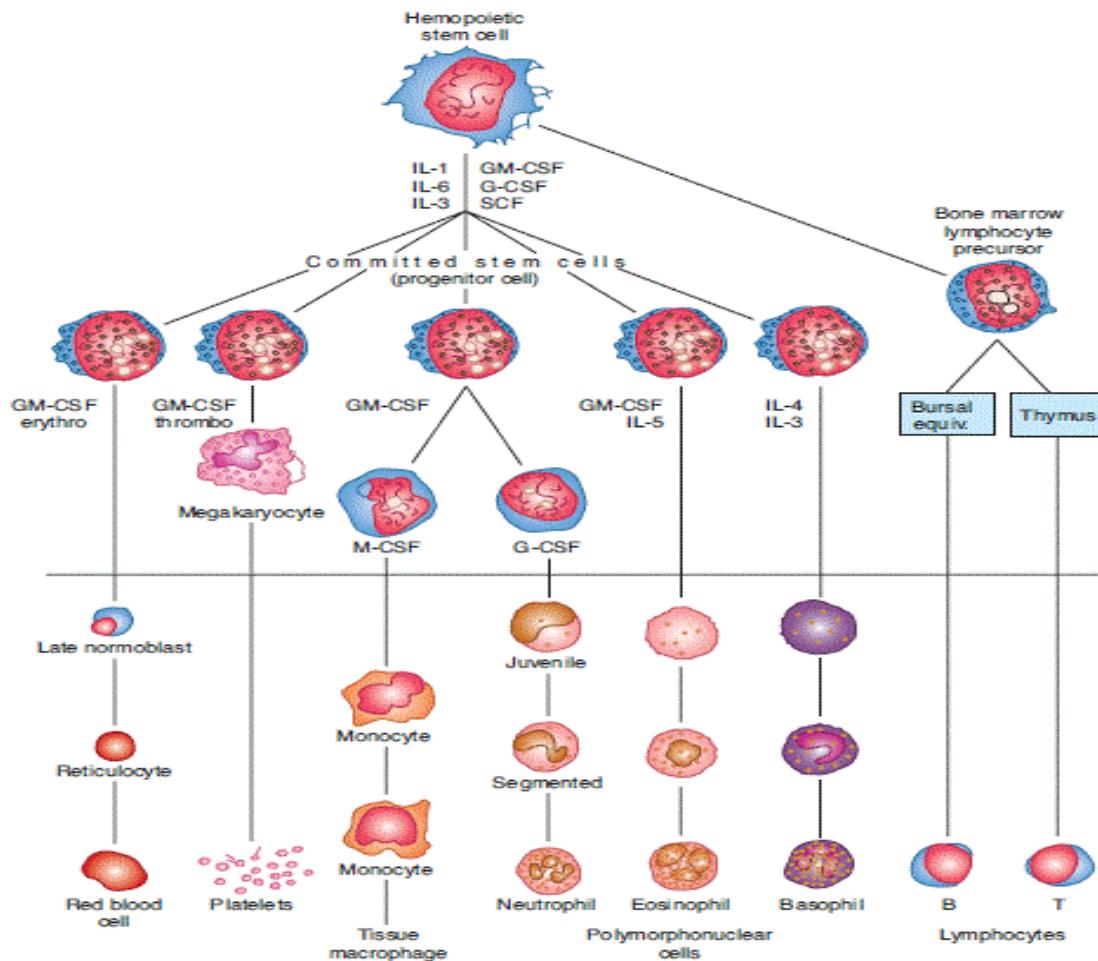


Figure 1.2: Development of various formed elements of the blood from bone marrow cells

Red blood cells

Normal red blood cells (erythrocytes), shown in Figure 1–27, are biconcave discs with a diameter of 7.2 microns and a thickness of 2.2 microns that contain one-third oxygen-carrying hemoglobin by volume. When oxygen combines with hemoglobin, the resulting oxyhemoglobin is bright red. Red blood cells discard their nuclei during development.

The typical red blood cell count is 4,600,000 - 6,200,000 cells per mm³ for males and 4,500,000-5,100,000 cells per mm³ for females. The number of red blood cells is a measure of the blood's oxygen-carrying capacity. With age, red blood cells become increasingly fragile and are damaged by passing through narrow capillaries. Macrophages in the liver and spleen phagocytize damaged red blood cells. Hemoglobin from the decomposed red blood cells is converted into heme and globin. Heme is decomposed into iron and biliverdin. Iron is recycled into new hemoglobin or stored in the liver. Some biliverdin is converted into bilirubin. Biliverdin and bilirubin are excreted in bile as bile pigments.

Erythropoiesis

This is the process of production of red blood cells. In the embryo and fetus, red blood cell production occurs in the yolk sac, liver, and spleen; in the adult it occurs in the red bone marrow. The average life span of a red blood cell is 120 days. The three cellular components of blood, that is red blood cells, white blood cells and platelets, originate from the same primitive or pluripotential haemopoietic stem cells (PHSC), from the bone marrow. The PHSC is uncommitted and can develop into any of the three cell types. The PHSC however differentiates (through mitotic divisions), to form committed stem cells. The committed stem cells at this stage are called colony-forming unit (CFU). A committed stem cell that produces erythrocytes is called a colony-forming unit- erythrocyte or CFU-E, while those that produce granulocyte and monocyte are called CFU-GM, those for platelets (megakaryocytes) are called CFU-M.

In erythropoiesis, large numbers of the first cell that can be identified as belonging to the red blood series, the proerythroblast are formed from the CFU-E stem cells under appropriate stimulation. Once the proerythroblast has been formed, it divides several more times and goes through many stages of development before it eventually forms many mature red blood cells. Thus, the proerythroblast goes through the following stages:

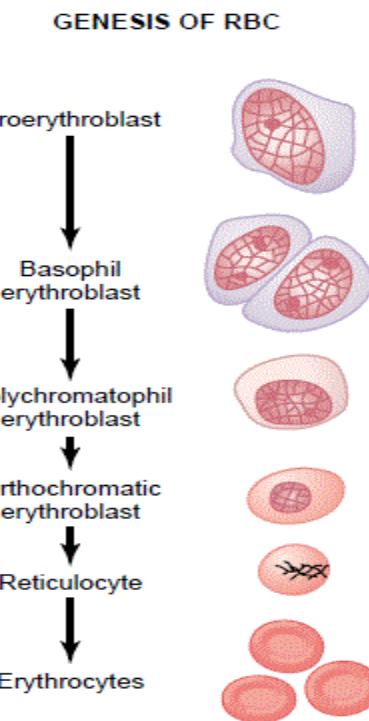


Figure 1.3: Genesis of normal red blood cells (RBCs)

As the proerythroblast undergoes successive division, the daughter cell becomes smaller than its precursor, and its nucleus occupies a smaller proportion of the total cell volume. These tend towards smaller cells and nuclei with successive cell types in the series, the early, intermediate and late erythroblast.

The late erythroblast loses its nucleus and thereby becomes a reticulocyte. The reticulocytes enter the blood by squeezing between the endothelial cells (diapedesis) of the sinusoids in the bone marrow. The cells lose their endoplasmic reticulum and mature into erythrocytes in one or two days. From proerythroblast to erythrocyte takes three to four days. For the red cell count to remain constant, the rate of production of red cells must equal the rate of destruction of old cells. The rate of production is indirectly controlled by the oxygen content of the blood.

Factors promoting erythropoiesis

Factors important in promoting erythropoiesis are erythropoietin, vitamins, iron, other hormones, proteins and certain trace elements.

Erythropoietin

This is a hormone that is also known as erythropoiesis stimulating hormone. It is the main regulator of erythropoiesis in man. It is a glycoprotein and has a molecular weight of 34,000. It is formed mostly in the kidneys (90%) and the remaining 10% is formed in tissues outside the kidneys, mainly in the liver. The main stimulus for the production of erythropoietin is oxygen deficiency (reduced oxygen delivery) to the tissues which can be caused by hypoxia, bleeding, anaemia etc. Erythropoietin then stimulates the haemopoietic tissues to form more red blood cells. Erythropoietin also causes the proerythroblasts to divide more rapidly and proceed to mature erythrocytes. The total number of red blood cells remains relatively constant due to a negative feedback mechanism utilizing the hormone erythropoietin, which is released in response to low oxygen levels detected in the kidneys and liver (Figure 4-3).

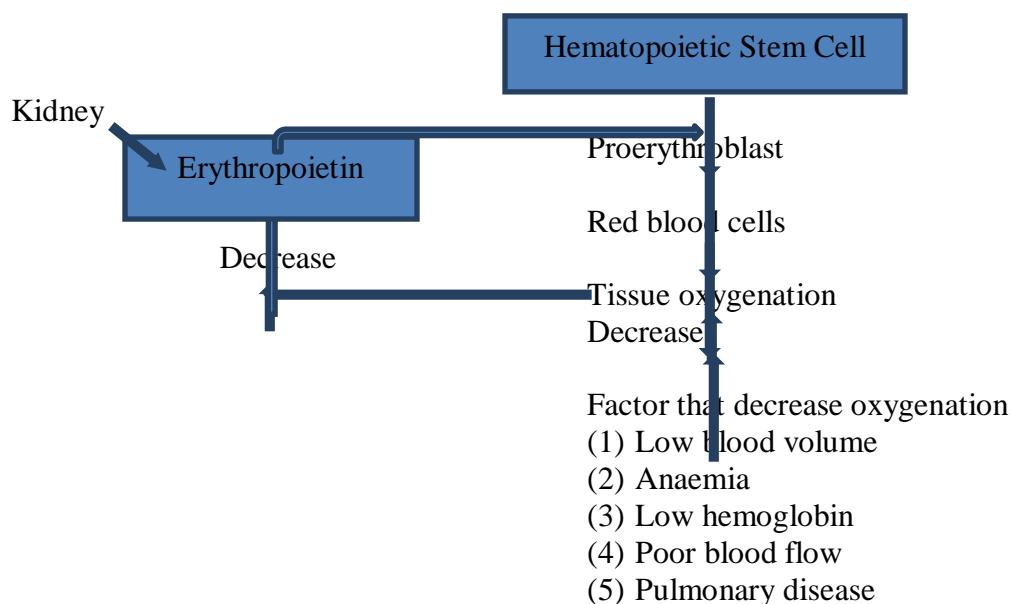


Figure 1.4. Function of the erythropoietin mechanism to increase production of red blood cells when tissue oxygenation decreases.

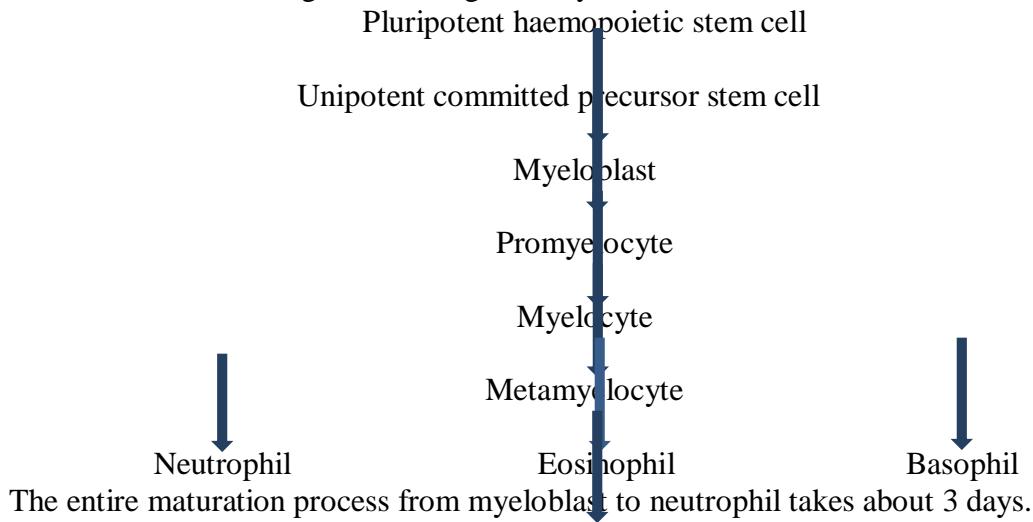
White blood cells

The leukocytes, also called white blood cells, are the mobile units of the body's protective system. White blood cells (leukocytes) help defend the body against disease. Five types of white

blood cells are in circulating blood and are distinguished by size, granular appearance of the cytoplasm, shape of the nucleus, and staining characteristics. The types of white blood cells are the granular neutrophils, eosinophils, and basophils, and the agranular monocytes and lymphocytes. Normally a cubic milliliter of blood contains 5,000 to 10,000 white blood cells.

Formation of granulocytes

The granulocytes are formed in the red bone marrow. The sequence of cell division/differentiation which gives rise to granulocytes is as follows:



Granulocyte and macrophage colony- stimulating factors.

The production of red and white blood cells is regulated with great precision in healthy humans. The production of granulocytes is rapidly increased in infections by bacteria, viruses, fungi or parasites. The proliferation and maturation of the cells that enter the blood from the marrow are regulated by glycoprotein growth factors or hormones that cause cells in one or more of the committed cell lines to proliferate and mature.

Three other factors, called colony-stimulating factors (CSFs) cause committed stem cells to proliferate and mature. These are

- (i) Granulocyte-macrophage CSF. (GM-CSF)
- (ii) Granulocyte CSF (G-CSF)
- (iii) Macrophage (M-CSF)

Interleukins also play important roles in haemopoiesis. Interleukins IL-1 and IL-6 followed by IL-3 act in sequence to convert pluripotent uncommitted stem cells to committed progenitor cells. Interleukins IL-4 and IL-5 also play their roles.

Neutrophils have red-staining fine cytoplasmic granules and a multilobed nucleus; they comprise 54-62% of leukocytes. It is a very motile and actively phagocytic cell that ingests bacteria and other microorganisms, small particulate matter and fibrin. The cytoplasmic granules of neutrophils appear to be the special types of lysosomes containing hydrolytic enzymes which are used to destroy bacteria and other microorganisms. Because of their motility, phagocytic activity and large numbers, neutrophils play a key role in the body's defense against bacterial invasion.

The neutrophils seek out, ingest and kill bacteria and have been called the body's first line of defence against bacterial infections. Neutrophils also release thromboxanes that are vasoconstrictors and platelet-aggregating agents.

Eosinophils have coarse granules that stain deep red, a bilobed nucleus, and make up only 1-3% of circulating leukocytes. They are weak phagocytes, and they exhibit chemotaxis. They are less motile than the neutrophils. The cytoplasmic granules of eosinophils contain many enzymes such as oxidases, peroxidases, and phosphatases, indicating that the primary function of the eosinophil is detoxification of foreign proteins and other substances. Eosinophils are more abundant in connective tissues than in the blood, particularly the lung, the mammary glands, omentum, and the inner wall of the small intestine.

Basophils have fewer granules that stain blue; they account for less than 1% of leukocytes. The basophils in the circulating blood are similar to the large tissue mast cells located immediately outside many of the capillaries in the body. Both mast cells and basophils liberate heparin into the blood, a substance that can prevent blood coagulation. The mast cells and basophils also release histamine, as well as smaller quantities of bradykinin and serotonin.

In allergic reactions, the antigen-antibody reaction cause mast cells or basophils to rupture and release exceedingly large quantities of histamine, bradykinin, serotonin, heparin, slow-reacting substance of anaphylaxis and a number of lysosomal enzymes. These substances then cause local vascular and tissue reactions that cause many, if not most, of the allergic manifestations.

Monocytes are the largest blood cells, have variably-shaped nuclei, and make up 3-9% of circulating leukocytes. They migrate into tissues, enlarge up to five times and develop numerous cytoplasmic granules (lysosomes). These cells are called macrophages and they are much more powerful phagocytes than neutrophils. Macrophages have a powerful lysosomal lipase which breaks down the lipid-rich cell membranes of many bacteria. Many macrophages become fixed within tissues. These stationary phagocytic cells are called tissue macrophage system.

Tissue macrophage are found virtually in all areas of the body especially in the skin and subcutaneous tissue, the lymph nodes, alveoli of the lungs, the liver sinuses (Kupffer cells), the spleen and marrow and in the brain.

Lymphocytes are long-lived, have a large, round nucleus, and account for 25-33% of circulating leukocytes. They are of two main types:

- (1) B-lymphocytes, which are for humoral immunity i.e. they synthesize circulating antibodies.
- (2) T-lymphocytes, which are processed by or in some way dependent on the thymus gland. They are responsible for cell-mediated immunity i.e. the production of lymphocytes which are sensitized against specific antigens.

The life of the granulocytes after being released from the bone marrow is normally 4 to 8 hours circulating in the blood and another 4 to 5 days in tissues where they are needed. The monocytes also have a short transit time, 10 to 20 hours in the blood, before wandering through the capillary membranes into the tissues. Once in the tissues, they swell to much larger sizes to become tissue macrophages, and, in this form, can live for months unless destroyed while performing phagocytic functions. The lymphocytes have life spans of weeks or months; this life span depends on the body's need for these cells. The platelets in the blood are replaced about once every 10 days; in other words, about 30,000 platelets are formed each day for each microliter of blood.

Platelets

Platelets are one of the formed elements of blood the others being red blood cells and white blood cells. Platelets are formed from the megakaryocyte cells in the marrow by pinching-off of bits of cytoplasm and extruding them into the circulation. Platelets are not nucleated and they have a diameter of $2\text{-}3\mu$. The normal platelet count is 200,000- 400,000 per mm^3 . Platelets contain glycogen, lysosomes and two types of granules: dense granules and alpha-granules. The dense granules contain ADP, serotonin and calcium. The alpha-granules contain clotting factors and other proteins. Platelets have the ability to collect at the site of injury (platelet aggregation) and discharge the contents of their granules (platelet release).

Functions of platelets

- (i) They prevent blood loss by adhering to the vessels walls and forming aggregate plugs.
- (ii) On damage, they undergo the release reaction and release amines (histamine, serotonin, adrenaline), adenine nucleotides (ADP) and phospholipids.
- (iii) They bring about clot retraction (platelet contractile protein).
- (iv) They contribute to endothelial integrity

The production of platelet is regulated by thrombopoietin or thrombopoietic stimulating factor (TSF) which is present in the blood. Thrombopoietin increases the formation of megakaryocytes from committed stem cells in the bone marrow.

Plasma and Plasma proteins.

Plasma

Plasma is the fluid portion of the blood. It is straw-coloured. It is part of the extracellular fluid, although it is found in the intravascular space. Its composition is similar to that of the interstitial fluid, except for a much higher concentration of proteins in the plasma.

Composition of plasma

Plasma is composed of

- (i) Water
- (ii) Electrolytes- Na^+ , K^+ , Cl^- , HCO_3^- , SO_4 , PO_4 , Ca^{++} , Mg^{++}
- (iii) Plasma proteins- albumin, globulins and fibrinogen
- (iv) Products of digestion- glucose, free- fatty acids, amino-acids
- (v) Hormones that have been released into the blood
- (vi) Dissolved gases, especially carbon dioxide and a little quantity of oxygen
- (vii) Metabolic waste products such as urea, uric acid, bilirubin.

Plasma proteins

The plasma proteins consist of albumin, globulin and fibrinogen. The total plasma protein concentration is 64-83g per liter (about 6-8g per 100ml). The globulin fraction can be subdivided into α_1 , α_2 , β_1 , β_2 , and γ globulins. The molecular weight of albumin is 69,000 while that of fibrinogen is 340,000. Because of their large molecular size, the plasma proteins do not normally pass through the capillary wall into the interstitial space. The proteins remain in the blood vessels and exert an osmotic force of about 25 mmHg across the capillary wall (oncotic pressure) that tends to pull the fluid from the interstitial space into the intravascular space.

Functions of plasma proteins

- (i) Exerts an osmotic pressure of 25 mmHg (oncotic pressure) that helps to pull water from the tissue spaces back into the blood.
- (ii) Helps to transport various substances, e.g. albumin- transports calcium, bilirubin, alpha-globulin- transports cortisol, thyroxine, Vit B₁₂. beta-globulin- transports iron (transferrin) cholesterol, lipids, insulin, the fat soluble vitamins A, D, and K.
- (iii) Plasma proteins act as blood buffers. They are responsible for 15% of the buffering capacity of the blood.
- (iv) The proteins contribute to the viscosity of the blood.
- (v) The globulins are the antibodies that defend the body against foreign antigens.

Blood groups.

Human beings can be divided into different groups based on the type of antigen on the surface of their red blood cells and the antibodies in their plasma. There are two main systems of blood group- the A.B.O. system and the Rhesus system.

The A.B.O. system

This system is based on the presence of A, B, or A and B agglutinogens (antigens) on the surface of the red blood cells. On the basis of these agglutinogens, human beings can be classified into four groups: groups A, B, AB and O. The plasma of each group contains agglutinin (antibody) that is opposite in name to the antigen on the surface of its red blood cells. For example, group A contains A antigen on the surface of its red blood cells and B antibody in its plasma. The distributions in the different groups are summarized in the table below

Blood Group	Agglutinogen	Agglutinin
A	A	Anti – B
B	B	Anti – A
AB	AB	None
O	None	Anti A and Anti B

The blood group antibodies are gamma globulins, mostly of the IgM types and they are produced by the same cells that produce antibodies to other antigens present or introduced into the body.

The A, B, O blood group is inherited in a Mendelian fashion. The three genes involved are A, B, and O. The six possible phenotypes with the corresponding blood groups are:

Phenotype	Blood Group
AA	A
AB	AB
BB	B
AO	A
OO	O
BO	B

Determination of blood group

Blood group can be determined using anti-A and Anti-B sera. A drop of the anti-serum is placed on a tile (or slide). The blood whose group is to be determined is diluted 1 in 20 with saline (using a white cell pipette of a haemocytometer). A drop of the diluted blood is added to the anti-sera and left for about 10 minutes. At the end of 10 minutes, the mixture is stirred with a glass rod and it is noted whether agglutination has taken place. The typical agglutination pattern is shown in the table.

RBC of Unknown Group	Anti- A	Anti-B	Blood Group
RBC	-	-	O
RBC	+	-	A
RBC	-	+	B
RBC	+	+	AB

- means no agglutination

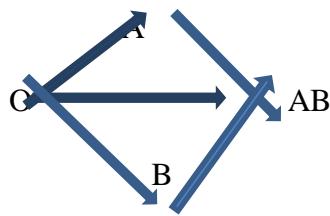
+ means agglutination is present

Rhesus blood group

In Rhesus blood group, there are six types of agglutinogens named C, D, E, and c, d, e. The first three are dominant and the last three are recessive. Of the dominant antigens, the main one is the D antigen. 85% of the population of all white people have the D agglutinogens and are Rhesus positive. The remaining 15% don't have D agglutinogens and are Rhesus negative. In American blacks, the percentage of Rh positives is about 95%, whereas in some African blacks, it is virtually 100%. Unlike in the A, B, O system, the Rhesus blood group has no naturally occurring antibody in the plasma to the D antigen. The antibody is only developed when a Rhesus negative person is exposed to a Rhesus positive blood. Any of the A, B, O, blood groups can be Rh positive or Rh negative. Thus, we can have A + ve, A -ve, B +ve, B-ve etc. Rhesus blood group is of great importance in women in relation to pregnancy. The problem is mainly in the Rhesus negative women. If she has been previously sensitized (by Rh positive blood transfusion or Rh positive baby where foetal and maternal blood mixed together at parturition), if the next pregnancy is an Rh positive foetus, the foetus may develop severe haemolysis and jaundice due to Rh incompatibility or be born dead (hydrops foetalis). An Rh positive woman does not have such problem.

Blood transfusion

This is the process whereby one person gives blood to be passed into the body of another person. The person who gives blood for someone else's use is called "donor" and the person to whom blood is given is called "recipient". Blood transfusion may be indicated in cases of excessive blood loss, severe anaemia or during surgical operation. To ensure that there is no agglutination, it is desirable that a recipient should be given blood of the same group as his own. Since this is not always possible, a recipient can be given blood from another group provided the agglutinins in the recipients' plasma will not react with the agglutinogens on the donors cells. For instance, a recipient who is group A cannot be given a group B blood since the Anti-B in the group A plasma will react with the B agglutinogens on the group B donor cells. Apart from people with the same blood group giving blood to themselves, the other possibilities in transfusion are as follows:



From the above diagram, it will be noted that group O can give blood to all the other groups, including group O, hence this group is called universal donor. Similarly, group AB can receive blood from all other groups; hence the group is called universal recipient. It is necessary to explain here that although blood group O contains anti-A and anti-B, it can be given to blood groups A, B and AB with A and/or B agglutinogens because the volume of the donor blood is far less than the total blood volume of the recipient. Hence, the agglutinin titre in the donor blood is considerably diluted by the larger volume of the recipient's blood so that it is no longer strong enough to cause agglutination.

Hazards of transfusion

Transfusion can be associated with some hazards, although, with great care, such hazards are indeed uncommon. The possible hazards are:

- (a) Incompatibility- this can be of the A B O; Rhesus; or expired blood types. Inappropriate storage (excessive heat or cold) can also cause incompatibility.
- (b) Overloading of the circulation- this occurs if large volume of blood is given too rapidly
- (c) Air embolism
- (d) Transmission of infection e.g. malaria, AIDS virus.
- (e) Allergic reaction
- (f) Sensitization, in case of Rh-positive blood to a Rh-negative person on the first occasion.
- (g) Febrile reaction due to pyrogens. This can be due to contamination of the blood giving set.

UNIT TWO - HAEMOSTASIS

CONTENTS

- 1.0** Introduction
- 3.0** Objectives
- 4.0** Main Content
 - 4.1** Haemostasis
 - 4.2** Vascular spasm
 - 4.3** Formation of platelet plug
 - 3.4** Formation of blood clot and clot retraction
 - 3.5** Repair of blood vessel endothelium
- 4.0** Conclusion
- 5.0** Summary
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- 6.1** Activity
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1.0 Introduction

The body is prone to injury from daily activities and there must be a way of regulating blood loss otherwise the body will lose the source of life. In this unit you will learn more about the process of how the body controls loss of blood.

2.0 Objectives

At the end of this unit, you should be able to:

- i. Explain the concept of Haemostasis
- ii. Describe the sequence of events that cumulate in haemostasis.
- iii. Explain the process of Vascular spasm
- iv. Describe the formation of platelet plug
- v. Discuss the formation of blood clot and clot retraction
- vi. Describe the repair process of blood vessel endothelium

3.0 Main Content

3.1 Haemostasis

This is the process by which blood loss from the body is prevented when a blood vessel is cut or ruptured. Following injury to a blood vessel, the sequence of events in haemostasis is as follows:

- i. Vascular spasm
- ii. Formation of platelet plug
- iii. Formation of blood clot
- iv. Growth of fibrous tissue into the clot to form a permanent seal at the point of vessel damage
- v. Removal of excess fibrous tissue (fibrinolysis)
- vi. Repair of blood vessel endothelium

3.2 Vascular spasm

This is a process in which the injured vessel contracts to narrow or obliterate its lumen, so as to reduce or stop blood loss altogether. Right after a blood vessel is injured, it undergoes a powerful vasoconstriction (vessel narrowing). Because the vasoconstriction is so strong and sudden, it is often called a vascular spasm. This spasm and narrowing of the vessel lumen immediately slows the rate of blood loss, because less blood is now flowing through the constricted, injured vessel. This spasm lasts about 20 to 30 minutes during which time, the next two processes- formation of platelet plug and formation of blood clot would have occurred thereby providing a more effective seal for the damaged vessel.

3.3 Formation of platelet plug

There are about 200,000 to 400,000 platelets per mm^3 of blood. When a vessel is cut open, the collagen fibers in its wall are torn. Platelets in the surrounding blood become sticky and attach to the shredded ends of the collagen fibers. As they pile up, a platelet plug is created that partially closes off the hole in the vessel wall. Platelets also release ADP and enzymes that cause formation of thromboxane A. Thromboxane A and ADP further cause the sticking together of platelets leading to platelet plug.

3.4 Formation of blood clot and clot retraction

This involves coagulation of the blood that comes out of the blood vessel at the site of injury.

Injury to the vessel wall creates a chemical called prothrombin activator. As its name indicates, prothrombin activator converts prothrombin (an inactive clotting enzyme) into an active clotting enzyme called thrombin. Thrombin acts upon fibrinogen, which are soluble or dissolvable within the bloodstream to form fibrin. Fibrin filaments are insoluble (not dissolvable) within the blood plasma. Hence, the fibrin filaments settle out of the blood and are deposited as a fibrin meshwork over the platelet plug. More circulating platelets, as well as a few red blood cells (RBCs), get stuck in this fibrin meshwork.

The process by which the body prevents blood loss occurs through two mechanisms to produce a definite fibrin clot. Disorders in either system can cause diseases that cause either too much or too little clotting. They are the Intrinsic and Extrinsic mechanisms. They involve the interplay and activation of proteins or clotting factors. They are;

Factor I = Fibrinogen

Factor II = Prothrombin

Factor III = Tissue factor

Factor IV = Calcium

Factor V = Labile factor

Factor VI - Does not exist as it was named initially but later on discovered not to play a part in blood coagulation.

Factor VII = Stable factor

Factor VIII = Antihemophilic factor A

Factor IX = Antihemophilic factor B or Christmas factor (named after the first patient in whom the factor deficiency was documented)

Factor X = Stuart Prower factor

Factor XI = Antihemophilic factor C

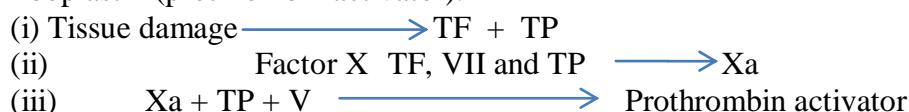
Factor XII = Hageman factor

Factor XIII = Fibrin stabilizing factor

Extrinsic Pathway

In the Extrinsic pathway, tissue trauma leads to release of two factors-tissue factors (TF), a proteolytic enzyme and tissue phospholipids, the latter is mainly from damaged cell membranes. Factor X, in the presence of tissue factors, factor VII and tissue phospholipids is converted to activated factor X.

Activated factor X reacts with tissue phospholipids and Factor V leading to formation of thromboplastin (prothrombin activator).



Where TF = Tissue factor

TP = Tissue phospholipids

VII= Factor VII

V = Factor V

Xa = Activated Factor X

Intrinsic Pathway

In the Intrinsic pathway,

- (a) contact of blood with collagen or a foreign surface converts Factor XII to activated factor XII, a proteolytic enzyme. Also, trauma leads to platelets aggregation and release of platelet phospholipid or platelet factor.
 - (b) Next, Factor XI is acted upon by activated Factor XII to form Activated Factor XI.
 - (c) Factor IX is acted upon by activated Factor XI and converted to activated Factor IX.
 - (d) Factor X is acted upon by activated Factor IX, Factor VII and platelet phospholipids and converted to Activated Factor X.
 - (e) Activated Factor X reacts with Factor V and platelet phospholipids to form thromboplastin (prothrombin activator).
- (i) Factor XII Collagen, foreign surface $\xrightarrow{\hspace{2cm}}$ XII_a
(ii) Factor XI XII_a $\xrightarrow{\hspace{2cm}}$ XI_a
(iii) Factor IX XI_a $\xrightarrow{\hspace{2cm}}$ IX_a
(iv) Factor X $\xrightarrow{\hspace{2cm}}$ IX_a + VII & PP X_a
(v) X_a + V + PP $\xrightarrow{\hspace{2cm}}$ prothrombin activator

Conversion of prothrombin to thrombin

Prothrombin is formed in the liver and vitamin K is required in its formation. Prothrombin is converted by prothrombin activator (formed in the extrinsic and intrinsic pathways) in the presence of calcium ions to thrombin. Platelets also play an important role in the conversion of prothrombin to thrombin.

Conversion of fibrinogen to fibrin

Fibrinogen is also formed in the liver. Thrombin, a proteolytic enzyme, acts on fibrinogen and converts it to fibrin monomer. The fibrin monomers join one another to form long fibrin threads. These fibrin threads form a mesh-work that traps blood cells, platelets and plasma. The initial fibrin thread can be easily broken, but it is acted upon by fibrin stabilizing factor (factor XIII). The factor XIII is first activated by thrombin and the activated factor XIII act on the fibrin threads to strengthen them so that they can no longer be broken easily.

Clot retraction

This is the final step in the clotting process. The clot formed above is soft and jelly-like. The fibrin threads in the clot contract a few minutes after the clot is formed and squeeze out most of the fluid (serum) so that what is left is a firm clot. Platelets are important in clot retraction and low platelets count can lead to failure of clot retraction.

Finally, excess fibrin that may be occluding part of the blood vessel lumen is removed (fibrinolysis) and the damaged endothelium is replaced by a new one.

Growth of fibrous tissue into the clot

The clot is soon invaded by fibroblasts leading to formation of dense fibrous tissue. The latter completes the final sealing of the cut in the blood vessel.

Fibrinolysis

If a small blood vessels is involved, the fibrous tissue may permanently occlude the entire lumen of the vessel, but if a big blood vessel is involved, the fibrous tissue at the site of vascular injury is retained, but excess fibrous tissue in clots that must have extended to the lumen of the vessel is dissolved by the enzyme plasmin, so that free flow of blood can occur once more.

3.5 Repair of blood vessel endothelium

This is the final step in the process of haemostasis. The damaged endothelium is replaced by the formation of a new lining.

4.0 Conclusion

- vii. Blood loss is control by several mechanical and chemical mechanisms. In this unit you have learnt that blood loss is controlled through vascular spasm, formation of blot clot, growth of fibrous tissue into the clot to form a permanent seal at the point of vessel damage, fibrinolysis and repair of blood vessel endothelium

5.0 Summary

In this unit, you have learnt that haemostasis is process by which blood loss from the body is prevented when a blood vessel is cut or ruptured through six main stages from the point of cut to the point of repairs of the blood vessels. You have also learnt about what happens at the different stages of repair.

6.0 Tutor Marked Assignments

6.1 Activity – See the instructions for Laboratory practicals as specified by the Facilitator

6.2 Answer the following questions.

- i. What is Haemostasis?
- ii. Explain Vascular spasm
- iii. Describe the formation of platelet plug
- iv. Discuss the formation of blood clot and clot retraction
- v. Describe the process of Repair of blood vessel endothelium

7.0 References and other resources

Fox SI. (2012). Human Physiology. 12th edition, Mc Graw Hill, New York.

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UNIT THREE - IMMUNE SYSTEM

CONTENTS

1.0 Introduction

2.0 Objectives

3.0 Main Content

- 3.1** Immunity
- 3.2** Active immunity
- 3.3** Mechanism of action of antibodies
- 3.4** Passive immunity
- 4.0** Conclusion
- 5.0** Summary
- 6.0** Tutor Marked Assignments
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- 7.0** References and other resources

1.0 Introduction

The body is able to survive in an environment with microorganisms and the toxins of these organisms that are often dangerous to the survival of the body. However the body's immune system helps to fight microorganisms and develop some resistance to them. In this unit, you are going to learn more about the different types of immunity and the mechanism of antibody function.

2.0 Objectives

At the end of this unit, you should be able to:

- i. Explain the concept of Immunity
- ii. Discuss different types of Immunity
- iii. The difference between Passive immunity and Active immunity
- iv. Discuss the Mechanism of action of antibodies

3.0 Main Content

3.1 Immunity

This is the ability of the human body to resist almost all type of organisms or toxic substances that tend to damage the tissue or organs. It is classified into 2 major groups:

(a) Active immunity and (b) Passive immunity.

3.2 Active immunity

This is further divided into innate and acquired immunity.

The innate immunity

This involves all the processes already present in the body of an organism that are directed at protecting the body of the organism, e.g. (i) the resistance of the skin to invasion of organism (ii) destruction in the stomach of foreign organism entering the gut through the mouth by acid secretion (iii) phagocytosis of bacteria and other foreign invaders by white cells or cells of the tissue macrophage system (iv) also present in the blood are certain chemicals such as lysosomes that attack foreign organisms or toxins.

Acquired immunity: This type of immunity is not present naturally in the body. There are two types of acquired immunity namely cellular and humoral immunity. It is the product of the body lymphocyte system.

Cellular immunity: It plays an important role in the body's defense against viral, bacteria, fungi infection and in transplant rejection. T-lymphocyte function may be suppressed by steroid hormones or by the drug azathioprine. Such drugs are used to prevent rejection of grafted tissue or organelles. Cellular immunity is mediated by T-lymphocytes. T- lymphocytes derive from the stem cell in bone marrow migrate to the thymus where it is processed and become immunologically competent. During this process, each lymphocyte T develop specific reactivity against one antigen, thus at the end of the process there are different T-lymphocytes with specific reactivity against millions of different antigen. These processed lymphocytes leave the thymus and spread throughout the body lodging in the lymphoid tissue all over the body. These T-cells have thousands of receptor molecules on its surface and antigens bind with these receptors. T-cells processed in the thymus are screened to ensure that when release into circulation they do not react with the body tissue, those that fail the test are phagocytized instead of begin released.

There are four major types of T-lymphocyte

- (1) Helper T cells
- (2) Cytotoxic or killer T cells
- (3) Suppressor T cells
- (4) Memory T cells

Helper T cell: They are the most numerous of the T cells and they constitute 70% of T-lymphocyte. They serve as the main regulator of all immune functions. They do this by forming series of products mediator called lymphokines or interleukins that act on the cell of the immune system. The important interleukin secreted by the Helper T cell are IL-2, IL-3, IL-4, IL-5, IL-6, granulocyte-monocyte cloning stimulating factor and the interferon. When this lymhokines are absent, the remainder of the immune system is paralyzed.

Helper T cells stimulate the growth of cytotoxic T cell and suppressor T cell. This is mediated by the interleukin -2 with IL-4 and IL-5 playing subsiding role. T cells also stimulate the B-cell growth and differentiation to form plasma cell and antibodies. IL-4, IL-5, IL-6 are responsible for this action. The lymhokines of the Helper T cells also ensure that macrophages slow down or stop their migration when they reach the site of attraction. They also activate the macrophages leading to increase and infective phagocytosis. The cellular T cells are mediated by the lymphocytes.

Cytotoxic cells: They are direct attack cell capable of killing microorganism. Each cell has antigen specific surface receptors that bind tightly to organism or cell that contain their specific binding antigen. They secrete hole-forming protein called perforins that punch large holes in the membrane of the attached cell leading to inflow of fluid into the cell and lysis. A single cytotoxic cell can kill hundreds of organism before its own death. Cytotoxic T cell play an important part in destroying cancer cell, heart transplant and other type of cells that are foreign to the body.

Suppressor T cells: They suppress the function of both cytotoxic and helper T cells. They regulate the activity of other cells preventing them from causing excessive immune reaction which may damage the body tissue. The process by which suppressing T cell limit the ability of immune to attack a person own tissue is known as immune tolerance.

Memory T (or B) cells: These are cells that have been exposed to an antigen and are readily converted to effector cells by later encounter with the same antigen.

Humoral immunity

This is mediated by B-lymphocytes. They are preprocessed in the liver during the mid foetal life and in the bone marrow in the late foetal life and after birth. After preprocessing, they migrate into the lymphoid tissue throughout the body. These cells differentiate into plasma cell and memory B cells. The mature plasma cells are responsible for the production of antibodies. These antibodies produced are called immunoglobulins and there are five classes of immunoglobulins-IgM, IgG, IgA, IgD, and IgE. IgG is the most abundant immunoglobulin in man (about 75% of the total). Most antitoxins and virus antibodies belong to this class of immunoglobulins. IgM are efficient in reacting with bacteria and foreign cells. IgA protect the mucus membrane. IgE is involved in hypersensitivity such as asthma and hay fever.

When an antigen is introduced into the body, antibodies appear in the blood after a few days. The antibody produced on this first contact with antigen increases rapidly to a peak which is not very high and then decline. If the same animal is injected with the same antigen, the response occurs sooner and the amount of antibody produced is much greater than the first exposure. This is the secondary immune response. The more rapid appearance of antibody and the greater production are due to the presence of long-lived B-lymphocytes called memory B cells.

3.3 Mechanism of action of antibodies

Antibodies act in two different ways: (i) by direct attack on the invader (ii) action of the complement system that destroys the invader. The direct action of antibodies is carried out in several ways which include: (i) agglutination (ii) precipitation (iii) neutralization and lysis.

These direct actions of antibodies attacking antigenic invader under normal condition are not strong enough to play a major role in protecting the body against the invader. Most of the protection form the amplifying effect of the complement system for antibodies action.

Complement system cell: Complement is a collective term of describing a system of 20 different proteins many of which are enzyme precursors. The principal actors of the system are 11 proteins designated C1-C9, B and D, shown in Figure 1-30. The enzyme precursors are normally inactive, but they can be activated in two ways: (i) the classical pathway (ii) alternate pathway.

The classical pathway is mediated when an antigen-antibody reaction occurs. The activated C₁ activates C₂, C₃, C₄, and so on, setting in motion a “cascade” of reactions and the enzyme produce cause the following effects:

- (1) Phagocytosis
- (2) Lysis
- (3) Agglutination
- (4) Neutralization
- (5) Chemotaxis
- (6) Activation of mast cells and basophils
- (7) Inflammatory effects

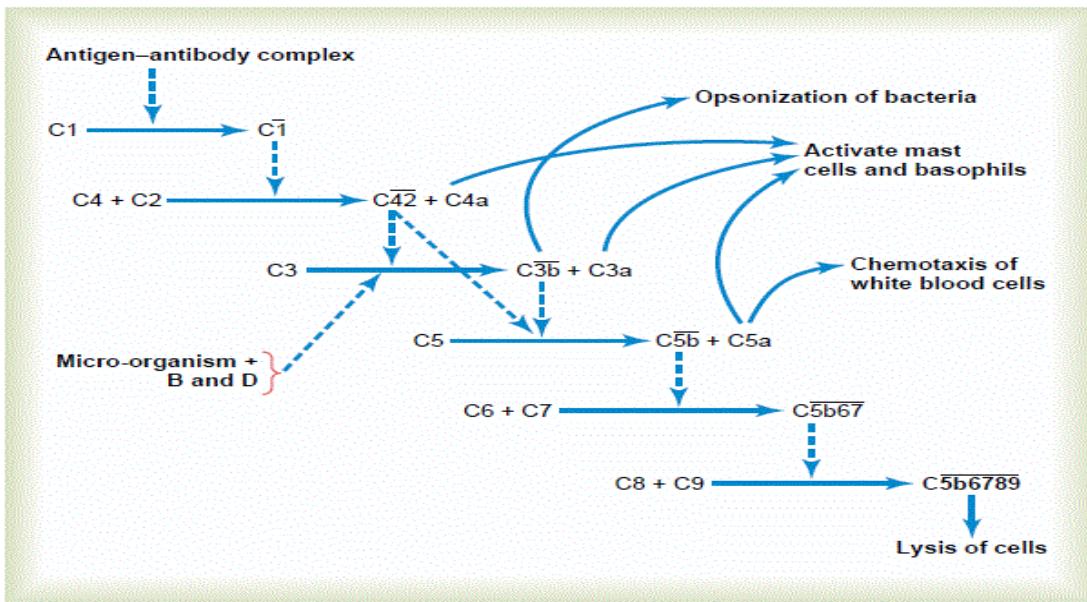


Figure 3.1: Cascade of reactions during activation of the classical pathway of the complement system.

In the alternate pathway, antigen-antibody complexes are not required to activate the system. This occurs in response to large polysaccharide molecules of some invading organisms. These substances react with complement B and D forming an activated product that activates factor C3 setting off the remainder of complement pathway. This leads to the release of the same enzymes and the same effects as in the classical pathway. Since the alternate pathway does not involve an antigen-antibody reaction, it can function even before a person is immunized against a particular organism.

3.4 Passive immunity

This can be achieved by injection of preformed antibody obtain from the plasma of another blood cell or of an animal that have already been actively immunized against a particular disease. Such antibody can be given in treatment of tetanus. Passive immunity can also be transferred from a mother to a newborn via colostrum.

4.0 Conclusion

The body is able to resist infections through active (innate or acquired) and passive immunity through active process of antibodies formation.

5.0 Summary

In this unit, you have learnt about the following:

- i. The concept of Immunity
- ii. Different types of Immunity
- iii. The differences between Passive immunity and Active immunity
- iv. The Mechanism of action of antibodies

6.0 Tutor Marked Assignments

6.1 Activity – As prescribed in the Laboratory assignment

6.2 Answer the following questions:

- i. Explain the concept of Immunity
- ii. Discuss different types of Immunity
- iii. Differentiate between Passive immunity and Active immunity and give examples of such as you see in your practice
- iv. Discuss the Mechanism of action of antibodies

7.0 References and other resources

Ganong WF. (2010). Review of Medical Physiology. 23rd edition, Mc Graw Hill, New York.

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MODULE 3 - Cardiovascular System

Introduction

The heart is the known life pump that sustains fluid circulation to all parts of the body for a lifetime. It is an important organ whose function is moderated by the special innervations. In this module, you are going to learn more about how the heart performs its functions and work in with the vessels to maintain the needed pressure for blood to flow round the body.

Module Objectives

At the end of this Module study session, you must be able to:

- i. Describe the structure of the heart and its components
- ii. Describe the systemic and the pulmonary circulation
- iii. Describe the pacemaker potential and the myocardial action potential
- iv. Describe the components of the electrocardiogram (ECG)
- v. Describe the short-term and long-term regulation of arterial blood pressure
- vi. Describe circulatory shock

Contents

Unit 1 Circulatory System

Unit 2 Cardiac Functioning

Unit 3 Electrocardiography

Unit 4 Cardiac Output and Control of Cardiac Output

Unit 5 Arterial Blood Pressure

Unit 6 Circulatory Shock

UNIT ONE - THE CIRCULATORY SYSTEM

CONTENTS

- 1.0** Introduction
- 2.0** Objectives
- 3.0** Main Content
 - 3.1** The concept of Haemodynamics
 - 3.2** The functional parts of the circulation
 - 3.3** The functional divisions of the circulation
- 4.0** Conclusion
- 5.0** Summary
- 6.0** Tutor Marked Assignments
- 6.1** Activity
- 6.2** Tutor Marked Tests
- 7.0** References and other resources

1.0 Introduction

There is a mechanism of fluid movement through the body that allows for exchange of required nutrients and exchange of different types of wastes. This unit covers the coordinated circulation of blood to different parts of the body.

2.0 Objectives

At the end of this unit, you should be able to:

- i. Explain the concept of Haemodynamics
- ii. Explain the functional parts of the circulation
- iii. Explain the functional divisions of the circulation

3.0 Main Content

3.1 Systemic and pulmonary circulation: Haemodynamics

The function of the circulation is to service the needs of the body tissues—to transport nutrients to the body tissues, waste products from the tissue to the excretory organs, hormones from one part of the body to another, and in general, to maintain an appropriate environment in all the tissue fluids of the body for optimal survival and function of the cells. The rate of blood flow through most tissues is controlled in response to tissues need for nutrients. The heart and circulation in turn are controlled to provide the necessary cardiac output and arterial pressure that are required for tissue blood flow.

The circulation is divided into the systemic circulation and the pulmonary circulation. The systemic circulation supplies blood to all the tissues of the body except the lungs, so it is also called the greater circulation or peripheral circulation.

3.2 Functional parts of the circulation

Arteries: Are blood vessels that carry blood away from the heart to the lungs and tissues. The arterioles are the last small branches of the arterial system; they act as control conduits through which blood is released into the capillaries, and because of their small diameter, they play a key role in vasoconstriction and vasodilatation. Most arteries and arterioles carry oxygenated blood, except the pulmonary artery which transports deoxygenated blood from right ventricle to the lungs.

Capillaries: They are microscopic blood vessels that allow the exchange of fluid, nutrients, electrolytes, hormones, and other substances between the blood and the tissue. To serve this role, the capillary walls are very thin and have numerous minute capillary pores permeable to water and other small molecular substances.

Veins: These are blood vessels that carry blood to the heart, from the lungs and tissues. They serve as a major reservoir of extra blood. Blood pressure in veins is extremely low as a result, valves formed by the tunica internal layer are necessary to prevent backflow. Most veins carry deoxygenated blood, except the pulmonary vein which transports oxygenated blood from the lungs to the left atrium. The venules collect blood from the capillaries, and they gradually coalesce into progressively larger veins.

3.3 Functional divisions of the circulation

Systemic circulation

Systemic circulation is a part of the cardiovascular system which is responsible for carrying oxygenated blood away from the heart to the body, and return deoxygenated blood back to the heart. Oxygen-rich blood from the lungs leaves the pulmonary circulation when it enters the left atrium through the pulmonary veins. The blood is then pumped through the mitral valve into the left ventricle. From the left ventricle, blood is pumped through the aortic valve and into the aorta, the body's largest artery. The aorta arches and branches into major arteries to the upper part of the body before passing through the diaphragm, where it branches further into arteries which supply the lower parts of the body. The arteries branch into smaller arteries, arterioles, and finally capillaries. Waste and carbon dioxide diffuse out of the cell into the blood, while oxygen and nutrients diffuses out of the blood into the interstitial fluid and then into the cell. The deoxygenated blood continues through the capillaries which merge into venules, then veins, and finally the venae cavae, which drain into the right atrium of the heart. From the right atrium, the blood travels through the pulmonary circulation to be oxygenated before returning again to the systemic circulation. Coronary circulation, blood supply to the heart muscle itself, is also part of the systemic circulation.

Pulmonary circulation

Pulmonary circulation is a part of the cardiovascular system which is responsible for carrying de-oxygenated from the heart to the lungs and then back to the heart for it to transfer the oxygenated blood to the rest of the body. Oxygen-depleted blood from the body leaves the systemic circulation when it enters the right atrium through the superior and inferior vena cavae. The blood is then pumped through the tricuspid valve into the right ventricle. From the right ventricle, blood is pumped through the pulmonary valve and into the pulmonary artery. The pulmonary artery splits into the right and left pulmonary arteries and travel to each lung. In the lungs, the blood travels through capillary beds on the alveoli where gaseous exchange occurs, removing carbon dioxide and adding oxygen to the blood. The alveoli are air sacs in the lungs that provide the surface for gas exchange during respiration. The oxygenated blood then leaves the lungs through pulmonary veins, which returns it to the left atrium, completing the pulmonary circuit.

After entering the left heart, the blood flows through the bicuspid valve into the left ventricle. From the left ventricle, the blood is pumped through the aortic valve into the aorta to travel through systemic circulation, delivering oxygenated blood to the body before returning again to the pulmonary circulation.

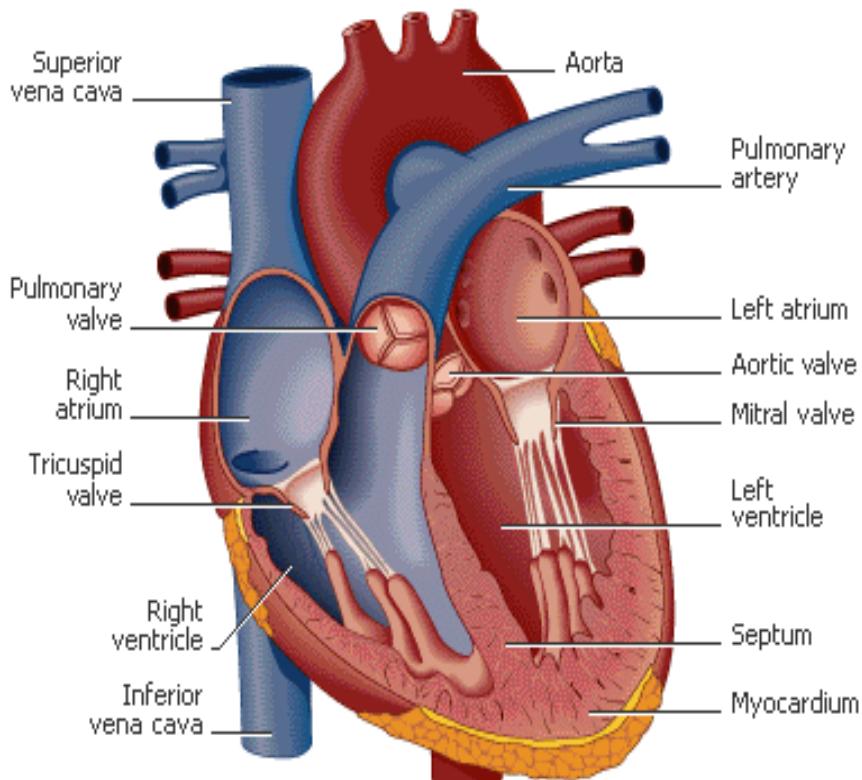


Figure 1.1: The Human Heart

4.0 Conclusion

With blood circulation through the arteries, veins and capillaries, circulation is divided into the systemic circulation and the pulmonary circulation. The systemic or greater circulation supplies blood to all the tissues of the body except the lungs, while the pulmonary circulation covers the movement of de-oxygenated blood from the heart to the lungs and then back to the heart for it to transfer the oxygenated blood to the rest of the body.

5.0 Summary

In this unit, you have learnt about the concept of Haemodynamics, the functional parts of the circulation and the functional divisions of the circulation.

6.0 Tutor Marked Assignments

6.1 Activity – Laboratory assignment

6.2 Answer the following questions:

- i. Explain the concept of Haemodynamics
- ii. Describe the functional parts of the circulation
- iii. Explain what happens in pulmonary and systemic circulation.

7.0 References and other resources

- Fox SI. (2012). Human Physiology. 12th edition, Mc Graw Hill, New York.
Ganong, W.F. (2010). Review of Medical Physiology. 23rd edition, Mc Graw Hill, New York.
Guyton, A.C, Hall J.E. (2001). Textbook of Medical Physiology. Harcourt International Edition , 10th edition, W.B. Saunders, Philadelphia.
Oyebola DO. (2002). Essential Physiology, Vol 1, Nihort Press.

UNIT TWO - CARDIAC FUNCTIONING

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- 1.0** Introduction
- 2.0** Objectives
- 3.0** Main Content
 - 3.1** The Cardiac Muscle
 - 3.2** The Cardiac Muscle Action Potential
 - 3.3** The Pacemaker cells
 - 3.4** The Cardiac Cycle
- 4.0** Conclusion
- 5.0** Summary
- 6.0** Tutor Marked Assignments
- 6.1** Activity
- 6.2** Tutor Marked Tests
- 7.0** References and other resources

1.0 Introduction

The heart is a life pump regulated by special innervations. In this unit, you are going to learn more about how the structuring of the heart supports its functions.

2.0 Objectives

At the end of this unit, you should be able to:

- i. Explain what in details The Cardiac Muscle
- ii. Discuss The Cardiac Muscle Action Potential
- iii. Explain in details The Pacemaker cells
- iv. Discuss The Cardiac Cycle

3.0 Main Content

3.1 The Cardiac Muscle

The heart is a muscular organ which weighs about 250-350 gm in an adult. It has four chambers, two atria and two ventricles. The heart consists of a specialized muscle called cardiac muscle.

Cardiac muscle is similar in structure to skeletal muscle in many ways; however, there are several important differences that can be discerned at the structural level. The electrical activity of cardiac muscle is very different from that of skeletal muscle.

Like skeletal muscle, cardiac muscle is striated. It contains the same basic contractile proteins forming thick and thin filaments that are organized into sarcomeres as they are in skeletal muscle, and the same sliding filament mechanism applies. Cardiac muscle fibers or cardiac cells (i.e. myocytes) also contain myofibrils, a network of T-tubules, and sarcoplasmic reticulum (SR). Force generation and its control by Ca^{2+} are also very similar to skeletal muscle, although cardiac muscle is less dependent on the release of Ca^{2+} from the sarcoplasmic reticulum, and the mechanism of sarcoplasmic reticulum Ca^{2+} release is different (i.e., calcium-induced -calcium release).

Cardiac muscle cells are similar to type I (slow oxidative) skeletal muscle fibers. Cardiac muscle cells depend primarily on oxidative phosphorylation to generate ATP. They are highly resistant to fatigue, but are also highly dependent on a continuous supply of oxygen. Cardiac muscle cells are much shorter than skeletal muscle fibers and they are sometimes branched. A typical ventricular muscle cell is roughly 100 microns long and about 20 microns in diameter.

Individual cardiac muscle cells are joined together by structures called intercalated discs, as shown in Figure 1-2. This is a very important distinction between cardiac and skeletal muscle. There are two types of membrane junctions in the intercalated discs. These are:

- (a) desmosomes, which are mechanical adhering junctions which hold the cells together.
- (b) gap junctions, which are low resistance electrical connections between adjacent cells.

Gap junctions allow electrical activity (e.g., action potentials) of one cell to spread to adjacent cells. Cardiac muscle cells are electrically coupled to one another, which allow the heart to contract as a unit (a functional syncytium).

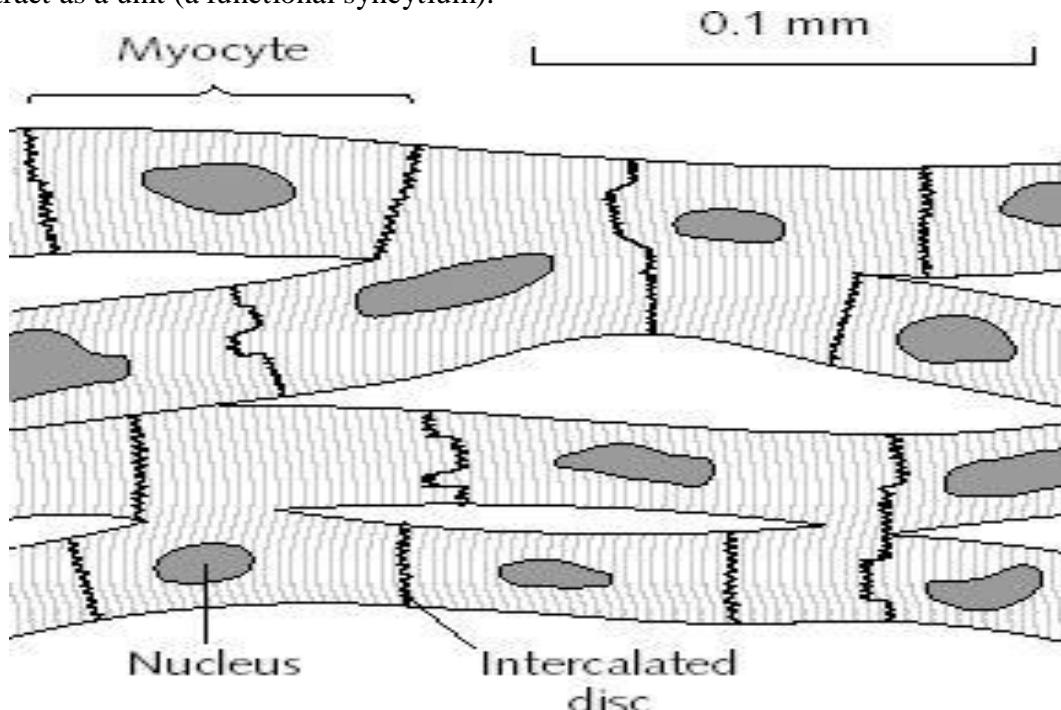


Figure 2.1: Diagrammatic section of cardiac muscle

3.2 The Cardiac Muscle Action Potential

The cardiac muscle has a distinct action potential which is different from that seen in skeletal muscle and is an important adaptation for the functions of the heart.

The cardiac action potential has five phases, as shown in Figure 1-3. During phase 0, membrane permeability to potassium decreases and fast sodium channels open allowing the influx of Na^+ , producing rapid depolarization from -90 mV to $+10\text{ mV}$. During phase 1, there is partial repolarization, because of a decrease in sodium permeability. Phase 2 is the plateau phase of the cardiac action potential. Membrane permeability to calcium increases during this phase, maintaining depolarization and prolonging the action potential. Membrane permeability to calcium decreases to some extent towards the end of phase 2, and the plateau is partially maintained by an inward sodium ion. Sodium flows into the cell through the sodium–calcium exchanger. The exchanger transfers three sodium ions into the cell in exchange for one calcium ion flowing out, and so produces a net inward flow of positive ions. As calcium channels inactivate towards the end of the plateau phase, an inward potassium ion produces repolarization in phase 3. The resting membrane potential in phase 4 is approximately -90 mV .

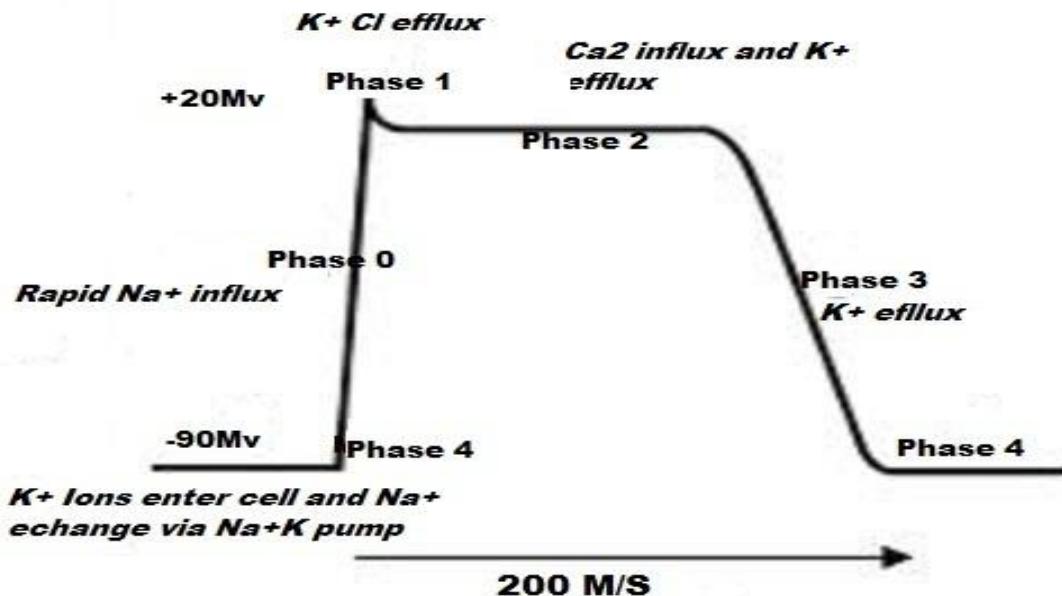


Figure 2.2: Phases of the Action Potential of a Cardiac Muscle Fibre. 0, depolarization; 1, rapid repolarization; 2, plateau phase; 3, late repolarization.

3.3 The Pacemaker cells

Pacemaker cells are found in the sinoatrial (SA) and atrioventricular (AV) nodes. However, the sinoatrial node has a faster rate of discharge and therefore ordinarily controls the rate of beat of the entire heart and is known as the cardiac pacemaker. The cells of the pacemaker have certain characteristics that enable it to exhibit automatic rhythmicity.

- (1) The resting membrane potential is -55 to -60 mV in sinoatrial node in comparison with -85 to -90 mV in ventricular muscle fibers.
- (2) The cell membranes of the sinus fibers are naturally leaky to sodium ions and allow the influx of Na^+ , thereby neutralizing much of the intracellular negativity.

Between heart beats, influx of Na^+ causes slowly rising membrane potential. When the membrane potential rises to a threshold voltage of about -40 mV , the calcium-sodium channels become activated, leading to rapid entry of both calcium and sodium ions thus eliciting the action potential. However the opening of the calcium and sodium channels is transient and they soon close and the simultaneous opening of K^+ channels leads to efflux of K^+ ions which causes repolarization effectively terminating the action potential. As the resting membrane potential reaches -55mV to -60mV , the K^+ ions channels close. The inward leaking of Na^+ ions overbalance the efflux of K^+ ions and the resting membrane potential rises again towards the threshold level for discharge. This process is repeated over and over throughout the lifetime of the individual.

3.4 The Cardiac Cycle: The cardiac events that occur from the beginning of one heartbeat to the beginning of the next are called the cardiac cycle or the series of events that occur during one complete heartbeat. Cardiac cycle is divided into two main phases; (i) ventricular diastole (ii) ventricular systole

Figure 2.3 shows the different events during the cardiac cycle. Ventricular diastole refers to ventricular relaxation phase. Events occurring during the diastole include; isovolumetric (isovolumic) relaxation, rapid passive filling, slow filling (diastasis), rapid active filling (atrial contraction).

After the ventricles have ejected the blood into the arteries, the aortic and pulmonary valves close. As the ventricles relax there is isovolumetric relaxation i.e. no change in volume as the ventricles relax, because all the four valves are closed. This relaxation with no change in volume leads to a reduction in the pressure in the ventricle. Simultaneously blood flowing into atria from inferior and superior vena cavae and the pulmonary veins cause an increase in the pressure in the atria. When the pressure in the atria rises above that in the ventricles, the atrio-ventricular valves are forced open and blood rushes rapidly into the ventricles. About 75 percent of blood entering the ventricles does so by this passive means (rapid passive filling). The remaining 25 percent is forced into the ventricles by contraction of atria (rapid active filling). At this point the ventricles begin to contract and there is sudden closure of the atrioventricular valves. (This gives rise to the first heart sound).

Ventricular systole refers to period of ventricular contraction. Events occurring during ventricular systole include; isovolumetric (isovolumic) contraction, ventricular ejection.

The ventricles continue to contract with four valves again closed. This phase is called the isovolumetric contraction. During this phase the pressure in the ventricles rises rapidly until they exceed that in pulmonary artery and aorta. The aortic and pulmonary valves are pushed open and blood is ejected into the aorta and pulmonary arteries (ventricular ejection). The ejection continues leading to drop of pressure in the ventricles until the pressure in the aorta and pulmonary artery exceeds that in the ventricles. There is thus a tendency for the blood to flow back which is prevented by closure of the aortic and pulmonary valves. (This gives rise to the second heart sound). Once the pulmonary and aortic valves are closed, all four valves are again closed and isovolumetric relaxation of the ventricles begins thereby completing the cardiac cycles. On average, the cycle is repeated every 0.8 seconds i.e. 72 cycles per minute.

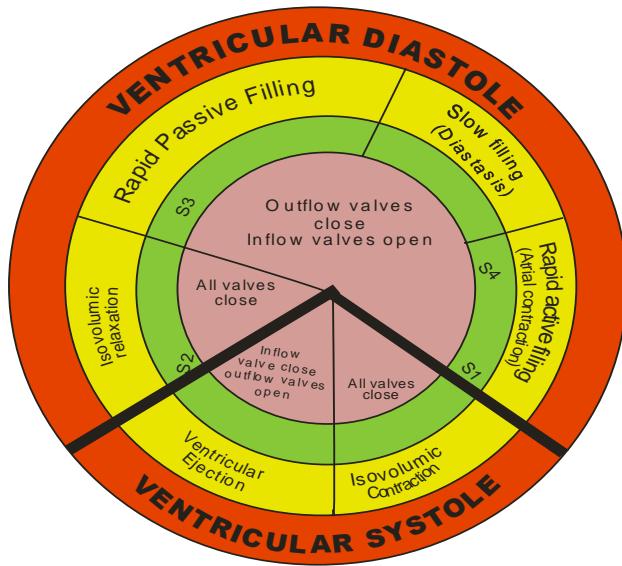


Figure 2.3: Annotated diagram of cardiac cycle

Wiggers diagram is a standard diagram in cardiovascular physiology to illustrate the haemodynamic consequences of cardiac cycle (Figure 1-5). The X-axis contains the time. The Y-axis contains; Blood pressure; ventricular pressure, aortic pressure and atrial pressure, Ventricular volume changes, Electrocardiogram, Phonocardiogram (optional).

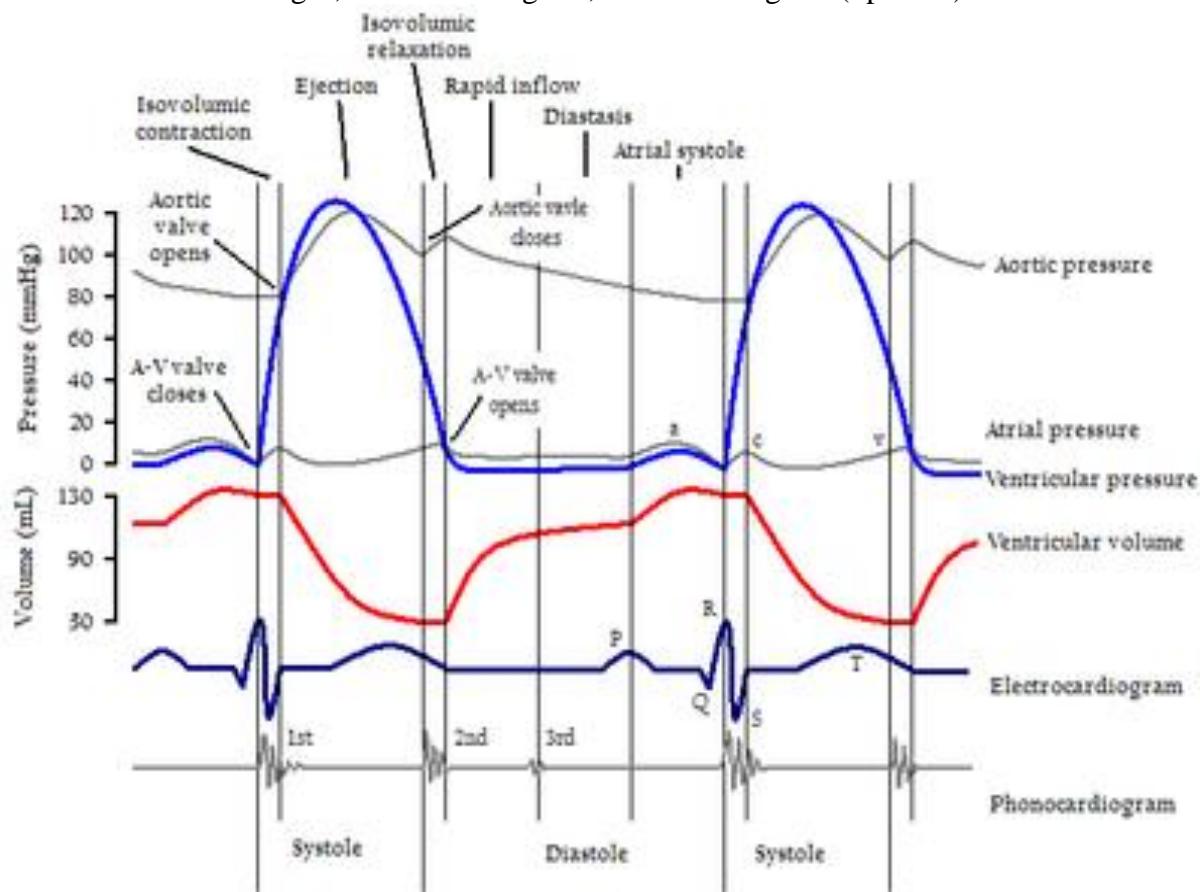


Figure 2.4: Wiggers Diagram

4.0 Conclusion

The heart is made of special cardiac muscles with a distinct action potential which is different from that seen in skeletal muscle and is an important adaptation for the functions of the heart.

5.0 Summary

In this unit you have learnt about the Cardiac Muscle, the Cardiac Muscle Action Potential, the Pacemaker cells and the Cardiac Cycle and you should be able to explain the describe how the the cardiac muscle is specially made to perform its unique functions within these contexts.

6.0 Tutor Marked Assignments

6.1 Activity- See Laboratory instructions

6.2 Answer the following questions:

- i. Explain in details The Cardiac Muscle
- ii. Discuss The Cardiac Muscle Action Potential
- iii. Explain in details The Pacemaker cells
- iv. Discuss The Cardiac Cycle

7.0 References and other resources

Fox SI. (2012). Human Physiology. 12th edition, Mc Graw Hill, New York.

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UNIT THREE - ELECTROCARDIOGRAPHY

CONTENTS

1.0 Introduction

2.0 Objectives

3.0 Main Content

3.1 Electrocardiography

3.2 ECG leads

4.0 Conclusion

5.0 Summary

6.0 Tutor Marked Assignments

6.1 Activity

6.2 Tutor Marked Tests

7.0 References and other resources

1.0 Introduction

The heart sustains some electrical charges that are measurable to explain the functioning of the heart. In this unit, you are going to learn about electrocardiography.

2.0 Objectives

At the end of this unit, you should be able to:

- i. Give detailed explanation about Electrocardiography
- ii. Explain the different waves and complexes that Electrocardiography is composed of.
- iii. Define ECG and list different types of ECG leads used in ECG recording

3.0 Main content

3.1 ELECTROCARDIOGRAPHY

Electrocardiography is a trans thoracic (across the thorax or chest) interpretation of the electrical activity of the heart over a period of time, as detected by electrodes attached to the outer surface of the skin and recorded by a device external to the body. By placing electric contact points called electrodes at suitable locations on or within the body, the electrical impulses could be detected, amplified and transcribed into graphic record by the instrument called electrocardiograph (ECG Machine). The graphic record of the heart electrical activities recorded from the body surface constitutes what is known as electrocardiogram (ECG) while the graphic record obtained directly from heart muscle is called electrogram. Electrocardiogram (ECG) is the graphic record of the electrical activities of the heart detected at the body surface by the aid of electrodes and lead system. The electrocardiogram (ECG) is simply a voltmeter that uses up to 12 different leads (electrodes) placed on designated areas of the body.

Electrical impulses of the heart are in form of waves of depolarization and repolarization. The waves represent the time-dependent electrical activities of the different regions of the heart that are transcribed on the graph paper as either upward (positive) or downward (negative) deflections separated by isoelectric lines. The pictogram formed from the deflections constitutes what is called electrocardiogram as denoted by PQRST complex, shown in Figure 1-6. The denotations can be measured in terms of magnitude, duration, orientation and shape. The various parameters had been standardized. Therefore, alterations in the standard pattern provide clues for the diagnosis of some cardiac lesions at a particular time.

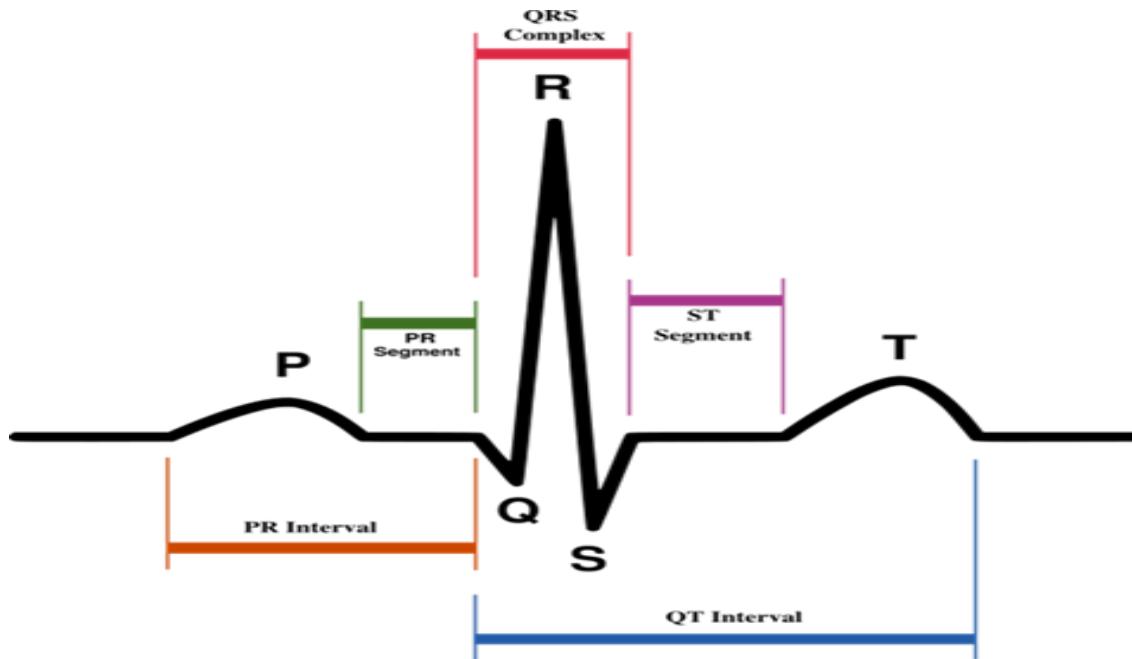


Figure 3.1: A normal electrocardiogram

The electrocardiogram is composed of waves and complexes. Waves and complexes in the normal sinus rhythm are the P wave, PR Interval, PR Segment, QRS Complex, ST Segment, QT Interval and T wave.

The P wave

The P wave is caused by atrial depolarization. The P wave is usually smooth and positive. The P wave duration is normally less than 0.12 sec and the amplitude is normally less than 0.25 mV. A negative P-wave can indicate depolarization arising from the AV node.

The P-R segment

The PR segment is the portion on the ECG wave from the end of the P wave to the beginning of the QRS complex. The PR segment corresponds to the time between the end of atrial depolarization to the onset of ventricular depolarization. It is an isoelectric segment, during which the impulse travels from the AV node through the conducting tissue (bundle branches, and Purkinje fibers) towards the ventricles.

The P-R interval

The PR interval is the portion of the ECG wave from the beginning of the P wave (onset of atrial depolarization) to the beginning of the QRS complex (onset of ventricular depolarization). It is normally 0.12 - 0.20 seconds.

The Q wave

This is the first negative deflection in ventricular depolarization (QRS complex).

The R wave

It is the first positive deflection in ventricular depolarization.

The S wave

This is the second negative deflection in ventricular depolarization or the first negative deflection after R wave.

The QRS complex

The QRS complex represents the time it takes for depolarization of the ventricles to occur. The normal QRS interval range is from 0.04 sec - 0.12 sec measured from the first deflection to the end of the QRS complex.

The ST Segment

It is the isoelectric line from the end of ventricular depolarization to the beginning of ventricular repolarization. No electrical activity is recorded during this period.

The T wave

The T wave is due to ventricular repolarization .The wave is normally round and positive.

The QT interval

The QT interval begins at the onset of the QRS complex and ends at the end of the T wave. It is the period from the onset of ventricular depolarization to the end of ventricular repolarization.

U wave

It refers to any wave between T and P- waves.

3.2 ECG leads

Lead may refer to the tracing of the voltage difference between two of the electrodes and is what is actually produced by the ECG recorder. Each will have a specific name. For example "Lead I" (lead one) is the voltage between the right arm electrode and the left arm electrode, whereas "Lead II" (lead two) is the voltage between the right limb and the feet. This rapidly becomes more complex as one of the "electrodes" may in fact be a composite of the electrical signal from a combination of the other electrodes. Twelve of these type of leads form a "12-lead" ECG.

There are three types of ECG leads used in ECG recording:

- i. Standard limb leads
- ii. Augmented unipolar limb leads
- iii. Chest (precordial) leads

Standard limb leads

The leads are grouped depending on their anatomical placement on the body surface. These include:

Limb (Extremity) Leads

In both the 5- and 12-lead configuration, leads I, II and III are called limb leads. The electrodes that form these signals are located on the limbs—one on each arm and one on the left leg. The limb leads form the points of what is known as **Einthoven's triangle** (Figure 1-7).

Lead I is the voltage between the (positive) left arm (LA) electrode and right arm (RA) electrode: $I = LA - RA$.

Lead II is the voltage between the (positive) left leg (LL) electrode and the right arm (RA) electrode: $II = LL - RA$.

Lead III is the voltage between the (positive) left leg (LL) electrode and the left arm (LA) electrode: $III = LL - LA$.

In a 12-lead ECG, all leads besides the limb leads are unipolar (aVR, aVL, aVF, V1, V2, V3, V4, V5, and V6).

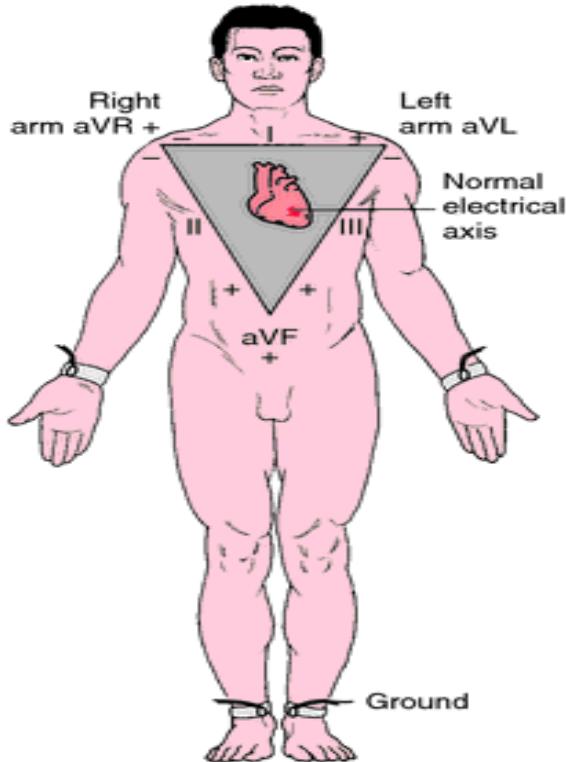


Figure 3.2: Einthoven triangle, illustrating the galvanometer connections for standard limb leads I, II and III.

Augmented unipolar limb leads

Augmented limb leads are aVF, aVL, aVR. They are described by Goldberger and are unipolar. The leads are connected by special mechanism, which allows for augmentation of the electrical activities of the heart. The positive pole of the augmented limb lead is at right arm for aVR, left arm for aVL and left leg for aVF. While recording from such a lead, the other limbs that are not used as the positive pole are connected to a central terminal or indifferent electrode which has zero potential. Thus, there is augmentation of the electrical activities by 50%. The lines of force of the augmented limb leads form an equilateral triangle.

Lead augmented vector right (aVR) has the positive electrode (white) on the right arm. The negative electrode is a combination of the left arm (black) electrode and the left leg (red) electrode, which "augments" the signal strength of the positive electrode on the right arm:

$$aV_R = RA - \frac{1}{2} (LA + LL)$$

Lead augmented vector left (aVL) has the positive (black) electrode on the left arm. The negative electrode is a combination of the right arm (white) electrode and the left leg (red) electrode, which "augments" the signal strength of the positive electrode on the left arm:

$$aV_L = LA - \frac{1}{2} (RA + LL)$$

Lead augmented vector foot (aVF) has the positive (red) electrode on the left leg. The negative electrode is a combination of the right arm (white) electrode and the left arm (black) electrode, which "augments" the signal of the positive electrode on the left leg:

$$aV_F = LL - \frac{1}{2} (RA + LA).$$

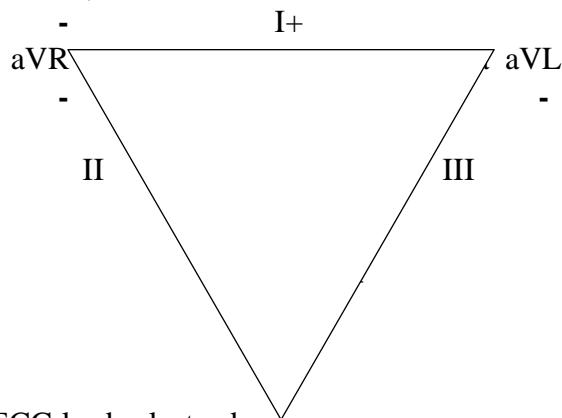


Figure 3.3: The standard ECG leads electrodes.

Chest (Precordial) leads

The electrodes for the precordial leads (V1, V2, V3, V4, V5 and V6) are placed directly on the chest (Figure 1-9). Because of their close proximity to the heart, they do not require augmentation. The precordial leads view the heart's electrical activity in the horizontal plane. The heart's electrical axis in the horizontal plane is referred to as the Z axis.

The chest leads are arranged on the chest wall in horizontal plane:

- V₁ : 4th intercostal space, right sternal edge
- V₂ : 4th intercostal space, left sternal edge
- V₃ : mid-way between V₂ and V₄
- V₄: 5th intercostal space, midclavicular line
- V₅: 5th intercostal space, anterior axillary line
- V₆: 5th intercostal space, mid-axillary line

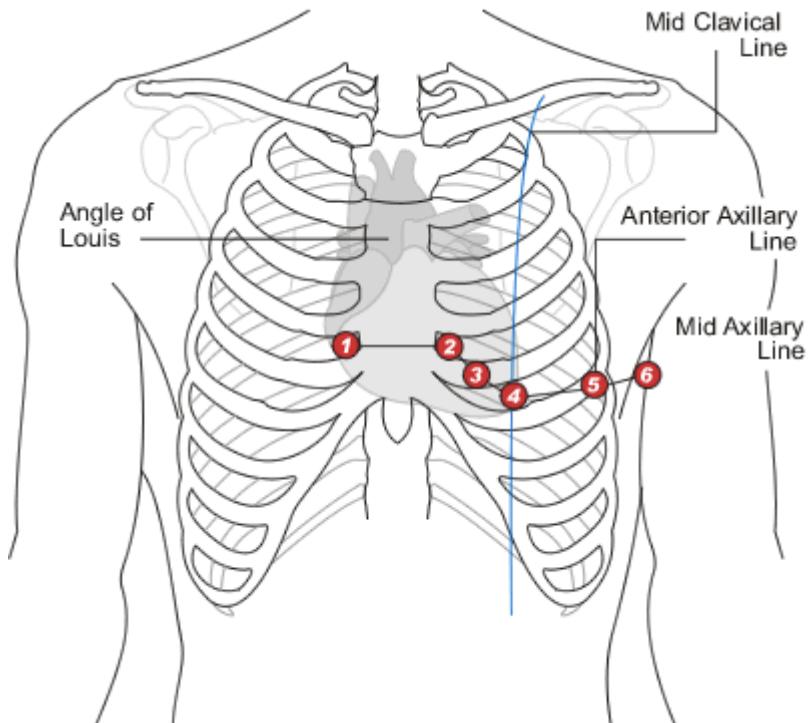


Figure 3.4: Chest lead positions

4.0 Conclusion

5.0 Summary

In this unit, you have learnt about Electrocardiography, the different waves and complexes that Electrocardiography is composed of, ECG and different types of ECG leads used in ECG recording. Please determine how much you have learnt to see how much you can recollect about each of these.

6.0 Tutor Marked Assignments

6.1 Activity – See Laboratory assignment as provided by the facilitator.

6.2 Answer the following questions:

- i. What is electrocardiography?
- ii. Explain the different waves and complexes of Electrocardiography
- iii. What are the different types of ECG leads used in ECG recording?

7.0 References and other materials

Fox SI. (2012). Human Physiology. 12th edition, Mc Graw Hill, New York.

Ganong, W.F. (2010). Review of Medical Physiology. 23rd edition, Mc Graw Hill, New York.

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UNIT FOUR - CARDIAC OUTPUT AND CONTROL OF CARDIAC OUTPUT

CONTENTS

- 1.0** Introduction
- 2.0** Objectives
- 3.0** Main Content
- 3.1** Cardiac Output
- 3.2** Control of cardiac output
- 3.3** Regulation of heart rate
- 3.4** Regulation of stroke volume
- 4.0** Conclusion
- 5.0** Summary
- 6.0** Tutor Marked Assignments
- 6.1** Activity
- 6.2** Tutor Marked Tests
- 7.0** References and other resources

1.0 Introduction

The ability of the body to get the desirable nutrients are subject to high well the heart sends its output out for every act of pumping. In this unit, you are going to learn more about per minute functioning of the heart as such relates to some of the measures that you take to determine the health status of clients. In this unit, you will cover the concept of cardiac output, regulation of the heart rate and the regulation of the stroke volume.

2.0 Objectives

At the end of this unit, you should be able to:

- i. Explain what Cardiac Output is
- ii. Discuss the Control of cardiac output
- iii. Explain how heart rate is regulated
- iv. Explain regulation of stroke volume and its determinants

3.0 Main content

3.1 Cardiac Output

Cardiac output is defined as the volume of blood ejected by each ventricle per minute. It is a function of heart rate and stroke volume. The heart rate is simply the number of heart beats per minute. The stroke volume is the volume of blood, in milliliters (mL), pumped out of the heart with each beat. Increasing either heart rate or stroke volume increases cardiac output.

Cardiac Output in mL/min = heart rate (beats/min) X stroke volume (mL/beat).

An average person has a resting heart rate of 70 beats/minute and a resting stroke volume of 70 mL/beat. The cardiac output for this person at rest is:

Cardiac Output = 70 (beats/min) X 70 (mL/beat) = 4900 mL/minute.

The average basal cardiac output is 5L per minute in adults. This can be increased tremendously in exercise or other conditions demanding increased blood supply to the body tissues.

Thus, cardiac output can be increased either by increasing the heart rate or by increasing the stroke volume or by increasing both heart rate and stroke volume.

3.2 Control of cardiac output

Since cardiac output is a product of heart rate and stroke volume, variations in cardiac output can be produced by changes in heart rate or stroke volume or both stroke volume and heart rate.

3.3 Regulation of heart rate

The sinoatrial (SA) node of the heart is innervated by both sympathetic and parasympathetic nerve fibers. Under conditions of rest the parasympathetic fibers release acetylcholine, which acts to slow the pacemaker potential of the SA node and thus reduce heart rate. Under conditions of physical or emotional activity sympathetic nerve fibers release norepinephrine which acts to speed up the pacemaker potential of the SA node thus increasing heart rate. Sympathetic nervous system activity also causes the release of epinephrine from the adrenal medulla. Epinephrine enters the blood stream, and is delivered to the heart where it binds with SA node receptors leading to further increase in heart rate.

3.4 Regulation of stroke volume

Stroke volume (SV) is the volume of blood pumped from one ventricle of the heart with each beat. The stroke volume is determined by two main factors:

- i. Nervous stimuli
- ii. End – diastolic length of cardiac muscle fibers.

Sympathetic nerve stimulation makes the myocardial muscle fibres contract with greater strength, while parasympathetic nerve stimulation has the opposite effect. Increase in strength of contraction without a concomitant increase in length of muscle fibre leads to increased stroke volume and reduced end –systolic volume. Increase in heart rate caused by catecholamines released by sympathetic stimulation is referred to as their chronotropic action, while their effect on the force of contraction is called their inotropic action. Factors that increase the force of cardiac contraction are said to be positively inotropic and those that decrease it are said to be negatively inotropic.

The end-diastolic length of cardiac muscle fibres is also an important determinant of cardiac output. The length of the cardiac muscle fibres is determined by how much filling of blood the ventricles received during diastole. The degree to which the ventricular muscle is stretched before it contracts is called preload. It has been shown that the more the cardiac muscle fibres are stretched before they contract, the greater is the force of contraction. This relationship holds as long as the muscle is not over-stretched to cause damage to the contractile tissues. The relationship of muscle length to the tension developed is known as Starlings law of the heart or Frank-Starling law.

4.0 Conclusion

Cardiac output is the volume of blood ejected by each ventricle per minute and this is the function of heart rate and stroke volume. The heart rate is the number of heart beats per minute.

5.0 Summary

In this unit, you have learnt about the cardiac output, the control of cardiac output, the regulation of heart rate and the regulation of stroke volume.

6.0 Tutor Marked Assignments

6.1 Activity – As given by the Facilitator

6.2 Answer the following questions:

- i. Explain what Cardiac Output is
- ii. Discuss the Control of cardiac output
- iii. Explain how heart rate is regulated
- iv. Explain the determinants and regulation of the stroke volume.

7.0 References and other resources

Fox SI. (2012). Human Physiology. 12th edition, Mc Graw Hill, New York.

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UNIT FIVE - ARTERIAL BLOOD PRESSURE

CONTENTS

1.0 Introduction

2.0 Objectives

3.0 Main Content

3.1 Arterial blood pressure

3.2 Determinants of arterial pressure

3.3 Measurement of arterial blood pressure

3.4 Regulation of arterial blood pressure

4.0 Conclusion

5.0 Summary

6.0 Tutor Marked Assignments

6.1 Activity

6.2 Tutor Marked Tests

7.0 References and other resources

1.0 Introduction

The nurse measures the arterial blood pressure of the clients as a basic assessment of the wellbeing of the person. In this unit, your knowledge of this procedure will be better enhanced.

2.0 Objectives

At the end of this unit, you should be able to:

- i. Explain the concept of Arterial blood pressure

- ii. Explain the determinants of arterial pressure
- iii. Describe how to measure arterial blood pressure accurately
- iv. Explain the regulatory process of arterial blood pressure

3.0 Main Content

3.1 Arterial blood pressure

The force which the blood exerts on the walls of the blood vessels is called blood pressure. This is the force exerted when the blood flows through the arteries. Arterial pressure changes continuously throughout each cardiac cycle. The highest pressure reached during systole is termed systolic arterial pressure and the lowest pressure reached during diastole is called diastolic arterial pressure. The pulse pressure is the difference between these two values i.e. systolic pressure – diastolic pressure. Mean arterial pressure is the average pressure during the cardiac cycle. Mean arterial pressure is given by the formula:

$$\text{Mean pressure} = \text{diastolic pressure} + \frac{1}{3} \text{ of pulse pressure}$$

Blood pressure is given by the formula: $B.P = C.O \times P.R.$ Where C.O is the cardiac output and P.R is the peripheral resistance.

Blood pressure can be varied by changing the cardiac output or by changing both PR and CO. Therefore, all factors affecting cardiac output and peripheral resistance will influence arterial pressure. The normal values of blood pressure for a given population show a fairly wide range in its distribution and also increase with age. The systolic blood pressure in person below 50 years of age ranges from 90 – 140 mm Hg, while the diastolic pressure ranges from 60-90 mm Hg. With increasing age, both systolic and diastolic pressures will increase.

Blood is pumped out of the heart at an average pressure of 120 mm Hg during systole.

3.2 Determinants of arterial pressure

There are some factors necessary for the maintenance of normal blood pressure, which are called local factors, mechanical factors or determinant of blood pressure. These factors are divided into two types called central factors and peripheral factors.

Central factors are related to the heart. These factors are (i) cardiac output and (ii) heart rate.

Peripheral factors are the factors pertaining to blood vessels. The following are the peripheral factors determining arterial blood pressure.

- (1) Peripheral resistance
- (2) Blood volume
- (3) Venous return
- (4) Elasticity of blood vessels
- (5) Velocity of blood flow
- (6) Diameter of blood vessels
- (7) Viscosity of blood

Cardiac output

Whenever the cardiac output is increased, the systolic blood pressure is increased and, when cardiac output is less, the systolic blood pressure is reduced. Cardiac output depends upon blood volume, venous return, heart rate and force of contraction. Cardiac output is directly proportional to blood volume. When blood volume increases, ventricular filling is more, cardiac output is

more and pressure rises. When the blood volume is reduced, the cardiac output is less and blood pressure falls.

Heart rate

Moderate changes in heart rate do not affect arterial blood pressure much. However, marked alteration in the heart rate affects the blood pressure by altering diastolic period and stroke volume.

Peripheral resistance

This is an important factor which maintains diastolic blood pressure. The diastolic blood pressure is directly proportional to peripheral resistance. When peripheral resistance is decreased, diastolic pressure is less and when peripheral resistance is more, the diastolic pressure rises.

Blood volume

Blood pressure is directly proportional to blood volume. Blood volume maintains the blood pressure through the venous return and cardiac output. If the blood volume is more, there is increase in venous return and cardiac output resulting in elevation of blood pressure. Blood pressure is increased in polycythaemia vera because of increased blood volume. The decrease in blood volume causes fall in blood pressure because of reduced cardiac output. This occurs in conditions like diarrhoea, vomiting and other conditions of dehydration and hemorrhage.

Venous return

Blood pressure is directly proportional to venous return. When venous return is more, there is increase in ventricular filling and cardiac output resulting in elevation of arterial blood pressure.

Elasticity of blood vessels

Blood pressure is inversely proportional to the elasticity of blood vessels. Due to the elastic property, the blood vessels are distensible and are able to maintain the pressure. When the elastic property is lost, the blood vessels become rigid and atherosclerosis causes elevated pressure. It occurs in old age. The deposition of cholesterol, fatty acids and calcium ions, produce rigidity of blood vessels and atherosclerosis leading to increased blood pressure.

Velocity of blood flow

The pressure in a blood vessel is directly proportional to the velocity of blood flow. If the velocity of the blood flow is more, the resistance is increased hence, the blood pressure is also increased.

Diameter of blood vessels

The arterial blood pressure is inversely proportional to the diameter of the blood vessels. If the diameter of arteries and arterioles decreases, the peripheral resistance is more and thereby, the blood pressure is elevated.

Viscosity of blood

Arterial blood pressure is directly proportional to the viscosity of blood. When viscosity of blood is increased, the resistance is increased and thereby the blood pressure increases. In

polycythemia and high content of plasma proteins, the viscosity of blood is increased causing increase in blood pressure. In anaemia, the reduced viscosity decreases the blood pressure.

3.3 Measurement of arterial blood pressure

The first documented measurement of blood pressure was accomplished by Stephen Hales (1677–1761), an English clergyman and physiologist. Hales inserted a cannula into the artery of a horse and measured the heights to which blood would rise in the vertical tube. The height of this blood column bounced between the systolic pressure at its highest and the diastolic pressure at its lowest, as the heart went through its cycle of systole and diastole. This method is invasive in that it involves penetrating the body tissues to reach the artery. Although the invasive technique is used frequently in experimental animals, it is not often suitable for use in man. Clinically, arterial blood pressure is measured indirectly by using a sphygmomanometer. The sphygmomanometer comprises an inflatable rubber cuff covered by a layer of non-distensible fabric and this is attached to a mercury manometer. The rubber cuff is usually wrapped around the upper arm (about the middle third of the upper arm). There is a rubber hand-pump attached to the rubber cuff and pressure in the cuff can be altered by pumping air into the cuff to increase its pressure or releasing the air through a needle valve to decrease the pressure (Figure 8-1).



Figure 5.1: Measurement of blood pressure: use of the sphygmomanometer

There are two methods of measuring arterial blood pressure using the sphygmomanometer. These are:

- i. By palpation
- ii. By auscultation

The two methods are often combined during sphygmomanometry (this is the process of measuring blood pressure using a sphygmomanometer). In the palpation method, the radial pulse is palpated and the palpating fingers are kept on the radial artery while the pressure in the sphygmomanometer cuff already wrapped round the arm is gradually increased. The reading of the mercury manometer at the point when the radial pulse can no longer be felt is the systolic pressure. The cuff pressure is increased further by about 50 mm Hg above the point of disappearance of the radial pulse. Then the second method, the auscultatory method, is carried out. At the peak of inflation of the cuff, a stethoscope is placed over the lower end of the branchial artery in the cubital fossa of the elbow joint (the artery is usually medial to the tendon of the biceps muscle at the cubital fossa). The pressure in the cuff is reduced gradually while the observer is listening with the stethoscope for any sound from the point of auscultation. When the cuff pressure has fallen to just below the systolic pressure, a clear, but often faint, tapping sound is suddenly heard. The cuff pressure at which the tapping sound is suddenly heard is the systolic pressure. As the cuff pressure is reduced further, the tapping sound becomes louder until it gets to a point when the sound becomes muffled and rapidly grows fainter. Finally, the sound disappears. The diastolic pressure is the pressure at which muffling occurs.

The sound heard at the cubital fossa during auscultation is called *Korotkoff* sounds. It is named after a Russian physiologist who first described these sounds in 1905. Korotkoff sound is produced at the peak of each systole by the transient and turbulent blood flow through the partially occluded branchial artery. It is not the same as heart sounds and it is not heard in a fully opened artery, in which flow is non-turbulent. This is why the sound disappears at pressure below the diastolic pressure when blood flow is no longer turbulent.

3.4 Regulation of arterial blood pressure

The maintenance of arterial blood pressure within a range of values consistent with health is mediated by two types of response. There are rapid, short-term adjustments and long-term adjustments.

Short-term adjustment are intended to correct temporary imbalances of pressure such as those caused by postural change, exercise or haemorrhage; short-term adjustment is usually a series of autonomic reflex responses mediated via the cardiovascular centres in the medulla i.e. baroreceptors reflex.

Long-term arterial blood pressure regulation is usually concerned with the balance between extracellular fluid and blood volume on the one hand and the renal mechanisms controlling urine output on the other hand. Renal urine output involves pituitary –adrenal cortical mechanisms which control water and sodium excretion by the kidney. Disturbances of this renal process may result in gradual increase in arterial blood pressure and if continued, it can lead to persistent elevation of blood pressure called hypertension.

Baroreceptor reflex

The baroreceptor reflex is one of the body's homeostatic mechanisms for maintaining blood pressure. It provides a negative feedback loop in which an elevated blood pressure reflexively causes heart rate to decrease and also causing blood pressure to decrease; likewise, decreased blood pressure activates the baroreceptors, causing heart rate to increase, and also causing an increase in blood pressure.

The baroreceptors are stretch receptors located in the carotid sinuses (the slightly widened areas of the internal carotid arteries at their points of origin from the common carotid arteries) and in the aortic arch (Figure 1-41). Impulses arising in the carotid sinus travel up through afferent fibres in the sinus nerve, which is a branch of the glossopharyngeal nerve (IXth cranial nerve) and synapse at the vasomotor center (VMC). Impulses arising from the aortic arch reach the VMC via afferent fibres in the vagus nerve (Xth cranial nerve).

When there is an increase in blood pressure, the baroreceptors are stretched, and this leads to increased discharge of afferent impulses through the IX and X cranial nerves to the VMC. These afferent impulses are inhibitory to the tonic activity of the VMC. Their effect is to reduce the sympathetic outflow to the arterioles.

This leads to vasodilatation and a reduction in blood pressure. In addition to the effects on the VMC, afferent impulses from the baroreceptors stimulate the cardioinhibitory centre, leading to a reduction in heart rate and force of contraction of the myocardium. The latter effects lead to a reduction in cardiac output. The combined effects of reduced peripheral resistance and cardiac output result in a decrease in blood pressure.

When there is a fall in blood pressure, the reverse of the above responses occur. There is reduced stretching of the baroreceptors, less inhibitory afferent impulses are sent to the VMC and cardiac centre. As a result of this, there is increased sympathetic discharge to the blood vessels resulting in vasoconstriction and increased peripheral resistance. There is also reduced stimulation of the cardioinhibitory centre so that heart rate and force of cardiac contraction are increased leading to increased cardiac output. The combination of increased peripheral resistance and cardiac output result in increased blood pressure. The response of the baroreceptors to increased or reduced blood pressure operate on a negative feedback mechanism and a careful adjustment of the responses to a rise or fall in blood pressure helps in maintaining a constant blood pressure.

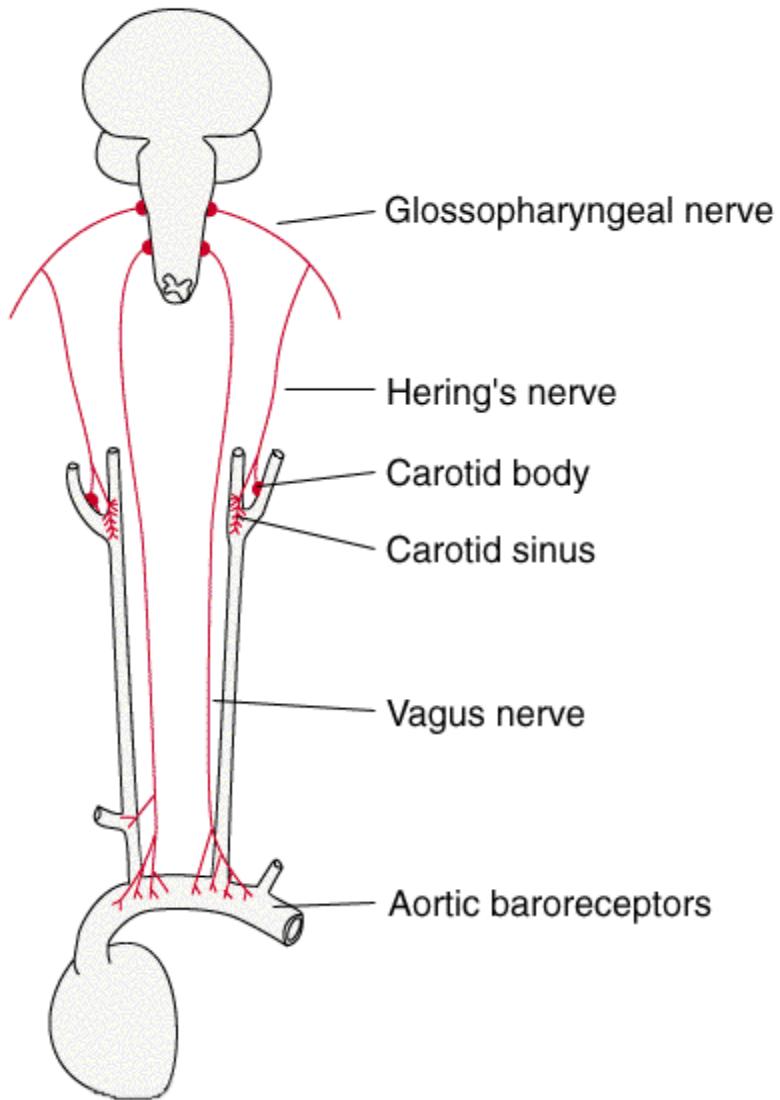


Figure 5.2: The baroreceptor system for controlling arterial pressure

Renin – angiotensin – aldosterone system

The kidneys play an important role in the long term regulation of arterial blood pressure. Kidneys regulate arterial blood pressure in two ways:

- (1) By regulation of extracellular fluid volume
- (2) Through renin-angiotensin mechanism

By regulation of extracellular fluid volume

When the extracellular fluid volume increases, the blood volume also increases. This will tend to increase the arterial blood pressure.

However, when the pressure is increased, the kidneys excrete more water and salt, particularly sodium. This reduces extracellular fluid volume and, in turn the arterial blood pressure is reduced.

Even slight increases in blood pressure can double the water excretion which is known as pressure diuresis. Elevated blood pressure also leads to sodium excretion, which is called pressure natriuresis. When blood pressure falls due to decreased extracellular fluid volume, the reabsorption of water from renal tubules is increased and the volume of extracellular fluid is restored.

Through renin – angiotensin mechanism

When there is a fall in blood pressure, special cells in the kidney collectively called juxtaglomerular apparatus detect the change and release renin into the bloodstream. Renin converts angiotensinogen the inactive forms of angiotensin, which is produced by the liver, to angiotensin I. Angiotensin I is converted to angiotensin II by angiotensin converting enzyme (ACE) in the lungs. Angiotensin II acts in two ways to increase arterial blood pressure.

(i) It causes constriction of arterioles in the body so that the peripheral resistance is increased, and blood pressure rises. Simultaneously, constriction of afferent arterioles in kidney causes retention of water and salts so that, the volume of extracellular fluid is increased. This in turn restores the normal blood pressure.

(ii) Angiotensin II also stimulates adrenal cortex to secrete aldosterone. This increases reabsorption of sodium from renal tubules. Sodium reabsorption is followed by water reabsorption and thereby extracellular fluid volume is increased and blood pressure becomes normal.

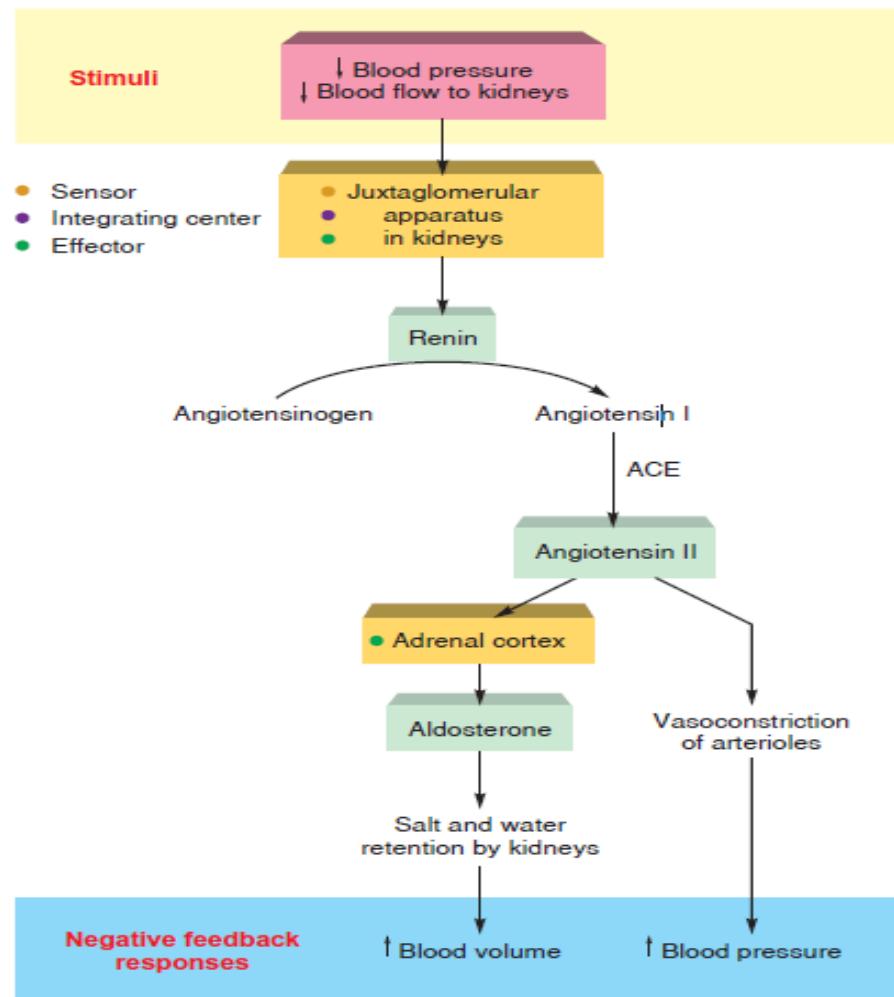


Figure 5.3: Renal regulation of blood pressure by renin - angiotensin mechanism

4.0 Conclusion

The force which the blood exerts on the walls of the blood vessels is called blood pressure. This is the force exerted when the blood flows through the arteries. Arterial pressure changes continuously throughout each cardiac cycle. The pressure is determined by cardiac and peripheral factors and it is also regulated with short-term adjustments and long-term adjustments and controlled by baroreceptors reflex and the renal angio-tensin mechanisms.

5.0 Summary

In this unit, you have learnt about the arterial blood pressure, determinants of arterial pressure, measurement of arterial blood pressure and the regulation of arterial blood pressure.

6.0 Tutor Marked Assignments

6.1 Activity – Laboratory and practical assignments as given by the Facilitator

6.2 Answer the following questions:

- i. What is Arterial blood pressure?
- ii. Explain the various factors that determine the arterial pressure.
- iii. Describe the process of measuring arterial blood pressure.
- iv. Explain how arterial blood pressure is regulated.

7.0 References and other resources

- Fox SI. (2012). Human Physiology. 12th edition, Mc Graw Hill, New York.
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UNIT SIX - CIRCULATORY SHOCK

CONTENTS

- 1.0** Introduction
- 2.0** Objectives
- 3.0** Main Content
- 3.1** Circulatory shock
- 3.2** Stages of shock
- 3.3** Types of shock
- 4.0** Conclusion
- 5.0** Summary
- 6.0** Tutor Marked Assignments
- 6.1** Activity
- 6.2** Tutor Marked Tests
- 7.0** References and other materials

1.0 Introduction

Shock is a state of compromise to life. Circulatory shock threatens life and if it is not managed as an emergency, it could result to loss of life. In this unit, you will learn more about circulatory shock as for you to understand the physiological bases on intervention.

2.0 Objectives

At the end of this unit, you should be able to:

- i. Define Circulatory shock
- ii. Explain the stages of shock
- iii. Explain different types of shock

3.0 Main Content

3.1 Circulatory shock

Circulatory shock is a state of inadequate tissue perfusion associated with or due to relative or absolute inadequacy of cardiac output. The essential signs of shock are rapid heartbeat (tachycardia/tachypnoea, both compensatory mechanisms), low blood pressure (hypotension), and signs of poor end-organ perfusion or "decompensation" (such as low urine output, confusion or loss of consciousness).

3.2 Stages of shock

There are four stages of shock

Compensatory (Compensating)

This stage is characterized by the body employing physiological mechanisms, including neural, hormonal and bio-chemical mechanisms in an attempt to reverse the condition. As a result of the acidosis, the person will begin to hyperventilate in order to rid the body of carbon dioxide (CO_2). CO_2 indirectly acts to acidify the blood and by removing it the body is attempting to raise the pH of the blood. The baroreceptors in the arteries detect the resulting hypotension, and cause the release of adrenaline and noradrenaline. Noradrenaline causes predominately vasoconstriction with a mild increase in heart rate, whereas adrenaline predominately causes an increase in heart rate with a small effect on the vascular tone; the combined effect results in an increase in blood pressure.

Renin-angiotensin system is activated and anti-diuretic hormone (ADH) is released to conserve fluid via the kidneys. These hormones cause the vasoconstriction of the kidneys, gastrointestinal tract, and other organs to divert blood to the heart, lungs and brain. The lack of blood to the renal system causes the characteristic low urine production. However the effects of the renin-angiotensin system take time and are of little importance to the immediate homeostatic mediation of shock.

Progressive (Decompensating)

Should the cause of the crisis not be successfully treated, the shock will proceed to the progressive stage and the compensatory mechanisms begin to fail. Due to the decreased perfusion of the cells, sodium ions build up within while potassium ions leak out. As anaerobic metabolism continues, increasing the body's metabolic acidosis, the arteriolar smooth muscle and precapillary sphincters relax such that blood remains in the capillaries. Due to this, the hydrostatic pressure will increase and, combined with histamine release, this will lead to leakage of fluid and protein into the surrounding tissues. As this fluid is lost, the blood concentration and viscosity increase, causing sludging of the micro-circulation. The prolonged vasoconstriction will also cause the vital organs to be compromised due to reduced perfusion. If the bowel becomes sufficiently ischemic, bacteria may enter the blood stream, resulting in the increased complication of endotoxic shock.

Refractory (Irreversible)

At this stage, the vital organs have failed and the shock can no longer be reversed. Brain damage and cell death are occurring, and death will occur imminently. One of the primary reasons that shock is irreversible at this point is that much cellular ATP has been degraded into adenosine in the absence of oxygen as an electron receptor in the mitochondrial matrix. Adenosine easily

perfuses out of cellular membranes into extracellular fluid, furthering capillary vasodilation, and then is transformed into uric acid. Because cells can only produce adenosine at a rate of about 2% of the cell's total need per hour, even restoring oxygen is futile at this point because there is no adenosine to phosphorylate into ATP.

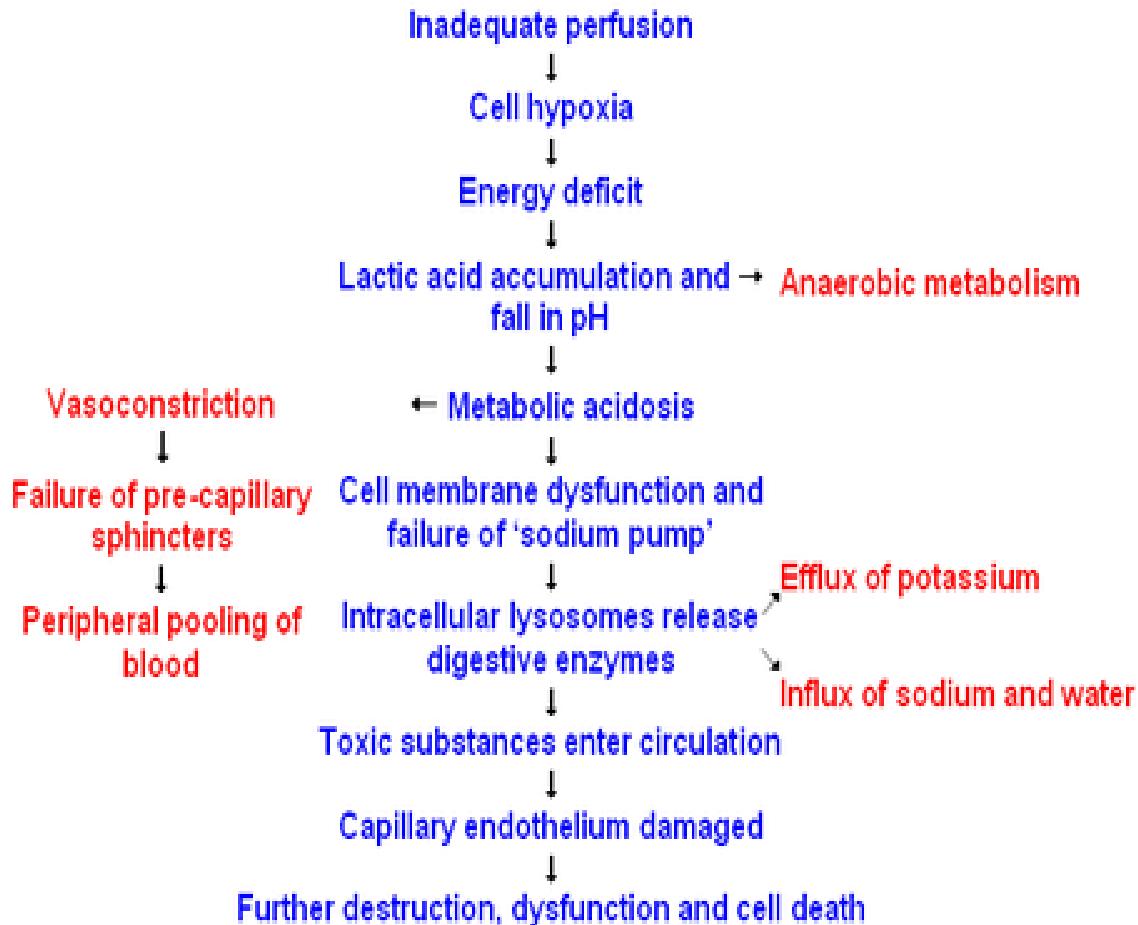


Figure 6.1: Effects of inadequate perfusion on cell function

3.3 Types of shock

There are four types of shock: hypovolemic, cardiogenic, distributive and obstructive shock

- i. Hypovolemic shock e.g. hemorrhage, trauma, surgery, burns, fluid loss- diarrhoea, and vomiting
- ii. Distributive shock/Vasogenic or low resistance shock e.g. fainting, anaphylaxis and sepsis .
- iii. Cardiogenic shock e.g. myocardial infarction, congestive heart failure.
- iv. Obstructive shock (obstruction to blood flow) e.g. tension pneumothorax, pulmonary embolism, cardiac tamponade.

Hypovolemic shock

In this form of shock, there is an absolute reduction of the intravascular blood volume. Therefore the amount of blood available for the heart to pump to the tissues is greatly reduced.

Venous return is reduced and therefore by Starlings law, the cardiac output is reduced. The symptoms of this shock is similar irrespective of the particular cause whether due to diarrhoea and vomiting, burns or haemorrhage. The symptoms are due to the body's attempts to compensate for the reduced blood volume. These symptoms and signs include:

- i. Cold skin particularly in the periphery, this is due to vasoconstriction of vessels to the skin in an attempt to shunt more blood to the heart and other vital tissues particularly the brain.
- ii. Pallor and Clamminess of the skin are also caused by the above compensatory mechanism
- iii. Thirst: The person feels an urge to drink. This is due to the stimulation of the thirst center located in the hypothalamus by hormones produced in response to depressed blood volume. The principal hormones involved are the antidiuretic hormone and angiotensin II.
- iv. Rapid respiration or air hunger. The diminished tissue perfusion leads to hypoxia which is detected by the chemoreceptors which in turn send signals to the respiratory center to increase the rate of respiration in order to take in more oxygen. This increased respiration also helps to increase venous return and therefore cardiac output via the thoracic pump
- v. A rapid thready (low volume) pulse. The pulse rate is greatly increased in order to compensate for the diminished stroke volume occasioned by the reduction of blood volume. Since cardiac output, $CO = HR \times SV$, in order to increase CO, the heart rate must increase greatly, the threadiness of the pulse i.e. the low volume is due to the diminished stroke volume.
- vi. The blood pressure is greatly reduced (hypotension). $BP = CO \times TPR$. Since CO depends on blood volume, the reduction in blood volume causes a decrease in cardiac output leading to a fall in blood pressure.

Distributive shock

In distributive shock there is a widespread vasodilatation which effectively increases the capacity of the circulation. Blood is trapped in non-essential areas of the body thereby being unavailable for circulation to the vital organs-heart, kidneys and brain. In these situations, the cardiac output is normal. There is thus a relative inadequacy of cardiac output. These forms of widespread vasodilation are usually caused by toxins in sepsis, chemicals produced in anaphylactic shock. In neurogenic shock a sudden widespread vasodilation occurs with pooling of blood in the veins. This effectively reduces the venous return and cardiac output and results in fainting. This usually occurs in situations of profound grief or overwhelming fear.

Septic shock

This refers to a bacterial infection widely disseminated to many areas of the body, with the infection being borne through the blood from one tissue to another and causing extensive damage.

Some of the typical causes of septic shock include the following:

- (i) Peritonitis caused by spread of infection from the uterus and fallopian tubes, sometimes resulting from instrumental abortion performed under unsterile conditions.
- (ii) Peritonitis resulting from rupture of the gastrointestinal system, sometimes caused by intestinal disease and sometimes by wounds.

- (i) Generalized body infection resulting from spread of a skin infection such as streptococcal or staphylococcal infection.
- (ii) Generalized gangrenous infection resulting specifically from gas gangrene bacilli, spreading first through peripheral tissues and finally by way of the blood to the internal organs, especially the liver.
- (iii) Infection spreading into the blood from the kidney or urinary tract, often caused by colon bacilli.

Some features often observed are:

- i. High fever.
- ii. Often marked vasodilation throughout the body, especially in the infected tissues.
- iii. High cardiac output in perhaps half of patients, caused by arteriolar dilation in the infected tissues and by high metabolic rate and vasodilation elsewhere in the body, resulting from bacteria toxin stimulation of cellular metabolism and from high body temperature.
- iv. Sludging of the blood, caused by red cell agglutination in response to degenerating tissues.

Cardiogenic shock

This is shock arising from the heart inability to generate enough force or beat frequently enough to maintain the cardiac output. Therefore, heart rate is reduced as occurs in heart block and other arrhythmia.

Obstructive shock

In this type of shock, the flow of blood is obstructed which impedes circulation and can result in circulatory arrest. Several conditions result in this form of shock.

Cardiac tamponade. In which fluid in the pericardium prevents inflow of blood into the heart (reduced venous return).

Constrictive pericarditis: The pericardium shrinks and hardens.

Tension pneumothorax: Through increased intrathoracic pressure, blood flow to the heart is prevented (decreased venous return).

Massive pulmonary embolism: It is the result of a thromboembolic incident in the blood vessels of the lungs and hinders the return of blood to the heart.

Aortic stenosis: This hinders circulation by obstructing the ventricular outflow tract.

4.0 Conclusion

Circulatory shock is a state of inadequate tissue perfusion associated with or due to relative or absolute inadequacy of cardiac output that present in four stages. The essential signs of shock are rapid heartbeat (tachycardia/tachypnoea, both compensatory mechanisms), low blood pressure (hypotension), and signs of poor end-organ perfusion or "decompensation" (such as low urine output, confusion or loss of consciousness). Hypovolemic shock e.g. hemorrhage, trauma, surgery, burns, fluid loss- diarrhoea, and vomiting, Shock can be hypovolumic, distributive shock/Vasogenic, Cardiogenic or Obstructive shock manifesting with varied signs and symptoms. The nurse is in a very

high position to detect, respond appropriately and save the life of a client in a state of shock by applying the knowledge of the pathology associated with shock.

5.0 Summary

In this unit, you have learnt about circulatory shock, stages of shock, types of shock and the signs and symptoms that the nurse must be able to pick and respond to promptly to save the client from loosing his/her life.

6.0 Tutor Marked Assignments

6.1 Activity

6.2 Answer the following questions:

- i. What is Circulatory shock
- ii. Describe the four stages of shock
- iii. Explain the different types of shock
- iv. Describe the compensatory mechanisms that act to raise blood volume during cardiovascular shock.
- v. Explain the physiological underpinnings of the signs and symptoms of shock.

7.0 References and other resources

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