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PATHOPHYSIOLOGY

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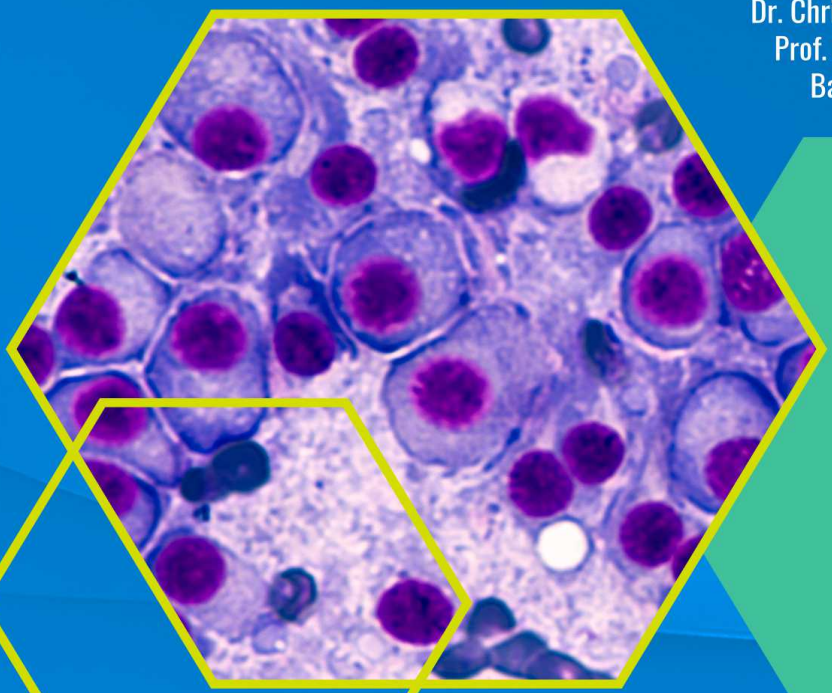

Pathophysiology

UU No 28 tahun 2014 tentang Hak Cipta

Fungsi dan sifat hak cipta Pasal 4

Hak Cipta sebagaimana dimaksud dalam Pasal 3 huruf a merupakan hak eksklusif yang terdiri atas hak moral dan hak ekonomi.

Pembatasan Pelindungan Pasal 26

Ketentuan sebagaimana dimaksud dalam Pasal 23, Pasal 24, dan Pasal 25 tidak berlaku terhadap:

i. Penggunaan kutipan singkat Ciptaan dan/atau produk Hak Terkait untuk pelaporan peristiwa aktual yang ditujukan hanya untuk keperluan penyediaan informasi aktual;
ii. Penggandaan Ciptaan dan/atau produk Hak Terkait hanya untuk kepentingan penelitian ilmu pengetahuan;
iii. Penggandaan Ciptaan dan/atau produk Hak Terkait hanya untuk keperluan pengajaran, kecuali pertunjukan dan Fonogram yang telah dilakukan Pengumuman sebagai bahan ajar; dan
iv. Penggunaan untuk kepentingan pendidikan dan pengembangan ilmu pengetahuan yang memungkinkan suatu Ciptaan dan/atau produk Hak Terkait dapat digunakan tanpa izin Pelaku Pertunjukan, Produser Fonogram, atau Lembaga Penyiaran.

Sanksi Pelanggaran Pasal 113

1. Setiap Orang yang dengan tanpa hak melakukan pelanggaran hak ekonomi sebagaimana dimaksud dalam Pasal 9 ayat (1) huruf i untuk Penggunaan Secara Komersial dipidana dengan pidana penjara paling lama 1 (satu) tahun dan/atau pidana denda paling banyak Rp100.000.000 (seratus juta rupiah).
2. Setiap Orang yang dengan tanpa hak dan/atau tanpa izin Pencipta atau pemegang Hak Cipta melakukan pelanggaran hak ekonomi Pencipta sebagaimana dimaksud dalam Pasal 9 ayat (1) huruf c, huruf d, huruf f, dan/atau huruf h untuk Penggunaan Secara Komersial dipidana dengan pidana penjara paling lama 3 (tiga) tahun dan/atau pidana denda paling banyak Rp500.000.000,00 (lima ratus juta rupiah).

Pathophysiology

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PATHOPHYSIOLOGY

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PREFACE

Pathophysiology is the study of functional disorders in diseased organisms, including the origin of disease, the course of disease, and its effects. Disease is an abnormal condition that causes the loss of normal healthy conditions. This course discusses the mechanisms of cell adaptation, the balance and processes of changes in fluid, electrolyte and acid-base balance, immune processes, degenerative processes, trauma, inflammatory processes, infectious processes, malignancy processes, shock processes, and genetic disorders and their interactions.

This book is indispensable for nursing students who will provide nursing care to patients. With an understanding of pathophysiology, a nurse can account for every independent nursing intervention carried out empirically and rationally. Because by using the basis of pathophysiology, nursing care ranging from nursing action plans to evaluation of nursing actions provided to patients becomes rational so that optimal success. If lacking in understanding pathophysiology, a nurse will have difficulty in making nursing care plans, understanding diagnostic tests, treatment of acute and chronic diseases, and disease prevention for patients and their families. Nurses who are able to recognise the pathophysiological signs and symptoms of their patients' conditions will be able to provide better quality follow-up care.

Instructional Objectives

After taking the pathophysiology course, students will be able to understand the concept of abnormal conditions that cause loss of normal healthy conditions and abnormalities in body structure and function.

Instructions for Study

1. Read and understand well the material descriptions presented in each learning activity. If any material is unclear, immediately ask the teacher.

2. Work on each discussion activity, practice questions well to train your ability to master conceptual knowledge and environmental literacy.
3. Understand the various terms in pathophysiology used in this book.
4. Success depends on the seriousness of learning, therefore do the exercises and assignments independently.
5. If you encounter difficulties, please contact the lecturer in charge of the pathophysiology course.

CONTENTS

UNIT 1 INTRODUCTION TO PATHOPHYSIOLOGY

LEARNING OBJECTIVES

After mastering the contents of this unit, you will be able to:

1. Define the pathophysiology
2. List the benefits of studying pathophysiology for nurses
3. Define the limits of normalcy
4. Define the disease limitation
5. Explain the interaction of disease, heredity and environment
6. Define the concept of disease
7. Identify the disease naming system
8. Explain the etiology or cause
9. List the signs and symptoms of disease

1. Definition of Pathophysiology

Pathophysiology is one of the sciences that specifically studies the impaired function of organisms affected by disease (Nair, 2009). Pathophysiology will discuss the origin of the disease, the process of the course of the disease and the consequences caused by the disease. Pathophysiology also studies the dynamic aspects of the disease process. Pathophysiology is also called the science that studies the process of changes or disorders of body functions due to a disease. For example, the pathophysiology of udema in patients with heart failure is the result of a process of fluid balance disturbance in the form of water and sodium retention due to obstructed return blood flow to the heart.

2. Benefits of Studying Pathophysiology for Nurses

Pathophysiology is one of the branches of medical science that is very important for nurses in carrying out their duties. The role and function of nurses is essential to assist patient in fulfilling basic needs that are impaired due to inability, unwillingness, or ignorance. Disruption of basic needs often occurs due to physical incapacity,

for example a client with a cruris fracture who cannot fulfil the needs of mobilization and ambulation. A professional nurse will be able to analyze the impact of the cruris fracture on the patient basic needs and provide nursing interventions according to their problem (Müller et al., 2020).

The analysis of the impact of disease on the fulfilment of basic needs studied in nursing pathophysiology is very important in analysing nursing problems that arise as a result of disease and identifying the causes so as to provide appropriate nursing interventions.

3. Limits of Normalcy

The normal state is difficult to explain in absolute terms because the normal state is a continuum that always moves between normal and abnormal states. The normal state in each individual may vary because each person is unique and intact. However, the normal state can be explained as an average value of various measurement variations. Differences or variations in the normal state in each individual are because (Smith & Germolec, 1999):

a. each individual has a different genetic makeup,
b. each individual has different experiences in interacting with the environment,
c. each individual has different physiological parameters.

These variations in normal values in reality come from different sources. Firstly, it is recognized that people differ from one another because of differences in their genetic makeup. Thus, there are no two people in the world, except those who come from the fertilization of the same ovum, having exactly the same genes. Secondly, there are differences related to the fact that people differ in their life experiences and interactions with the environment. Thirdly, even in a single individual, there are many physiological parameters in which the body's regulatory mechanisms function. Based on the above reasons, being normal is not determined by an absolute value but based on a certain range of values. For example,

the normal blood glucose level is 70–140 mg/dl or the normal leucocyte level is 5,000–10,000/mm3.

4. Disease

Disease can be defined as a form of life outside normal boundaries. The most useful benchmark of these normal limits relates to the individual's ability to fulfil the demands of adaptation to changes in the external environment in order to maintain a fixed internal environment (Hyochol Ahn, 2017). Thus, maintaining a constant internal state (homeostasis) is an important feature of a normal body. The maintenance of the stability of the physical and chemical state of the internal fluid environment that washes the body cells in a very regular and coordinated manner is a homeostatic concept. Homeostasis can be achieved when there is physiological and psychological balance.

Physiological balance is achieved when all body systems work synergistically to meet physiological needs such as oxygen, fluids and electrolytes and nutrients. Perfect fulfilment of physiological needs requires normal psychological functioning. The physiological and psychological aspects influence each other in maintaining a state of homeostasis. If the physiological aspect is disturbed, the psychological aspect may also be disturbed, and vice versa. For example, a person who is psychologically stressed may lose their appetite and thus may be unable to fulfil their nutritional needs. There are also psychosomatic diseases such as insomnia and gastritis. Disruption of homeostasis due to instability in physiological and psychological aspects is the cause of disease (McClain & McManus, 2018).

5. Interaction of Disease, Heredity and Environment

Disease is an abnormal form of life that causes interference in the fulfilment of basic needs. The process of disease occurrence is influenced by various factors, both intrinsic and extrinsic. Environmental changes are extrinsic factors that trigger disease. Extrinsic factors can cause disease if the individual's intrinsic capacity for self-defence is not commensurate with environmental

changes (Hyochol Ahn, 2017). Extrinsic factors include infectious agents, mechanical trauma, toxic chemicals, radiation, extreme weather, nutritional problems and psychological problems. Intrinsic factors include age, gender, and previous illnesses.

Diseases are partly caused by environmental factors, but on the other hand diseases are also caused by inherited genetic disorders (hereditary). In between, there are also diseases that are an interaction between genetic and extrinsic factors. These diseases only appear in adulthood after interacting with the environment even though they already have genetic abnormalities from birth (McPhee et al., 2005). For example, coronary artery disease is more common in close families and is influenced by extrinsic factors such as smoking, stress and food consumption, just like diabetes and hypertension.

6. The Concept of Disease

Disease or illness is defined as a condition in which there is an abnormal state of the body, leading to the loss of normal healthy conditions. Another definition of a disease is a change in an individual that causes the parameters (characteristics) of their health to change beyond normal limits (McPhee et al., 2005). Parameter changes in the body Those parameter changes in our body include breathing, airway, vision, and abdominal parameters (Wilkins., 2013).

a. Breathing parameters

   Normal breathing parameters are when inhaling and exhaling without obstruction. When the parameters change such as when the patients experience shortness of breath when inhaling and exhaling this means that they are sick or have an illness.

b. Airway parameters

   The airway parameters of a normal child are not excessive secretions. If the parameters change, such as the child has a lot of nasal secretions, it means that the child is sick or has a disease.

c. Vision parameters

Normal vision parameters occur when our eyes do not produce secretions and the vision is clear, but if the parameters change such as secretions and blurred vision, the eyes are sick or have a disease.

d. Abdominal parameters

Normal abdominal parameters mean no pain in the stomach. However, if the parameters change such as when you experience pain, fullness or burning, it means that you are sick or have a disease.

7. Disease Naming System

There are many types of diseases. Generally, diseases are named after the scientific name or the name of the bacteria that causes them, such as typhoid or typhoid because the cause is the bacteria Salmonella typhi. Naming diseases is also commonly done by adding prefixes or suffixes to a condition. Such as hypertension, hypothyroidism, and so on. The disease naming system used today generally also has a decades-old history, even centuries that have long been forgotten or covered by modern meanings.

a. Primary and secondary (Huether et al., 2020)

1) Primary. Primary means abnormally high blood pressure with no apparent cause. Terms that have similar meanings to the word primary are essential, idiopathic, and cryptogenic. The word primary is also used to identify or distinguish between the beginning and advanced stages of a disease. For example, primary cancer means early cancer.

2) Secondary. Secondary means abnormally high blood pressure as a result or complication of another disease such as renal arteriostenosis.

b. Acute and chronic (Huether et al., 2020)

1) Acute is a term used to describe the rapid and frequent progression of disease without rapid resolution. The

word acute is also used to describe a condition in which the patient's illness is severe and obvious.

2) Chronic is a term used to describe the slow or prolonged progression of the disease over months or even years with an invisible or hidden disease process.

c. Benign and malignant (McPhee et al., 2005)

1) Benign is the terminology used to classify certain diseases according to their condition and impact. For example, a benign tumour describes the results of a tissue biopsy examination and rarely results in death unless it presses or presses on vital organs such as the brain.

2) Malignant is the terminology used for the classification of certain diseases that spread from their site of origin or infiltrate and are often deadly.

d. Prefix addition

Some diseases are named by adding a prefix such as (Murray et al., 1964):

1) *ana* means absence, for example *ana*phylaxis;
2) *dis* means deviation, for example patellar *dis*location;
3) *hyper* means excess over normal, for example *hyper*pigmentation;
4) *hypo* means deficiency below normal, for example *hypo*glycaemia;
5) *meta* means change to another form, for example *meta*plasia.

e. Additional suffixes

Some diseases are named by adding suffixes such as:

1) *itis* means inflammation, for example periton*itis*;
2) *penia* means absent, for example thrombocyto*penia*;
3) *oma* means tumour, for example carcin*oma*;
4) *osis* means a condition that is not necessarily pathological, for example osteoarth*osis*;
5) *cytosis* means the number of cells increases, for example leuco*cytosis*;

6) *oid* means something similar, for example rheumat*oid*;
7) *opathy* means the abnormal shape loses its characteristics, for example lymphaden*opathy*.
8) *Ectasis* means dilatation, for example bronchi*ectasis*.
9) *Plasia* means growth disorder, for example hyper*plasia*

f. Eponymy

The naming of a disease is related to the person who first described the disease state or related to the place. For example: Graves' disease, Hodgkin's disease, Crohn's disease.

g. Syndromes (Iorga & Dara, 2019)

A syndrome is a collection of signs, symptoms, or a combination of lesions. Diseases that cannot be recognised or diagnosed have eponymised names.

1) Cushing syndrome is a syndrome that occurs due to a tumour in the pituitary gland which results in obesity, hirsutism, and hypertension.
2) Nephrotic syndrome is a syndrome that occurs due to abnormalities in the glomerulus or due to other kidney diseases that can be seen in the form of edema throughout the patient's body. Laboratory examination results found albuminuria and hypoalbuminemia.

8. Etiology or cause

Etiology is the cause of a disease or a series of events that cause the patient's illness. Another definition of etiology is the determination of the cause of a phenomenon including the identification of factors that cause disease (Huether & McCance, 2012).

Disease also involves the problem of cause relationships. It is explained that the cause relationship can be absolute or non-absolute (exclusive).

Experts have concluded that in general the etiological causes of illness are:

a. genetic abnormalities;

b. infectious agents such as bacteria, viruses, parasites, and fungi;
b. chemicals and radiation; and
c. trauma or forced labour.

9. Signs and symptoms of disease

Clinical signs and symptoms as biological changes due to disease include(McPhee et al., 2005):

a. signs of disease that are objectively observable manifestations of disease such as coughing, diarrhoea, vomiting and loose stools;
b. symptoms that are subjective changes due to disease that cannot be observed by others such as nausea, dizziness, and abdominal pain; and
c. complications that are new or separate processes that arise secondary to some change from the original condition.

SUMMARY

Pathophysiology is one of the sciences that specifically studies the impaired function of organisms affected by disease. Pathophysiology is also called the science that studies the process of changes or disorders of body functions due to a disease. A professional nurse will be able to analyze the impact of the cruris fracture on the patient basic needs and provide nursing interventions according to their problem. being normal is not determined by an absolute value but based on a certain range of values. For example, the normal blood glucose level is 70–140 mg/dl or the normal leucocyte level is 5,000–10,000/mm3. Disease can be defined as a form of life outside normal boundaries. The most useful benchmark of these normal limits relates to the individual's ability to fulfil the demands of adaptation to changes in the external environment in order to maintain a fixed internal environment. There are also psychosomatic diseases such as insomnia and gastritis. Disruption of homeostasis due to instability in physiological and psychological aspects is the cause of disease. The process of disease occurrence is influenced by various factors, both intrinsic and extrinsic. Environmental changes are extrinsic factors that trigger disease. Extrinsic factors can cause disease if the individual's

intrinsic capacity for self-defence is not commensurate with environmental changes. Generally, diseases are named after the scientific name or the name of the bacteria that causes them, such as typhoid or typhoid because the cause is the bacteria Salmonella typhi. Naming diseases is also commonly done by adding prefixes or suffixes to a condition. Disease or illness is defined as a condition in which there is an abnormal state of the body, leading to the loss of normal healthy conditions. Another definition of a disease is a change in an individual that causes the parameters (characteristics) of their health to change beyond normal limits. Etiology of a disease is the cause of a disease or a series of events that cause the patient's illness. Another definition of etiology is the determination of the cause of a phenomenon including the identification of factors that cause disease. Signs and symptoms of disease are as biological changes due to disease include signs of disease that are objectively observable, and subjective changes due to disease that cannot be observed by others such as nausea, dizziness, and abdominal pain; and complications that are new or separate processes that arise secondary to some change from the original condition.

KEY TERMS

Pathophysiology
Benefits of studying pathophysiology for nurses
Limits of normalcy
Disease limitation
Interaction of disease, heredity and environment
Concept of disease
Disease naming system
Etiology or cause
Signs and symptoms of disease

REVIEW QUESTION

ASSIGNMENT

Have a discussion with your friends about the cases below, then present the cases that have been discussed. Here is a situation that can be discussed about COVID 19:

Situation: COVID-19 is a respiratory disease caused by infection with the SARS-CoV-2 virus.

1. Explain what COVID-19 is and how the SARS-CoV-2 virus spreads. Discuss the ways the virus is transmitted, such as through respiratory droplets produced when coughing, sneezing, or talking, as well as contact with contaminated surfaces.
2. Discuss the common symptoms of COVID-19, including fever, dry cough, fatigue and respiratory distress. Remind that symptoms can vary from mild to severe, and some individuals may show no symptoms at all.
3. Discuss complications that may arise from COVID-19, such as pneumonia, severe acute respiratory syndrome (SARS), organ failure or blood clotting problems. Emphasise vulnerable groups, such as the elderly or individuals with underlying medical conditions.
4. Explain important precautions, such as regular hand washing, wearing a face mask, social distancing, and avoiding crowds. Discuss the importance of COVID-19 vaccination and promote vaccine awareness to the community.
5. Discuss the care given to COVID-19 patients, including isolation, symptomatic treatment to alleviate symptoms, and medical treatment given in more serious cases. Also explain the importance of close health monitoring and following guidelines set by health authorities.
6. Mention the psychological impacts of the COVID-19 pandemic, such as stress, anxiety and depression. Discuss the importance of mental support and the possible long-term impact on people's mental health.
7. Explain the nurse's role in managing COVID-19 patients, including patient supervision and care, monitoring symptoms, providing emotional support, and educating patients and their families on necessary precautions and treatments.

FORMATIVE TEST

1. Pathophysiology is the study of:
    a) Diagnosis of disease
    b) Treatment of disease
    c) Biological processes that occur in disease
    d) Signs and symptoms of disease

2. One of the differences between pathophysiology and etiology is:
   a) Pathophysiology is concerned with the causes of disease, whereas etiology is concerned with biological changes in the body.
   b) Pathophysiology is related to biological changes in the body, while etiology is related to the cause of disease.
   c) Pathophysiology is related to disease prognosis, while aetiology is related to biological changes in the body.
   d) Pathophysiology is related to disease diagnosis, while aetiology is related to the signs and symptoms of disease.

3. At the cellular level, pathophysiological changes can occur due to:
   a) Tissue damage
   b) Bacterial infection
   c) Chronic inflammation
   d) Vitamin deficiency

4. One example of pathophysiological changes at the organ level is:
   a) Changes at the cellular level
   b) Changes at the molecular level
   c) Changes at the systemic level
   d) Changes at the organ level

5. The process of pathogenesis refers to:
   a) The cause of a disease
   b) The course and progression of the disease
   c) Symptoms and signs of disease
   d) Diagnosis and treatment of disease

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UNIT 2. MECHANISMS OF CELL ADAPTATION

LEARNING OBJECTIVES

After mastering the contents of this unit, you will be able to:

1. Explain the cell structure
2. Define the cell injury
3. Classifying the cell injury based on the causes
4. Define the cell adaptation
5. Identify the mechanism of cell adaptation
6. Comparing the forms of adaptation
7. Explain the cell death

1. CELL STRUCTURE

Cells contain an organized physical structure called organelles consisting of two main parts, namely the Nucleus and Cytoplasm which are both separated by the core membrane. The following is presented in the picture of the cell and its parts (Hammer, 2018):

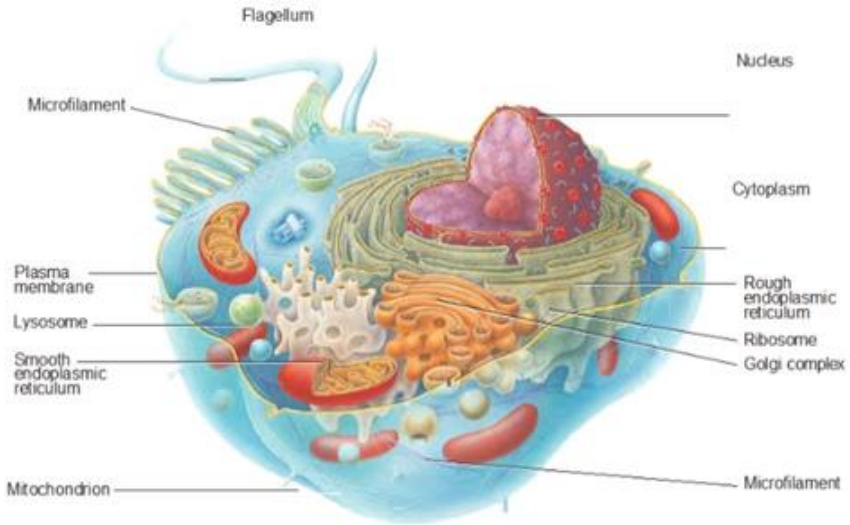


Figure 1: Cell Parts (Müller et al., 2020)

Some important cell parts and their functions to know (Folb, 2009):

a. Nucleus

Known as the "command center" of the cell, the nucleus is a large organelle that stores the DNA (deoxyribonucleic acid) of the cell. The nucleus controls all cell activities, such as growth and metabolism, using the genetic information of the DNA. Inside the nucleus are smaller structures called nucleoli, which is also a house for RNA (ribonucleic acid). RNA helps relay DNA commands throughout the cell and serves as a template for protein synthesis.

b. Ribosomes

Ribosomes are the protein factories in cells. Consisting of two subunits, ribosomes can be found floating freely within the cytoplasm of the cell or embedded within the endoplasmic reticulum. Using templates and instructions provided by two different types of RNA, ribosomes synthesize various proteins that are essential for cell survival.

c. Endoplasmic reticulum

The endoplasmic reticulum (ER) is a membranous organelle that shares part of its membrane with the nucleus. Some parts of the ER, known as the rough ER, are studded with ribosomes and are involved in protein manufacturing. The rest of the organelle is referred to as the smooth ER and functions to produce important lipids (fats).

d. Golgi apparatus

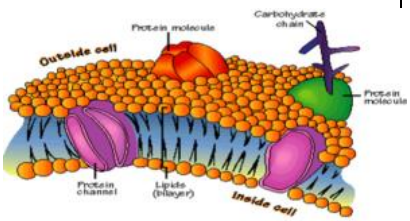
If proteins from the rough ER require further modification, they are transported to the Golgi apparatus (or Golgi complex). Like the ER, the Golgi apparatus consists of a folded membrane. It searches the protein's amino acid sequence for a specific "code" and modifies it. These processed proteins are then stored in the Golgi or packaged in vesicles for shipment elsewhere in the cell.

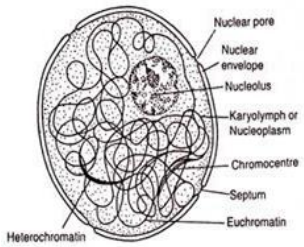
e. Mitochondria

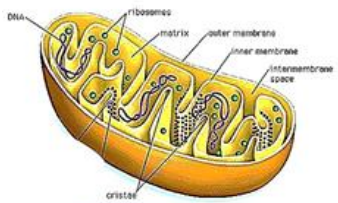
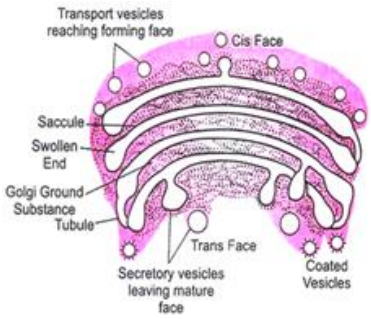
As the “powerhouse” of the cell, mitochondria are oval-shaped organelles found in most eukaryotic cells. As the site of cellular respiration, mitochondria function to convert molecules such as glucose into energy molecules known as ATP (adenosine triphosphate). ATP fuels cellular processes by breaking high-energy chemical bonds. Mitochondria are most abundant in cells that require large amounts of energy to function, such as liver and muscle cells.

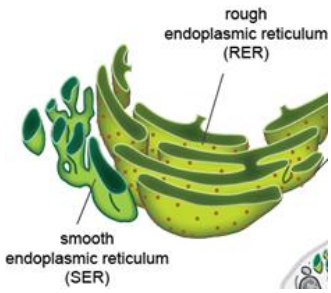
f. Lysosomes are the digestive organs of the cell

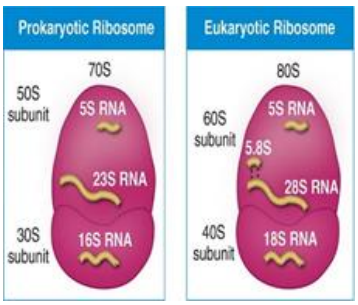
Table 1. Structure and Functions of Cells (Kumari & Bhandari, 2017)

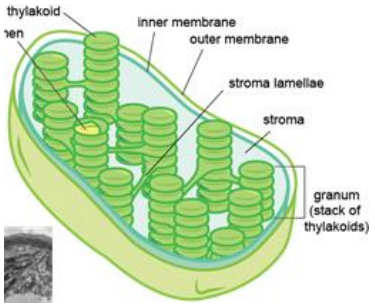
Cell Organelle	Occurrence/Characteristic & Structure	Function
Cell Membrane/Plasma Membrane	• Present in both plant cell and animal cell. • Selectively Permeable: Allows the materials in and out of the cell according to the requirement of the cell.  • Made up of bilipid layer and protein (Fluid Mosaic Model)	• Encloses the contents of the cell. • Provides shape: animal cell. • Allows transport: by Diffusion and Osmosis.

Cell Wall	• Present only in a plant cell. • Hard and rigid. • Fully permeable. • Made up of Cellulose in plant and peptidoglycan in bacteria.	• Protection • Gives shape and turgidity.
Cytoplasm	• Contains 80-90% water and many organic and inorganic compounds. • Colloidal, Viscous, Jelly like fluid inside the cell.	• Contains enzymes responsible for all the metabolic activity taking place inside the cell.
Nucleus (Director/Brain of the Cell)	• Covered by a double membranous nuclear membrane in a Eukaryotic Cell. • Contains DNA, RNA, Protein, nucleolus, and Chromatin network.  Fig. 8.1 Structure of a nucleus.	• Controls the activity of the cell. • Starts cell division. • It has the chromosomes or DNA which controls the hereditary characters

Mitochondria (The Power House of The Cell/Storage Batteries)	• Double membranous structure. • Autonomous body as contains its own DNA. • Self-duplicates • The main seat of respiration. • Stores energy in the form of ATP molecules.  MITOCHONDRIA-STRUCTURE	
Golgi Bodies (Shipping Department of Cell)	• Discovered by Camillo Golgi in 1898. • Originates from RER. • Contains Sac like Cisternae and Vesicles. • Has two faces–cis face or receiving face and trans face or supplying face.  	• Modification, Packaging, and transport of materials • Synthesis of lysosomes, plasma membrane

Endoplasmic Reticulum (Framework of Cell)	• A network of membranes. • RER bears ribosomes and appears rough • SER does not have ribosomes  	• Forms the skeletal framework of the cell. • Transport of materials from one cell to other. • Provides a surface for the synthesis of material– Proteins in RER and Lipids in SER. • Formation of lysosomes, Golgi bodies and vacu oles • Membrane Biogenesis • Detoxification of harmful substances in the liver.
Vacuole	• Arise from ER and GB • Surrounded by tonoplast and filled with cell sap	• Store cell sap which may be liquid or solid food, toxic byproduct. • Provide rigidity and turgidity to plant cell

Lysosomes (Suicidal bags of Cell, natural scavenger, cellular housekeeper)	• Membrane-bound organelles • Present in all animal cells and few plant cells • Tiny circular single membrane-bound structures filled with digestive enzymes	• Intracellular digestion of food in unicellular organisms.
Ribosomes (Protein Factories)	• Without a membrane • Consist of two subunits–60S and 40S in eukaryote both made up of RNA 	• Synthesis of Proteins
Plastids	• Double membrane-bound Types-1. Leucoplast–Colourless plastid; 2. Chromoplast–Coloured Plastid–blue, red, yellow. 3. Chloroplast–Green plastid	• Chloroplast–Perform Photosynthesis–Helps in the release of oxygen

	Autonomous self-duplicating body  	• Chromoplast– impart colour to flowers which help in pollination • Leucoplast– Storage • Amyloplast– Store starch • Aleuroplast– Store Protein • Elaioplast–Store fat

2. Cell Injury

A human body is susceptible to a wide variety of injuries at any time, which means that the injuries are experienced by cells. Cell injury occurs when a cell can no longer adapt to a stimulus (Hensley et al., 2000). This can happen if the stimulus is too long or too severe. Cells can recover from injury or die depending on the cell and the magnitude and type of injury. Here are the various causes of cell injury (Hensley et al., 2000).

a. Hypoxia

Hypoxia is cell injury due to a decrease in oxygen concentration. Hypoxia can occur due to loss of blood supply due to blood flow disorders. It can also be due to the loss of blood's ability to transport oxygen such as due to anemia or poisoning. The cell adaptation response to hypoxia depends on the severity of the hypoxia.

b. Chemicals

Chemicals including drugs cause changes to various cell functions, such as energy-producing functions, digesting lipids and proteins so that cells become damaged and die. For

example, gastric ulcers (wounds on the stomach) often occur due to frequent consumption of analgesic drugs and corticosteroids. This causes gastric mucosal cells to be injured and damaged and eventually ulcers (wounds) occur.

c. Physical agents

Physical agents such as mechanical trauma, low temperature and too high temperature, radiation and electrical trauma. All of these physical agents can cause changes or shifts in cell structure resulting in disruption of cell function which eventually leads to cell death

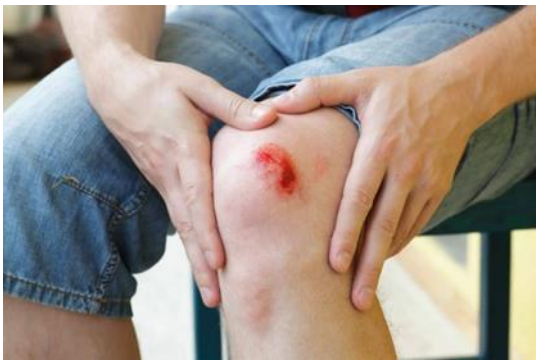


Figure 2: Body Parts Damaged by a Physical Agent

d. Microbiological agents

Microbiological agents are various types of bacteria, viruses, mycoplasmas, chlamydia, fungi and protozoa that secrete exotoxins that can damage the cell wall so that the cell wall function is disrupted and eventually cause cell death.

e. Immune mechanisms

Immune mechanisms are often the cause of damage to cells. For example, allergic diseases are often experienced by elderly patients or due to other immune reactions that cause itching or skin cell damage.

3. Definition of Cell Adaptation

Cell adaptation is changes undergone by cells in response to physiological (e.g., increased muscle mass after exercise, increased number of breast epithelial cells during pregnancy) or pathological (e.g., Barett's esophagus disease due to chronic exposure to stomach acid) stimuli. These changes usually make it easier for cells to tolerate adverse environments.

Continued stress can lead to cellular injury (e.g., critical hypertrophy of the left ventricle will cause myofibril damage and may eventually lead to heart failure).

4. Mechanism of Cell Adaptation

In order for the cell to continue to perform its function, the cell must carry out an adaptation mechanism when it gets injured so that the cell can survive. In terms of cell workload, according to (Krisanova N. V. et al., 2016), cell adaptation can be divided into:

a. Adaptation to increased cell workload

b. Adaptation to decreased cell workload

The following are the forms of adaptation carried out by cells (Hidayat, 2023):

1) Increase in cell size (hypertrophy)

Hypertrophy is defined as the enlargement of a tissue or organ due to the enlargement of its cells that is not accompanied by an increase in the function of the organ or tissue. Hypertrophy can be physiologic and pathologic. For example, pathologic hypertrophy conditions can be seen in heart muscle tissue that has an increased workload such as in patients who have suffered from hypertension for years. While physiologic hypertrophy conditions such as skeletal muscles in bodybuilders are deliberately formed as a result of lifting heavy weights.

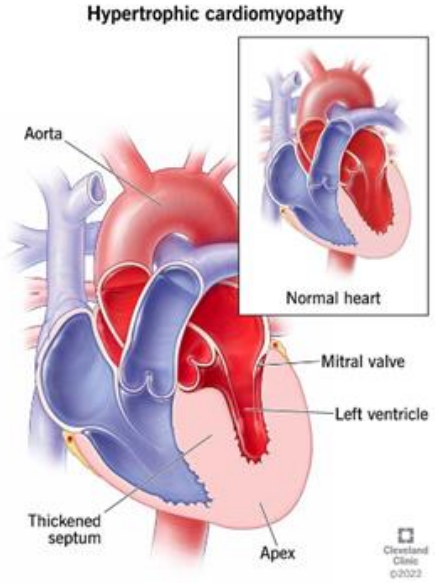
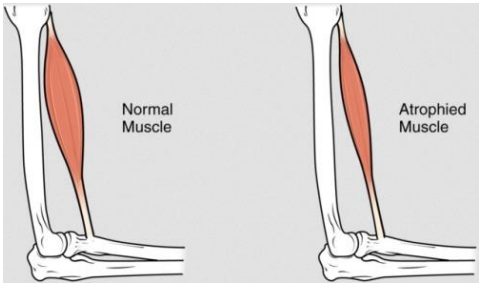


Figure 3: Pathologic Hypertrophy of the Heart Muscle

2) Reduction in cell size (atrophy)

Atrophy is an event where the organ or tissue that is formed grows to a fixed normal limit and then shrinks. It can be physiologic, for example in the aging process where all parts of the body appear to shrink gradually. It is clearer if seen in the elderly who experience endocrine atrophy so that their hormone products decrease. Pathological atrophy can occur in the muscles of individuals who are immobilized so that the muscles are never moved so that the muscles will get smaller.



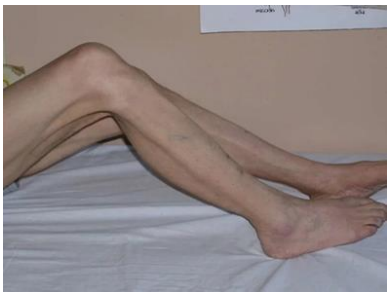
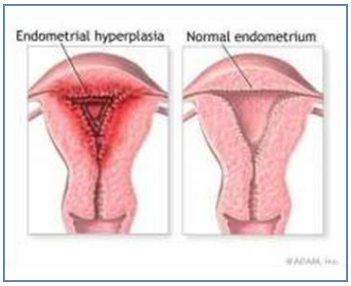


Figure 4: Muscle Atrophy

3) Increase in the number of cells (hyperplasia)

Hyperplasia occurs because of an absolute increase in a tissue or organ that causes enlargement of the tissue or organ and the function of the organ or tissue also increases. This can only occur in labile cells such as epidermal cells or blood cells. It does not occur in permanent cells such as skeletal muscle, nerve and heart cells. An example of physiologic hyperplasia is the enlargement of uterine cells when a woman is pregnant so that the fetus can grow bigger inside. Whereas pathologic hyperplasia usually occurs due to excessive hormonal stimuli such as endometrial hyperplasia due to uncontrolled estrogen hormone release and is a precursor to malignant proliferation.



Figures 5a & 5b: Physiologic Hyperplasia, Fetal-Appropriate Uterine Enlargement

4) Cell change (metaplasia)

A form of adaptation that occurs in the form of changing certain types of mature cells into other types of mature cells. For example, thoracic epithelial cells that can secrete are replaced by layered flat epithelial cells that cannot secrete which occurs in the respiratory tract of a smoker. This is unfavorable because the lender which is a means of protecting the respiratory tract against dust bacteria and foreign objects is not formed so that the respiratory tract is prone to infection.

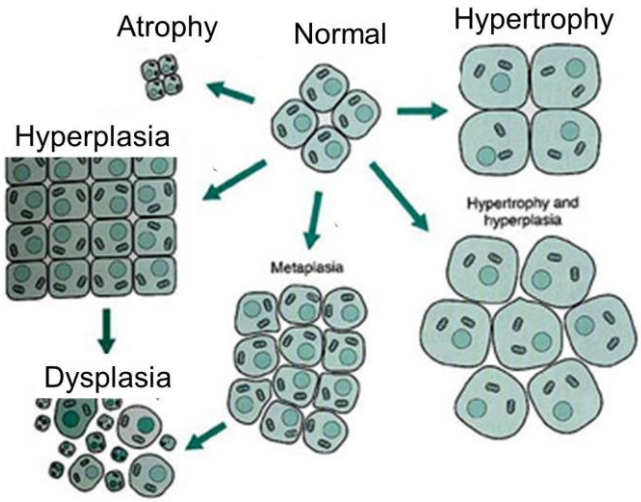


Figure 5. The Forms of Adaptation Carried Out by Cells

5. Cell Death

Previously we discussed that injury and cell death can be caused by lack of oxygen (hypoxia), chemicals, physical agents, microbiological agents and immune mechanisms. Based on the level of damage, cell injury or injury is grouped into 2 main categories, namely reversible injury (degeneration) and irreversible injury (cell death)(Hensley et al., 2000). Reversible injury is a condition when the cell can return to its original function and morphology if the damaging stimulus is removed. Meanwhile, irreversible injury is a

condition when the damage continues, so that the cell cannot return to its original state and the cell will die (Hidayat et al. 2023).

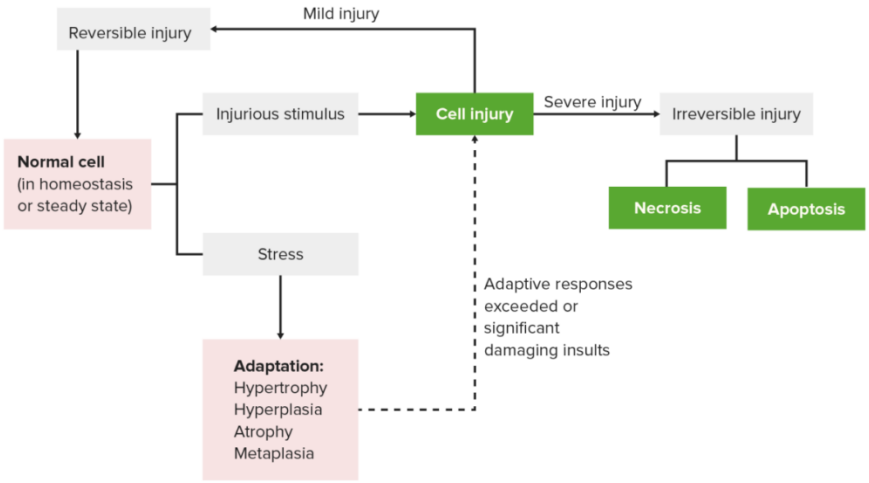


Figure 6. Cellular Response to Stress and Injury

Lack of oxygen (hypoxia) is the most common cause of cellular injury and death. The following conditions can cause problems such as ischemia, thrombosis, embolism, infarction and necrosis (Thompson et al., 2007). These injuries are reversible in some circumstances, or may progress to become permanent (irreversible) (Willis et al., 2014).

a. Ischemic

Ischemic is a lack of blood supply in a localized area. It is reversible, with the tissue returning to normal function once oxygen is reintroduced. Ischemic usually occurs in the presence of atherosclerosis, which is a narrowing of the blood vessels due to the accumulation of lipids or fat. An example of this condition is angina pectoris in the heart which has clinical symptoms in the form of pain in the left chest and disappears at rest (Huether et al., 2020).

b. Thrombosis

Thrombosis is the formation of a clot on the inner lining

(endothelium) of blood vessels. Thrombosis can restrict blood flow or completely block a blood vessel. Thrombosis can also occur in the endothelial lining of the heart. Thrombosis in an artery can stop blood flow to the area drained by the vessel and cause ischemia or infarction of the area.

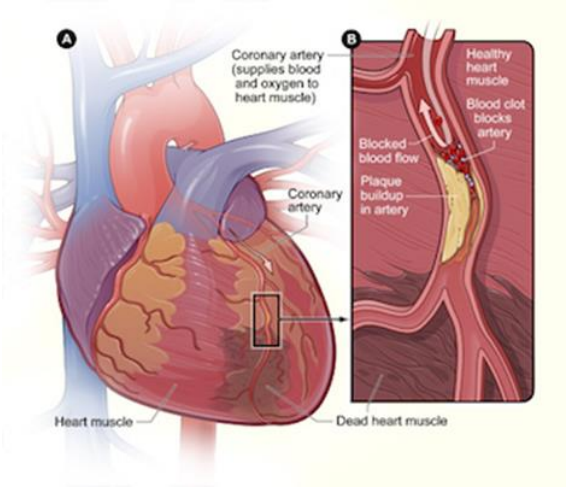


Figure 7. Thrombosis

c. Embolism

An embolism is a collection of a blood clot (thrombus) or other substance such as cholesterol that breaks away from a major blood vessel and enters the bloodstream where it can go anywhere and cause various problems including stroke, coronary heart disease, kidney failure or pulmonary embolism (Huether et al., 2020).

Figure 8: Thrombus-derived Embolism

d. Necrosis (Lamb et al., 2016)

Necrosis is a state of biochemical and morphologic changes (appearance) of cells due to injury to cells so that they cannot recover (irreversible). Necrosis is also called cell death (cellular death) which can occur throughout the body (somatic death) or limited to a tissue only in certain cells (Nair, 2009).

SUMMARY

Cells are the smallest structural and functional unit of the human body, damage to cells can lead to tissue damage. Cellular adaptation is the ability of cells to respond to different types of stimuli and adverse environmental changes. These adaptations include hypertrophy (enlargement of individual cells), hyperplasia (increase in cell number), atrophy (reduction in cell size and number), metaplasia (transformation from one type of epithelium to another), and dysplasia (irregular cell growth). Tissues adapt differently depending on the replicative characteristics of the cells that make up the tissue. For example, labile tissues such as skin can replicate rapidly, and therefore can also regenerate after injury, whereas permanent tissues such as nerve tissue and the heart cannot regenerate after injury. If cells cannot adapt to adverse environmental changes, cell death occurs physiologically in the form of apoptosis, or pathologically, in the form of necrosis. This article provides an overview of the main cellular adaptation mechanisms and their various consequences in the human body. Reversible and irreversible injuries will be experienced by cells at any time with various causes such as hypoxia, physical agents, chemicals, microbiological agents and immune mechanisms. Therefore, cells must carry out adaptation mechanisms in various forms such as atrophy, hyperplasia, hypertrophy and metaplasia

KEY TERMS

Cell structure
Cell injury
cell adaptation
Mechanism of cell adaptation
Cell death

REVIEW QUESTION

ASSIGNMENT

Have a discussion with your friends about the cases below, then present the cases that have been discussed.

1. Discuss the role of cell adaptation in wound healing and tissue regeneration. How are cells able to adapt and regenerate after injury?
2. What is the role of cell adaptation in stress tolerance? Explain the mechanism of cell adaptation to oxidative stress.
3. How is cell adaptation related to the development of diseases and pathological conditions? Give examples of cell adaptations that occur in specific disease cases.

FORMATIVE TESTS

1. A 45-year-old man was admitted to the emergency room due to electric shock while repairing a short circuit cable, causing wounds and injuries to the arm area.
   The cause of the injury is...
   a. Physical Agent
   b. Chemical
   c. Microbiology
   d. hypoxia
   e. Poisoning

2. A 60-year-old woman was admitted to the ICCU due to blockage of the coronary arteries of the heart. It is known that this mother has long suffered from hypertension since 10 years ago. After echocardiography examination, it was found that the heart was

enlarged (Cardiomegaly). In the enlargement of the heart there is a process of pathological adaptation of cells called....

a. Hypertrophy
b. Atrophy
c. Hyperplasia
d. Metaplasia
e. Cell Necrosis

3. A 60-year-old man has been hospitalized for a year because of a stroke that caused paralysis of the right lower extremity. Because it has never been moved so that the leg muscles shrink. In the shrinking of leg muscles, there is a pathological adaptation of cells called...

a. Hypertrophy
b. Atrophy
c. Hyperplasia
d. Metaplasia
e. Cell Necrosis

4. A 45-year-old man was admitted to the internal medicine ward for diabetes mellitus and gangrene. When performing gangrene wounds, black dead tissue is found and must be removed immediately so as not to spread. Black dead tissue in gangrene wounds is called....

a. Necrosis
b. Ischemic
c. Thrombosis
d. Embolism
e. Atrophy

5. A 40-year-old woman was admitted to the emergency room with symptoms of stroke. After CT-Scan examination, it was found that there was a blockage in the blood vessels in the brain. Blockage of cerebral blood vessels can be obtained from debris from a fatty substance called...

a. Necrosis

b. Ischemic
c. Thrombosis
d. Embolism
e. Atrophy

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UNIT 3. BALANCE AND IMBALANCE PROCESSES OF FLUIDS, ELECTROLYTES, AND ACIDS BASES

LEARNING OBJECTIVES

After mastering the contents of this chapter, you will be able to:

explain the balance of fluids and electrolytes
explain the body fluid distribution
identify materials contained in body fluids (electrolytes and non-electrolytes)
explain fluids and electrolytes in the body
explain mechanisms for regulating fluid and electrolyte balance
list the factors affecting fluid and electrolyte balance
explain the imbalance of fluid and electrolyte
define the edema
define acid and base balance
explain the regulation of acid and base balance
list the imbalance acids bases

1. BALANCE OF FLUIDS AND ELECTROLYTES

Fluid and electrolyte balance means the normal distribution of total body water and electrolytes to all parts of the body (Huether & McCance, 2012). Fluid and electrolyte balance are interdependent; if a problem occurs with one of them, it will affect the other. Fluids and electrolytes are necessary in order to maintain a healthy body condition. Fluid and electrolyte balance in the body is one part of homeostatic physiology. Fluid and electrolyte balance involves the composition and movement of various body fluids. Body fluids are solutions consisting of water (solvent) and certain substances (solutes). Electrolytes are chemical substances that produce electrically charged particles called ions when in solution. Fluids and electrolytes are essential for maintaining the body's balance or homeostasis. Body electrolytes contain chemical components. Body electrolytes are

positively charged (cations) and negatively charged (anions). Electrolytes are essential for many body functions, including neuromuscular function and acid-base balance (Huether & McCance, 2012).

2. BODY FLUID DISTRIBUTION

Water is the largest component of the human body. The percentage of body fluid depends on a person's age, gender and degree of nutritional status. As a person grows, the percentage of fluid to body weight decreases (Juffrie, 2017).

Table 2. Body Fluid Distribution

Fluid distribution	**Male Adult**	**Female Adult**	**Infant**
tal body water (%)	60	50	75
Intracellular	40	30	40
Extracellular	20	20	35
- Plasma	5	5	5
- Intersisial	15	15	30

Proportion of Body Fluid

The percentage of total body fluid varies according to the individual and depends on age, body fat condition, sex (RAJESHWARI, 2023).

Consider the following description.

Table 3. Percentage of Body Fluid by Age and Gender

No.	Age	Percentage
1.	Infant (newborn).	75 %
2.	Adults: a. Male (20-40 years old) b. Female (20-40 years old)	 60 % 50 %
3.	Elderly	45-50 %

For adults, approximately 40% of the body weight or 2/3 of its TBW is inside the cell (intracellular fluid/ICF), the rest, or 1/3 of TBW, or 20% of its body weight is outside the cell

(extracellular) is divided into 15% interstitial fluid, 5% intravascular fluid and 1-2% transcellular (Curtis & Bartels, 2021).

Body fluids are divided into two major groups, namely: intracellular fluid and extracellular fluid. Intracellular fluid is fluid that is inside the cells throughout the body. Meanwhile, extracellular fluid is fluid that is outside the cells and consists of three groups, namely: intravascular fluid (plasma), interstitial fluid, and transcellular fluid. Intravascular fluid (plasma) is fluid in the vascular system, interstitial fluid is fluid located between cells, while transcellular fluid is a special secretion fluid such as cerebrospinal fluid, intraocular fluid, and gastrointestinal secretions.

a. Intracellular fluid

   In adults, about 2/3 of the fluid in the body is intracellular. In contrast, in infants, only half of their body weight is intracellular fluid (Curtis & Bartels, 2021).

b. Extracellular fluid

   The relative amount of extracellular fluid decreases with age, to about one-third of the total volume in adults. Extracellular fluid is divided into interstitial fluid and intravascular fluid.

   Interstitial fluid is the fluid that surrounds cells and includes fluid contained between body cavities (transcellular) such as cerebrospinal, pericardial, pleural, synovial joint, intraocular, and digestive tract secretions.

   Meanwhile, intravascular fluid is the fluid contained in blood vessels, in this case blood plasma.

3. MATERIALS CONTAINED IN BODY FLUIDS (ELECTROLYTES AND NON-ELECTROLYTES) (Huether & McCance, 2012)

All body fluids are aqueous solutions of solvents, dissolved substances (solutes)

a. Water

Water is the main component of the human body. The average adult male contains almost 60% of his body weight in water and the average woman contains 55% of her body weight in water.

b. Solutes

In addition to water, body fluids contain two types of solutes (dissolved substances) electrolytes and non-electrolytes.

1) Electrolytes

Electrolytes are substances that dissociate (separate) in solution and will conduct electricity. Electrolytes dissociate into positive and negative ions and are measured by their capacity to bind to each other (milliequivalents/liter). The number of cations and anions, measured in milliequivalents, in a solution is always the same. mol/L) or by molecular weight in salts (millimoles/litre mEq/L).

a) Cations

Cations are ions that form a positive charge in solution. The main extracellular cation is sodium (Na^{+}), while the main intracellular cation is potassium (K^{+}). A pump system is present in the cell wall of the body that pumps sodium outward and potassium inward(S. Huether, 2013).

b) Anions

Anions are ions that form a negative charge in solution. The main extracellular anion is chloride (Cl^{-}), while the main intracellular anion is phosphate ion ($PO4_{3}$).

2) Non-electrolytes

Non-electrolytes are substances such as glucose and urea that do not dissociate in solution and are measured by weight (milligrams per 100 ml-mg/dl).

Other non-electrolytes of clinical importance include creatinine and bilirubin(S. E. Huether et al., 2020).

4. FLUIDS AND ELECTROLYTES IN THE BODY

In order to maintain health and life, humans require fluids and electrolytes in the right amounts and proportions in various body tissues. This can be achieved by a series of complex physicochemical maneuvers. Water occupies a large proportion of the body. A person weighing 70 kg can have about 50 liters of water in the body. Water makes up 75% of an infant's body weight, 70% of an adult man's body weight, and 55% of an elderly man's body. Because women have relatively large fat stores (relatively water-free), the water content in the female body is 10% less than that of men. Water is stored in two main compartments in the body, namely: intracellular fluid (CIS) and extracellular fluid (CES).

a) Intracellular fluid (CIS)

CIS is the fluid that resides in cells throughout the body. It serves as an important medium for chemical processes. The amount is about 2/3 of the total body fluid or 40% of body weight. The most cation electrolytes are K+, Mg+, a little Na+. The most anion electrolytes are HPO 2-, proteins, a little HCO-, SO 2-, Cl-.

b) Extracellular fluid (CES)

CES is the fluid that exists outside the cells and makes up about 30% of the total body fluid. CES includes intravascular fluid, interstitial fluid, and transcellular fluid. Interstitial fluid is present in the intercellular space, blood plasma, cerebrospinal fluid, lymph, and serous cavity and joint fluid. However, the amount is too small to play a role in fluid balance. In order to maintain the body's chemical and electrolyte balance and maintain a normal pH, the body carries out a two-way exchange mechanism between the CIS and CES. The electrolytes that play a role are cations and anions.

a. Main Electrolytes of the Human Body

Non-electrolytes are solutes that do not decompose in solution and are not electrically charged, such as: protein, urea, glucose, oxygen, carbon dioxide and organic acids. The body's electrolytes include sodium (Na+), potassium (K+), calcium (Ca++), magnesium (Mg++), chloride (Cl-), bicarbonate (HCO3-), phosphate (HPO42-), sulphate (SO42-).

The concentration of electrolytes in body fluids varies from one part to another, but although the concentration of ions in each part is different, the law of electrical neutrality states that the number of negative charges must equal the number of positive charges. The composition of body electrolytes in both the intercellular and plasma is detailed in the table below.

Table 4. Composition of Body Electrolytes in Both the Intercellular and Plasma

No.	Electrolytes	Extracellular	Interstitial	Intracellular Plasma
1.	Cations: Sodium (Na+) Potassium (K+)	144,0 mEq 5,0 mEq	137,0 mEq 4,7 mEq	10 mEq 141 mEq
	Calcium (Ca++) Magnesium (Mg ++)	2,5 mEq 1,5 mEq	2,4 mEq 1,4 mEq	0 31 mEq
2.	Anion: Chloride (Cl-) Bicarbonate (HCO3-) Phosphate (HPO42-) Sulfate (SO42-) Protein	107,0 mEq 27,0 mEq 2,0 mEq 0,5 mEq 1,2 mEq	112,7 mEq 28,3 mEq 2,0 mEq 0,5 mEq 0,2 mEq	4 mEq 10 mEq 10 mEq 1 mEq 4 mEq

b. Functions of Fluids and Electrolytes in the Body

1) Function of Fluids in the Body

In the metabolic processes that occur in the body, water has these main functions:

a) to carry nutrients such as carbohydrates, vitamins, and minerals that carry oxygen to the cells of the body;

b) to remove by-products of metabolism and can also be said to play a role in metabolic processes such as carbon dioxide (CO) and also nitrate compounds;

c) to moisturize body tissues such as the eyes, mouth, and nose, lubricant in joint fluid;

d) to catalyze cell biological reactions;

e) to protect the organs and tissues of the body and will also help in maintaining blood pressure and solute concentration;

f) as a heat regulator to keep the body temperature at an ideal condition of ± 37C.

2) Function of Electrolytes in the Body

Several functions of electrolytes in our body including:

a) to assist in the transfer of fluid between the room inside the cell and outside the cell, especially in the presence of sodium. If the amount of sodium in the CES increases, a certain amount of fluid will move toward the CES for fluid balance.

b) to regulate the acid-base balance and determine the pH of the blood with the buffer system;

c) with the difference in electrolyte composition in the CES and CIS, there will be a transfer that produces nerve implants and results in muscle contraction.

5. MECHANISMS FOR REGULATING FLUID AND ELECTROLYTE BALANCE

Fluid regulation in the body encompasses the reciprocal relationship between a number of components, including water in the body and its fluids, fluid parts, fluid spaces, membranes, transport systems, enzymes, and tonicity. Fluid and electrolyte circulation occurs in three stages. Firstly, blood plasma travels throughout the body via the circulatory system. Secondly, interstitial fluid and its components move between blood capillaries and cells. Finally, fluid and substances move from the interstitial fluid into the cells. Meanwhile, the mechanism of movement of body fluids takes place in three processes, namely: diffusion, osmosis, and active transport.

a. Diffusion

   Diffusion is the movement of a solution from an area of high concentration to an area of low concentration by crossing a semipermeable membrane. In this process, fluids and electrolytes enter across the membrane that separates the two compartments so that the concentration in both compartments is balanced. The speed of diffusion is influenced by three things, namely molecular size, solution concentration, and solution temperature.

b. Osmosis

   Osmosis is the movement of a liquid across a semipermeable membrane from an area of low concentration to an area of high concentration. In this process, the liquid crosses the membrane to dilute both sides of the membrane. This osmotic difference is partly influenced by the uneven distribution of proteins. Due to its large molecular size, the colloid osmotic pressure (oncotic pressure) is imbalanced so that the liquid is drawn into the intravascular space.

c. Active Transport

   Active transport is the transport process used by molecules to move across the cell membrane against its concentration

gradient. In other words, active transport is the movement of particles from one concentration to another regardless of their level. This process requires energy in the form of adenosine triphosphate (ATP). ATP is useful for maintaining the concentration of sodium and potassium ions in the extracellular and intracellular spaces through a process called the “sodium-potassium” pump.

Regulation of fluid balance occurs through the mechanism of thirst, anti-diuretic hormone (ADH), aldosterone hormone, prostaglandins, and glucocorticoids. The following is an explanation of this regulation.

a. Thirst

Thirst is a conscious desire for fluid. Thirst usually arises when plasma osmolality reaches 295 mOsm/kg. Osmoreceptors located in the hypothalamic thirst center are sensitive to changes in osmolality in extracellular fluid. If the osmolality increases, the cells will contract and the sensation of thirst will appear due to dehydration conditions. The mechanism is as follows:

1) Decreased renal perfusion stimulates the release of renin, which in turn produces angiotensin II. Angiotensin II stimulates the hypothalamus to release neuronal substrates responsible for continuing the sensation of thirst.
2) Osmoreceptors in the hypothalamus detect an increase in osmotic pressure and activate the neural network resulting in the sensation of thirst.
3) Thirst can be induced by localized dryness of the mouth due to hyperosmolar status. In addition, thirst can also arise to relieve the uncomfortable sensation of dryness due to decreased salivation.

b. ADH hormone

This hormone is formed in the hypothalamus and stored in the neurohypophysis of the posterior pituitary. The main stimuli for ADH secretion are increased osmolality and

decreased extracellular fluid. In addition, secretion can also occur under conditions of stress, trauma, surgery, pain, and on the use of some types of anaesthetics and drugs. This hormone increases water reabsorption in the collecting duct so as to retain water and maintain extracellular fluid volume. ADH is also referred to as vasopressin because it has a minor vasoconstrictive effect on arterioles that can increase blood pressure.

c. Aldosterone hormone

This hormone is secreted by the adrenal glands and acts on the renal tubules to increase sodium absorption. Sodium retention results in water retention. Aldosterone release is stimulated by changes in potassium concentration, serum sodium levels, and the rennin-angiotensin system.

d. Prostaglandins

Prostaglandins are naturally occurring fatty acids found in many tissues and play a role in inflammatory responses, blood pressure control, uterine contractions, and gastrointestinal motility. In the kidney, prostaglandins regulate renal circulation and sodium reabsorption.

e. Glucocorticoids

Glucocorticoids increase the reabsorption of sodium and water thereby increasing blood volume and resulting in sodium retention. Therefore, changes in glucocorticoid levels result in changes in blood volume balance (Tambayong, 2000).

Fluid intake in adult individuals ranges from 1500-3500 ml/day. Meanwhile, the fluid expenditure is 2300 ml/day. Fluid expenditure can occur through several organs, namely the skin, lungs, digestion, and kidneys.

a. Skin

Fluid expenditure through the skin is regulated by the work of sympathetic nerves that stimulate the activity of sweat glands. The stimulation of the sweat glands is caused by muscle activity, high ambient temperature and feverish

conditions. Fluid expenditure through the skin is known as insensible water loss (IWL). The same applies to the lungs. While fluid expenditure through the skin ranges from 15-20ml/24 hours or 350-400 ml/day.

b. Lungs

The increased amount of fluid output through the lungs is a form of response to changes in breathing rate and depth due to movement or febrile conditions. The IWL for the lungs is 350-400 ml/day.

c. Digestion

Under normal conditions, the amount of fluid lost through the digestive system each day ranges from 100-200 ml. The overall IWL calculation is 10-15 ml/kg BW/24 hours, with an additional 10% of normal IWL every 10C increase in temperature.

d. Kidney

The kidneys are the main fluid-excreting organ in the body. In adult, the kidneys excrete approximately 1500 ml per day.

Electrolyte balance is very important because the total electrolyte concentration will affect fluid balance, and electrolyte concentration affects cell function. Electrolytes play a role in maintaining fluid balance, acid-base regulation, facilitating enzyme reactions, and transmitting neuromuscular reactions. The most abundant electrolytes in the body are cations and anions.

a. Cations

Cations present in the body include:

1) Sodium (Na+)

Sodium is the main cation in the CES. The normal concentration of sodium is regulated by ADH and aldosterone (in the extracells). Sodium not only moves into and out of cells, but also moves between the two major fluid compartments. Sodium plays a role in the regulation of fluid balance, impulse

transmission and muscle contraction. The main function of sodium is to help maintain fluid balance, especially intracellular and extracellular, using the "sodium-potassium pump" system. Regulation of sodium ions is done by sodium intake, the hormone aldosterone and urine output.

2) Potassium (K+)

Potassium is the main cation found in the CIS. Potassium sources are bananas, broccoli, oranges and potatoes. Potassium is important for maintaining acid-base balance, as well as regulating heart impulse transmission and muscle contraction. The balance of potassium is regulated by the kidneys by alteration and replacement with potassium ions in the renal tubules.

3) Calcium (Ca2+)

Forms salts together with phosphate, carbonate, flouride in bones and teeth to make them hard and strong, improves nerve and muscle function, increases the effectiveness of the blood clotting process by activating prothrombin and thrombin. Sources: milk with high calcium, fish with bones, vegetables, etc.

b. Anions

Anions found in the body include:

1) Chloride (Cl-)

Chloride is one of the largest anions in extracellular fluid. Chloride functions to maintain blood osmotic pressure. The normal value of chloride is 95-105 mEq/l.

2) Bicarbonate (Cl-)

Bicarbonate is the main chemical buffer in the body found in extracellular and intracellular fluids. Regulation of bicarbonate is carried out by the kidneys. The normal value of bicarbonate is 22-26

mEq/l.

3) Phosphate (PO42-)

Phosphate is a buffer anion in intracellular and extracellular fluids. Phosphate helps the growth of bones and teeth and maintains their integrity. In addition, phosphate also helps with neuromuscular work, carbohydrate metabolism, and acid-base regulation. The action of phosphate is regulated by parathyroid hormone and activated by vitamin D.

6. FACTORS AFFECTING FLUID AND ELECTROLYTE BALANCE

Factors that affect fluid and electrolyte balance include age, activity, climate, diet, stress, illness, medical actions, medications, and surgery.

a. Age

Individual fluid intake varies with age. In this case, age affects body proportions, body surface area, metabolic needs, and body weight. Infants and children in their infancy have a greater proportion of body fluids than adults, hence the amount of fluid required and the amount of fluid lost are also greater than adults. The high fluid requirement in infants and children is also influenced by their high metabolic rate and the condition of their kidneys, which are less regulated than those of adults. Fluid loss may occur due to large fluid output from the skin and respiration. In elderly, fluid and electrolyte imbalances are often caused by cardiac problems or renal impairment.

b. Activity

A person’s life activity greatly affects fluid and electrolyte requirements. Activity causes an increase in metabolic processes in the body. This results in increased fluid loss through sweating. Thus, the amount of fluid needed also increases. In addition, insensible water loss also increases the rate of breathing and activation of sweat glands.

c. Climate

Normally, individuals living in environments where the climate is not too hot will not experience extreme fluid loss through the skin and breathing. In this situation, the fluid loss is generally unnoticeable (also known as insensible water loss, or IWL). The amount of IWL varies from individual to individual, influenced by environmental temperature, metabolic rate and age. Individuals living in high temperature environments or in areas with low humidity will experience more fluid and electrolyte loss. Similarly, people who work hard in high temperature environments may lose as much as five litres of fluid per day through sweat. Generally, people who are used to being in hot environments will lose as much as 700 ml of fluid per hour when in a hot place, while people who are not used to being in hot environments can lose up to two litres of fluid per hour.

d. Diet

A person's diet also affects fluid and electrolyte intake. If food intake is not balanced, the body tries to break down protein stores by first breaking down fat and glycogen stores. This condition causes a decrease in albumin levels.

e. Stress

Stressful conditions affect the body's fluid and electrolyte needs. During stress, the body experiences increased cellular metabolism, increased blood glucose concentration, and muscle glycolysis. This mechanism results in water and sodium retention. In addition, stress also causes an increase in the production of anti-diuretic hormones which can reduce urine production.

f. Illness

Illness greatly affects the body's fluid and electrolyte balance, for example: Trauma such as burns will increase water loss through IWL, kidney and cardiovascular disease greatly affect the process of regulating the body's fluid and

electrolyte balance.

g. Medical Actions

Some medical treatments have secondary effects on fluid and electrolyte requirements. Suctioning of gastric juices may cause a decrease in calcium and potassium levels.

h. Medications

Excessive use of some medications such as diuretics and laxatives can cause increased fluid loss in the body, resulting in fluid deficiency. In addition, the use of diuretics causes sodium loss so potassium levels will increase. The use of corticosteroids can also cause sodium and water retention in the body.

i. Surgery

Clients undergoing surgery are at high risk of fluid imbalance. Some clients may lose a lot of blood during the operative period, while others may experience fluid overload due to excessive intravenous fluid intake during surgery or secretion of the hormone ADH during times of stress due to anesthetic drugs.

7. IMBALANCE FLUID AND ELECTROLYTE

Imbalance fluid and electrolyte can occur when the body's compensatory mechanisms are unable to maintain homeostasis.

Fluid imbalance can be in the form of fluid volume deficits or vice versa.

a. Fluid volume deficit (FVD)

Fluid volume deficit is an imbalance condition characterized by a deficiency of fluid and electrolytes in the extracellular space, but the proportion between the two (fluid and electrolytes) is close to normal. This condition is also known as hypovolaemia. In hypovolaemia, the osmotic pressure changes so that the interstitial fluid becomes empty and intracellular fluid enters the interstitial space, disrupting cell life. In general, the condition of fluid volume deficit (dehydration) is divided into three, namely:

isotonic dehydration, hypertonic dehydration, and hypotonic dehydration.

1) Isotonic dehydration
   This occurs when the amount of fluid lost is proportional to the amount of electrolytes lost. Plasma Na+ levels are 130-145 mEq/l.
2) Hypertonic dehydration
   This occurs when the amount of fluid lost is proportional to the amount of electrolytes lost. Plasma Na+ levels are 130-150 mEq/l.
3) Hypotonic dehydration
   This occurs when the amount of fluid lost is less than the amount of electrolytes lost. The Na+ level in blood plasma is 130 mEq/l.

Excessive extracellular fluid loss can cause several changes. These include a decrease in extracellular volume (hypovolaemia) and changes in hematocrit. Basically, this condition can be caused by many factors, such as lack of fluid intake, high intake of solvents (e.g., protein and chloride or sodium) that can lead to excessive urine excretion, profuse sweating over a long period of time, and other abnormalities that cause excessive urine output.

Furthermore, dehydration conditions can be categorized according to its severity, i.e., mild, moderate, and severe dehydration.

1) Mild dehydration
   In this condition, fluid loss reaches 5% of body weight or about 1.5-2 litres. A fluid loss of 5% in older children and adults is categorised as severe dehydration. Excess fluid loss may take place through the skin, gastrointestinal tract, faeces, lungs or blood vessels.
2) Moderate dehydration
   This condition occurs when fluid loss reaches 5-10% of body weight or about 2-4 litres. The serum

sodium level is around 152-158 mEq/l. One of the symptoms is sunken eyes.

3) Severe dehydration

This condition occurs when fluid loss reaches 4-6 litres. Serum sodium levels range from 159-166 mEq/l. In this condition the patient may experience hypotension.

b. Fluid volume excess (FVE)

Fluid volume excess (overhydration) is an imbalance condition characterized by excess (retention) of fluid and sodium in the extracellular space. This condition is also known as hypervolemia. Overhydration is commonly caused by impaired renal function. The most common manifestations of this condition are increased blood volume and oedema. Oedema occurs due to increased hydrostatic pressure and decreased osmotic pressure. Edema often appears in the eyes, fingers and ankles. Pitting oedema is oedema that appears in peripheral areas. If the area is pressed, a depression will form that does not disappear immediately after the pressure is released. This is because the transfer of fluid to the tissues through the pressure point of pitting oedema does not show a thorough fluid overload. In non-pitting oedema, on the other hand, fluid within the tissue cannot be transferred to the area by finger pressure. This is because non-pitting oedema does not indicate extracellular fluid overload, but rather conditions of infection and trauma that cause fluid collection and coagulation at the tissue surface. Excess vascular fluid increases hydrostatic pressure and fluid pressure on the interstitial surface. Anasarka oedema is oedema that is present throughout the body. Manifestations of pulmonary oedema include sputum accumulation, dyspnoea, cough, and wet rales.

Electrolyte imbalance include these following conditions.

a. Hyponatremia and hypernatremia

Hyponatremia is a deficiency of sodium levels in the extracellular fluid which causes changes in osmotic pressure. This change results in the movement of fluid from the extracellular to the intracellular space so that the cells become swollen. Hyponatremia is commonly caused by kidney disease, Addison's disease, sodium loss through digestion, excessive sweat output, dieresis, and metabolic acidosis. Other causes related to fluid overload are syndrome of inappropriate antidiuretic hormone (SIADH), increased fluid intake, hyperaldosteronism, diabetic ketoacidosis, oliguria, and psychogenic polydipsia. Signs and symptoms of hyponatremia include anxiety, postural hypotension, postural dizziness, nausea, vomiting, diarrhoea, tachycardia, seizures and coma. Laboratory findings for this condition are serum sodium level <136 mEq/l and urine specific gravity <1.010. On the other hand, hypernatremia is an excess of sodium levels in the extracellular fluid leading to increased extracellular osmotic pressure. This condition results in the movement of intracellular fluid out of the cell. Causes of hypernatremia include excessive sodium intake, impairment of thirst sensation, dysphagia, diarrhoea, excessive fluid loss from the lungs, polyuria due to diabetes insipidus. Signs and symptoms include dry skin, dry lip mucosa, pyrexia, agitation, seizures, oliguria, or anuria. Laboratory findings for this condition are serum sodium >144 Meq/l, urine specific gravity >11.30.

b. Hypokalaemia and hyperkalaemia

Hypokalaemia is a deficiency in potassium levels in the extracellular fluid which causes potassium to

move out of the cells. As a result, hydrogen and potassium ions are retained in the cells and cause disturbances or changes in plasma pH. Symptoms of potassium deficiency are first seen in the muscles, bowel distension, decreased bowel noise, and irregular pulse. Laboratory examination reveals a serum potassium value of <3.0 mEq/l. Meanwhile, hyperkalaemia is an excess of potassium in the extracellular fluid. This case is rare, but even if it is, it will certainly be very dangerous for life because it will hinder the transmission of heart impulses and cause a heart attack. When hyperkalaemia occurs, one of the efforts that can be made is to give insulin because insulin can help push potassium into cells. Signs and symptoms of hyperkalaemia include anxiety, irritability, irregular heart rhythm, hypotension, parasthesias, and weakness. In laboratory examination, the serum potassium value is found to be >5 mEq/l, while in ECG examination, the T wave is peaked, QRS is widened, and PR is elongated.

c. Hypocalcaemia and hypercalcaemia

Hypocalcaemia is a deficiency of calcium in the extracellular fluid. If prolonged, this condition can lead to osteomalacia as the body will try to fulfil its need for calcium by taking it from the bones. Signs and symptoms of hypocalcaemia include spasm and tetany, increased gastrointestinal motility, cardiovascular disorders and osteoporosis. Laboratory findings for this condition include serum calcium levels <4.5 mEq/l or 10 mg/100 ml as well as prolonged Q-T interval. In addition, hypocalcaemia can also be assessed from positive Trosseau and Chvostek signs. On the other hand, hypercalcaemia is an excess of calcium in the

extracellular fluid. This condition causes a decrease in muscle and nerve excitability which in turn leads to flaccidity. Signs and symptoms of hypercalcaemia include decreased muscle excitability, anorexia, nausea, vomiting, weakness and lethargy, back pain and cardiac arrest. Laboratory findings include serum calcium levels >5.8 mEq/l or 10 mg/100 ml and elevated BUN due to fluid deprivation. X-rays showed generalised osteoporosis as well as diffuse bone cavities.

d. Hypomagnesemia and hypermagnesemia

Hypomagnesemia occurs when the serum magnesium level is less than 1.5 mEq/l. Generally, this condition is caused by excessive alcohol consumption, malnutrition, diabetes mellitus, liver failure, poor intestinal absorption. Signs and symptoms include tremors, hyperactive profunda tendon reflexes, confusion, disorientation, hallucinations, seizures, tachycardia and hypertension. Laboratory findings for this condition include serum magnesium levels <1.4 mEq/l. On the other hand, as its name suggest, hypermagnesemia is a condition of increased magnesium levels in the serum. Although it is quite rare, this condition can affect people with kidney failure, especially those taking magnesium-containing antacids. Signs and symptoms of hypermagnesemia include cardiac arrhythmia, depression of profunda tendon reflexes, respiratory depression. Laboratory findings for this condition include serum magnesium levels >3.4 mEq/l.

e. Hypochloraemia and hyperchloraemia

Hypochloraemia is a decrease in serum chloride ion levels. Specifically, this condition is caused by excessive loss of gastrointestinal secretions, such as

vomiting, diarrhoea, dieresis, and nasogastric suction. Signs and symptoms resemble metabolic alkalosis, with apathy, weakness, mental confusion, cramps and dizziness. The laboratory finding for this condition is a chloride ion value >95 mEq/l. On the other hand, hyperchloraemia is an elevated serum chloride ion level. It is often associated with hypernatremia, especially when there is dehydration and kidney problems. Hyperchloraemia causes a decrease in bicarbonate resulting in an acid-base imbalance. Furthermore, this condition can lead to weakness, lethargy and Kussmaul's breathing. The laboratory finding is a chloride ion value >105 mEq/l.

f. Hypophosphataemia and hyperphosphataemia

Hypophosphataemia is a decreased level of phosphate in the serum. This condition may result from decreased intestinal phosphate absorption, increased phosphate excretion, and increased bone phosphate uptake. Hypophosphataemia can occur due to alcoholism, malnutrition, diabetic ketoacidosis and hyperthyroidism. Signs and symptoms include anorexia, dizziness, paresthesias, muscle weakness, and occult neurological symptoms.

The laboratory finding for this condition is a phosphate ion value <2.8 mEq/dl. On the other hand, hyperphosphataemia is an increased level of phosphate ions in the serum. This condition may appear in cases of renal failure or when parathyroid hormone levels decrease. In addition, hyperphosphatemia can also result from excessive phosphate intake or abuse of phosphate-containing laxatives. Since calcium levels are inversely proportional to phosphate, the signs and symptoms

of hyperphosphatemia are similar to those of hypocalcaemia, namely increased central nervous system excitability, muscle spasm, convulsions and tetany, increased intestinal motility, cardiovascular problems such as decreased cardiac contractility/symptoms of heart failure, and osteoporosis. Laboratory findings are phosphate ion values >4.4 mg/dl or 3.0 mEq/l.

8. EDEMA

Edema is an abnormal accumulation of fluid in the interstitial spaces (spaces between cells) or tissues of the body that causes swelling. Under normal conditions in general, body fluids that are outside the cells will be stored in two rooms, namely blood vessels and interstitial spaces. If there is a disturbance in the balance of body fluid regulation, fluid can accumulate excessively in the interstitial space, causing oedema. However, if the fluid is very excessive, excess fluid can sometimes gather in the third space, namely body cavities such as the chest abdomen and abdominal cavity.

You need to know that this swelling condition generally occurs in some parts of the body that are very active. And one of the body parts in question is the feet, and some parts of the body around the feet. The causes themselves include:

a. blood clots in the legs,
b. the occurrence of enlarged veins,
c. not moving for a long period of time,
d. extremely hot weather,
e. burns,
f. pressure that interferes with blood flow.

9. ACID AND BASE BALANCE

Acid-base balance is a state in which the concentration of hydrogen ions produced is equal to the concentration of hydrogen ions released by the cell. In the process of life, acid

balance at the molecular level is generally associated with weak acids and weak bases, as well as at very low levels of H+ ion or OH^- ion concentration.

The acid-base balance is a hydrogen ion balance. Although production will continue to produce very large amounts of hydrogen ions, it turns out that the concentration of hydrogen ions is maintained at a low level of pH 7.4. The acidity (pH) of human blood normally ranges from 7.35 to 7.45. The human body is able to maintain a balance of acids and bases so that metabolic processes and organ functions can run optimally.

The acid-base balance in the human body is regulated by two organ systems, namely the lungs and kidneys. The lungs play a role in the release (excretion of CO2) and the kidneys play a role in the release of acids. Acids and bases are two classes of chemical substances that are very important in everyday life. In relation to acid-base properties, solutions are grouped into three groups, namely acidic, basic, and neutral. Acids and bases have different properties, so we can determine the nature of a solution. The acid-base nature of a solution can also be determined by measuring its pH. pH is a parameter used to express the acidity of a solution. Acidic solutions have a pH of less than 7, basic solutions have a pH of more than 7, while neutral solutions have a pH of 7. The pH of a solution can be determined with a pH indicator or with a pH meter. According to this explanation, it explains about acid-base balance and various factors or things related to acid-base balance.

Acids are defined as substances that can give H^+ ions to other substances (referred to as proton donors), while bases are substances that can accept H^+ ions from other substances (referred to as proton acceptors). An acid can only release protons if there is a base that can accept the released protons. An example of an acid is hydrochloric acid (HCL), which ionises in water to form hydrogen ions (H^+) and chloride ions (CL^-) likewise, carbonic acid (H_2CO^3) ionises in water to form H+ ions and bicarbonate ions (HCO_3^-). Strong acids are acids that

dissociate rapidly and mainly release large amounts of H^+ ions in solution, an example is HCL. Weak acids have less tendency to dissociate their ions and therefore release less H^+, an example is H_2CO^3.

Bases are ions or molecules that accept hydrogen ions. For example, bicarbonate ion (HCO_3^-), is a base because it can combine with one hydrogen ion to form carbonic acid (H_2CO^3).1 Proteins in the body also function as bases because some of the amino acids that make up proteins with a negative final charge readily accept hydrogen ions. The hemoglobin protein in red blood cells and proteins in other body cells are the most important bases of the body. Strong bases are bases that react rapidly and strongly with H^+. It therefore quickly removes it from solution. A typical example is OH^-, which reacts with H^+ to form water (H_2O). A typical weak base is HCO_3^- because HCO_3^- binds to H^+ much weaker than OH^-. Most acids and bases in extracellular fluids that are associated with normal acid-base regulation are weak acids and bases.

Acid-base balance is important for the body because it can affect the function of vital organs. Severe acid-base balance disorders can affect the survival of patients. The acidity (pH) of human blood normally ranges from 7.35 to 7.45. The human body is able to maintain a balance of acid and base so that metabolic processes and organ functions can run optimally. The acid-base balance in the human body is regulated by two organ systems, namely the lungs and kidneys. The lungs play a role in the release (excretion of CO_2) and the kidneys play a role in the release of acid.

Some principles related to acid-base balance that we need to know are explained below.:

a. The term acidosis refers to the condition of pH < 7.35 while alkalosis when pH > 7.45.
b. CO_2 (carbon dioxide) is a gas in the blood that acts as an acid component. CO_2 is also a respiratory component. The normal value is 40 mmHg.

c. HCO_3 (bicarbonate) acts as an alkaline component and is also known as a metabolic component. The normal value is 24 mEq/L.
d. Acidosis means that there is an increase in the amount of acidic components or a decrease in the amount of basic components.
e. Alkalosis means that there is an increase in the amount of basic components or a decrease in the amount of acidic components.

10. REGULATION OF ACID AND BASE BALANCE

The regulation of hydrogen ion balance is in some ways similar to the regulation of other ions in the body, for example, to achieve homeostatis. There must be a balance between hydrogen ion intake or production and the removal of hydrogen ions from the body. And as with other ions, the kidneys play a key role in the regulation of hydrogen ions. However, the proper regulation of extracellular fluid hydrogen ion concentration involves much more than the simple elimination of hydrogen ions by the kidneys. There are also many acid-base buffering mechanisms involving the blood, cells and lungs that are necessary to maintain normal hydrogen ion concentrations in extracellular and intracellular fluid. There are various mechanisms that help regulate hydrogen ion concentration, with particular emphasis on the control of renal hydrogen ion secretion and the reabsorption, production and excretion of bicarbonate ions by the kidneys, a key component of the acid-base control system in various body fluids.

Hydrogen ion concentration and pH of normal body fluids and the changes that occur in acidosis and alkalosis. Blood hydrogen ion concentration is normally maintained within strict limits of a normal value of about 0.00004 mEq/litre (40 nEq/litre).6 Normal variations are only about 3 to 5 mEq/litre, but under extreme conditions, hydrogen ion concentration can vary from as low as 10 nEq/litre to as high as 160 nEq/litre

without causing death. Since the normal hydrogen ion concentration is low and in small amounts this is impractical, usually the hydrogen ion concentration is expressed on a logarithmic scale, using the unit pH. pH is related to the hydrogen ion concentration.

The normal pH of arterial blood is 7.4, while the pH of venous blood and interstitial fluid is about 7.35 due to the extra amount of carbon dioxide (CO2) liberated from tissues to form H2CO3.3 Since the normal pH of arterial blood is 7.4 a person is expected to experience acidosis when the pH falls below this value and to experience alkolysis when the pH increases above 7.4. The lower limit of pH at which a person can live more than a few hours is about 6.8 and the upper limit is about 8.0. Intracellular pH is usually slightly lower than plasma pH because cellular metabolism produces acids, mainly H2CO3.3 Depending on the cell type, the pH of intracellular fluid is thought to range between 6.0 and 7.4. Tissue hypoxia and poor blood flow to the tissues can lead to acid collection and that can lower the intracellular pH. Urine pH can range from 4.5 to 8.0 depending on the acid-base status of the extracellular fluid. An extreme example of an acidic body fluid is HCl which is excreted into the stomach by the oxytocic (parietal cells) of the gastric mucosa.

The regulation of acid-base balance is organised through the coordination of 3 systems, i.e., buffer system, lung system, and renal system.

a. Buffer System

A chemical acid-base buffer system in body fluids, which immediately combines with acids or bases to prevent excessive changes in hydrogen ion concentration. This buffer system neutralises excess hydrogen ions, is temporary and does not perform elimination. The main function of buffer systems is to prevent pH changes caused by the influence of fixed and organic acids on extracellular fluid. As a buffer, this system has limitations, such as:

1) It cannot prevent pH changes in extracellular fluid

caused by increased CO2.

2) This system only functions when the respiration system and the respiratory system control centre are working normally.
3) The ability to organise a buffer system depends on the availability of bicarbonate ions.

There are four buffer systems as explained below.

1) The bicarbonate buffer is a dapar system in the extracellular fluid mainly for changes caused by non-bicarbonates.
2) Protein buffers are aqueous systems in extracellular and intracellular fluids.
3) Haemoglobin buffer is a solvent system in erythrocytes for carbonic acid changes acid load.
4) Phosphate buffers are aqueous systems in the urinary system and intracellular fluid.

Chemical systems can only address temporary acid-base imbalances. If chemical buffers are not enough to correct the imbalance, then pH control will be continued by the lungs which respond quickly to changes in blood H ion levels due to stimulation of chemoreceptors and respiratory centres, then maintain levels until the kidneys eliminate the imbalance. The kidneys are able to regulate the H ion imbalance slowly by secreting H ions and adding new bicarbonate to the blood because it has a phosphate and ammonia reservoir.

The elimination process is carried out by the lungs and kidneys. The mechanism of the lungs and kidneys in supporting the performance of the buffer system is by regulating the secretion, excretion, and absorption of hydrogen and bicarbonate ions and forming additional buffers (phosphate, ammonia). For the long term, excess acid or base is excreted through the kidneys and lungs while for the short term, the body is protected from pH changes by the buffer system. The buffer mechanism aims

to maintain blood pH between 7.35- 7.45.

b. Lung System

The lungs, under the control of the cerebral medulla, control carbon dioxide, and therefore also control the carbonic acid content of the extracellular fluid. The lungs do this by adjusting ventilation in response to the amount of carbon dioxide in the blood. An increase of the partial pressure of carbon dioxide in the arterial blood (PaCO2) is a strong stimulant for respiration. Of course, the partial pressure of carbon dioxide in the arterial blood (PaCO2) also affects respiration. However, the effect is not as clear as that produced by PaCO2. In states of metabolic acidosis, respiratory frequency is increased, leading to greater elimination of carbon dioxide (to reduce excess acid). In states of metabolic alkalosis, respiratory frequency is decreased, leading to retention of carbon dioxide (to increase acid load).

c. Renal System

To maintain acid-base balance, the kidneys must excrete non-volatile acid anions and replace HCO3-. The kidneys regulate acid-base balance by secretion and reabsorption of hydrogen ions and bicarbonate ions. In this mechanism of regulation by the kidneys, three systems play a role: carbonic acid buffering, phosphate buffering and ammonia formation. Hydrogen ions, CO2 and NH3 are excreted into the tubule lumen with the help of energy generated by the sodium pump mechanism in the basolateral tubule. In this process, carbonic acid and sodium are released back into the circulation to be able to function again. The proximal tubule is the main site of bicarbonate reabsorption and acid expulsion.

Hydrogen ions are highly reactive and readily combine with negatively charged ions at very low concentrations. Even at very low levels, hydrogen ions have a great effect on biological systems. Hydrogen ions

interact with various biological molecules so that they can affect protein structure, enzyme function and membrane excitability. Hydrogen ions are very important in the normal functioning of the body for example as a mitochondrial proton pump in the oxidative phosphorylation process that produces ATP.

Hydrogen ion production is very much because it is generated continuously in the body. The acquisition and excretion of hydrogen ions vary greatly depending on diet, activity and health status. Hydrogen ions in the body come from food, drink, and the body's metabolic processes. In the body hydrogen ions are formed as a result of carbohydrate, protein and fat metabolism, anaerobic glycolysis or ketogenesis.

11. IMBALANCE ACID-BASE

Acid-base balance (pH) disorder is a condition when the levels of acids and bases in the blood are unbalanced. This condition can interfere with the work of various organs of the body. The body uses various mechanisms to regulate the acid-base balance in the blood. These mechanisms involve the lungs, kidneys and the buffer system. The regulation of blood pH balance in the lungs occurs during the breathing process. Humans breathe by inhaling oxygen (O2) and removing carbon dioxide (CO2). CO2 is an acidic substance so the amount of CO2 released will affect the blood pH balance, either acidosis or alkalosis. Acidosis and alkalosis caused by disorders of the lungs or breathing are called respiratory acidosis and respiratory alkalosis.

Acidosis and alkalosis can also occur if the production of acids and bases in the body is not balanced. The condition occurs when the kidneys are unable to remove excess acids or bases from the body. Acidosis and alkalosis due to either of the above two conditions are called metabolic acidosis and metabolic alkalosis.

The following are the types of acid-base balance disorders

a. Respiratory Acidosis

Respiratory acidosis is excessive blood acidity due to the build-up of carbon dioxide in the blood as a result of poor lung function or slow breathing. Poor lung function or slow breathing. The speed and depth of breathing control the amount of carbon dioxide in the blood. Under normal circumstances, if carbon dioxide accumulates, the pH of the blood will drop and the blood will become acidic. High levels of carbon dioxide in the blood stimulate the brain that regulates breathing, resulting in faster and deeper breathing.

Respiratory acidosis occurs when the lungs cannot adequately remove carbon dioxide. This can occur in severe diseases affecting the lungs. Respiratory acidosis can also occur when diseases of the nerves or muscles of the chest cause interference with the respiratory mechanism. The first symptoms are headache and drowsiness. If the condition is getting worse, the drowsiness will progress to stupor and coma. Stupor and coma can occur within moments if breathing is stopped or if breathing is severely impaired; or after hours if breathing is less impaired. The kidneys attempt to compensate for the acidosis by retaining bicarbonate, but this process takes several hours or even days. The diagnosis is usually made based on the results of blood pH and carbon dioxide measurements from arterial blood. Treatment for respiratory acidosis aims to improve the function of the lungs. Medicines to improve breathing can be given to patients with lung diseases such as asthma and emphysema. In patients with severe respiratory distress, artificial respiration with the help of a mechanical ventilator may be necessary.

b. Metabolic Acidosis

Metabolic acidosis is excessive blood acidity, characterised by low levels of bicarbonate in the blood. When the increase in acidity exceeds the pH buffering system, the blood will actually become acidic. As the blood pH decreases, breathing becomes deeper and faster as the body attempts to reduce the excess acid in the blood by decreasing the amount of carbon dioxide. Ultimately, the kidneys also attempt to compensate by excreting more acid in the urine. But both mechanisms can be overridden if the body continues to produce too much acid, resulting in severe acidosis and coma.

The causes of metabolic acidosis can be:

1) Excess acid production

   In diabetic acidosis or lactic acidosis, acid production may exceed the ability of the kidneys to absorb and excrete H+.

2) Lack of saline reserves

   Wasted HCO_3 ion loss through the kidneys or intestines leads to hypocarbonatraemia and metabolic acidosis.

3) Lack of acid excretion

   It may occur in chronic kidney disease where the kidneys fail to excrete normally produced acid.

Mild metabolic acidosis can be asymptomatic, but patients usually experience nausea, vomiting and fatigue. Breathing becomes deeper or slightly faster, but most sufferers do not notice this.

As the acidosis getting worse, the patient begins to feel extreme fatigue, drowsiness, increased nausea and confusion. As the acidosis getting worse, blood pressure may drop, leading to shock, coma and death. The diagnosis of acidosis is usually made based on the results of blood pH measurements taken from arterial blood (radial artery at the wrist). Arterial blood is used as an example because

venous blood is not accurate for measuring blood pH. To determine the cause, carbon dioxide and bicarbonate levels in the blood are measured. Additional tests may be needed to help determine the cause. For example, high blood sugar levels and the presence of ketones in the urine usually indicate an uncontrolled diabetes. The presence of toxic substances in the blood suggests that the metabolic acidosis is due to poisoning or overdose. Sometimes microscopic examination of urine and measurement of urine pH are performed.

Treatment of metabolic acidosis depends on the cause. For example, diabetes is controlled with insulin or poisoning is treated by removing the toxic material from the blood. Sometimes dialysis is necessary to treat overdose or severe poisoning. Metabolic acidosis can also be treated directly. In mild acidosis, only intravenous fluids and treatment of the cause are required. In severe acidosis, bicarbonate may be given intravenously, but bicarbonate only provides temporary relief and can be harmful.

c. Respiratory Alkalosis

Respiratory alkalosis is a condition where the blood becomes alkaline due to rapid and deep breathing, resulting in low carbon dioxide levels in the blood. Rapid and deep breathing is called hyperventilation, which causes too much carbon dioxide to be removed from the bloodstream. Respiratory alkalosis can make the patient feel anxious and can cause itching around the lips and face. If the condition worsens, muscle spasms and loss of consciousness may occur. Treatment is directed at improving ventilation. Pharmacological preparations are used as indicated. For example, bronchodilators help reduce bronchial spasm, and antibiotics are used for respiratory infections. Pulmonary hygiene measures are performed, when required, to clear the respiratory tract of

mucus and drainage of mucus. Adequate hydration is indicated to keep the mucous membranes moist and hence facilitate secretion removal. Supplemental oxygen is given when required. Mechanical ventilation used judiciously can improve pulmonary ventilation. Unwise use of mechanical ventilation may lead to such rapid carbon dioxide excretion that the kidneys are unable to eliminate excess biocarbonate quickly enough to prevent alkalosis and seizures. For this reason, the increase in PaCO2 should be decreased slowly. Laying the patient in a semifowler position facilitates chest wall expansion.

d. Metabolic Alkalosis

Metabolic alkalosis is a state where the blood is alkaline due to high levels of bicarbonate. Metabolic alkalosis occurs when the body loses too much acid. An example is the loss of a certain amount of stomach acid during a prolonged period of vomiting or when stomach acid is aspirated with a gastric tube. In rare cases, metabolic alkalosis occurs in people who consume too much base from substances such as bicarbonate of soda. In addition, metabolic alkalosis can occur when the loss of large amounts of sodium or potassium affects the kidneys' ability to control the acid-base balance of the blood.

The main causes of metabolic alkalosis:

1) Use of diuretics (thiazide, furosemide, ethacrinic acid)
2) Loss of acid due to vomiting or gastric emptying
3) Overactive adrenal glands (Cushing's syndrome or due to corticosteroid use).

Metabolic alkalosis may cause irritability, muscle twitching and muscle spasms; or no symptoms at all. In severe alkalosis, prolonged muscle contractions (cramps) and spasms (tetany) may occur. Metabolic alkalosis is usually treated with fluids and electrolytes (sodium and potassium). In severe cases, intravenous ammonium chloride is given.

SUMMARY

Body fluids are solutions composed of water (solvent) and certain substances (solutes). Electrolytes are chemical substances that produce electrically charged particles called ions when in solution. Body fluids are divided into two major groups viz: intracellular fluid and extracellular fluid. The total body fluid volume (total body water-TBW) is approximately 60% of a man's body weight and 50% of a woman's body weight. This volume depends on body fat content and age.

The mechanism of action of fluids and electrolytes in the body is through three processes: diffusion, osmosis, and transport. Body fluids are distributed between two compartments: intracellular and extracellular. Intracellular fluid is approximately 2/3 or 40% of body weight, while extracellular fluid is 20% of body weight. Fluid expulsion occurs through the body's organs, namely the kidneys, skin, lungs, and gastrointestinal tract.

Normal body fluid and electrolyte balance is the result of a dynamic balance between incoming food and drink with a balance involving a large number of organ systems. As more body fluids and electrolytes are consumed, more fluids are excreted.

There are nine factors that affect fluid and electrolyte requirements in the body, namely age, activity, climate, diet, stress, disease, medical treatment, medication, and surgery. Disorders of fluid and electrolyte balance in the body can be influenced by two factors, namely excess and deficiency of fluids and electrolytes.

Acid-base balance is a state in which the concentration of hydrogen ions produced is equal to the concentration of hydrogen ions released by the cell. In the process of life, acid balance at the molecular level is generally associated with weak acids and weak bases, as well as at very low levels of H+ ion or OH- ion concentration.

The normal acidity (pH) of human blood ranges from 7.35 to 7.45. The human body is able to maintain a balance of acids and bases so that metabolic processes and organ functions can run optimally.

There are 2 main abnormalities in acid-base balance, namely acidosis or alkalosis. Acidosis is a condition in which the blood

contains too much acid (or too little base) and often causes a decrease in blood pH. Alkalosis is when the blood has too much base (or too little acid) and sometimes causes an increase in blood pH. Acidosis and alkalosis are categorised as metabolic or respiratory, depending on the underlying cause. Metabolic acidosis and metabolic alkalosis are caused by an imbalance in the formation and removal of acids or bases by the kidneys. Respiratory acidosis or respiratory alkalosis is mainly caused by lung disease or respiratory abnormalities.

KEY TERMS

Balance of fluids and electrolytes
Body Fluid Distribution
Materials Contained in Body Fluids (Electrolytes and Non-Electrolytes)
Fluids and Electrolytes in the Body
Mechanisms for Regulating Fluid and Electrolyte Balance
Factors affecting fluid and electrolyte balance
Imbalance of Fluid and Electrolyte
Edema
Acid and Base Balance
Regulation of Acid and Base Balance
Imbalance Acids Bases

REVIEW QUESTION

ASSIGNMENT

Have a discussion with your friends about the cases below, then present the cases that have been discussed.

Situation: You are a nurse in the intensive care unit (ICU) of a hospital. A 65-year-old patient, who has just undergone major surgery, has a disturbed water and electrolyte balance. The patient has a history of hypertension and type 2 diabetes. The patient is currently dehydrated and has elevated blood sodium levels. The doctor asks you to monitor the patient's condition closely and provide appropriate care.

Discuss the situation by considering the following:

1. Identify factors that may have contributed to the patient's dehydration, given his medical history.

2. Explain the mechanism underlying the patient's elevated blood sodium level (hypernatremia).
3. Discuss the symptoms and signs of dehydration and its impact on the patient's health.
4. How will you monitor the patient's condition to assess his fluid and electrolyte requirements? Describe the parameters that you will look out for.
5. Discuss the treatment steps you would take to address dehydration and restore normal water and electrolyte balance in the patient.
6. What are the complications that can occur if the patient's water and electrolyte disturbances are not treated promptly?

FORMATIVE TESTS

1. What happens to the body when it is dehydrated?
    a. There is a decrease in sodium levels in the blood
    b. There is an increase in sodium levels in the blood
    c. There is a decrease in potassium levels in the blood
    d. There is an increase in potassium levels in the blood

2. Electrolyte disturbances that often occur in conditions of excessive vomiting are:
    a. Hypokalaemia (decreased potassium levels in the blood)
    b. Hyperkalaemia (increased potassium levels in the blood)
    c. Hyponatremia (decreased levels of sodium in the blood)
    d. Hypernatremia (increased levels of sodium in the blood)

3. What causes hyponatremia?
    a. Lack of sodium in the diet
    b. Excess sodium in the diet
    c. Excessive fluid loss
    e. Excessive fluid accumulation

4. What are the signs and symptoms of hyperkalaemia?
    a. Muscle spasms and pain
    b. Muscle weakness and confusion

c. Palpitations and irregular heartbeat
d. High body temperature and thirst

5. Acid-base disorders that occur when the blood pH is below 7.35 are:
   a. Metabolic acidosis
   b. Metabolic alkalosis
   c. Respiratory acidosis
   d. Respiratory alkalosis

6. What causes metabolic alkalosis?
   a. Excessive loss of stomach acid
   b. Accumulation of lactic acid in the body
   c. Loss of sodium in the blood
   d. Accumulation of sodium in the body

7. What are the signs and symptoms of respiratory acidosis?
   a. Confusion and shortness of breath
   b. Muscle weakness and rapid heart rate
   c. Chest pain and shortness of breath
   d. Pale skin and weak heart rate

8. Electrolyte disorders that often occur in diabetes mellitus are:
   a. Hyperglycaemia (increased blood glucose levels)
   b. Hypokalaemia (decreased levels of potassium in the blood)
   c. Hyponatremia (decreased levels of sodium in the blood)
   d. Hypernatremia (increased levels of sodium in the blood)

9. What causes hypokalaemia?
   a. Excessive fluid loss
   b. Excessive fluid accumulation
   c. Potassium deficiency in the diet
   e. Excess potassium in the diet

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UNIT 4 THE PROCESS OF IMMUNITY

LEARNING OBJECTIVES

After mastering the contents of this chapter, student will be able to:

Define the Immunology
Define the Functions of the Immune System
Classifying the Immunologic Response
Identify the Antibodies (Immunoglobulin/Ig)
Contrast the Immune Deficiency and Inflammation
Identify the symptoms of Immunodeficiency
Explain the Immunodeficiency Treatment
Recall the Prevention of Immunodeficiency

1. Definition of Immunology

Immunology comes from the Latin language, namely *Immunis* and *Logos*, *Immun* which means immune and *logos* which means science (Smith & Germolec, 1999). Immunology is the study of immunity. Immunity is protection from diseases, especially infectious disease (Smith & Germolec, 1999). The cells and molecules involved in protection make up the immune system. While the response to welcome foreign agents is called the immune response. Immunology is a broad branch of biomedical science that includes the study of all aspects of the immune system in all organisms (Kumar, 2014).

The immune system is working correctly, it protects the body against bacterial and viral infections, and destroys cancer cells and other foreign substances in the body. If the immune system is weakened, its ability to protect the body is also reduced, allowing pathogens, including viruses that cause colds and flu, to thrive in the body. The immune system also provides surveillance against tumor cells, and inhibition of this system has also been reported to increase the risk of developing some cancers (Kumar, 2014).

2. Functions of the Immune System

The Immune System is the single most important system that never shirking its duties and constantly performing tasks and its activities. It protects the body all the time from all kinds of invaders that could potentially cause disease to our body. It works for the body like a well-armed fighting force(Hammer, 2018).

Each organ system, organ or group of cells in the body represents the whole in a perfect division of labor. Any failure in the system will destroy this order. The immune system is indispensable to our body. The immune system is a collection of cells, tissues, and organs consisting of:

1. The body's first line of defense–This is the part that can be seen by the body and is on the surface of the human body such as skin, tears, saliva, nose hair, sweat, mucosal fluids, hair.
2. Second line of defense–This is the part that cannot be seen such as the thymus, spleen, lymphatic system, bone marrow, white blood cells/leukocytes, antibodies, and hormones.

All these parts of the immune system work together to fight the entry of viruses, bacteria, fungi, worms, and other parasites that enter the body through the skin, nose, mouth, or other parts of the body (Kuba & Kubová, 2005).

The functions of the immune system include:

1. Protect the body from disease-causing invasions by destroying and eliminating microorganisms or foreign substances (bacteria, parasites, fungi, and viruses, as well as tumors) that enter the body
2. Removing dead or damaged tissue or cells for tissue repair
3. Recognize and eliminate abnormal cells.

And the main targets are pathogenic bacteria and viruses. Leukocytes are the main immune cells (besides plasma cells, macrophages, and mast cells).

3. Immunologic Response

An immune response is the body's response in the form of a complex sequence of events to an antigen, to eliminate the antigen.

This response can involve a variety of cells and proteins, especially macrophage cells, lymphocyte cells, complement and cytokines that interact with each other in a complex manner. The body's defense mechanisms consist of non-specific defense mechanisms and specific defense mechanisms.

Stages of Immune System Response (Wang et al., 2015):

1. Detection and recognition of foreign bodies. Immune system can detect foreign bodies & protect the body from damage caused by it, but cannot recognize foreign objects that enter the body.
2. Communication with other cells to respond. Cells have developed complex communication mechanisms so that they can receive messages, transfer information across the plasma membrane, and then produce changes within the cell in response to the message.
3. Recruitment of help and coordination of response. Innate immunity occurs immediately, when circulating innate cells recognize a problem. Adaptive immunity occurs later, as it relies on the coordination and expansion of specific adaptive immune cells. Immune memory follows the adaptive response, when mature adaptive cells, which are highly specific to the original pathogen, are retained for later use.
4. Destruction or suppression of invaders. The process of antibodies attaching to an invader may be referred to as 'opsonisation'. Some antibodies can bind to and inactivate toxins. Others can bind to the surface of microbes and prevent them from attaching to body cells (thus preventing the virus from entering the host cell).

Immune response functions (McPhee et al., 2005)

a. Defense: against foreign bodies/microbes. There are two types of endocytosis are designated based on the size of the vesicle formed. Pinocytosis (cell drinking) involves the ingestion of fluids, bits of the plasma membrane, and solute molecules through formation of small vesicles; such as bacteria, through formation of large vesicles (vacuoles). Phagocytes are the

white blood cells that protect the body by ingesting harmful foreign particles and help initiate an immune response.

b. Homeostasis: elimination of useless cells/debris. The synthesis of proteins and hormones and transport out of the cell, isolation and removal of waste products from the cell, performance of metabolic processes, breakdown and disposal of cellular debris and foreign bodies proteins (antigens), and maintenance of cell structure and motility.

c. Surveillance: in charge of being alert and recognizing changes and quickly removing abnormal cells.

Based on the response, two main types of immune response are recognized

1. Specific and Non-specific Immune Response (Innate Immune) Responses

   Specific immune response is a defense mechanism aimed specifically at one type of antigen, therefore it cannot play a role against other types of antigens. Specific immunity is able to re-recognize antigens it has encountered (has memory), so that subsequent exposure will increase the effectiveness of the body's defense mechanisms.

   There are 2 specific immune systems, namely:

   a. Humoral specific immune system. The role in the humoral immune system is B lymphocytes or B cells. B t cells are found in the serum. The main function of this antibody is for defense against viral infections, bacteria (extracellular), and can neutralize the toxin.

   b. Cellular specific immune system. The role in the cellular specific immune system is T lymphocytes or T cells. Unlike B cells, T cells are made up of several cell subsets that have different functions. The main function of specific immune cells is for defense against bacteria that live intracellularly, viruses, fungi, parasites, and malignancies.

Specific immunity can occur as follows (Kuba & Kubová, 2005):

a. Natural
    1) Natural Passive. Passive natural immunity is the transfer of antibodies or sensitized white blood cells from the body of an immune person to another immune person, for example through the placenta and colostrum from mother to child.
    2) Active natural immunity can occur when a microorganism naturally enters the body and causes the formation of antibodies or sensitized cells.
b. Artificial (Nair, 2009)
    1) Passive. Passive artificial immunity is done by giving serum, antibodies, antitoxins for example in tetanus, diphtheria, gangrene, snake bites and immune deficiency or giving cells that have been sensitized to tuberculosis and hepatic.
    2) Active. Active artificial immunity can be generated by vaccination through the administration of tetanus toxoid, microorganism antigens both dead and alive.

The specific defense system against foreign bodies/microbes consists of several components, namely: Lymphocytes

a. B lymphocytes (B cells). The process of formation and maturation of B cells occurs in the bone marrow. B cells play a role in the formation of humoral immunity by forming antibodies. B cells can be divided into:
    1) Plasma B cells, function to form antibodies.
    2) Memory B cells, function to remember antigens that have entered the body and stimulate the formation of plasma B cells in the event of a second infection.
    3) Splitting B cells, which form plasma B cells and reminder B cells.

b. T lymphocytes (T cells). The process of T cell formation occurs in the bone marrow, while the maturation process occurs in the thymus gland. T cells play a role in the formation of cellular immunity, namely by attacking antigen-producing cells directly.
T cells also help the production of antibodies by plasma B cells. T cells can be divided into:
   1) Killer T cells, function to attack pathogens that enter the body, infected body cells, and cancer cells directly.
   2) Helper T cells stimulate the formation of plasma B cells and other T cells and activate macrophages to phagocytose.

   Suppressor T cells reduce and stop the immune response by decreasing antibody production and reducing killer T cell activity. Suppressor T cells will work after the infection has been successfully treated.

2. Non-specific Immune Response (Innate Immunity)

Non-specific immune response (innate immunity) is a natural immunity that has existed since birth. This immunity is not intended for only one type of antigen, but for a variety of antigens, so it is not a special defense for certain antigens(McPhee et al., 2005).

Non-specific immune responses consist of:

a. Physical/mechanical defense. Skin, mucous membranes, respiratory tract cilia, coughing, sneezing will prevent the entry of various pathogenic germs into the body. Damaged skin for example by burns and mucous membranes damaged by cigarette smoke will increase the risk of infection.
b. Biochemical defense. The material secreted by the airway mucosa, skin sebaceous glands, skin glands, ears, spermin in semen, contains materials that play a role in the body's biochemical defense. HCL acid in

gastric juice, lysozyme in sweat, saliva, tears and milk can protect the body against various gram-positive germs by destroying their cell walls. Breast milk also contains lactoferrin and neuraminic acid which have antibacterial properties against E. coli and staphylococcus. Lysozyme released by macrophages can destroy gram-negative germs and this is reinforced by complement. Lactoferrin and transferrin in serum can bind to iron needed for the life of pseudomonas germs.

c. Humoral defense. Various materials in the circulation contribute to the body's humoral defenses. These materials are:

1) Complement. Complement activates phagocytes and helps destructive bacteria and parasites because:
   a) Complement can destroy bacterial cell membranes
   b) Is a chemotactic factor that directs macrophages to the bacterial site
   c) Other complement components deposited on the surface of bacteria make it easier for macrophages to recognize and phagocytose (opsonization).

2) Interferon. Interferon is a glycoprotein produced by various human cells containing the nucleus and released in response to viral infection. Interferon has anti-viral properties by inducing cells around virus-infected cells to become resistant to the virus. In addition, interferon can also activate Natural Killer cells (NK cells). Cells that are infected by the virus or become malignant will show changes on their surface. These changes will be recognized by NK cells

which then kill them. Thus, the spread of the virus can be prevented.

3) C-Reactive Protein (CRP). The role of CRP is as an opsonin and can activate complement. CRP is formed by the body during infection. CRP is a protein whose levels increase rapidly (100 x or more) after acute infection or inflammation. CRP plays a role in non-specific immunity, because with the help of Ca++ it can bind to various molecules found in many bacteria and fungi.

d. Cellular defense. Phagocytes/macrophages and NK cells play a role in the cellular non-specific immune system.

1) Phagocytes. Although various cells in the body can perform phagocytosis, the main cells that play a role in non-specific defense are mononuclear cells (monocytes and macrophages) and polymorphonuclear cells such as neutrophils. Phagocytic cells also interact with complement and the specific immune system. The destruction of germs occurs at several levels as follows: Chemotaxis, capture, feeding (phagocystosis), killing and digestion. Chemotaxis is the movement of phagocytes to the site of infection in response to various factors such as bacterial products and biochemical factors released upon complement activation. Antibodies as well as complement C3b can enhance phagocystosis (opsonization). Antibody-bound antigens will be more easily recognized by phagocytes to be destroyed. This is made possible by the presence of receptors for the Fc fraction of immunoglobulins on the surface of phagocytes.

2) Natural Killer Cell (NK cell). NK cells are lymphoid cells found in the circulation and do

not have the characteristics of lymphoid cells of the specific immune system, so they are called non-B non-T cells (NBNT cells) or third population cells. NK cells can destroy cells containing viruses or neoplasm cells and interferon has an influence in accelerating the maturation and political effects of NK cells.

4. Antibodies (Immunoglobulin/Ig)

Antibodies are formed when an antigen enters the body. Antigens are protein compounds present in foreign cell pathogens or cancer cells. Antibodies are also called immunoglobulins or serum protein globulins, because they function to protect the body through the immune process. Antibodies are protein compounds that function against antigens by binding to them, to be captured and destroyed by macrophages. An antibody works specifically for certain antigens. Because the type of antigen in each disease germ is specific, different antibodies are needed for different types of germs. Therefore, different types of antibodies are needed to protect the body from various germs (Smith & Germolec, 1999).

Antibodies are composed of two identical polypeptide chains, namely two light chains and two heavy chains. The four chains are connected to each other by disulfide bonds and the shape of the molecule is like the letter Y. Each arm of the molecule has an antigen binding site (Smith & Germolec, 1999).

Some of the ways antibodies work in inactivating antigens are(Kuba & Kubová, 2005):

a. Neutralization. In immunological terms, this refers to the ability of antibodies to block sites on bacteria or viruses that they use to enter their target cells. One example of this in biology is neutralising antibodies by blocking virus binding sites, enveloping bacteria and or co-opsonising them).
b. Agglutination of particles containing antigens. Agglutination reactions result in visible aggregates of antibody–antigen

complexes when the antibody or antigen is conjugated to a carrier such as a microbe.

c. Precipitation (settling) of soluble antigens. Precipitation is enhanced when the antibody has a high affinity for the antigen. Although most antibodies bind antigens with high affinity, even high-affinity binding uses relatively weak noncovalent bonds, so individual interactions will often break and new interactions will occur.

d. Complement fixation (complement activation). Complement activation is regulated to eliminate dying cells without further activation of other innate or adaptive immune components. Complement is only activated in cases of pathogen infection. During infection, complement causes inflammation, opsonisation, phagocytosis, and destruction of the pathogen and results in the activation of adaptive immune responses.

Antibodies can be divided into five types as shown in the table below.

Table 5. Antibody Types and Their Characteristics

No	Antibody Type	Characteristics
1.	IgM	First released into the bloodstream upon first infection (primary immune response)
2.	IgG	Most abundant in the blood and produced upon second infection (secondary immune response). Flows through the placenta and provides passive immunity from the mother to the fetus.
3.	IgA	Found in tears, saliva, sweat and mucous membranes. Prevents infection on epithelial surfaces. Found in colostrum which serves to prevent infant mortality due to gastrointestinal infections
4.	IgD	Found on the surface of B lymphocytes as a receptor and functions to stimulate antibody formation by plasma B cells.
5.	IgE	Found bound to basophils in the blood circulation and mast cells (mastocytes) in tissues that influence cells to release histamine and are involved in allergic reactions.

5. Immunodeficiency

Immune deficiency is a condition where the body is unable to fight off infections and diseases. This is caused by a weakened or compromised immune system. This makes you susceptible to viral, bacterial, and fungal viral and bacterial infections(Wang et al., 2015). The immune system includes organs such as the lymph nodes, bone marrow, spleen, and tonsils. These organs process and release lymphocytes, which are white blood cells classified as B cells and T cells. B and T cells fight foreign substances that carry so-called antigens, such as bacteria, viruses, cancer cells and parasites. Immunodeficiency impairs the body's ability to defend itself and fight against these antigens.

Immunodeficiencies are divided into two (Rezaei et al., 2008):

a. Primary immunodeficiencies are immune system disorders that a person is born with or are inherited disorders due to family medical history or genetic changes.
b. Secondary immunodeficiencies are immune system disorders that a person develops later in life due to certain environmental factors. Secondary immunodeficiencies are more common than primary ones.

a. Causes of Immunodeficiency.

The most common cause of primary immunodeficiency is hereditary, passed down from one or both parents. The only risk factor for this disorder is having a family member with a history of primary immunodeficiency. If you have a primary immunodeficiency and are planning to have offspring, it's a good idea to consult a doctor or get genetic counseling. Secondary immunodeficiencies can be caused by various things, including(Smith & Germolec, 1999):

1) Chronic diseases such as diabetes or cancer
2) Severe burns
3) HIV infection that causes AIDS

4) Leukemia, a cancer that starts in the bone marrow cells that causes hypogammaglobulinemia, a type of secondary immunodeficiency
5) Malnutrition, which affects up to 50 percent of the population in underdeveloped countries and makes people susceptible to respiratory infections and diarrhea

Immunodeficiency is not only caused by disease, but there are other conditions known as by:

a. Age. Aging can weaken your immune system. As we age, some organs that produce or process white blood cells shrink and become less efficient.
b. Side effects of cancer drugs and treatment methods such as chemotherapy can also be a cause of secondary immunodeficiency.
c. Protein deficiency. Protein is essential for immunity. The body also produces proteins while you sleep that help the body fight infections. For this reason, lack of sleep can reduce your immunity(Smith & Germolec, 1999).

6. Symptoms of Immunodeficiency

Each form of immunodeficiency has unique symptoms that can be acute (sudden and short-term) or chronic (occurring over the long-term), and the symptoms can vary from person to person. The body with an immunodeficiency is likely to experience more frequent, longer-lasting infections, and experience infections that someone with a healthy immune system would not likely experience(Wang et al., 2015).

In general, the symptoms of immunodeficiency are:

a. Frequent and recurrent pneumonia, bronchitis, sinus infections, ear infections, meningitis, skin infections
b. Inflammation of internal organs
c. Blood disorders, such as low platelet count or anemia
d. Conjunctivitis (pink eye)
e. Chronic gum disease (gingivitis)

f. Fungal infection
g. Slow body growth and development
h. Digestive problems, such as loss of appetite, nausea, diarrhea
i. Autoimmune disorders, such as lupus, rheumatoid arthritis or type 1 diabetes(Smith & Germolec, 1999)

7. Immunodeficiency Treatment

Immunodeficiency treatment revolves around preventing infections, treating infections, and strengthening the immune system (Huether et al., 2020). Antibiotics and immunoglobulin therapy are two frequently used treatments. Antiviral drugs such as oseltamivir and acyclovir or interferon drugs are also sometimes used in treatment. A bone marrow transplant is possible if your bone marrow does not produce enough lymphocytes.

8. Prevention of Immunodeficiency (Rezaei et al., 2008)

Primary immunodeficiency can be controlled and symptoms relieved with medication, but it cannot be prevented (Huether et al., 2020). Since it is caused by genetic changes, there is no way to prevent it. When you or your child has a weak immune system, you can take the following steps to prevent infection:

a. Practice a clean lifestyle. Wash hands with soap after using the toilet and before eating.
b. Keep your teeth clean. Brush your teeth at least twice a day.
c. Eating a healthy and balanced diet can help prevent infections.
d. Be physically active as exercise is important for your overall health.
e. Get enough sleep. Try to go to bed and wake up at the same time every day, and get the same number of hours of sleep every night.
f. Manage stress. Some studies show that stress can inhibit the immune system. Keep stress at bay with massage, meditation, yoga, or taking up a hobby.
g. Avoid or stay away from people with colds or other infections and avoid crowds.

9. Disorders of the Immune System

People born with certain genes, your immune system may react to substances in the environment that are normally harmless. These substances are called allergens. Having an allergic reaction is the most common example of an overactive immune system. Dust, mould, pollen and food are examples of allergens.

Some conditions caused by an overactive immune system are:

a. Allergies

Allergy or hypersensitivity is an exaggerated immune response to compounds that enter the body(Smith & Germolec, 1999). These compounds are called allergens. Allergens can be dust, pollen, insect bites, cat hair, and certain types of food, such as shrimp. The process of allergy begins with the entry of allergens into the body which then stimulates plasma B cells to secrete IgE antibodies. Allergens that first enter the body will not cause allergies, but the IgE formed will bind to mastocytes. As a result, when the allergen enters the body for the second time, the allergen will be bound to IgE that has bound to mastocytes. Mastocytes then release histamine which plays a role in the inflammatory process. This inflammatory response results in allergic symptoms such as sneezing, itchy skin, watery eyes, runny nose, and difficulty breathing. Allergy symptoms can be stopped by administering antihistamines.

b. Autoimmunity

Autoimmunity is a disorder of the immune system in which the antibodies produced attack the body's own cells because they are unable to distinguish between the body's own cells and foreign cells (Smith & Germolec, 1999). Autoimmunity can be caused by the failure of the T cell maturation process in the thymus gland. Autoimmunity causes several disorders, namely(Wang et al., 2015):

1) Diabetes mellitus is caused by antibodies attacking beta cells in the pancreas that produce the hormone insulin. This causes the body to lack the hormone insulin,

causing blood sugar levels to rise.

2) Myasthenia gravis is caused by antibodies that attack striated muscles, causing them to become damaged.
3) Addison's disease is caused by antibodies that attack the adrenal glands. This results in weight loss, lower blood sugar levels, fatigue, and increased skin pigmentation.
4) Memory loss.
5) Lupus. Lupus is caused by antibodies that attack the body itself. In people with lupus, antibodies attack the body in two ways, namely (Wang et al., 2015):
   a) Antibodies attack body tissues directly. For example, antibodies that attack red blood cells, causing anemia.
   b) Antibodies combine with antigens to form bonds called immune complexes. Under normal conditions, foreign cells whose antigens have been bound by antibodies will then be captured and destroyed by phagocytic cells.

   However, in people with lupus, these foreign cells cannot be destroyed by phagocytic cells properly. The number of phagocytic cells will actually increase while releasing compounds that cause inflammation. This inflammatory process will cause various symptoms of lupus. If it occurs in the long term, organ function will be disrupted.
6) Arthritis (rheumatoid arthritis). Arthritis is an autoimmune disease that causes prolonged inflammation of the joints. The disease usually affects multiple joints and is characterized by inflammation of the synovial membrane and joint structures, muscle atrophy, and bone thinning.
7) AIDS. AIDS (Acquired Immuno Deficiency Syndrome) is a collection of various diseases caused by a weakened immune system. It is caused by HIV (Human

Immunodeficiency Virus) infection that attacks helper T cells that stimulate the formation of plasma B cells and other types of T cells. This results in a reduction in the body's ability to fight off germs. Helper T cells are the main target of HIV because they have CD4 molecules as receptors on their surface. Infection begins when glycoprotein molecules on the surface of HIV attach to CD4 receptors on the surface of helper T cells. Next, HIV enters the helper T cell by endocytosis and begins to multiply(Wang et al., 2015). Then, new viruses exit the infected T cells by exocytosis or cell lysis. The number of T cells in normal people is around 1,000 cells/mm3 of blood, while in people with AIDS, the number of T cells is only around 200 cells/mm3. This condition makes AIDS patients susceptible to various diseases such as tuberculosis, meningitis, blood cancer, and memory loss. HIV positive patients can generally still live normally and appear healthy, but can transmit the virus appear healthy, but can transmit the HIV virus. AIDS patients are HIV positive patients who have shown symptoms of AIDS. The time it takes an HIV positive person to become an AIDS patient is relatively long, which is between 5-10 years. There are even HIV-positive people who have not become AIDS patients in their lifetime. This is because the HIV virus in the body takes time to destroy the patient's immune system. When the immune system has been destroyed, HIV positive patients will show symptoms of AIDS.

SUMMARY

The body is often exposed to infectious agents such as bacteria, viruses and fungi. However, this does not always cause disease. This is because in the body there is an immune system that is often referred to as the immune response. The immune response in the body is a system. In this immune system, there are several components that have different functions and

ways of working. In general, immune responses can be divided into 2 major groups, namely non-specific/non-adaptive/innate immune responses; and specific/adaptive immune responses. The immune system in the body is very important to protect the body from pathogens or disease-causing agents. The incidence of immunodeficiency in an individual will make that individual susceptible to disease. The first immune response to a pathogen attack is the innate/non-specific/non-adaptive immune response. The nature of the non-specific immune response is that it has been formed before infection, reacts to all pathogens, the response time is not long (only a few hours), but this response is able to distinguish between body proteins and pathogens. There are many components of the non-specific immune response, including the surface epithelium, phagocytic cells, NK cells and complement proteins, each of which has its own mode of action. Antibodies consist of several classes, namely IgA, IgG, IgM, IgD and IgE, each of which has a unique structure and function. Antibodies have specific working dynamics for primary and secondary infection events. Memory immune response is a distinctive ability possessed by specific immune responses, so that the body can react more quickly in eliminating pathogens from the body.

KEY TERMS

Immunology
Immune System
Immunologic Response
Antibodies (Immunoglobulin/Ig)
Immune Deficiency and Inflammation
Symptoms of Immunodeficiency
Immunodeficiency Treatment

REVIEW QUESTION

Assignment:

Have a discussion with your friends about the cases below, then present the cases that have been discussed

1. In this material, students are given a structured assignment to make a paper on autoimmune diseases. Students can choose one

autoimmune disease. The paper is made to discuss the selected autoimmune disease, starting from its mechanism, the condition of the disease in Indonesia, to the therapies available to sufferers. The paper is then discussed together to gain new knowledge together.

2. Here is a situation that can be discussed regarding immune deficiency and inflammation:
   You are a physician in the immunology department of a hospital. A 40-year-old patient presents with recurrent infections and unexplained chronic inflammatory problems. The patient has symptoms such as fatigue, frequent fever, recurrent upper respiratory tract infections, and joint pain. After a series of examinations, you suspect the patient has an immune disorder and an underlying chronic inflammatory condition.
   Discuss the situation by considering the following:
   1. Identify possible causes of the patient's immune deficiency. Discuss the types of immune deficiency that may be involved based on the symptoms.
   2. Explain the mechanism and impact of chronic inflammation on the human body. What causes chronic inflammation?
   3. Discuss the impact of immune deficiency on the patient's ability to fight infection and how this relates to the patient's symptoms.
   4. How would you verify the diagnosis of immune deficiency in such a patient? Describe the examinations or tests that may be required.
   5. Discuss possible treatment approaches to manage the immune deficiency and address the patient's chronic inflammation.

FORMATIVE TESTS

a. What is immunology?
b. What is an immune response?
c. Describe the properties of non-specific immune responses
d. List the components that make up the non-specific immune response

e. How do dendritic cells work as APCs?
f. How do complement proteins work?
g. Describe the types of hypersensitivity diseases.
h. In your opinion, what is the condition of hypersensitivity disease in Indonesia?
i. Is hypersensitivity disease a problem in Indonesia?

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UNIT 5 DEGENERATIVE DISEASE

LEARNING OBJECTIVES

After mastering the contents of this chapter, you will be able to:

1. Clarifying of The Degenerative Diseases
2. Mention of the Theories of Ageing
3. Summarizing the Mechanism of Degenerative
4. List the Classified of Degenerative diseases
5. List of Other Types of Degenerative Diseases

1. DEGENERATIVE DISEASES

Degenerative disease is the process of gradual loss of nerve cell function without a known cause (Kuba & Kubová, 2005). This condition results in nerve cells that previously functioned normally becoming worse until they do not function at all. Degenerative disease indicates a more rapid process of deterioration of neurons, myelin and tissues with consequent degenerative products and violent cell destruction reactions (Hensley et al., 2000). (REFF) Such diseases indicate a decrease in nerve cell survival and result in faster cell death. Degenerative disease is a disorder in which there is a gradual decline in function or damage to the body's structure. or damage to body structures that occurs gradually. This process of damage can be caused by age-related wear and tear or by an unhealthy lifestyle. (REFF)

2. Theories of Ageing

Ageing is defined as a process that transforms a healthy adult into a frail, vulnerable person with a reduction in most physiological system reserves and exponentially increased susceptibility to disease and death. Aging is a process of progressive decline in the function and maximum reserve capacity of all organs of the body, including the skin. This natural decline in skin function is often complicated and accelerated by a number of chronic environmental stressors, such as exposure to ultraviolet (UV) and infrared (IR) radiation and environmental carcinogens from air pollution in major cities

(Nishino et al., 2014).

The mechanism of ageing is complex and not fully understood. However, cumulative oxidative stress and chronic inflammation are the main features that have been theorized to play an essential role in age progression and chronic degenerative diseases. Numerous normal cell metabolic processes in the human body (digesting food, breathing, alcohol and drug metabolism), besides genetic or environmental factors such as air pollutants, cigarette smoking, toxins, and radiation, generate toxic compounds called free radicals. Free radicals are oxygen-containing ions, molecules, or atoms with one or more unpaired electrons in the outermost orbit (valence shell). These molecular species are highly reactive, unstable, and capable of existing independently, thus, harmfully modifying deoxyribonucleic acid (DNA), proteins, and lipids and triggering several types of human diseases.

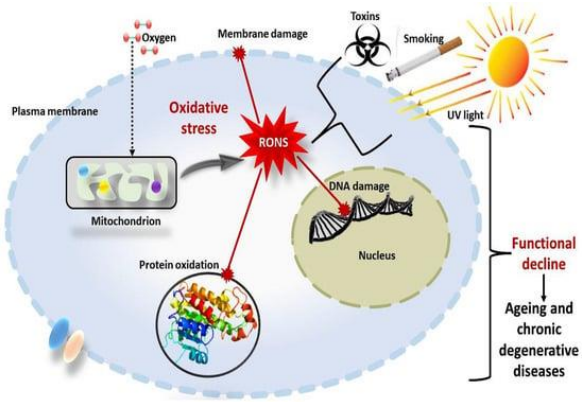

Figure 9. Schematic Representation of Oxidative Stress (Huether et al., 2020)

Oxidative stress is a phenomenon elevated with ageing and degenerative diseases. It involves the accumulation of reactive oxygen and nitrogen species (RONS) in cells and tissues, harmfully modifying deoxyribonucleic acid (DNA), proteins and lipids and triggering ageing and chronic degenerative diseases.

Theory of Aging

The process of aging proceeds slowly. The exact time limit between the cessation of physical growth and the start of the aging process is not clear, but generally around the middle of the second decade, signs of skin aging begin to appear. Various theories on the aging process have been proposed and explained as follow.

a. Free Radical Theory

The free radical theory of aging was first introduced by Denham Harman in 1956, who stated that the normal aging process is a result of tissue damage due to free radicals. Harman stated that mitochondria, as generators of free radicals, are also targets of free radical damage. Free radicals are chemical compounds containing unpaired electrons that are formed as a byproduct of various cellular processes or normal metabolism involving oxygen. Examples are reactive oxygen species (ROS) and reactive nitrogen species (RNS) generated during normal metabolism. Because their electrons are unpaired, free radicals will chemically seek other electron pairs by reacting with other substances, especially with proteins and unsaturated fats. Structures within cells such as mitochondria and lysosomes are also enveloped by fat-containing membranes, making them easily disrupted by free radicals.

b. DNA Repair Theory

This theory was proposed by Hart and Setlow in 1974 They showed that there are differences in the pattern of “repair” lanes or repair of ultraviolet (UV) light-induced DNA damage in various cultured fibroblasts. Fibroblasts in species that have the longest maximum lifespan show the greatest rate of DNA repair, and this correlation can be shown in various mammals and primates. The theory of DNA repair or more precisely mitochondrial DNA repair is closely related to the theory of free radicals. Because, most free radicals (especially ROS) are generated through oxidative phosphorylation that occurs in the mitochondria. Mitochondrial DNA (mtDNA) mutations

and ROS generation in the mitochondria mutually influence each other, forming a “vicious cycle” that exponentially multiplies oxidative damage and cellular dysfunction, ultimately leading to cell death. Human mtDNA mutations mainly occur after the mid-thirties, accumulating with age and rarely exceeding 1%. The low number of mtDNA mutations accumulated is due to the repair process of oxidative damage, which is the cause of accelerated aging.

c. Pacemaker or Endocrine Theory

This theory says that the aging process is regulated by pacemakers, such as the thymus, hypothalamus, pituitary, and thyroid glands that produce hormones, and in turn regulate the hormonal balance and regeneration of human body cells. The aging process occurs due to changes in the balance of the hormonal system or a decrease in the production of certain hormones.

d. Glycosylation Theory REFF

This theory states that non-enzymatic glycosylation processes that produce glucose-protein linkages called advanced glycation end products (AGEs) can lead to the build-up of proteins and other modified macromolecules that cause dysfunction in aging animals or humans. Glycated proteins show functional changes, including decreased enzyme activity and decreased degradation of abnormal proteins. As humans age, AGEs accumulate in various tissues, including collagen, haemoglobin and the lens of the eye.

e. Telomere Elongation Theory REFF

Every cell has the ability to divide to maintain its function and slow down death. This ability to divide occurs until the cells are dense enough to meet each other, to then stop dividing, to then stop dividing, a phenomenon called “contact inhibition”. Once the cells have lost the ability to divide again. The cells will then enlarge, survive for a while, and then slowly die. Each time the cell divides, the telomeres get shorter and shorter, until one day they can no longer shorten. Telomeres

that are already very short will become a signal to trigger proliferative aging or apoptosis, thus contributing to the appearance of the aging phenotype.

f. Immunity Theory

The immune system has two main roles: defense against external attacks and internal immunological surveillance. Aging of the immune system is generally characterized by reduced numbers of memory T cells, reduced populations of naive T cells, and impaired humoral and cellular immunity. Chronic inflammatory conditions, reduced immunity to a number of exogenous antigens, and increased autoreactivity appear to impair the ability to resist attacks from the environment. In the aging process, an increase in the amount of reactive oxygen species (ROS) in the cells leads to oxidative stress and plays a role in triggering mild inflammation. This ROS imbalance contributes to the aging of the immune system, beginning with the reduction of the natural immune response and leading to the disruption of the adaptive immune response. These abnormalities appear to contribute to the increased incidence of infections and malignancies in the elderly.

g. Mechanism of Degenerative

Free radicals are atoms or molecules containing unpaired electrons. Electrons normally exist in pairs in specific orbitals in atoms or molecules. Free radicals, which contain only a single electron in any orbital, are usually unstable toward losing or picking up an extra electron, so that all electrons in the atom or molecule will be paired.

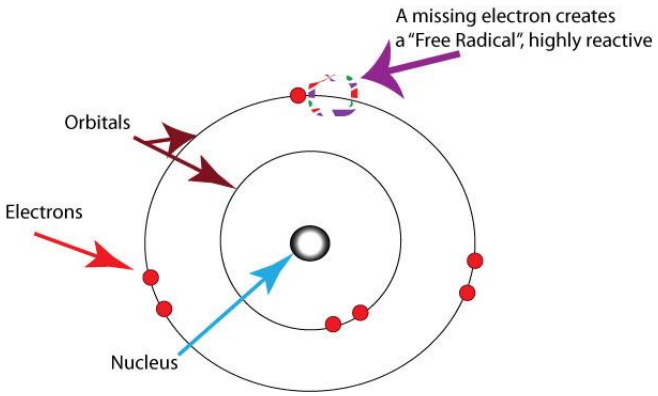

Figure 10. Free Radical Molecule

Free radical molecules cause cross-linking by stealing electrons in proteins (collagen), DNA or any molecule, ion or atom-creating a chain reaction that leads to aging and disease.

The unpaired electron does not imply charge; free radicals can be positively charged, negatively charged, or neutral. Damage occurs when the free radical encounters another molecule and seeks to find another electron to pair its unpaired electron. The free radical often pulls an electron off a neighboring molecule, causing the affected molecule to become a free radical itself. The new free radical can then pull an electron off the next molecule, and a chemical chain reaction of radical production occurs. The free radicals produced in such reactions often terminate by removing an electron from a molecule which becomes changed or cannot function without it, especially in biology. Such an event causes damage to the molecule, and thus to the cell that contains it (since the molecule often becomes dysfunctional). The chain reaction caused by free radicals can lead to cross-linking of atomic structures. In cases where the free radical-induced chain reaction involves base pair molecules in a strand of DNA, the DNA can become cross-linked. DNA cross-linking can in turn lead to various

effects of aging, especially cancer. Other cross-linking can occur between fat and protein molecules, which leads to wrinkles. Free radicals can oxidize LDL, and this is a key event in the formation of plaque in arteries, leading to heart disease and stroke. These are examples of how the free-radical theory of aging has been used to neatly "explain" the origin of many chronic diseases.

Free radicals that are thought to be involved in the process of aging include superoxide and nitric oxide. Specifically, an increase in superoxide affects aging whereas a decrease in nitric oxide formation, or its bioavailability, does the same.

Antioxidants are helpful in reducing and preventing damage from free radical reactions because of their ability to donate electrons which neutralize the radical without forming another. Ascorbic acid, for example, can lose an electron to a free radical and remain stable itself by passing its unstable electron around the antioxidant molecule.

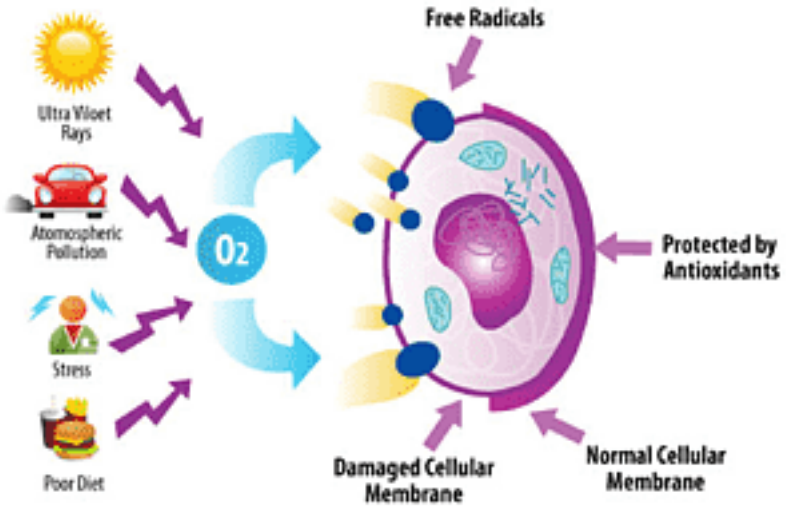

Figure 11. Antioxidants Reduce and Prevent Damage Cell from Free Radical Reactions

This has led to the hypothesis that large amounts of antioxidants, with their ability to decrease the numbers of free radicals, might lessen the radical damage causing chronic diseases,

and even radical damage responsible for aging.

The free radicals may originate from metabolism within the body but can also be external radicals. Antioxidant mechanisms can delay/inhibit the free radical reaction in at least 2 ways, namely:

a. Antioxidants capture free radicals. Known as primary antioxidants, for example vitamins E, C and flavonoids
b. Binds to metals, captures oxygen, converts hydroperoxides to non-radical species and absorbs UV light. radicals and absorb UV light. These antioxidants are known as secondary antioxidants.

Free radicals are compounds/molecules that contain more than one free electron. This causes the free radical to be highly reactive. Free radicals are reactive oxygens species (ROS). All molecules that contain oxygen with high reactivity properties are grouped into ROS. Some types of ROS include the hydroxyl radical, the superoxide anion radical, hydrogen peroxide, singlet oxygen, nitric oxide radical, hypochlorite radical, and lipid peroxides.

Under normal conditions, these free radicals can actually be beneficial, among others

including: fighting inflammation & bacteria and playing a role in regulating smooth muscle tone in organs. Excessive exposure to free radicals can occur from: ultraviolet light,

cigarette smoke, air pollution, food, insecticides and stress. Excessive free radicals are a factor that causes cellular degeneration. This will facilitate the occurrence of degeneration diseases, among others: diabetes mellitus, autonomic heart disease, cataract senilism cancer, stroke, dementia and others.

The adverse effects of free radicals can be reduced with antioxidants. Antioxidants will provide hydrogen atoms to free radicals so that they will reduce the reactivity of the free radicals. Some sources of antioxidants are indigenous antioxidants such as superoxide dismutase (SOD), glutathione peroxidase and catalase. Exogenous antioxidants such as vitamins E, C, beta-carotene and vitamin E.

3. Classified of Degenerative Diseases (Langrish et al., 2014)

Some of the most common types of degenerative diseases are:

a. Cardiovascular disease is divided into 2 diseases, they are:

1) Hypertension. Hypertension is a disease in which arterial blood pressure is abnormally high, during systole or during diastole. Patients who have blood pressure exceeding 140/90 mmHg are thought to have high blood pressure. This condition must be diagnosed and treated, as it causes permanent injury to the arteries and, subsequently, leads to other severe diseases of organs such as stroke, heart attack, chronic heart failure, and arterial aneurysms.

2) Coronary disease. Coronary disease, or coronary insufficiency, is a disease in which there is total or partial obstruction of one or more arteries that irrigate the heart muscles are coronary blood vessels. The blockage of the blood vessels is caused by the process of atherosclerosis or the accumulation of fat/plaque in the blood vessels so that the diameter of the blood vessels is getting smaller and harder/stiffer. The process of atherosclerosis occurs slowly over time, but in people with high levels of plaque in the blood, this process in the blood vessels becomes faster and more numerous. Blocked heart blood vessels can cause the death of heart cells because they do not get enough nutrients and oxygen intake. Heart cells that have died cannot be repaired. Symptoms that can be found in this disease:

a) Chest pain, characterized by pain in the left chest, pain radiating to the left hand and chin. In some cases, chest pain can be atypical such as pain in the solar plexus, pain radiating to the back, and pain radiating to the right arm.

b) Sensation of heaviness in the chest such as being hit by a heavy object, sharp and stabbing pain in the chest, and squeezing.

c) Heart palpitations.
d) Pain and shortness of breath occur with strenuous activity and subside after resting.
e) Sometimes, at first the patient is not aware of having CHD because the pain felt is only brief

b. Neoplastic/Cancer

Cancer is a group of diseases characterized by uncontrolled cell division. Cancer is caused by abnormal cells that continue to grow, multiply and spread throughout the body. While there are many factors known to contribute to the formation of cancer cells, the exact cause has yet to be discovered. And these cells generally invade other biological tissues, be it by direct growth in adjacent tissues (invasion) or migration of cells to distant sites (metastatis). Usually, the uncontrolled growth is due to DNA damage, causing mutations of vital genes that control cell division. However, it takes several mutations to turn a normal cell into a cancer cell. Generally, these mutations are caused by chemical or physical agents called carcinogens. Mutations can be spontaneous (acquired) or inherited (germline mutations). Because of this, cancer can cause many different symptoms depending on its location, malignancy and metastatic factors. Usually, a diagnosis can be made when there has been microscopic examination of tissue obtained by biopsy. Once diagnosed, cancer is treated with surgery, chemotherapy, radiation.

The causes of people getting cancer are due to genes, diet, viruses, environmental pollution, immune system, old age, and smoking.

c. Nervous system

1) Parkinson's. Parkinson's is a degenerative disease that results in loss of muscle control because neurons cannot function normally. But the cause of the abnormalities in neuron function has yet to be determined. However, scientists have been able to compile a list of risk factors, such as environmental toxins and oxidative stress

(Huether & McCance, 2012).

2) Alzheimer's. Alzheimer's is also a common degenerative disease that results in decreased intellectual function. The exact cause of this disease is yet to be discovered. But, scientists are pretty sure of the theory that the metals iron, aluminium, and copper are the main culprits (Huether & McCance, 2012).
3) Huntington's. Huntington's is a disease characterized by mental and physical deterioration leading to death. Individuals with this disease initially lack coordination and then eventually lose a steady gait, coordinated movements, and mental abilities.
4) Amyotrophic lateral sclerosis. Amyotrophic lateral sclerosis (ALS) is a disease caused by the death of neurons that control voluntary muscles. Initially, there is a weakening of the arms or legs. Eventually, people with ALS will lose the ability to use their hands and feet, speak, and swallow.
5) Multiple sclerosis. Multiple sclerosis is a neurodegenerative disease characterized by the gradual accumulation of focal plaques of demyelination, mainly in the periventricular regions of the brain (Foguem et al., 2018).
6) Batten. Batten disease is a neurodegenerative disorder characterized by excessive accumulation of lipofuscin in cells and tissues. The accumulation of lipofuscin is caused by pathological mutations in genes (e.g., CLN3 gene, in the juvenile type of the disease). The disease begins at the age of five to eight years. Some symptoms include seizures, ataxia, visual impairment, and clumsiness.
7) Stroke. Stroke is a functional brain disease in the form of nerve paralysis (neurologic deficit) due to impaired blood flow to one part of the brain. Stroke is defined as a brain disease where the blood supply to the brain

stops due to blockage or bleeding. Mild symptoms of stroke are shown by momentary paralysis, while severe symptoms can cause loss of consciousness and death. Stroke can be either ischemic or hemorrhagic. In an ischemic stroke, blood flow to the brain is stopped due to a blood clot blocking the blood vessel (atherosclerotic). tic). In bleeding (hemorrhagic) stroke, the blood vessel bursts, resulting in abnormal blood flow. And, the blood seeps into the brain and damages

d. Diabetes mellitus (DM) type 2

Diabetes mellitus is a disease characterized by high levels of glucose or sugar in the blood caused by the body being unable to use glucose or sugar in the blood as a source of energy. This disease consists of several types, the most common type that can be found is type 2 diabetes mellitus (McPhee et al., 2005).

Classic symptoms:

1) Thirsty. Patients will feel thirsty quickly and drink often. Patients often do not realize this as a symptom because they feel that drinking a lot is good for kidney function.
2) Frequent urination (BAK). Often sufferers think that the cause of frequent urination is because they drink a lot of water and not the result of a disease. In addition, this symptom can also interfere with sleep at night because you wake up back and forth to urinate.
3) Feeling hungry quickly. This happens because the body cannot use the sugar in the blood as an energy source, even though the sugar level in the blood is already high. Because there is no source of energy, the body feels hungry so it always wants to eat.
4) Symptoms due to complications from this disease appear as a result of starvation of the body's cells. Long-term starvation causes the cells to die.
5) Tingling at the tips of the fingers and toes. If this

symptom appears, it means that there has been damage to the nerve endings. Complaints will gradually get worse so that they feel numb or numb. If it is numb, the patient often does not realize if his leg is injured.

6) Blurred vision. This can be caused by abnormalities of the retina, cornea, or lens of the eye.
7) Wounds that are difficult to heal. Cells in the body are difficult to repair themselves to close wounds that occur. In addition, high sugar levels are favored by germs, making infection easy and complicating wound closure.

Risk factors that can cause this disease include: the habit of eating sweet foods, excess body weight, genetic, infrequent exercise.

The causes of glucose not being utilized in the body in type 2 diabetes are(McPhee et al., 2005):

1) Insulin resistance in cells. In order for cells to use glucose from the blood, insulin is needed. In patients with this disease, it is found that the cells become less sensitive to insulin. Although there is insulin in the body, the cells cannot use it. This leads to high blood sugar levels.
2) Low insulin production by the pancreas. Insulin is produced by the beta cells of the pancreas. Insufficient insulin production causes the body to be unable to use glucose in the blood.

e. Uric acid (Huether et al., 2020)

Uric acid is the metabolic waste of purine substances that come from the food we consume. This is caused by the breakdown of cells in the blood.

In fact, purines themselves are substances found in every foodstuff found in the body of living things. In other words, every living thing must have purines in its body. Then the substance is transferred into the body when eating these creatures. Vegetables and fruits contain purines. This is

because purines are produced from certain diseases or the destruction of body cells that occur normally.

Symptoms experienced by people with gout are tingling, linu, joint pain (joints affected by uric acid look swollen, reddish, and hot), feeling extreme pain at night and in the morning when you wake up.

4. Other Types of Degenerative Diseases (Wilkins., 2013)

Some Other Types of Degenerative Diseases are

a. Macular Degeneration. Macular degeneration is a medical condition caused by damage to the macula. Affected individuals may experience blurred vision in the center of the visual field. Over time, vision deteriorates and may end in blindness. Risk factors include genetic factors, poor diet, physical inactivity, and smoking.

b. Osteoarthritis (OA). OA is a degenerative disease that causes damage to the cartilage tissue in the joints which is characterized by changes in the bone. Osteoarthritis is a non-inflammatory degenerative joint disease that occurs mainly in the elderly. It is characterized by degeneration of articular cartilage, hypertrophy of the bone at the edge, and changes in the synovial membrane. It is accompanied by pain and stiffness, especially after prolonged activity. Anti-inflammatory drugs are given to relieve the pain(McPhee et al., 2005). Risk factors for this disease are genetics, women, history of joint impact, age and obesity. Symptoms that can be found in this disease are:

1) Pain in the joints especially after exertion and improves after resting.
2) Sometimes stiffness can be found in the morning, lasting no more than 30 minutes.
3) These symptoms make it difficult to carry out daily activities and work. Generally, the affected joints are those that support the body such as the knees, pelvis and back.

To diagnose this disease, a physical examination of the affected joints and supporting examinations are needed to rule out the possibility of other diseases. Supporting examinations that can be performed include x-rays of the affected joints and laboratory tests. On roentgen, changes in the shape of the affected joints can be found.

c. **Osteoporosis**. **Osteoporosis** is a degenerative disease involving the bones. This condition is characterized by highly porous bones. As such, an individual with osteoporosis has an increased risk of fractures. It usually affects elderly women and causes a curved back due to compression fractures of the backbone(McPhee et al., 2005). Osteoporosis is a degenerative bone disease characterized by low bone mass and thinning of bone tissue. This can cause bones to become brittle and break easily. Diagnosis of this disease is based on bone mass. It is called osteoporosis if the bone mass is <-2.5 standard deviations (SD) of normal bone mass, and called osteopenia if the bone mass is between -1 to -2.5 SD. Since this disease does not give symptoms until a fracture occurs, it is important to be screened to prevent this disease. In addition, sufferers should also be self-reliant and make adjustments so that they do not fall easily, for example, the bathroom uses a rough floor. Osteoporosis can be caused by: decreased calcium absorption in post-menopausal women, age over 70 years, chronic disease, and deficiency of bone-building substances such as calcium, vitamin D

d. **Duchenne muscular dystrophy**. Duchenne muscular dystrophy (DMD) is a degenerative disease characterized by progressive muscle **degeneration**. This leads to muscle weakness. It may manifest in children aged 2 or 3 who may have difficulty jumping, running and walking. It is a genetic disorder associated with a genetic mutation on the X chromosome that codes for the protein dystrophin. Without enough functional dystrophin, which helps keep muscle cells intact, the muscles tend to be fragile and prone to damage.

SUMMARY

Degenerative diseases are diseases that accompany the aging process as people age and lead unhealthy lifestyles. However, they can also occur at a young age, resulting in a decline in health status that is usually followed by disease. The causes of diseases are often unknown, including a group of diseases that are influenced by genetic factors or at least occur in one family member (familial factors), so they are often called heredodegenerative diseases. Premature shrinkage of cellular function. Diseases Degenerative diseases can be prevented by minimising the risk factors that cause them. The main risk factors for degenerative diseases are an unhealthy diet, lack of exercise, smoking, and physical activity, smoking, and increased stress and exposure to degenerative disease triggers. Some examples of degenerative diseases include diabetes mellitus (DM), osteoarthritis (OA), osteoporosis, coronary heart disease (CHD), gout, stroke, and hyperlipidaemia (high cholesterol and fat). The main risk factors for degenerative diseases are unhealthy diet, lack of physical activity, and smoking. Currently, it can be said that external factors have a higher potential to cause degenerative diseases than internal factors (genetics or heredity).

KEY TERMS

Degenerative Diseases
Theories of Ageing
Mechanism of Degenerative
Classified of Degenerative Diseases
Other Types of Degenerative Diseases

REVIEW QUESTION

ASSIGNMENT

Have a discussion with your friends about the cases below, then present the cases that have been discussed. Here is a situation that can be discussed about degenerative diseases:

Situation: You are a health researcher studying degenerative diseases. You have a research team consisting of geneticists, neuroscientists, and other biomedical science experts. Your team is interested in studying the causes,

mechanisms and treatment strategies of certain degenerative diseases, such as Alzheimer's disease or Parkinson's disease.

Discuss the situation with the following in mind:

1. Explain what a degenerative disease is and name some examples of common degenerative diseases.
2. Identify the risk factors associated with the degenerative disease your team is researching.
3. Describe the degeneration process that occurs in the organ or tissue associated with the disease.
4. Discuss the role of genetic mutations, accumulation of plaques or protein aggregates, inflammation and other factors in the development of degenerative diseases.

FORMATIVE TESTS

1. A 54-year-old man presented with complaints of joint pain that had been experienced for several years. A cut of the patella reveals white, cautery-like deposits and histological examination reveals long needle-shaped crystals. Which of the following options is the most likely diagnosis?
   A. Osteoarthritis
   B. Osteoporosis
   C. Rheumatoid arthritis
   D. Gouty arthritis
   E. Paget's disease
2. The main manifestations of Parkinson's disease are:
   A. Tremor at rest
   B. Akinesia
   C. Rigidity
   D. Postural instability
   E. Micrographia
3. The following statements are incorrect:
   A. The aetiology of Parkinson's disease is multifactorial
   B. Clinical features are caused by lesions in the basal ganglia, in the substantia nigra leading to motor deficits
   C. Postural instability is caused by proprioceptive disorders

D. Higher incidence in males
E. Death is usually caused by immobility

4. In rheumatoid arthritis, we can find:
   A. Osteoporosis of the bone
   B. Widened joint gap
   C. Swelling of the joint capsule
   D. Ankylosis
5. In gouty arthritis, you can find:
   A. 1.Erosion of the joint surface
   B. 2.Osteoporosis
   C. 3.Subchondral cyst
   D. 4.Punched-out lesion
6. Synonyms of osteoarthritis, except:
   A. Osteoarthritis
   B. Hyperthropic arthritis
   C. Degenerative arthritis
   D. Spondyloarthrosis
   E. Sondylitis
7. The following statements are true for Parkinson's disease, except:
   A. Chronic, non-progressive disease
   B. For rigidity, infrared is given
   C. For balance training, coordination is better hydrotherapy
   D. To prevent pneumonia complications with breathing exercises
   E. To improve function with cane use
8. Radiological examination is important to establish the diagnosis of osteoarthritis:
   A. Symmetrically narrowed joint space
   B. Subchondral sclerosis
   C. Joint erosion
   D. Osteophytes at the joint edge

A 70-year-old male patient came to the neurological polyclinic. At the entrance to the examination, he was seen walking with small steps often stopped, lack of arm swing, oily face without expression.

9. What disease is impressed by this inspection?

A. Stroke
B. Guillain Barre syndrome
C. Parkinson's
D. Spondylosis
E. Spinal cord lesions

10. The neurological examination of this disease may reveal the presence of:
A. Essential tremor
B. Tremor of rest
C. Bradycardia
D. Postural hypotension
E. Relaxation

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UNIT 6 THE INFLAMMATORY PROCESS

LEARNING OBJECTIVES

After mastering the contents of this chapter, you will be able to:

1. Illustrate of Inflammation
2. Summarize the Causes of Inflammation
3. Explain the Pathophysiology of inflammation
4. Repeat the Signs of Inflammation
5. Focus the Classification of Inflammation
6. Explain the Healing Process of Inflammation

1. Inflammation

Inflammation is a local protective reaction caused by injury or tissue damage, which functions to destroy, reduce or confine (sequester) both the injuring agent and the injured tissue. Inflammation is the body's response to tissue damage, such as from a scratch or hard impact(Huether & McCance, 2012). The inflammatory process is a collection of four symptoms: dolor (pain), rubor (redness), calor (heat) and tumor (swelling). Inflammation prevents the spread of infection and speeds up wound healing. Inflammation is a response to infection, antigen challenge or tissue injury that is designed to eradicate microbes or irritants and to potentiate tissue repair. Excessive inflammation may, however, lead to tissue injury and can, if severe, cause physiological decompensation, organ dysfunction and death. Inflammation can be divided into two major categories—acute and chronic—based on timing and pathological features (Hammer, 2018).

The inflammatory reaction also serves as a danger signal and as a command for white blood cells (neutrophils and monocytes) to phagocytose microbes that infect the body. Inflammation is a physiological response to infection and tissue injury, inflammation also initiates pathogen killing, tissue repair process and helps restore homeostasis at the site of infection or injury. If the anti-inflammatory response fails to regulate, it can result in chronic

injury and aid in the development of associated diseases. Inflammation can be divided into two, namely acute and chronic. Acute inflammation has a more rapid onset and duration. Acute inflammation occurs with a duration of several minutes to several days, characterized by the presence of plasma protein exudate fluid as well as the accumulation of predominantly neutrophilic leukocytes. Chronic inflammation has a longer duration of duration of days to years. The type of chronic inflammation is determined by an increase in the number of lymphocytes and macrophages that are associated with vascular proliferation and fibrosis (McPhee et al., 2005).

2. Causes of Inflammation

Inflammation can occur acutely or chronically. Acute inflammation involves several factors. The acute inflammatory response is initiated by a variety of endogenous and exogenous stimuli that result in injury to the vascularized tissue (Huether & McCance, 2012). Response to injury starts with active hyperemia with increased blood flow to the wound or injured tissue and subsequent dilatation of arteries and capillaries. This is facilitated by prostaglandins, leukotrienes and nitric oxide. Dilatation of arteries and capillaries causes blood to stagarthritis, and even cancer. These undesirable events occur due to the release of phagocytosis enzymes from phagocytic cells, such as phagocyte oxydase, inducible nitric oxyde synthase, and lysosomal protease, which produce free radicals and superoxide compounds that can cause injury to the surrounding tissue(Wilkins., 2013).

Two main components of inflammation 1) Vascular stage, causes an increase in blood flow, changes in small blood vessels in the microcirculation. 2) Cellular stage Causes migration of leukocytes from the circulation, activation to eliminate harmful agents. Cellular stage of inflammation is characterized by changes in the endothelial cells lining the blood vessels and movement of phagocytic leukocytes to the area of injury or infection. Metabolism of arachidonic acid produces prostaglandins that have effects on

blood vessels, nerve endings, and on blood vessels, nerve endings, and on cells involved in inflammation. Steroid drugs inhibit the phospholipase A2 enzyme so that no arachidonic acid. The absence of arachidonic acid means that there is no formation of prostaglandins. While AINS (non-steroidal) drugs inhibit cyclooxygenase (cox-1 and cox-2) or selectively inhibit cox-2 only so that no pain mediators are formed. Formation of pain mediators, namely prostaglandins and thromboxane. The occurrence of continuous (chronic) inflammation can also lead to tissue damage and is responsible for the mechanism of occurrence of several diseases(Nair, 2009).

3. Pathophysiology of Inflammation

The immune response to tissue injury or infection can be divided into innate and adaptive responses. The innate immune system mounts the initial response to tissue invasion. The previously discussed phases of vasodilatation, increased vascular permeability and cellular infiltration are part of the innate immune response. Inflammation is a physiological response to various stimuli such as infection. Inflammation begins with acute inflammation which is the initial response to tissue damage. Acute inflammation has 2 main components, namely vascular changes and cell activity. Vascular changes include vasoconstriction within seconds of the injury, followed by vasodilation of the arterioles resulting in increased blood flow, leading to rubor and caloric symptoms that are typical signs of inflammation(Smith & Germolec, 1999).

Small blood vessels become more permeable and protein-rich fluid will flow out into extravascular tissues, increasing blood viscosity and slowing blood flow. Once the blood vessels are static, leukocytes especially neutrophils begin to cluster on the vascular surface of the endothelium. Endothelial cell contraction leads to the formation of intercellular gaps in post capillary venules causing an increase in vascular permeability. Endothelial cell contraction occurs immediately after binding with histamine, bradykinin, leukotrienes for 15-30 minutes, which is followed by an increase in TNF and IL-

1. Increased vascular permeability leads to the flow of protein-rich fluids as well as blood cells into extravascular tissues. This will result in increased osmotic pressure of interstitial fluid, and fluid into the tissue resulting in the accumulation of protein-rich fluid called exudate, and edema as a manifestation of inflammation(Kuba & Kubová, 2005).

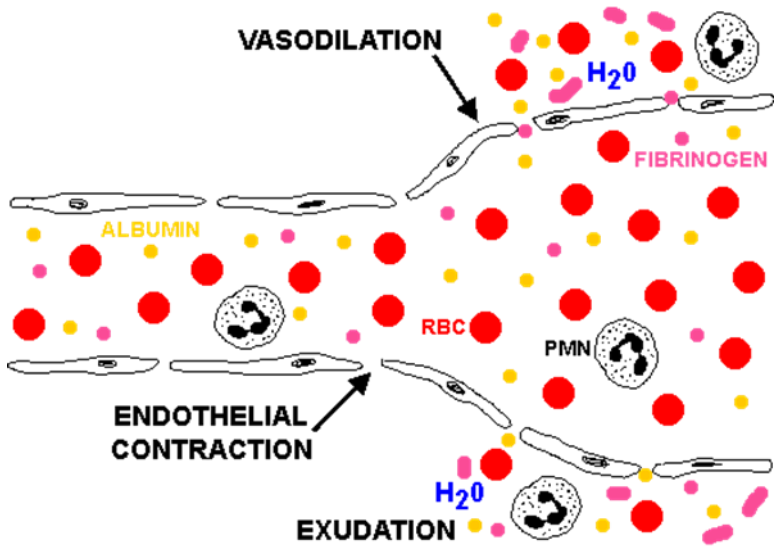

Figure 12. The Process of Exudation of Inflammation

Inflammation is a localized reaction of tissues or cells to a stimulus. to a stimulus. If there is an injury, there is a stimulus to release certain chemicals that stimulate changes in the tissue as a manifestation of tissue as a manifestation of inflammation, including histamine, serotonin, bradykinin, leukotrienes and prostaglandins. Cyclooxygenase (COX) is an enzyme that is found in the biosynthetic pathway of prostaglandins, thromboxane. This enzyme was discovered in 1988 by Dr. Daniel Simmons, a researcher from Harvard University. Cyclooxygenase is divided into two, namely COX-1 and COX-2. COX-1 as a housekeeping gene in almost all tissues normal tissues, while the COX-2 enzyme is responsible for

the inflammatory mechanisms and pain (Ungurianu et al., 2017). COX-2 forms PGE2 and PGI2 which can cause the occurrence of several biological processes, namely increased capillary permeability, pyretic agents and hyperalgesia. and hyperalgesia.

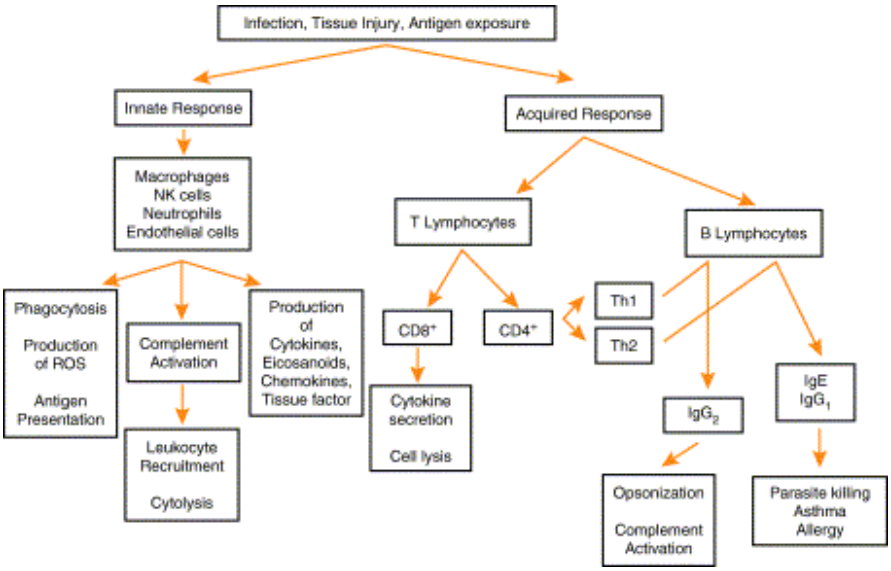

Figure 13. Mechanism of Inflammation

4. Some Signs of Inflammation

According to Wilson (McPhee et al., 2005), common signs that occur in the inflammatory process are rubor (redness), tumour (swelling), calor (excessive local heat), dolor (pain), and funcolaesa (impaired function/loss of function of the affected tissue). The explanation of the signs of inflammation is as follows:

a. **Rubor or redness.** Redness or rubor is usually the first thing that is seen during inflammation seen when experiencing inflammation. When an inflammatory reaction artery that supply blood to the area widen, therefore blood flows more widen, therefore more blood flows into the local microcirculation. local microcirculation. Blood vessels that were previously empty or partially empty are stretched rapidly and filled with blood. This situation is called hyperemia or

congestion causing a local red color due to acute inflammation (Huether & McCance, 2012). Usually redness (rubor) is usually the first thing seen in the area that has inflammation. When the inflammatory reaction starts, the artery that supplying blood to the area are dilated, thus more blood flows into the local microcirculation. Vessels that were previously empty or partially empty stretch rapidly and fill up with blood. This condition is called hyperemia or congestion causes local red color due to acute inflammation. The onset of hyperemia is the beginning of an inflammatory reaction regulated by the body through the release of mediators such as histamine. or prostaglandin.

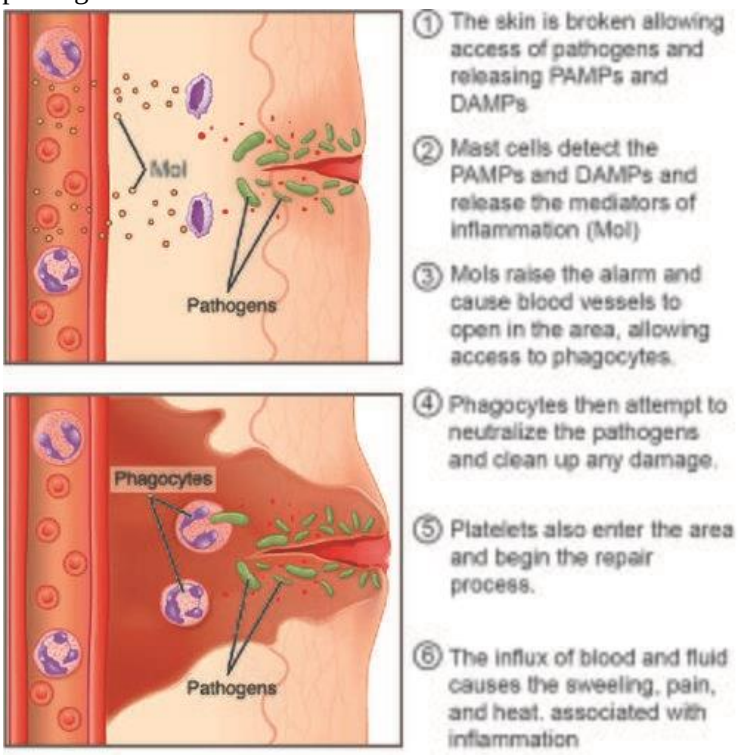

Figure 14. Inflammation Process

b. **Heat or increase in body temperature.** Heat is a reaction on the surface of the body, namely the skin that occurs along with redness due to inflammation. Heat and redness occur simultaneously. Feeling heat is caused because the amount of blood is greater at the site of inflammation than in other areas around the inflammation. This heat phenomenon occurs when it occurs on the surface of the skin. Meanwhile, when it occurs deep inside the body cannot be seen and felt. The area of inflammation on the skin becomes hotter than around it, this happens because the blood with a temperature of 37oC is more blood is channelled to the surface of the area affected by inflammation more than to normal areas. more than to normal areas (Hidayat, 2023).

c. **Dolor or pain.** Pain or dolor from inflammatory reactions is produced by various mechanisms. Pain due to inflammation can be caused by stretching of the tissue due to edema resulting in an increase in local pressure which can cause pain, and the presence of the release of chemicals or pain mediators such as prostaglandins, histamine, bradykinin which can stimulate peripheral nerves around the inflammation so that pain is felt. Changes in local pH or concentration of certain ions can stimulate the nerve endings to release certain chemicals such as histamine or other mediators that cause swelling and pain. Mediators that cause swelling and inflammation in the tissue resulting in increased local pressure can cause pain.

d. **Tumor or swelling.** A symptom of acute inflammation is a tumour or swelling. The most obvious symptom in inflammation is swelling which is caused by an increase in capillary permeability, the presence of increased blood and fluid flow to the injured tissue so that plasma proteins can escape from the blood vessels into the interstitial space. This occurs due to increased permeability capillary walls as well as the channelling of fluids and cells from the circulation to the injured tissue. In inflammation, the capillary walls become

more permeable and are more easily traversed by leukocytes and proteins, especially albumin. by leukocytes and proteins, especially albumin, followed by larger molecules so that tissue plasma contains larger molecules so that tissue plasma contains more protein which then leaves the capillaries and into the tissue causing the tissue to become swollen (Huether et al., 2020).

e. **Functio Laesa.** Functio laesa is an inflammatory reaction characterized by with pain accompanied by abnormal circulation due to accumulation and increased blood flow resulting in resulting in an abnormal local chemical environment and make the inflamed tissue not function normally. Functionality is the impairment of tissue function as consequence of an inflammatory process. Movement that occurs in area, whether done consciously or reflexively, will experience will be inhibited by pain, intense swelling, and physically resulting in reduced tissue motion.

5. CLASSIFICATION OF INFLAMMATION

a. Acute Inflammation

Acute inflammation is an immediate response to injury that is designed Upon arrival at the site of injury, leukocytes clear any invading microbes and begin the process of breaking down the necrotic tissue. Examples of acute inflammation can be seen in boils, pimples, and recent wounds.

This process has two main components namely (Hammer, 2018):

1) **Vascular changes**: changes in the capillaries of blood vessels that resulting in increased blood flow (vasodilation) and structural changes that allow plasma proteins to leave the circulation. Structural changes that allow plasma proteins to leave the circulation (increased vascular permeability).

2) **Cellular events**: emigration of leukocytes from the microcirculation and their accumulation at the focus of

injury (cellular recruitment and activation). The cascade of events in acute inflammation is integrated by the local release of chemical mediators(McPhee et al., 2005).

Vascular changes and cell recruitment determine three of the five classic local signs of acute inflammation: heat (calor), red (rubor), and swelling (tumor). Two additional cardinal features of acute inflammation, namely pain (dolor) and loss of function (function laesa), occur due to mediator expansion and leukocyte-mediated damage

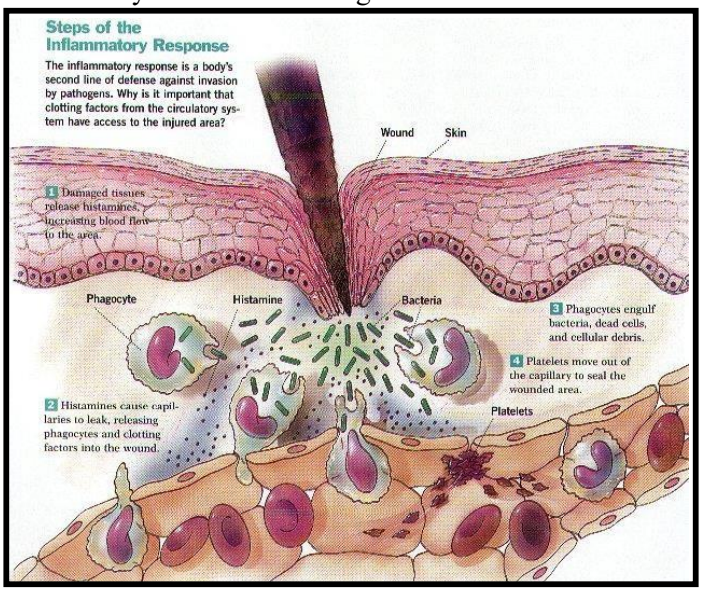

Figure 15. Mechanism of Inflammation Due to Injury

b. Chronic inflammation

Chronic inflammation can be thought of as long-lasting inflammation in which active inflammation, tissue damage and healing occur simultaneously (Saltiel & Olefsky, 2017). Contrary to acute inflammation which is distinguished by vascular changes, edema and overwhelming neutrophilic infiltrates (Hammer, 2018). Chronic inflammation is characterized by the following:

1) Mononuclear cell infiltration (chronic inflammation), including macrophages, lymphocytes, and plasma cells
2) Tissue destruction, mostly organized inflammation
3) Repair, involving proliferation of new blood vessels (angiogenesis) and fibrosis

Chronic inflammation occurs if the antigen persists in the tissue. The manifestation of chronic inflammation is severe tissue damage, leading to dysfunction. The onset of chronic inflammation is influenced by the type of antigen and where the predominant immune reaction occurs. In cases of chronic inflammation, there is involvement of elements of the adaptive immune system (delayed-type hypersensitivity), namely lymphocytes.

In chronic inflammation, macrophages play a role in:

a. Phagocytosis of antigens or cellular debris, such as degenerated neutrophils
b. after the inflammation is under control activation of T lymphocytes through antigen presentation and cytokine secretion.

Chronic inflammation is inflammation of long duration (several weeks or months) in which inflammation, tissue damage and repair occur simultaneously. Chronic inflammation occurs when the acute inflammatory process fails, and when antigens persist. Persisting antigens lead to continuous activation and accumulation of macrophages. Macrophages play a role in repairing damaged parenchymal tissue.

Phagocytosis is performed on cell debris and other materials that have not been degraded by neutrophils. The result may be a return to normal tissue structure, or fibrosis leading to tissue dysfunction. causing tissue dysfunction.

Chronic inflammation can occur under several circumstances such as persistent infections, immune-mediated inflammatory diseases, or exposure to various potentially toxic agents, both external and internal to the body. For example, exogenous

agent silica particles are inanimate and non-biodegradable which, if inhaled over a long period of time, can lead to an inflammatory lung disease called silicosis.

The following are some of the etiologies of chronic infections:

1) viral infection.
2) persistent microbial infections, mostly characterized by the presence of a select set of microorganisms. These organisms have weak direct pathogenicity, but in particular can cause an immune response called slow hypersensitivity which can culminate in a granulomatous reaction
3) exposure to potentially toxic agents.
4) autoimmune diseases

Table 6. Type of Inflammation (McPhee et al., 2005)

	Acute	**Chronic**
Causes	Pathogens, damaged tissue	Persistent acute inflammation, foreign body, autoimmune reaction
Cells involved	Neutrophils, mononuclear cells (monocytes, macrophages)	Mononuclear cells (monocytes, macrophages, plasma cells, lymphocytes) fibroblasts
Onset	Immediately	Slow
Duration	Several days	Several months–years
Outcome	Resolution, abscess, chronic inflammation	Tissue damage, fibrosis

6. HEALING PROCESS OF WOUND

Healing is restoring the integrity of injured tissue and preventing the organism from deregulating homeostasis. Wound healing has evolved from ancient times. The application of closure materials aims to stop bleeding and protect the wound from environmental irritants such as water and electrolyte disturbances. According to Cohen (2001)(Wilkins., 2013), acute wounds will achieve normal healing through a healing process that is expected within a certain

time to achieve restoration of anatomical integrity and function. Acute wounds usually occur in normal, healthy individuals, and can be closed primary or allowed to heal secondary. Most wounds that occur as a result of trauma to an organ or tissue can be categorized as acute wounds.

The wound healing process is dynamic with the ultimate goal of restoring tissue function and integrity. By understanding the biology of wound healing, we can infer that the wound healing process is an accumulation of processes including coagulation, matrix and basic substance synthesis, angiogenesis, fibroplasias, epithelialization, contraction, and remodeling. However, this complex process is broadly divided into three phases of wound healing (Figure 16): the inflammatory phase, the proliferation phase, and the maturation phase (Cohen, 2001).

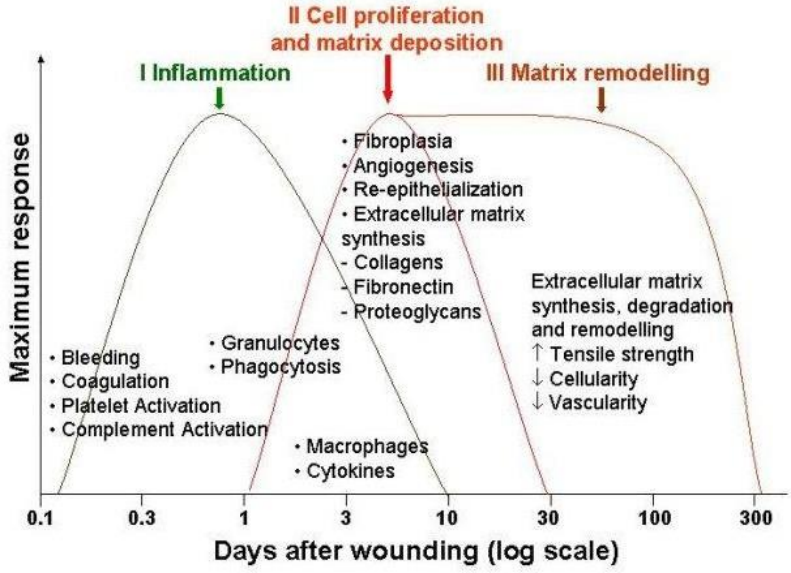

Figure 16. Wound Healing Phase Chart (Torre, 2006)

Wound healing is a quality of tissue life that is also related to tissue regeneration. The phases of wound healing are described as occurring in surgical wounds.

a. Inflammatory Phase. The inflammatory phase begins after injury and ends on day 3-4. The two stages in this phase are hemostasis and phagocytosis. As a result of constriction of blood vessels, resulting in blood clotting to cover the wound. This is followed by vasodilation leading to increased blood flow to the wound area which is restricted by white blood cells to invade the wound and destroy bacteria and debris. Approximately 24 hours after the wound most of the phagocytic cells (macrophages) enter the wound area and secrete angiogenesis factors that stimulate the formation of epithelial daughters at the end of the wound vessels so that re-formation can occur as shown in Figure 17.

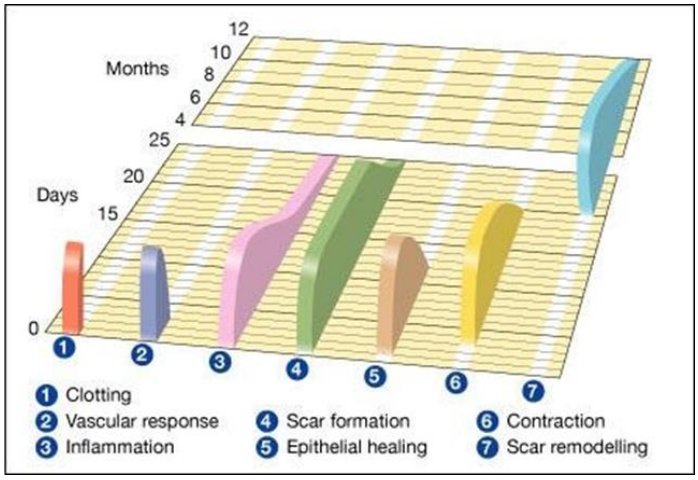

Figure 17. Phase of Wound Healing

b. Proliferation Phase. Begins on day 3 or 4 and ends on day 21. Fibroblasts rapidly synthesize collagen and basic substance. A thin layer of epithelial cells forms across the wound and blood flows through it, this new tissue is called granulation tissue.

c. Maturation Phase. The final phase of healing, beginning on day 21 and can continue until the wound is completely healed. New collagen coalesces, compressing blood vessels in the healing wound, resulting in a flat and thin scar.

Factors that interfere with wound healing are as follows (Huether & McCance, 2012):

a. Nutrition. Normal wound healing requires proper nutrition. The physiological process of wound healing depends on the availability of protein, vitamins (especially vitamins A and C) and the trace minerals zinc and copper. Collagen is a protein formed from amino acids that fibroblasts obtain from dietary protein obtained by fibroblasts from proteins eaten. Vitamin C is required to synthesise collagen. Vitamin A may reduce the negative effects of steroids on wound healing. The microelement zinc is required for epithelial formation, collagen (zinc) synthesis and holding collagen fibres together.
b. Age. Ageing can interfere with all stages in wound healing. Vascular changes interfere with circulation to the blood, decreased liver function impaired synthesis of clotting factors, slowed inflammatory response, decreased antibody and lymphocyte formation, less collagen tissue soft, less elastic scar tissue. Although the wound healing stage in elderly clients occurs at a slower rate, the physiological aspects of wound healing are no different from younger clients.
c. Impaired oxygenation. Low arterial oxygen pressure will interfere with the synthesis of collagen synthesis and epithelial cell formation. If the local circulation of blood flow is poor, tissues fail to obtain the required oxygen. Decreased Hb in the blood will reduce the level of arterial oxygen in the capillaries and impair tissue repair.
d. Smoking. Smoking reduces the amount of functional Hb in the blood thereby decreases tissue oxygen. Smoking can increase aggregation of platelets and cause hypercoagulation. Smoking interferes with normal cell mechanisms that can increase the release of oxygen into tissues.
e. Medications. Steroids decrease the inflammatory response and slow down the synthesis of collagen. Anti-inflammatory drugs suppress protein synthesis, wound contraction, epithelialisation and inflammation.

f. Diabetes. Chronic disease causes small blood vessel disease that can impair tissue perfusion. Diabetes causes haemoglobin to have a greater affinity for oxygen, so that haemoglobin fails to release oxygen to tissues. Hyperglycaemia impairs the ability of leucocytes to phagocytose and also promotes the overgrowth of fungal and yeast infections.

g. Radiation. The process of formation of vascular and fibrous abdominal tissue will occur in unirradiated skin tissue. The tissue is easily damaged and lack of oxygen.

SUMMARY

Inflammation is part of the immune response. This mechanism is only needed under certain conditions for a short period of time. For example, when a part of the body has an open wound, the inflammation mechanism will help remove damaged cells and speed up the healing process. Conversely, when inflammation occurs for longer than necessary, it tends to be detrimental. Inflammation is a protective response to injury or tissue damage by destroying, reducing, or containing foreign agents or compounds that enter to maintain body homeostasis and remove necrotic cells and tissues that result from cell damage. Removing such foreign substances or objects is important to initiate the healing process. Through various other mechanisms, inflammatory cells in the blood vessels trigger swelling in the damaged area of the body and cause swelling, redness, and pain. Inflammation can be uncomfortable, but it is essential to the healing process. Controlling the inflammatory response is key to treating many disease symptoms.

KEY TERMS

Inflammation
Causes of Inflammation
Pathophysiology of Inflammation
Signs of Inflammation
Classification of Inflammation
Healing Process of Inflammation

REVIEW QUESTION
ASSIGNMENT

Have a discussion with your friends about the cases below, then present the cases that have been discussed. Here is a situation that can be discussed about degenerative diseases:

Here is a situation to discuss about inflammation:

Situation: You are a general practitioner working in a medical centre. A 45-year-old patient presents with complaints of pain and swelling in the knee joint. After performing a physical examination and analysing the patient's medical history, you suspect that the patient has an inflammatory problem in the joint. Discuss the situation with the following in mind:

1. Explain what inflammation is and what its main role is in the body's immune response.
2. Discuss the possible causes of the inflammation in the patient's knee joint. What are the risk factors to be aware of?
3. Describe the symptoms that typically occur with joint inflammation conditions, such as pain, swelling and limitation of movement.
4. How will you confirm the diagnosis of inflammation in the patient? What kind of tests or examinations would you perform?
5. Explain how inflammation can develop into more serious conditions, such as rheumatoid arthritis.
6. What is the difference between acute inflammation and chronic inflammation?
7. How important is a healthy lifestyle and long-term care in the management of inflammation? Discuss the role of diet, physical activity and stress management.

FORMATIVE TESTS

1. What is inflammation...
    A. Localised reaction of living tissues to injury by mobilising all forms of the body
    B. Systemic reaction of living tissues to injury by mobilising all forms of body defences

C. Local reaction of living tissue to injury by mobilising all forms of body defences
D. Local reaction of living tissue to injury by mobilising all forms of body resistance

2. The following are cardinal signs of inflammation, except....
   A. Calorific
   B. Rubor
   C. Dolor
   D. Fulor

3. Which of the following is not an inflammatory etiology?
   A. Chemical Agents and Physical Agents
   B. Necrotic Tissue
   C. Inflammatory Reactions
   D. Microbial Infection

4. Which one is not a mediator of inflammation...
   A. Leukotrienes
   B. Platelets
   C. Histamine
   D. Prostaglandins

5. Exudate, Transudate, Edema and Pus fall under the category of...
   A. Classic Signs
   B. Cardinal Signs
   C. Non-classical Marks
   D. Non-Cardinal Mark;

6. Recoverability is practically absent, for example in: heart muscle, striated muscle, nerve tissue, glomerulus are Cell Types....
   A. Labile Cell
   B. Permanent Cell
   C. Fluctuating Cell
   D. Stable Cell

7. When damaged/dead, it is always replaced by similar cells, e.g., surface cells, bone marrow, and spleen, including cell types....
   A. Stable Cell
   B. Fluctuating Cells
   C. Labile Cell
   D. Permanent Cell

8. Cell regeneration is...
   A. Replacement of damaged/dead cells due to injury with similar types of cells
   B. Replacement of damaged/dead cells due to injury with the same type of cells
   C. Replacement of damaged/dead cells with advanced cell types
   D. Replacement of damaged/dead cells caused by injury with different cell types
   E. Tissue Repair is...

9. Healing by way of replacement with epidermal tissue
   A. Healing by replacement with connective tissue
   B. Healing by replacement with muscle tissue
   C. Healing by replacement with new tissue

10. Chronic inflammation consists of...
   A. Serous, Fibrotic, Soporific, and Granulomatous
   B. Serous, Fibrotic, Suppurative, and Granulosis
   C. Serous, Fibrotic, Suppurative, and Granulomatous
   D. Serous, Suppurative Fibrosis, and Granulomatous

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UNIT 7 INFECTION PROCESS

LEARNING OBJECTIVES

After mastering the contents of this chapter, student should be able to:

1. Define Inflammation
2. Repeat the Host Factors in Infection
3. Explain Line of Body Defence
4. State the Mechanism of Infection Transmission
5. Explain the Incubation Period
6. List the Stages of the Infectious Process
7. Clarify the Bacterial Virulence Facto
8. State the Opportunistic and Nosocomial Infections

1. INFECTION

Infection is a disease caused by pathogenic microbes and is very dynamic. Microbes as living things have a way of surviving by multiplying in a suitable reservoir and are able to find other new reservoirs by spreading or moving. The spread of pathogenic microbes is certainly very detrimental to people who are in good health, more so for people who are sick. Healthy people will become sick and people who are sick and are in the process of nursing care in the hospital will get an "additional patient burden" from the spread of these pathogenic microbes (Wilkins., 2013).

Infection is a disease caused by pathogenic microorganisms and has a dynamic nature. In developing countries such as Indonesia, infection is still in the main range of causes of high mortality in hospitals (Konoralma 2019). Dorland's medical book (2012) states that infection is the entry of pathogenic organisms into body tissues and reproduces in them, causing inflammation(Hammer, 2018).

2. HOST FACTORS IN INFECTION

The requirement for the onset of infection is that infectious microorganisms must be able to attach, occupy or enter the host and multiply at least to some extent (Huether & McCance, 2012). Therefore, it is not surprising that in the course of evolution, animal species including humans have developed certain defence mechanisms in various places related to the environment:

a. *Skin and oropharyngeal mucosa.* The main boundary between the environment and the human body is the skin. Intact skin has a keratinized layer or horny layer on the outer surface and a flat layered epithelium as a means barrier that is very good against infection. However, iris, abrasion or maceration (such as in body folds that are always wet) can allow infectious agents to enter. The skin also has the ability to decontaminate itself. In physical decontamination, organisms that are attached to the outer layer of the skin (assuming that they don't die if they become dry) are released as the skin layer sloughs off. Chemical decontamination occurs due to sweating and secretion of sebaceous glands that cleanse the skin of germs. The normal flora found on the skin causes biological decontamination by inhibiting the breeding of other organisms attached to the skin.

b. *Gastrointestinal tract*

1) The gastric mucosa is glandular and not a good mechanical barrier. There are often small defects or erosions in the lining of the stomach, but they do not have much significance in the infectious process because the atmosphere of the stomach itself is very unsuitable for many microorganisms. This is largely due to the high acidity of the stomach, in addition to the stomach tending to transfer its contents to the small intestine in a relatively rapid process.
2) The lining of the small intestine is also not a good mechanical barrier and can easily be penetrated by

many bacteria. However, the peristaltic movement to push the intestinal contents is so fast that the bacterial population in the lumen is kept small.

3) The inner lining of the colon is not mechanically good either. At this place the propulsion is not fast and there is a relative stagnation of the intestinal contents. The main defense against microorganisms is through the large number of normal flora that inhabit the colon and coexist with the host. These numerous normal bacteria compete for food or they actually secrete antibacterial substances (antibiotics).

c. Respiratory tract

The epithelium of the airway, such as the nasal lining, nasopharyngeal lining, trachea and bronchi, consists of tall cells, some of which secrete mucus, but most are equipped with cilia on the surface of their lumen(McPhee et al., 2005). These small protrusions vibrate like whips with movements directed towards the mouth, nose and outside the body. If microorganisms are inhaled, they tend to adhere to the mucosal blanket produced from the mucus, to be scavenged. This protective action is enhanced by the presence of antibodies in the secretions. If some agents evade these defenses and reach the air spaces in the lungs, then there are always alveoler macrophages which are another line of defense (Kemenesi et al., 2020).

3. LINE OF BODY DEFENCE

a. Inflammation. If an infectious agent manages to penetrate one of the body's barriers and enter the tissues, the next line of defense is an acute inflammatory reaction where the humoral (antibodies) and cellular aspects of the body's defenses come together.

b. Lymph vessels. Lymph flow in acute inflammation is accelerated so that infectious agents spread rapidly along the

lymph vessels along with the lymph flow. Sometimes this leads to lymphangitis, but more often the agents are carried directly to the lymph nodes, where they are rapidly phagocytosed by macrophages. In this situation, the lymph fluid flowing to the center through the lymph nodes can be free of these agents.

c. Last defense (primary vein). If the spread of the infectious agent is not stopped at the lymph node or if the agent directly enters the vein at its primary site, infection of the bloodstream can occur.

Bacterial explosions in the bloodstream are actually not uncommon, and these so-called bacteremia events are usually dealt with quickly and effectively by macrophages of the monocyte–macrophage system (McPhee et al., 2005). Septicemia or blood poisoning occurs if the bacteremia condition persists resulting in the incoming organisms being so large and resistant enough that the macrophage system is overpowered. These resident organisms produce symptoms of malaise, weakness, fever, etc. In severe conditions called septicopyemia or pyemia for short, where the organisms reach such large numbers that they circulate in clots and take up space in many organs and cause numerous microabscesses, the bacteremia can be severe(McPhee et al., 2005).

4. MECHANISM OF INFECTIO TRANSMISSION

Transmission of infections can be largely prevented through the use of evidence-based infection control guidelines. The concept of the chain of infection has provided the basis for understanding pathogen transmission to prevent infection. Few germs can fly–almost all germs must be carried from one place to another. Most infection control efforts are aimed at preventing the transfer of germs from reservoirs to susceptible hosts. All types of precautions (standard, contact, droplet and airborne) are designed to break the transmission pathway. Direct and indirect contact is the most common mode of transmission in healthcare settings–from the hands of caregivers and items passed from one patient to another. In

outline, the transmission mechanism of pathogenic microbes to a suspectable host can occur in two ways.

a. *Direct transmission*. Direct transmission by pathogenic microbes to the appropriate *port d'entrée* of the host. Examples are touching, biting, kissing, or the presence of droplet nuclei during sneezing, coughing, talking, or during blood transfusion with blood contaminated with pathogenic microbes.
b. *Indirect transmission*. Transmission of pathogenic microbes through this method requires the presence of "intermediary media" in the form of goods/materials, air, water, food/drinks, and vectors.

As for indirect transmission, namely micro-bacteria transmission that requires intermediary media, including:

a. *Vehicle-borne*

   In this category, the intermediary medium of transmission is contaminated goods/materials such as eating and drinking utensils, surgical/obstetric instruments, laboratory equipment, infusion/transfusion equipment.
b. *Vector-borne*

   As an intermediary medium of transmission is the vector (insect), which transfers pathogenic microbes to the host in the following ways
   1) *Mechanical way*

      On the legs of insects that become vectors attached feces/sputum containing pathogenic microbes, then land on food/drink, which will then enter the gastrointestinal tract of the host.
   2) *Biological way*

      Before entering the host's body, microbes undergo a breeding cycle in the body of the vector/insect, then the microbes move to the host's body through a bite.
c. *Food-borne* Food and beverages are intermediary media that have proven to be quite effective in suggesting the spread of

pathogenic microbes to the host, namely through the entrance (*port d'entrée*) of the gastrointestinal tract.

d. *Water*-borne

The availability of clean water both quantitatively and qualitatively, especially for hospital needs, is an absolute must. Water quality, which includes physical, chemical, and bacteriological aspects, is expected to be free from pathogenic microbes so that it is safe for human consumption. Otherwise, as one of the intermediary media, water is very easy to spread pathogenic microbes to the host, through the entrance (*port d'entrée*) of the gastrointestinal tract and other entrances.

e. *Air-borne*

Air is absolutely necessary for everyone, but unfortunately air that has been contaminated by pathogenic microbes is very difficult to detect. Pathogenic microbes in the air enter the host's airway in the form of droplet nuclei released by the patient (reservoir) when coughing or sneezing, talking or breathing through the mouth or nose. While dust is a particle that can fly with floor/soil dust.

5. INCUBATION PERIOD

The incubation period is the time interval between exposure to a pathogen until symptoms first appear. The incubation period is the time span from when the pathogen enters the human body until the onset of clinical symptoms characterized by fever(McPhee et al., 2005). With respect to infectious diseases, the incubation period is the time required for the pathogen to multiply until it can cause symptoms in its host. Duration of the incubation period (blue line on top left) versus the onset of symptoms and clinical signs of disease. The incubation period is not always the same and depends on the individual. Incubation is also called the budding period, the period from the entry of germs into the body (time of infection) to the time of disease onset. Each disease has a different incubation period (Wilkins., 2013). Disease transmission can occur during the incubation period.

The incubation period for some common diseases includes:

PATHOGEN	In hours	In days	In weeks	In years
Botulism	12–36 hours			
Cholera		3–6 days		
Conjunctivitis		1–3 days		
Diphtheria		2–5 days		
Amoeba dysentery			2–4 weeks	
Bacillary dysentery		1–7 days		
Dengue hemorrhagic fever		4–5 days		
Gonnorhea		2–5 days		
Infectious hepatitis			2–6 weeks	
Shingles			1–2 weeks	
Influenza			1–3 days	
Salmonella food poisoning	6–12 hours			
Lymphogranuloma venereum			2–5 weeks	
Morbili/measles		10–14 days		
Morbus hansen/leprosy				3–5 years
Epidemic parotitis		12–25 days		
Poliomyelitis		7–12 days		
Pertussis/whooping cough		7–20 days		
Syphilis		10–90 days		
Tetanus		7 days		
Tuberculosis			4–12 weeks	
Typhoid abdominalis			1–2 weeks	
Varicella			2–3 weeks	
Variola		7–15 day		
Botulism	12–36 hours			

The length of the incubation period is affected by:

a. **Type of microorganism** (McPhee et al., 2005)

Each disease has a specific incubation period, depending on the causative agent. Sometimes this incubation time is constant, while in some other diseases the incubation time is uncertain. In some venereal diseases, the incubation period is generally constant, for example: Gonorrhoe (2–5 days), Lues (3–4 weeks) and molle ulcer (1–2 days).

In general, infectious diseases that run acutely have an indeterminate incubation period. Another factor that influences whether the incubation period is constant or not is the unknown period of transmission. In chronic diseases such as tuberculosis and leprosy. Usually, the incubation period is not clear, because we do not know when the contamination occurred.

b. **Virulence** or ferocity of microorganisms and Number of microorganisms

These two factors are related to each other. Virulence is the strength of a microorganism or the ferocity of a microorganism. The more microorganisms that invade the body, the more virulent the microorganism is. The number of microorganisms that enter depends on the mode of transmission. The virulence of a microorganism can be seen from the severity of the disease it causes (Sutaryo et al., 2018). In general, it can be said that the more severe the symptoms of the disease, the more virulent the microorganism that causes it, but this is not always true because however a person's immune system can also affect it.

c. **The speed of proliferation** of microorganisms and the speed of toxin formation from microorganisms(Wang et al., 2015). This is related to virulence. Virulent microorganisms will multiply faster and form toxins, if the atmosphere allows.

6. STAGES OF THE INFECTIOUS PROCESS

The infectious process is one of the most dynamic forms of interaction between microbes and a macroorganism that has developed during evolution. The process proceeds with a constant change of cause-and-effect relationships. Conventionally, it can be divided into several stages.

The penetration of the microorganism into the macroorganism, its adaptation at the entrance gate and adhesion. The starting point of the infection process is the introduction and adaptation of microbes (from late Latin. *Adaptatio*-adaptation) at the site of the entrance gate of infection, as well as adhesion of microbes to the cells of the macroorganism. Entrance gates are tissues and organs through which microbes enter the body. In most cases, microbes enter the microorganism through damaged skin and intact mucous membranes permeable to microbes.

a. **Colonization** and formation of enzymes, toxins and other products during the life and reproduction of microorganisms, which leads to disruption of homeostasis due to local and generalized inflammation. The second stage is colonization (from Lat. Colonia–settlement)–horizontal colonization of the skin and mucous membranes at the site of the entrance gate of infection. In the infectious process, the spread of microbes occurs not only horizontally, on the surface of the cells, but also in the depths of the cells and tissues of the macroorganism. The ability of microbes to penetrate the cells of a macroorganism is called penetration. In this case, the multiplication of microbes and the formation of new generations of the pathogen under favorable conditions, as well as the release of metabolic products of microbes, their enzymes and toxins and, in addition, the formation of toxic decomposition products of macroorganism cells that have local or long-term damaging effects on tissues and organs.

b. The third stage is **dissemination** (from the Latin. *Disseminare*–scatter, spread) i.e., the spread of microbes beyond the primary focus of the introduction and colonization of microbes by the hematogenous pathway, bronchogenic or

perineural, along the nerve trunks, which leads to the generalization of the infectious process (generalization is a transition from general to particular, spreading throughout the macroorganism).

c. The fourth stage is **the mobilization of the protective factors** of the macroorganism. In response to the penetration of microbes and their pathogenic effect, the macroorganism mobilizes all initially non-specific and then specific protective factors inherent in it, the action of which is aimed at neutralizing both the microbes themselves and their toxins and at restoring impaired homeostasis in the macroorganism.

d. The fifth stage **is the end and outcome of the infectious process**. In most cases, sanitation of the macroorganism occurs (from the English. Sanative-, healing) that is, the complete release of the macroorganism from the microbe and the acquisition of a new quality by it–the formation of immunity. In some cases, the infectious process ends in death. In those cases when equilibrium is established between the microbe and the macroorganism, carrier state formation takes place.

As a result of the action of many factors, the infectious process does not always go through all its inherent stages and can end already in the early stages, for example, proceeding in an abortive form of an infectious disease in vaccinated or in persons who have previously undergone this disease. Another example is the defeat of the mucous membranes of the urogenital tract in gonorrhea without subsequent generalization of the infection, or colonization of the mucous membranes in intestinal diseases without subsequent generalization of the infection. In diphtheria, the infectious process is also limited by adhesion, colonization and production of exotoxin (histotoxin). The penetration of bacteria into the blood does not occur. If for extracellular parasites the process is limited by adhesion and colonization, then for obligate and facultative intracellular parasites, an important condition is their penetration into the cell and subsequent intracellular multiplication.

The infectious process can occur at all levels of the organization of the biological system of a macroorganism. In addition, each higher level includes lower levels. First of all, the multi-level system of the infectious process includes the body level or the infectious process itself, since infection is a system of reactions that arise in a susceptible macroorganism. The subordinate levels are the tissue-organ, cellular (the interaction of the microbial cell and the host cell) and the subcellular or molecular level, which is based on the competitive interaction of the biological molecules of the microbe and the macroorganism. As a result of the interaction of the microbe with the macroorganism, first of all, the cell suffers in which the microbe makes the gaps through which it subsequently penetrates the macroorganism. The interaction process itself occurs at the level of complementary structures of the microbial macromolecules and the eukaryotic cells of the macroorganism.

7. BACTERIAL VIRULENCE FACTORS

Transmission: The first stage of the infection loop is the entry of microorganisms into the host via one or more routes: respiratory, digestive, urogenitalia, or injured skin. After entry, the pathogen must pass through various host defense systems before it can live and multiply within the host. Examples of host defense systems include acidic conditions in the stomach and urogenital stream, phagocytosis by white blood cells, and various hydrolytic and proteolytic enzymes that can be found in the salivary glands, stomach, and small intestine (Molebogeng X. Rangaka et al., 2017). Bacteria that have a polysaccharide capsule on the outside of their body such as Streptococcus pneumoniae and Neisseria meningitidis have a greater chance of survival.

a. **Attachment:** Some bacteria such as Escherichia coli use their pili to attach to their host cell surface. Other bacteria have adhesion molecules on their cell surface or cell walls that are hydrophobic so that they can attach to the host cell membrane. Attachment increases virulence by preventing the bacteria from being carried away by mucus or body organs due to fluid flow such as in the urine stream and digestion.

b. **Invasive ability:** Invasive bacteria are bacteria that are able to

enter into host cells or penetrate the surface of mucosal glands so that they can spread from the initial point of infection. This invasive ability is supported by the possession of enzymes that degrade the extracellular matrix such as collagenase.

c. **Bacterial toxins:** Some bacteria produce toxins which can be divided into two types viz: endotoxins and exotoxins. Exotoxins are proteins secreted by both gram-positive and gram-negative bacteria. On the other hand, endotoxins are lipopolysaccharides that are not secreted but exist in the cell wall of gram-negative bacteria."

The types of microorganisms that cause infections are divided into our categories, namely (Nair, 2009):

A. *Bacteria.* Bacteria are the most common cause of infection. Hundreds of species of bacteria can cause disease in humans and can live in the body. Bacteria can enter through air, soil, water, food, fluids and other body tissues or inanimate objects.

B. *Viruses.* Viruses mainly contain nucleic acid and therefore must be in living cells to be produced.

C. *Parasites*. Parasites that live in other living organisms, including the parasite group are protozoa, worms, and arthropods.

D. Fungi. Fungi consist of yeast and mold.

8. OPPORTUNISTIC and NOSOCOMIAL INFECTIONS

Opportunistic Infections. The concept of opportunistic infections reflects the existence of many microorganisms that we don't think will do much to a healthy individual, but given the wrong environment, will change and cause infectious diseases(Longo et al., 2014). Such organisms are called opportunistic, because they seem to take advantage of the particular circumstances of the host. Endogenous infectious agents are opportunistic organisms that permanently reside in the host. Opportunistic infections arise when some factor or group of factors

compromise the host's intrinsic defences mechanisms or by altering the ecology of normal resident microorganisms.

Various conditions that can lead to opportunistic infections:

a. Patients with malnutrition disorders
b. Patients with immunologic disorders
c. Patients receiving antimicrobial therapy
d. Patients receiving adrenal corticosteroid therapy

Nosocomial Infection. Nosocomial comes from the Greek language, from the word *nosos* which means disease and *komeo* which means care. *Nosokomion* means a place to treat/hospital. So nosocomial infection can be defined as an infection that is acquired or occurs in a hospital. Nosocomial infections are currently one of the causes of increased morbidity and mortality in hospitals. Nosocomial rates are one of the benchmarks of hospital service quality. A hospital's operational license can be revoked due to the high incidence of nosocomial infections (Inweregbu et al., 2005). Even insurance companies do not want to pay the costs incurred due to nosocomial infections.

Some things that contribute to the occurrence of nosocomial infections are:

a. Other patients who are also in the nursing process
b. Staff (doctors, nurses, etc.)
c. Medical equipment used
d. The place (room/ward/room) where the patient is treated
e. The place/room where the patient underwent acute medical treatment (operating room, delivery room, etc.)
f. Food or drink served
g. The hospital environment in general.

The object of nosocomial infection control is the entry of pathogenic microbes that can come from the elements mentioned above.

SUMMARY

Infection is a disease caused by pathogenic microbes and is very dynamic. Microbes as living things have a way of surviving by multiplying in a suitable reservoir and are able to find other new reservoirs by spreading or moving. The requirement for the onset of infection is that infectious microorganisms must be able to attach, occupy or enter the host and multiply at least to some extent. Septicemia or blood poisoning occurs if the bacteremia condition persists resulting in the incoming organisms being so large and resistant enough that the macrophage system is overpowered. The concept of the chain of infection has provided the basis for understanding pathogen transmission to prevent infection. Few germs can fly–almost all germs must be carried from one place to another. Most infection control efforts are aimed at preventing the transfer of germs from reservoirs to susceptible hosts. All types of precautions (standard, contact, droplet and airborne) are designed to break the transmission pathway. The incubation period is the time span from when the pathogen enters the human body until the onset of clinical symptoms characterized by fever. With respect to infectious diseases, the incubation period is the time required for the pathogen to multiply until it can cause symptoms in its host. The penetration of the microorganism into the macroorganism, its adaptation at the entrance gate and adhesion. Entrance gates are tissues and organs through which microbes enter the body. In most cases, microbes enter the microorganism through damaged skin and intact mucous membranes permeable to microbes. The first stage of the infection loop is the entry of microorganisms into the host via one or more routes: respiratory, digestive, urogenitalia, or injured skin. After entry, the pathogen must pass through various host defense systems before it can live and multiply within the host. Endogenous infectious agents are opportunistic organisms that permanently reside in the host. Opportunistic infections arise when some factor or group of factors compromise the host’s intrinsic defences mechanisms or by altering the ecology of normal resident microorganisms.

KEY TERMS

Infection
Host Factors in Infection
Line of Body Defence
Mechanism of Infection Transmission
Incubation Period
Stages of the Infectious Process
Bacterial Virulence Factors
Opportunistic and Nosocomial Infections

REVIEW QUESTION

ASSIGNMENT

Have a discussion with your friends about the cases below, then present the cases that have been discussed. Here is a situation that can be discussed about infection:

Situation: You are a nurse in the emergency room of a hospital. A 30-year-old patient presents with symptoms of high fever, cough, and difficulty breathing. The patient claims to have just returned from a trip to a malaria-endemic area. You must perform an initial assessment of the patient and determine the appropriate treatment steps.

Discuss the situation by considering the following:

1. Identify possible causes of infection in the patient, given the history of travelling to malaria endemic areas. What are the infectious diseases to consider?
2. Discuss the patient's symptoms and indications of infection. Explain why a high fever, cough and difficulty breathing can be signs of a serious infection.
3. How will you assess and monitor the patient's condition? Explain what tests or examinations you might perform to establish a diagnosis and monitor response to treatment.
4. Discuss the treatment steps you will take for the patient. Is it necessary to administer antibiotic therapy or anti-malarial drugs? What other measures may be needed to manage the patient's symptoms?

FORMATIVE TEST

1. What causes influenza infection?
   a. Bacteria
   b. Parasites
   c. Virus
   d. Fungi

2. What is the main mode of transmission of hepatitis A infection?
   a. Through insect bites
   b. Through sexual contact
   c. Through contaminated food or drink
   d. Through contaminated air

3. What causes Salmonella infection?
   a. Viruses
   b. Bacteria
   c. Parasites
   d. Fungi

4. What causes Malaria infection?
   a. Bacteria
   b. Virus
   c. Parasites
   d. Fungi

5. What is the causative organism of Tuberculosis infection?
   a. Mycobacterium tuberculosis bacteria
   b. Influenza virus
   c. Plasmodium parasite
   d. Candida fungus

6. What is the main mode of transmission of HIV virus infection?
   a. Through contaminated air
   b. Through insect bites
   c. Through sexual contact

d. Through contaminated food or drink

7. What is the main mode of transmission of E. coli bacterial infection?
   a. Through insect bites
   b. Through sexual contact
   c. Through contaminated air
   d. Through contaminated food or drink

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UNIT 8 NEOPLASM

LEARNING OBJECTIVES

After mastering the contents of this chapter, student will be able to:

1. State the Definition of Neoplasm
2. State the Characteristics of Neoplasms
3. Explain Neoplasm Cell Metabolism
4. List of Classification by Biological Properties of Tumors
5. List of the Effects of Neoplasms
6. State the Clinical features of neoplasms
7. State the Causes of neoplasm
8. Explain the Pathophysiology of Neoplasm
9. Explain the Diagnosis and Treatment of Neoplasms
10. Explain the Preventive Measures for Neoplasms
11. State the Nature of benign and malignant tumors
12. State the Biology of Tumor Growth
13. List Causes of Cancer
14. Explain the Pathophysiology of neoplasms (Cancer)
15. Explain the Development of Normal Cells into Cancer Cells

1. Definition of Neoplasm

A neoplasm is a mass of abnormal cells formed by cells that grow continuously in an indefinite manner, uncoordinated with surrounding tissues and useless for the body(McPhee et al., 2005). Similarly, a neoplasm, as defined by Willis in 1950, is an abnormal mass of tissue that grows excessively and uncoordinated with normal tissue growth and continues to do so even though the design that triggered the change has stopped. The fundamental thing about the origin of neoplasms is the loss of responsiveness to normal growth control factors. Neoplastic cells are called transformed because they continue to grow, seemingly indifferent to the regulatory influences that control normal growth. In addition, neoplasms behave like parasites and compete with normal cells and tissues for their metabolic needs(Snodgrass et al., 2018). To some extent, neoplasms have autonomy and more or less continue to grow

independent of the local environment and nutritional status of the host. Some neoplasms require endocrine support, and such dependence can sometimes be exploited to the detriment of the neoplasm. All neoplasms depend on the host for nutrition and blood flow(Wilkins., 2013).

In common medical usage, neoplasms are often referred to as tumors, and the science of tumors is called oncology (from *onkos*, tumor and *logos*, science). In oncology, the division of neoplasms into benign and malignant categories is important. This division is based on an assessment of the likely behavior of the neoplasm. A tumor is said to be benign (beniga) if its microscopic and macroscopic features are considered relatively innocent, which implies that the tumor will be localized, cannot spread elsewhere, and can generally be removed by local surgery in which the patient generally survives. However, it should be noted that benign tumors can cause more than just a localized lump, and sometimes they cause serious illness. Malignant tumors are collectively called cancer, derived from the Latin word for crab with a tumor cling tightly to all surfaces it touches, like a crab. Malignant, when applied to neoplasms, indicates that the lesion can invade and damage nearby structures and spread to distant sites (metastesis) and cause such death.

2. Characteristics of Neoplasms (M. J. Kim et al., 2022)

In general, neoplasms have the following characteristics:

a. Infiltrative growth: that is, growth that branches out and invades into the surrounding healthy tissue, so that it resembles a crab man (cancer), so that in malignant tumors the tissue cannot move from its base.

b. Residual (recurrence): i.e., tumors that have been removed or that remain after treatment, if there are tumor cells left behind then the tumor cells will grow and become large to form a tumor in the same place. Benign tumors will not experience recurrence, because benign tumors have skin layer (capsule)(Wilkins., 2013).

c. Metastatic (scatter): this is the process of detachment and

causes malignant neoplasms. Malignant neoplasm cells proliferate and are able to break away from the parent tumor (primary tumor) and form secondary tumors. The area of secondary growth is called the metastatic area.

d. There is growth and enlargement of the tumor. In benign tumors the growth is rather slow and does not enlarge quickly, while in malignant tumors, the tumor grows quickly and enlarges. In malignant tumors, multi-cell division occurs at the same time so that a cell can have 3 or 4 daughter cells.

e. Changes in the cell nucleus. The ratio of this to the cytoplasm is between 1:1 or 1:2. In normal cells the ratio is 1:4. This change is not because the size of the cell nucleus increases, but because the amount of cell cytoplasm decreases. Sometimes the shape of the cell nucleus changes shape for example: chromatin increases so that become rough picture and group on the edge of the core or nucleolus increases in size.

f. Anaplasia is a cell that loses differentiation (differential), tumor cells in a malignant state when dividing themselves will undergo changes so that they may not reach the original cell.

g. Loss of polarity: polarity means opposite or contradictory properties. A normal tissue is composed of normal cells and usually forms a certain arrangement, for example epithelial cells that suckle the epidermis of the skin the arrangement consists of: basal layer, spinosum layer, granulosum layer and so on. So there is polarity. In malignant tumors it is found that the location of one cell against another is no longer regular for example in cancer of the uterine mouth, the layered epithelial layer is not clearly stratified.

h. Causing death. Malignant tumors if not treated will cause the death of the sufferer even though it is only located in the leg, while in benign tumors the patient does not experience death unless the tumor is located in vital body organs such as the brain and heart.

3. Neoplasm Cell Metabolism (E. K. Kim et al., 2021)

In neoplasm metabolism, there are several things that are important for us to know, namely(Hammer, 2018):

a. Energy Source

Neoplasm cells get energy mainly from anaerobic glycolysis because the cell's ability to oxidize is reduced, even though it has complete enzymes for oxidation. Unlike normal tissue cells which enzyme composition is different, the enzyme composition of all neoplasm cells is more or less the same (uniform) (Huether et al., 2020).

b. Enzyme Arrangement

Normal cells prioritize function (which produces energy by catabolism) over reproduction (which requires energy for anabolism). Neoplasm cells prioritize reproduction rather than performing their functions, so the arrangement of enzymes for catabolism is no longer important. Therefore, the enzyme arrangement of neoplasm cells is uniform.

c. Competitive Struggle

Growing tissues require materials to form protoplasm and energy for that purpose. Neoplasm cells seem to be given priority to get amino acids so that other body cells will experience a shortage. This may explain why patients with malignant tumors in the last stages experience cachexia. Cachexia is excessive weight loss. It is caused by the depletion of adipose tissue and muscle mass in the body. A person with cachexia will experience drastic weight loss without trying to diet or exercise.

4. Classification by Biological Properties of Tumors

All tumors, both benign and malignant, have two basic components: parenchyma and stroma. The parenchyma is the proliferative cells of the tumor, which exhibit growth properties and varied functions resembling those of the original cells, for example, the production of collagen, mucin, or keratin. Stroma is the support of tumor

parenchyma consisting of connective tissue and blood vessels. The presentation of food to tumor cells through blood vessels by diffusion.

Based on their biological properties, tumors can be divided into benign tumors and malignant tumors, as well as tumors that are in between benign and malignant called “intermediate” (Assarzadegan & Montgomery, 2021).

a. Benign Tumors

Benign tumors are slow-growing and usually have a capsule. They do not grow infiltratively, do not damage surrounding tissues and do not spread to distant sites. Benign tumors are generally perfectly curable except for tumors that secrete hormones or are in very important places, for example in the spinal cord which can cause paraplegia or in the brain nerves which compress brain tissue.

Benign neoplasms are made up of cells with the cellular structure of their origin, the cells of benign neoplasms are more cohesive compared to malignant neoplasms. Growth occurs from the center of the benign mass, usually resulting in a well-defined border. Benign tumors cause effects in the form of obstruction, pressure and secretion. Benign tumors within an enclosed space such as the skull can cause serious distress that can lead to death. Intestinal obstruction may result from the growth of a benign tumor in that location.

b. Malignant Tumors

Malignant tumors are generally fast-growing, infiltrative and destructive to the surrounding tissues. In addition, they can spread throughout the body through the lymph flow or bloodstream and often cause death (Nair, 2009).

Malignant neoplasms have a typical cell structure, with abnormal division and nuclear chromosomes, malignant cells lose differentiation or resemble their cell of origin. The tumor cells are incoherent, and as a result, the growth pattern is irregular; no capsule is formed, and separation from the

surrounding tissue is difficult to see.

c. Intermediate

Between 2 groups of benign tumors and malignant tumors there is a small group of tumors that have local invasive properties but little metastatic ability. Such tumors are called locally aggressive tumors of low-grade malignant tumors. An example of this tumors is basal cell carcinoma of the skin.

Neoplasms can also be classified based on their stage of development. Staging is an attempt to describe how far the disease has progressed at that point. The benefits of staging are to indicate treatment, assess, determine treatment methods, and facilitate information exchange between treatment centers.

5. Effects of Neoplasms

Benign tumors have effects on the patient due to three possibilities, because of its position, secondary complications, and excessive hormone production (Ortmann et al., 2015).

a. Position of the Tumor

Proliferation of tumor cells will form a mass that can compress the surrounding tissue. The suppressed tissue will become atrophic. Adenomas of adenoids will compress the trachea and interfere with breathing. Tumors in the ureter or kidney cup will cause urinary obstruction. Intracranial tumors such as meningiomas can cause increased intracranial pressure (Huether & McCance, 2012).

b. Secondary Complications

Bleeding can occur in benign tumors in the mucous membranes, such as papillomas in the digestive tract and urinary tract. In stemmed benign tumors such as a subserosal myoma or an ovarian cystadenoma, the stem may rotate and cause severe pain. Pedunculated tumors of the intestine may cause intussusception (invagination).

c. Excessive Hormone Production

Benign tumors of the endocrine glands can produce excessive hormones so that the consequences of excess hormones will arise in patients. Malignant tumors can cause disorders in patients due to their position and secondary complications as in benign tumors. Excessive hormone production in malignant tumors of the endocrine glands may not occur because the cells are poorly differentiated and do not form hormones. Instead, there may be deficiency due to destruction of normal cells by tumor cells. The most important thing in malignant tumors is the destruction of surrounding tissue by infiltrative growth and the occurrence of metastasis. Some of these variations are influenced by the patient's reaction to the tumor. Some patients seem to be resistant to spread and perhaps the immunologic power of the cells resists the growth and spread of cancer cells such as a local inflammatory reaction with histiocyte changes in regional lymph nodes.

Malignant tumors are most likely to cause death due to cachexia, which is very weak, weight loss and poor general condition. This situation makes the patient very susceptible to other diseases such as pneumonia. There is usually a relationship between the amount of malignancy of the tumor and the severity of cachexia. Heavy tumors with a lot of spread usually cause severe cachexia. Friedel (1965) argues that cachexia is caused by severe anemia due to excessive destruction of red blood cells. Friedel (1965) argues that cachexia is caused by various factors that occur in the state of malignant tumors such as: starvation, the occurrence of ulcers with bleeding, secondary infections, destruction of important body organs such as the liver or lungs by pain, lack of sleep and anxiety of the patient.

6. Clinical Features of Neoplasms

The effect of the tumor on the patients is explained as follows. As a result of the local mass of tumor tissue that grows, it

causes pressure on the important instruments around it, for example, blood vessels, nerves, visceral tracts, ducts and solid devices that cause various complications(Qu et al., 2021). In general, cancer patients become thin followed by weakness, anemia, and anorexia. The coexistence (collection of symptoms) is caused by metabolic abnormalities, not from dietary needs, but as a result of the action of soluble factors such as cytoxins produced by the tumor. Fungal activity is more typical in benign tumors than in malignant tumors/cancerous tumors, because malignant tumors are undifferentiated cells, so their ability is lost.

Tumors can cause various symptoms and clinical signs can generally be:

a. often feeling unwell,
b. feeling very tired,
c. fever and chills,
d. no appetite,
e. weight loss without apparent cause, and
f. night sweats.

However, each tumor has different indications depending on the type and location of growth. For example, brain tumors can cause symptoms of unbearable headaches, sudden vomiting, and convulsions. While the symptoms of benign lung tumors can take the form of ongoing and worsening coughing up blood, shortness of breath, chest pain and fatigue.

There are also malignant tumors that do not even cause symptoms until they reach an advanced stage, such as cervical cancer and liver cancer. Therefore, you are advised to always be vigilant and check with your doctor if you experience a condition that feels odd even though it seems mild at first glance.

7. Causes of Neoplasm

Tumors are caused by mutations in the DNA of cells. A build-up of mutations is required for a tumor to appear. Mutations that activate oncogenes or suppress tumor suppressor genes can eventually lead to tumors (Schwarz et al., 2023). Cells have mechanisms that repair

DNA and other mechanisms that cause cells to destroy themselves through apoptosis when DNA is damaged too severely. Mutations that hold genes for these mechanisms can also cause cancer. A mutation in one oncogene or one tumor-blocking gene is usually not enough to cause a tumor. A combination of several mutations is required. Apoptosis is the active process of cell death characterized by cleavage of chromosomal DNA. Condensation of chromatin, and fragmentation of the nucleus and the cell itself. Mutations that suppress genes for these mechanisms can usually lead to cancer.

Aging leads to more mutations in DNA. This means that tumor prevalence increases with aging. This is also the case for older people with tumors, most of which are malignant. For example, if a 20-year-old woman has a tumour in her chest, it is most likely a benign tumour. However, if the woman is 70 years old, it is most likely a malignant tumour. Two properties of malignant tumor cells (cancer) are the ability to invade the local tissue where the malignant tumor grows (locally) and metastasize/spread far from the parent tumor. Invasion and metastasis are the main biologic properties of malignant tumors. Theories of the causes of neoplasms is explained below.:

a. Somatic mutation theory

   Abnormalities in genes arise due to mutational changes, which may be induced by carcinogenic substances, and the presence of hereditary factors. There is evidence that people with certain chromosomal abnormalities are prone to certain neoplasms, for example leukemia cases are more frequent in people with trisomy, especially trisoma 2.1 retinoblastoma is common in people with deletion-D syndrome (on part of chromosome 13). People with chronic myelocytic leukemia have Philadelphia chromosome (translocation of chromosome 22) to more than 90%.

b. Aberrant or epigenetic differentiation theory

   Abnormalities arise due to disruption of the regulation of normal genes. The incidence of malignant neoplasms increases during growth and development. Dermoite cysts,

hamartomas, and teratomas are neoplasms that arise due to disruption of embryonal growth and development.

c. Viral theory

Viruses are cited as a possible cause of malignant neoplasms in humans. They are called oncogenic viruses. There is evidence to suggest that viruses alter the genes of infected cells, which then alter the derivatives of the cells. The 2 oncogenic viruses are DNA and RNA viruses.

d. Cell selection theory

Neoplasms develop step by step, through the process of mutation, this process can stop and is reversible (when the stimulus is no longer present). Immunodeficiency increases the risk of neoplastic growth.

e. Other factors in carcinogenesis

1) Living habits and culture

Gastric carcinoma is more common in Japan than in the United States. While carcinomas of the intestine, breast, prostate occur less in Japan than the United States. However, after Japanese people lived in America, this difference disappeared.

2) Diet

Low fiber diet habits can cause colon carcinoma and gastric carcinoma.

3) Sex life

Cervical carcinoma is more common in women who have had sex since young, let alone changing partners. Breast carcinoma is more common in women who do not have children, who are younger at the time of first menstruation or late menopause.

4) Habits

The habit of drinking alcohol can trigger asophageal carcinoma. Smoking habit triggers the occurrence of lung carcinoma; 9-10 cigarettes/day has a 4x greater chance and >20 cigarettes/day has a 10x greater chance.

5) Hormones

When levels of certain hormones are elevated for a long time, they can trigger carcinoma of the breast, endometrium, vagina, or thyroid.

8. Pathophysiology of Neoplasma (Schwarz et al., 2023)

Cancer is a diverse class of diseases that differ greatly in terms of their causes and biology. Any organism, even plants, can get cancer. Almost all known cancers arise gradually, as defects accumulate in the cancer cells and their daughter cells.

Everything that replicates has the possibility of defects (mutations). Unless the prevention and repair of defects is properly addressed, the defects will remain, and may be passed on to daughter cells. Normally, the body guards against cancer by various methods, such as apoptosis, helper molecules (some DNA polymerases), senescence, and others. However, these correction methods often fail, especially in an environment that makes the defect more likely to appear and spread. For example, such environments contain damaging substances, called carcinogens, periodic injuries (physical, thermal, etc.), or environments that make it impossible for cells to survive, such as hypoxia. Cancer is therefore a progressive disease, and these progressive defects slowly accumulate until the cell begins to act contrary to its proper function in the organism. Cell defects, as the cause of cancer, are usually self-amplifying, eventually multiplying exponentially. For example:

a. mutations in the defect-repairing apparatus can cause cells and their cells to accumulate defects more quickly,
b. mutations in signalling equipment (endocrine) can send defect-causing signals to surrounding cells, and
c. mutations can cause cells to become neoplastic, causing them to migrate and damage healthier cells. Mutations can cause cells to become immortal, see telomeres, making damaged cells can make healthy cells damaged forever.

9. Diagnosis and Treatment of Neoplasms

In addition to asking about the history of the disease, symptoms and examining the physical condition, the doctor will include several types of examinations to confirm the patient's diagnosis, these examinations include (Schwarz et al., 2023):

a. complete blood test and organ function evaluation,
b. CT, MRI or PET scan to confirm the location and extent of tumor spread.
c. chest X-ray,
d. biopsy or tumor sampling which is used to confirm whether or not the tumor is malignant.

If you are diagnosed with a specific tumor, your doctor will assist you in determining the appropriate treatment. The method of treatment depends on the type, location, and malignancy of the tumor.

There are a number of treatment methods for malignant tumors. Commonly recommended measures include:

a. surgical removal,
b. chemotherapy,
c. radiotherapy,
d. biological therapy,
e. targeted therapy which only seeks out and attacks cancer cells.

Patients generally require a combination of 3 methods, namely surgical removal, chemotherapy and radiotherapy. If the malignant tumor is still in one location and has not spread, the cancer will usually be removed through a surgical procedure. Benign tumors can also generally be removed but if they do not interfere with organ performance and do not adversely affect health at all, benign tumors sometimes do not need to be removed.

The earlier a tumor is detected, the higher the patient's chances of recovery. Therefore, all tumors (malignant or benign) should be diagnosed and treated immediately as they have the potential to cause various health complications if left untreated.

10. Preventive Measures for Neoplasms

There is no prevention method that can provide total protection from the appearance of tumors. However, there are a number of simple steps that we can take to lower our risk of developing cancer (Vyazovichenko et al., 2022). These steps include:

a. quit smoking,
b. exercise regularly,
c. implement a healthy and balanced diet, such as increasing the consumption of fiber foods (especially vegetables) and reducing the consumption of fatty foods or those containing preservatives,
d. maintain a healthy body weight to avoid obesity,
e. limit the consumption of alcohol,
f. avoid exposure to chemical compounds containing raccoons, for example by wearing a mask when riding public transportation,
g. minimize exposure to radiation,
h. undergo regular check-ups, and
i. undergo vaccinations needed to prevent cancer, such as the HPV vaccine.

SUMMARY

A neoplasm is a mass of abnormal cells formed by cells that grow continuously in an indefinite manner, uncoordinated with surrounding tissues and useless for the body. Neoplasms are often referred to as tumors, and the science of tumors is called oncology (from onkos, tumor and logos, science). In general, neoplasms have the following characteristics: infiltrative growth, residual (recurrence), metastatic (scatter), growth and enlargement of the tumor, changes in the cell nucleus, loses differentiation (Anaplasia), loss of polarity, and causing death. Neoplasm cells get energy mainly from anaerobic glycolysis because the cell's ability to oxidize is reduced, even though it has complete enzymes for oxidation. Neoplasm cells prioritize reproduction rather than performing their functions, so the arrangement of enzymes for catabolism is no longer important. Based on their biological properties, tumors can be divided into benign tumors and

malignant tumors, as well as tumors that are in between benign and malignant called “intermediate”. Benign tumors are slow-growing and usually have a capsule. They do not grow infiltratively, do not damage surrounding tissues and do not spread to distant sites. Malignant tumors are generally fast-growing, infiltrative and destructive to the surrounding tissues. In addition, they can spread throughout the body through the lymph flow or bloodstream and often cause death. Intermediate, between 2 groups of benign tumors and malignant tumors there is a small group of tumors that have local invasive properties but little metastatic ability. Benign tumors have effects on the patient because of its position, secondary complications, and excessive hormone production. As a result of the local mass of tumor tissue that grows, it causes pressure on the important instruments around it, for example, blood vessels, nerves, visceral tracts, ducts and solid devices that cause various complications. Tumors are caused by mutations in the DNA of cells. A build-up of mutations is required for a tumor to appear. Mutations that activate oncogenes or suppress tumor suppressor genes can eventually lead to tumors. Cells have mechanisms that repair DNA and other mechanisms that cause cells to destroy themselves through apoptosis when DNA is damaged too severely. Cancer is a diverse class of diseases that differ greatly in terms of their causes and biology. Any organism, even plants, can get cancer. Almost all known cancers arise gradually, as defects accumulate in the cancer cells and their daughter cells. Diagnosis of Neoplasms by asking about the history of the disease, symptoms and examining the physical condition, the doctor will include several types of examinations to confirm the patient’s diagnosis, these examinations include complete blood test and organ function evaluation, CT, MRI or PET scan to confirm the location and extent of tumor spread, chest X-ray, and biopsy or tumor sampling. Treatment of Neoplasms commonly recommended measures include surgical removal, chemotherapy, radiotherapy, biological therapy, targeted therapy which only seeks out and attacks cancer cells. There is no prevention method that can provide total protection from the appearance of tumors. However, there are a number of simple steps that we can take to lower our risk of developing cancer include: quit smoking, exercise regularly, implement a healthy and

balanced diet, such as increasing the consumption of fiber foods (especially vegetables) and reducing the consumption of fatty foods or those containing preservatives, maintain a healthy body weight to avoid obesity, limit the consumption of alcohol, avoid exposure to chemical compounds containing raccoons, for example by wearing a mask when riding public transportation, minimize exposure to radiation, undergo regular check-ups, and undergo vaccinations needed to prevent cancer, such as the HPV vaccine..

KEY TERMS

Definition of Neoplasm
Characteristics of Neoplasms
Neoplasm Cell Metabolism
Classification by Biological Properties of Tumors
Effects of Neoplasms
Clinical Features of Neoplasms
Causes of Neoplasma
Pathophysiology of Neoplasma
Diagnosis and Treatment of Neoplasms
Preventive Measures for Neoplasms
Classification and Naming of Neoplasms
Classification on the Basis of Cell/Tissue Origin
Effects of Neoplasms
Nature of Benign and Malignant Tumors
Biology of Tumor Growth
Causes of Cancer
Pathophysiology of Neoplasma (Cancer)
Development of Normal Cells into Cancer Cells

REVIEW QUESTION

Assignment

Have a discussion with your friends about the cases below, then present the cases that have been discussed.

1. A boy, 4 years old, weighing 10 kg was admitted to the paediatric

surgery clinic with the main complaint of a lump on the right side of the abdomen, known to the patient's parents since 1 year ago. The lump has been getting bigger since 6 months ended. Appetite decreased and body weight decreased. There was no vomiting and defecation disorder. No complaints of abdominal pain, sometimes accompanied by urine mixed with blood. There is no history of trauma. Physical examination results: there was a lump in the right abdomen, palpable hard mass, and fixed in the retroperitoneum area, not moving with breathing. RT: no abnormalities found. Weight loss. This patient was accompanied by hypospadias.46. In the above case, the clinical diagnosis led to the suspicion of a tumour,

Question:

a. The first supporting examination performed in the above case is.
b. In the above case, to be able to distinguish from other tumours, the spread of the abdomen, lymph nodes, surrounding organs, vena cava, and contra-lateral renal function can be determined. The appropriate examination is.
c. In the above case, if the abdominal CT scan examination is not clear whether the tumour is from the kidney or hepar, the most appropriate supporting examination is.

2. A man of Chinese descent, 60 years old, came for consultation at The Surgical Department of Dr. Wahidin Sudirohusodo Hospital with a chief complaint of progressive dysphagia, which had lasted for 12 months, initially disturbed when eating solid food and then continued with liquid food. There is no odynophagia, only complains of frequent heartburn. Lately there is sometimes melena. She claims to be getting thin.
   a. The most likely diagnosis is.....
   b. To strengthen the diagnosis, the important examination recommended is...
   c. To determine the stage, the necessary examinations are....a cytological examination of lambent smear
   d. If the PA examination reveals an "Adenocarcinoma", then there is a possibility of an associated with the disease....

FORMATIVE TEST

1. What are the main risk factors associated with lung cancer?
    a. Excessive sun exposure
    b. Tobacco smoking
    c. Air pollution
    d. Viral infection

2. What is the most common type of cancer among women worldwide?
    a. Breast cancer
    b. Ovarian cancer
    c. Cervical cancer
    d. Colorectal cancer

3. What is metastasis in the context of cancer?
    a. Formation of a primary tumour
    b. Spread of cancer cells to other parts of the body
    c. Early screening for cancer detection
    d. Use of radiation therapy to destroy cancer cells

4. What are the main risk factors associated with skin cancer?
    a. Air pollution
    b. Excessive sun exposure
    c. Consumption of foods that are high in fat
    d. Exposure to nuclear radiation

5. What is chemotherapy?
    a. Surgical removal of tumours
    b. Use of drugs to destroy cancer cells
    c. Radiation therapy to destroy cancer cells
    d. Early detection of cancer through medical examination

6. What is the most common type of cancer among men worldwide?
    a. Prostate cancer
    b. Lung cancer

c. Liver cancer
d. Melanoma skin cancer

7. What is a Pap smear test?
   a. A blood test to detect cancer
   b. X-ray examination to look at internal organs
   c. Ultrasound examination to detect tumours
   d. Screening to detect cervical cell changes that may indicate cervical cancer

8. What is metastatic cancer?
   a. Cancer that is confined to one organ
   b. Cancer that has spread to nearby organs
   c. Cancer that has spread to other parts of the body
   d. Cancer that can be completely cured through surgery

9. What is a genetic risk factor in cancer development?
   a. Exposure to harmful chemicals
   b. Unhealthy lifestyle
   c. Family history of cancer
   d. Poor environmental factors

10. What is primary prevention of cancer?
    a. Therapies used after a cancer diagnosis
    b. Measures to prevent cancer before it occurs
    c. Routine screening for early cancer detection
    d. Treatment

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UNIT 9 THE PROCESS OF SHOCK

LEARNING OBJECTIVES

After mastering the contents of this chapter, student should be able to:

1. Define Shock
2. Mention Classifications and Causes of Shock
3. Mention the General assessments for shock
4. Explain the Pathophysiology of Shock
5. Explain the stages of shock
6. Repeat the Complications of shock

1. SHOCK

Shock is a life-threatening manifestation of circulatory failure. Circulatory shock leads to cellular and tissue hypoxia resulting in cellular death and dysfunction/failure of vital organs. Effects of shock are reversible in the early stages, and a delay in diagnosis and/or timely initiation of treatment can lead to irreversible changes, including multiorgan failure (MOF) and death (Neaz, 2019).

There are the stages of shock here:

a. A state of hypoperfusion/hypotension (low blood pressure)
b. Oxygen does not get to the tissues (causing global hypoxia)
c. Cells don't function property (they shift into anaerobic metabolism when they don't get enough oxygen). Anaerobic metabolism results in the production of lactate and ultimately leads to metabolic acidosis.
d. Organs start to fail.

Shock is a clinical syndrome due to circulatory system failure with insufficient supply of oxygen and other metabolic substrates to the tissues and failure to remove metabolic waste (McPhee et al., 2005).

2. CLASSIFICATIONS AND CAUSES OF SHOCK

Based on the components of the circulatory system, there are several types of shock(Kuba & Kubová, 2005)

a. Hypovolemic Shock
   Hypovolemic shock, the most common type of shock, is caused by insufficient circulating volume, usually as a result of bleeding, although severe vomiting and diarrhea are also potential causes.
b. Cardiogenic Shock
   Cardiogenic shock is caused by the failure of the heart to pump properly, either due to heart muscle damage through myocardial infarction or through heart valve problems, congestive heart failure, or dysrhythmias.
c. Obstructive Shock
   Obstructive shock is caused by the obstruction of blood flow outside the heart. This usually occurs due to decreased venous return, but can also be caused by aortic blockage.
d. Distributive Shock
   Distributive shock is caused by abnormal distribution of blood to tissues and organs, and includes septic, anaphylactic and neurogenic causes.
e. Septic Shock
   Septic shock is the most common cause of distributive shock and is caused by excessive systemic infection that cannot be cleared by the immune system, resulting in vasodilation and hypotension.
f. Anaphylaxis shock
   Anaphylactic shock is caused by a severe reaction to an allergen, leading to the release of histamine which causes widespread vasodilation and hypotension.
g. Neurogenic shock
   Neurogenic shock results from damage to the central nervous system, which impairs cardiac function by reducing heart rate and loosening vascular tone, resulting in severe hypotension.

3. GENERAL ASSESSMENTS FOR SHOCK

As evaluating a patient in shock, there are some clinical signs and symptoms must be assessed regardless of which classification of shock you are dealing with (Neaz, 2019). These symptoms include:

1. weakness, which is caused by due to tissue hypoxia and acidosis,
2. feeling thirsty, which is caused by hypovolemia (in particular by the relatively low amount of fluid in the blood vessels),
3. pallor due to catecholamine-induced vasoconstriction and/or red blood cell loss,
4. tachycardia, which is caused by the effects of catecholamines on the heart,
5. tachypnea (increased respiratory rate) which caused in response to stress, catecholamines, acidosis, and hypoxia 5,
6. diaphoresis (sweating) which is caused by the effect of catecholamines on sweat glands 6,
7. decreased urine output which is caused by hypovolemia, hypoxia, and circulating catecholamines (important to remember in inter-hospital transfers),
8. weakened peripheral pulse which include weak pulse caused by vasoconstriction, rapid heart rate, and blood volume loss,
9. hypotension which is caused by hypovolemia, either absolute or relative 9,
10. altered consciousness (confused, agitated, rebellious, unconscious) which is caused by decreased cerebral perfusion, acidosis, and catecholamine stimulation,
11. respiratory arrest which is caused by critical organ failure due to blood and fluid loss, hypoxia, and sometimes arrhythmias due to catecholamine stimulation.

4. PATHOPHYSIOLOGY OF SHOCK

a. Hypovolemic Shock

Hypovolemic shock is one of the most common cardiac complications. In hypovolemic shock, reduced intravascular blood volume causes circulatory dysfunction and inadequate

tissue perfusion. Vascular fluid volume loss causes extreme tissue hypoperfusion (Gould et al., 1993). The pathophysiology of hypovolemic shock includes the following processes.

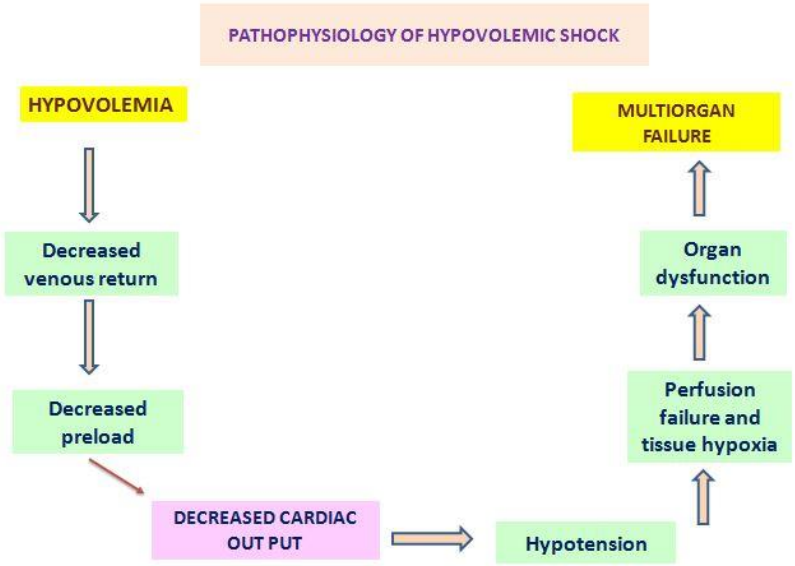

Figure 18. Pathophysiology of Hypovolemic Shock

Hypovolemic shock begins with fluid loss. Fluid loss can be either internal or external fluid loss. The compensatory mechanism carried out by the body is the decrease in arterial blood pressure that occurs will activate the body's compensatory mechanism in an effort to increase the body's intravascular volume. This will affect venous return due to decreased arterial blood pressure. The blood filling (preload) returning to the heart is reduced and consequently affects the stroke volume which becomes reduced. Cardiac output becomes decreased due to the decrease in stroke volume. arterial pressure, reduced mean arterial pressure follows a gradually decreasing cardiac output. As a result, blood flow to organs and cells decreases. Impaired cell nutrition. When

tissue perfusion decreases, nutrient and oxygen delivery to cells will be reduced, which may eventually lead to multiple organ dysfunction syndrome (Neaz, 2019).

b. Cardiogenic Shock

Cardiogenic shock occurs when the heart's ability to contract and to pump blood is impaired and the supply of oxygen is inadequate for the heart and tissues.

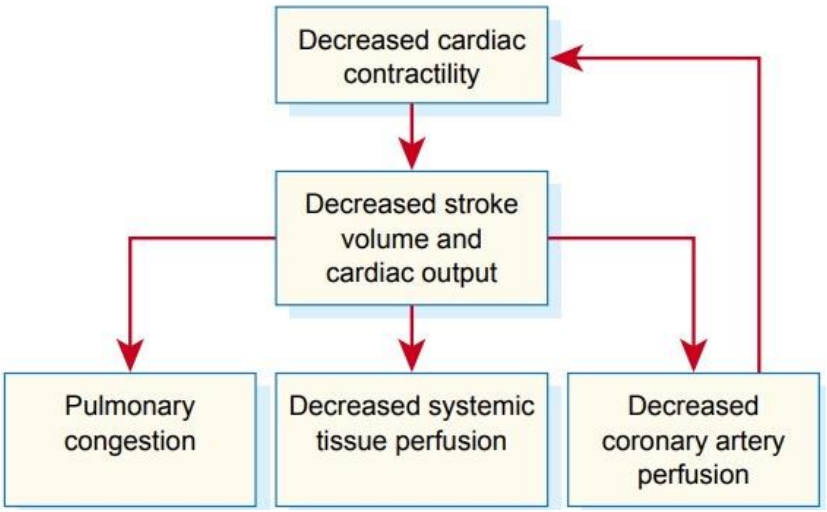

Figure 19. Pathophysiology of Cardiogenic Shock

It is preceded by the inability of the myocardial muscle to contract. When the myocardium cannot contract sufficiently to maintain an adequate cardiac output, the stroke volume decreases and the heart cannot expel an adequate volume of blood with each contraction. Subsequently pulmonary congestion occurs, blood backs up behind the weakened left ventricle, increasing preload and causing pulmonary congestion. The next step is the compensation stage. In addition, to compensate for the reduced stroke volume, heart rate increases in an attempt to maintain cardiac

output. The resulting reduced stroke volume causes coronary artery perfusion and collateral blood flow to decrease. Ultimately there is an increase in cardiac workload. All these mechanisms increase cardiac workload and promote left-sided heart failure. Ultimately myocardial hypoxia occurs, cardiac output decreases, and triggers compensatory mechanisms to prevent decompensation and death.

c. Neurogenic Shock

Neurogenic shock is a distributive type of shock. In neurogenic shock, vasodilation occurs as a result of a loss of balance between parasympathetic and sympathetic stimulation. It is a type of shock (a life-threatening medical condition in which there is insufficient blood flow throughout the body) that is caused by the sudden loss of signals from the sympathetic nervous system that maintain the normal muscle tone in blood vessel wall (Kuba & Kubová, 2005)s. The patient experiences the following that results in neurogenic shock.

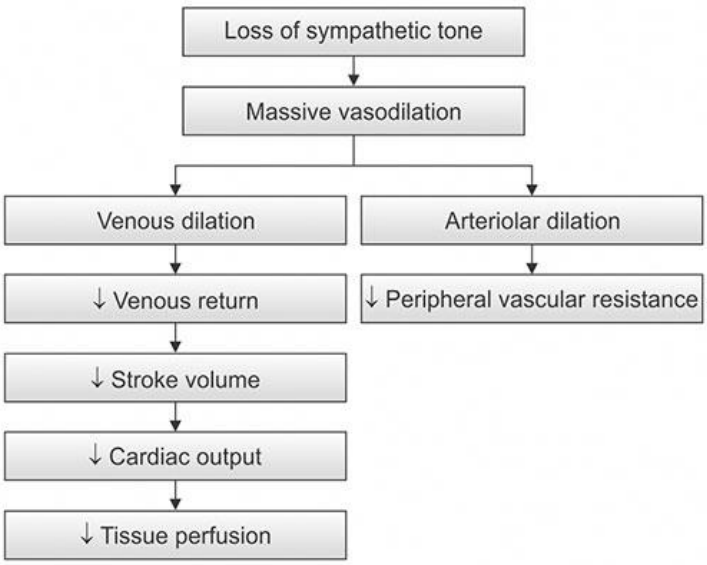

Figure 20. Pathophysiology of Neurogenic Shock

Neurogenic sympathetic shock causes vascular smooth muscle to constrict, and parasympathetic stimulation causes vascular smooth muscle to relax or expand. This results in vasodilation. The patient has predominant parasympathetic stimulation causing vasodilation that lasts for a long period of time, leading to a relative hypovolemic state. And there is hypotension. Even if the blood volume is sufficient, but because the blood vessels are dilated; the blood volume is displaced, resulting in a state of hypotension (low blood pressure). Cardiovascular changes. The excessive parasympathetic stimulation that occurs in neurogenic shock causes a drastic decrease in the patient's systemic vascular resistance and bradycardia. Inadequate perfusion. Inadequate blood pressure leads to insufficient perfusion of tissues and cells, which is common to all states of shock(Nair, 2009).

d. Anaphylactic Shock

Anaphylactic shock occurs rapidly and is life-threatening. Anaphylactic shock is a systemic, type I hypersensitivity reaction that often has fatal consequences. Anaphylaxis causes the immune system to release a flood of chemicals that can cause a person to go into shock (Reber et al., 2017).

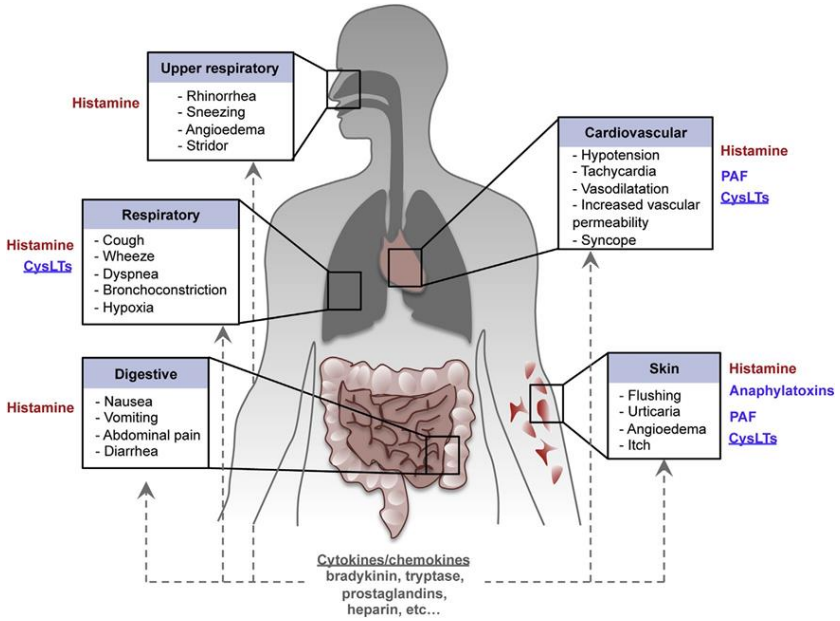

Figure 21. Pathophysiology of Anaphylactic Shock

Anaphylaxis occurs in a person after re-exposure to an antigen for which the person has produced specific IgE antibodies.

1. Re-exposure. Upon re-exposure to a sensitizing allergen, the allergen can crosslink mast cells or allergen-specific IgE bound to the surface of basophils resulting in cellular degranulation as well as de novo synthesis of mediators.
2. Binding. Immunoglobulin E (IgE) binds to antigens (foreign materials that trigger allergic reactions).
3. Activation. Antigen-bound IgE then activates FcεRI receptors on mast cells and basophils.
4. Release of inflammatory mediators. This leads to the release of inflammatory mediators such as histamine.
5. Histamine release. Many signs and symptoms of anaphylaxis are due to the binding of histamine to its

receptors; binding to H1 receptors mediates pruritus, rhinorrhea, tachycardia and bronchospasm.

6. Prostaglandin D2. Prostaglandin D2 mediates bronchospasm and blood vessel dilatation, the main manifestations of anaphylaxis.
7. Leukotriene C4. Leukotriene C4 is converted to LTD4 and LTE4, mediators of hypotension, bronchospasm, and mucus secretion during anaphylaxis in addition to acting as a chemotactic signal for eosinophils and neutrophils.

e. Septic Shock

Sepsis is a systemic response to infection. It is manifested by two or more of the SIRS (Systemic Inflammatory Response Syndrome) criteria as a consequence of documented or presumed infection. Septic shock is associated with sepsis. It is characterized by symptoms of sepsis plus hypotension and hypoperfusion despite adequate fluid volume replacement.

The pathophysiology of sepsis involves an evolving process. The following shows the process of how sepsis works its way inside of our body.

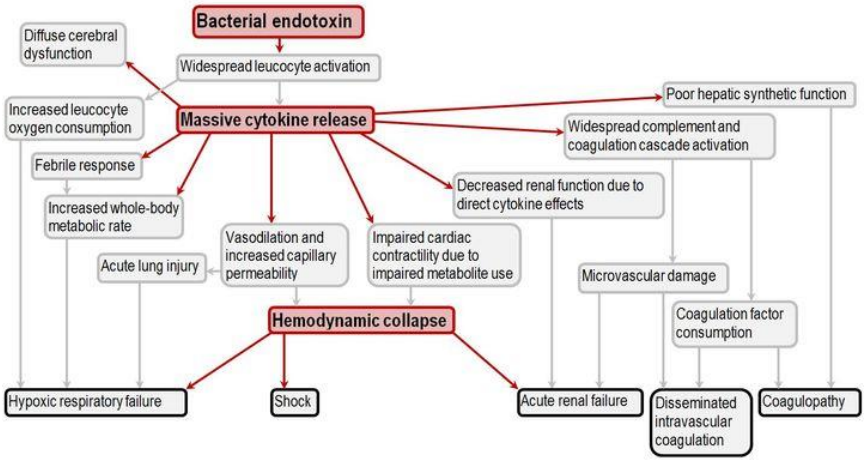

Figure 22. Pathophysiology of Septic Shock

Microorganisms invade the body tissues and in turn, patients exhibit an immune response.

The immune response provokes the activation of biochemical cytokines and mediators associated with an inflammatory response. Increased capillary permeability and vasodilation interrupt the body's ability to provide adequate perfusion, oxygen, and nutrients to the tissues and cells. Proinflammatory and anti-inflammatory cytokines released during the inflammatory response and activates the coagulation system that forms clots whether or not there is bleeding. The imbalance of the inflammatory response and the clotting and fibrinolysis cascades are critical elements of the physiologic progression of sepsis in affected patients.

f. Obstructive Shock

Obstructive shock refers to anatomical obstruction of the major blood vessels of the heart (e.g., superior vena cava, inferior vena cava, and pulmonary veins) leading to decreased venous return and/or excessive afterload (e.g., the force that the left ventricle must overcome to expel blood through the aortic valve), resulting in decreased cardiac output. Shock describes circulatory failure and ineffective tissue perfusion that can lead to reversible cellular injury, or if prolonged, irreversible cellular injury. There are four different types of shock: obstructive, distributive (including anaphylactic, septic and neurogenic shock), cardiogenic, and hypovolemic shock. Shock is a life-threatening condition and requires immediate medical attention (see Figure 23).

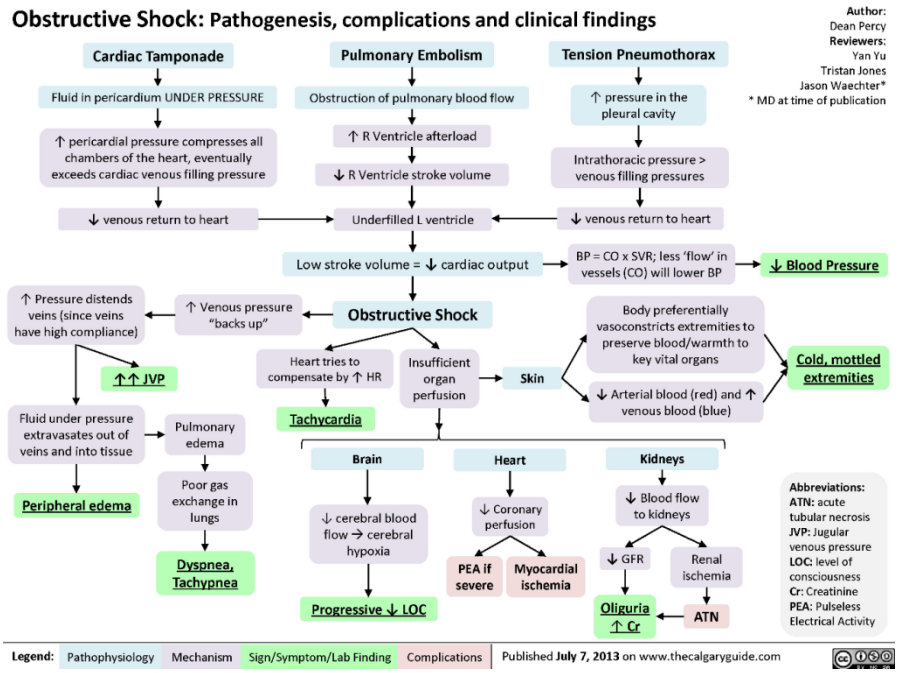

Figure 23. Obstructive Shock: Pathogenesis, Complication and Clinical Findings

g. Distributive Shock

In most cases, inflammatory mediators play a major role in the development of distributive shock. Distributive shock, also known as vasodilatory shock, refers to systemic vasodilation and decreased blood flow to vital organs such as the brain, heart, and kidneys. It can also cause fluid to leak from the capillaries into the surrounding tissues as a result. Distributive shock is one of the four broad classifications of disorders that cause inadequate tissue perfusion. Inflammatory cytokines released in sepsis and toxic shock syndrome induce systemic vasodilation and capillary leakage, as well as cardiomyopathy. Systemic release of histamine in anaphylaxis produces similar effects. The interaction between catecholamines and adrenergic receptors in blood vessels is

critical in other causes of distributive shock. Both norepinephrine and epinephrine stimulate alpha-1 receptors on arterioles to cause vasoconstriction and regulate blood pressure. In the case of neurogenic shock, the sympathetic nervous system is impaired, leading to reduced delivery of catecholamines to these receptors. Cortisol is a key regulator of alpha-1 receptor expression on the arteriolar surface, but this becomes impaired in patients with adrenal insufficiency. As a result, the factors leading to vasodilation and shock are multimodal and complex. This requires careful history taking and physical examination to elucidate the underlying cause and a multi-system approach to treatment (Figure 24).

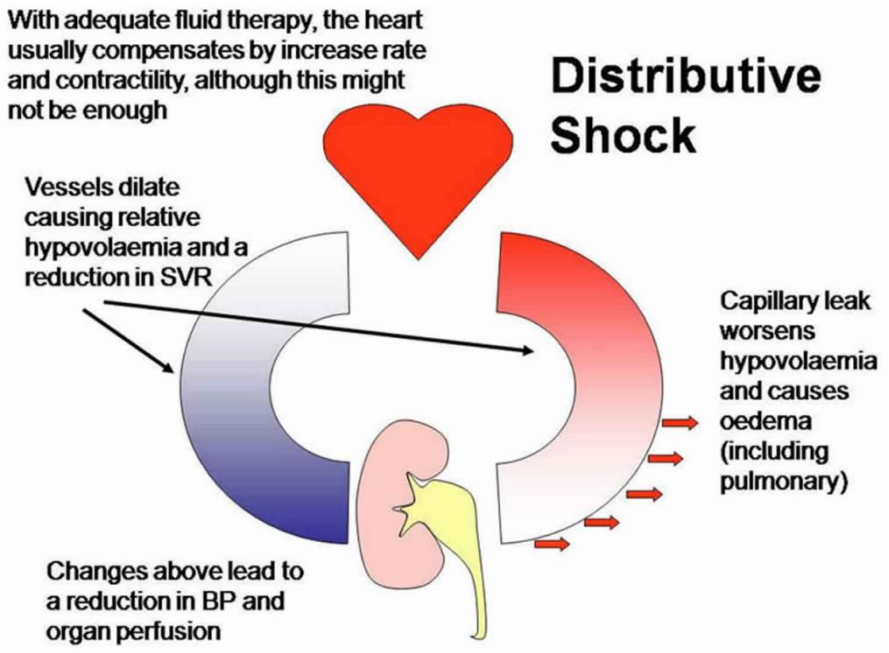

Figure 24. Distributive Shock

1. THE STAGES OF SHOCK

Hypoxia at the cellular level causes a series of physiologic and biochemical changes, resulting in acidosis and a decrease in

regional blood flow, which further worsens the tissue hypoxia. In hypovolemic, obstructive, and cardiogenic shock, there is a decrease in cardiac output and decreased oxygen transport. In distributive shock, there is decreased peripheral vascular resistance and abnormal oxygen extraction. Shock is a spectrum of physiologic changes, ranging from early stages, which are reversible to the final stages, which are irreversible with multiorgan failure and death. Generally, shock has the following three stages, pre-shock, shock, and end-organ dysfunction.

a. **Pre-shock or compensated shock**–As the name suggests, this stage is characterized by compensatory mechanisms to counter the decrease in tissue perfusion. In this stage, vital organ function is maintained by increasing sympathetic reflexes, resulting in increased systemic resistance, increased heart rate resulting in increased CO; and increased secretion of vasopressin, RAAS (renin-angiotensin aldosterone system) which causes the kidneys to retain water and sodium in the circulation. At this stage, the body is still able to compensate for absolute or relative fluid loss. During this phase, the patient is still able to maintain adequate blood pressure as well as cerebral perfusion as the sympathetic nervous system increases heart rate and respiration and delivers blood to the core of the body through vasoconstriction and microcirculation, precapillary sphincters narrow and decrease blood flow to areas of the body with a high tolerance to decreased perfusion, e.g., skin. Clinical symptoms in shock with this compensatory stage are tachycardia, restlessness, coldness, slow capillary filling, agitation and anxiety, narrowed pulse pressure, decreased blood flow to the gastrointestinal (GI) system: nausea, vomiting thirst. The onset of early signs of hypoxia: pale and clammy skin–this is due to a decreased sense of microcirculation.

b. **Shock**–During this stage, most of the classic signs and symptoms of shock appear due to early organ dysfunction, resulting from the progression of the pre-shock stage as the

compensatory mechanisms become insufficient. Decompensated shock is defined as the late phase of shock in which the body's compensatory mechanisms (such as increased heart rate, vasoconstriction, increased respiratory rate) are unable to maintain adequate perfusion to the brain and vital organs. It occurs when blood volume is reduced by more than 30%. The patient's compensatory mechanisms actively fail and cardiac output decreases resulting in decreased blood pressure and cardiac function. Several mechanisms occur in the decompensation phase, such as worsening tissue perfusion leading to a significant decrease in O2, resulting in anaerobic metabolism so that lactate production increases causing lactic acidosis. This condition is aggravated by the accumulation of CO2 which becomes carbonic acid. Acidemia will inhibit myocardial contractility and response to catecholamines. In addition, there is a metabolic disturbance of the energy dependent Na+/K+ pump at the cellular level, causing cell membrane integrity to be compromised, lysosomal and mitochondrial function to deteriorate which can result in cell damage. In this decompensated stage, blood flow is slow, the kinin chain and coagulation system are damaged, which will be exacerbated by platelet aggregation and thrombus formation with the risk of bleeding. The release of vascular mediators, such as histamine, serotonin and cytokines, leads to the formation of oxygen radicals and platelet aggregating factors. The release of mediators by macrophages causes vasodilation of arterioles and increased capillary permeability, thus decreasing venous return and preload which results in decreased cardiac output. Symptoms in this decompensated stage include tachycardia, very low blood pressure, poor peripheral perfusion, acidosis, oliguria, and decreased consciousness. Altered mental status, tachypnea, labored and irregular breathing, weak to absent peripheral pulse, decreased body temperature, and cyanosis.

c. **End-organ dysfunction**–This is the final stage, leading to irreversible organ dysfunction, multiorgan failure, and death. This stage is an advanced stage of shock that does not receive proper and sustainable treatment. Irreversible shock is the terminal phase of shock. This phase is the point of no return as there is rapid damage to the cardiovascular system and the patient's compensation mechanisms have failed. At this stage, there will be damage and cell death that can result in MOF (multiple organ failure). At this stage, the body will run out of energy due to the depletion of ATP (adenosine triphosphate) reserves in the cells. Clinical symptoms of this stage include palpable pulse, unmeasured blood pressure, anuria, and signs of organ failure MODS–multiple organ dysfunctions).

5. COMPLICATIONS OF SHOCK

Shock is a serious medical condition that occurs when there is insufficient blood flow to the body's organs and tissues, resulting in an inadequate supply of oxygen and nutrients. Complications of shock can vary, depending on the type of shock and the severity of the condition. The following are some of the common complications associated with shock:

1. Organ Dysfunction/Failure: Prolonged or severe shock can lead to dysfunction or failure of vital organs such as the heart, lungs, kidneys, liver or digestive system. Inadequate blood flow and oxygen supply can lead to cellular damage and dysfunction.
2. Acute Respiratory Distress Syndrome (ARDS): In severe cases of shock, the lungs may be affected, leading to ARDS. ARDS is characterised by severe lung inflammation and impaired oxygen exchange, resulting in respiratory failure.
3. Kidney Injury: Shock can lead to reduced blood flow to the kidneys, leading to acute kidney injury (AKI). AKI can lead to decreased urine output, electrolyte imbalance and build-up of waste products in the blood.

4. Disseminated Intravascular Coagulation (DIC): DIC is a condition where the blood clotting mechanism becomes overactive and widespread clotting occurs throughout the body. This can deplete clotting factors and cause abnormal bleeding.
5. Multiple Organ Dysfunction Syndrome (MODS): In severe shock, multiple organ systems can be affected, leading to a condition called multiple organ dysfunction syndrome. This occurs when two or more organs fail and can be life-threatening.
6. Infections: Shock weakens the immune system, making the body more susceptible to infections. Sepsis, a severe systemic infection, is a common complication of shock.
7. Heart Arrhythmia: Electrocution can disrupt the normal electrical activity of the heart, leading to abnormal heart rhythms, such as ventricular tachycardia or fibrillation.
8. Metabolic Acidosis: Inadequate tissue perfusion during shock can lead to the build-up of lactic acid and other acidic metabolites, leading to metabolic acidosis.
9. Neurological Complications: Prolonged or severe shock can affect the brain, leading to cognitive impairment, confusion, delirium or even coma.

It is important to note that specific complications may vary depending on the underlying cause of the shock (e.g., septic, cardiogenic, hypovolaemic, etc.) and individual patient factors. Prompt and appropriate management of shock is essential to minimise the risk of complications and improve outcomes.

SUMMARY

Shock is a life-threatening manifestation of circulatory failure. Circulatory shock leads to cellular and tissue hypoxia resulting in cellular death and dysfunction/failure of vital organs. Effects of shock are reversible in the early stages, and a delay in diagnosis and/or timely initiation of treatment can lead to irreversible changes, including multiorgan failure (MOF) and death. Based on the components of the circulatory system, there are several

types of shock: hypovolemic Shock, cardiogenic shock, obstructive shock, distributive shock, septic shock, anaphylaxis shock, and neurogenic shock. Hypovolemic shock, the most common type of shock, is caused by insufficient circulating volume, usually as a result of bleeding, although severe vomiting and diarrhea are also potential causes. Cardiogenic shock is caused by the failure of the heart to pump properly, either due to heart muscle damage through myocardial infarction or through heart valve problems, congestive heart failure, or dysrhythmias. Obstructive shock is caused by the obstruction of blood flow outside the heart. This usually occurs due to decreased venous return, but can also be caused by aortic blockage. Distributive shock is caused by abnormal distribution of blood to tissues and organs, and includes septic, anaphylactic and neurogenic causes. Septic shock is the most common cause of distributive shock and is caused by excessive systemic infection that cannot be cleared by the immune system, resulting in vasodilation and hypotension. Anaphylactic shock is caused by a severe reaction to an allergen, leading to the release of histamine which causes widespread vasodilation and hypotension. Neurogenic shock results from damage to the central nervous system, which impairs cardiac function by reducing heart rate and loosening vascular tone, resulting in severe hypotension. As evaluating a patient in shock, there are some clinical signs and symptoms must be assessed regardless of which classification of shock you are dealing with. These symptoms include: weakness, feeling thirsty, pallor, tachycardia, diaphores, decrease urine output, weaken peripheral pulse, hypotension, altered consciousness, and respiratory arrest. Complications of shock can vary, depending on the type of shock and the severity of the condition. The following are some of the common complications associated with shock: organ dysfunction/failure, acute respiratory distress syndrome (ARDS), kidney injury, Disseminated Intravascular Coagulation (DIC), Multiple Organ Dysfunction Syndrome (MODS), infections, heart arrhythmia, metabolic acidosis, and neurological complications

KEY TERMS

Shock

Classifications and Causes of Shock

The Four Classifications of Shock

General Assessments for Shock
Pathophysiology of Shock
The Stages of Shock
Complications of Shock
Opportunistic and Nosocomial Infections

REVIEW QUESTION
ASSIGNMENT

Have a discussion with your friends about the cases below, then present the cases that have been discussed. Here is a situation that can be discussed about Shock:

Situation:
A 60-year-old male patient, Mr. Johnson, presented to the emergency department with complaints of severe chest pain and shortness of breath. Mr. Johnson had a history of coronary heart disease and had undergone angioplasty. He also had type 2 diabetes which was controlled with oral hypoglycaemic medication. On examination, Mr. Johnson's blood pressure was recorded as 80/50 mmHg, pulse rate of 130 beats per minute, and rapid breathing with oxygen saturation of 88% in room air. He looks agitated and pale.

Discuss the following with the nursing students:

1. Identify the possible types of shock experienced by Mr. Johnson based on the signs and symptoms.
2. Explain the pathophysiology of the shock that occurred in this patient.
3. Discuss the risk factors that can lead to shock in patients like Mr. Johnson.
4. List the emergency care steps that need to be taken to manage shock in this patient.
5. How can nurses support and care for patients with shock?
6. Discuss the possible complications of shock in this patient.

7. List the signs and symptoms that need to be monitored periodically to monitor the patient's response to treatment and identify worsening of the condition.

FORMATIVE TEST

1. Shock is a medical condition characterised by:
   a) High blood pressure
   b) Low blood pressure
   c) Slow heartbeat
   d) Rapid heartbeat

2. Cardiogenic shock results from:
   a) Excessive bleeding
   b) Heart failure
   c) Systemic infection
   d) Significant fluid loss

3. Risk factors that can lead to hypovolaemic shock include:
   a) Renal failure
   b) Heart disease
   c) Significant blood loss
   d) Lung infection

4. Neurogenic shock results from disorders of:
   a) Respiratory system
   b) Nervous system
   c) Digestive system
   d) Circulatory system

5. One of the signs and symptoms of shock is:
   a) Increased body temperature
   b) Decrease in body temperature
   c) Increased appetite
   d) Decreased frequency of breathing

6. The first steps to be taken in handling shock are:
    a) Provide oxygen
    b) Inserting an intravenous drip
    c) Address the cause of shock
    d) Assist the patient to lie down

7. Septic shock is caused by:
    a) Significant blood loss
    b) Bacterial infection in the blood
    c) Renal failure
    d) Myocardial infarction

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UNIT 10. GENETIC DISORDERS AND INTERACTIONS

LEARNING OBJECTIVES

After mastering the contents of this chapter, you will be able to:

1. Define the genetic disorders
2. State the classification of genetic disorders
3. Explain genetic disorders and diseases caused by dominant body chromosome factors
4. Explain genetic disorders and diseases caused by autosomal recessive factors
5. Explain genetic disorders and diseases linked to sex chromosomes/gonosomes
6. Explain genetic disorders and diseases caused by the effect of chromosomal aberrations
7. State the test to determine genetic abnormalities

a. Definition

Genetics is also called the science of heredity, derived from the word *genos* (Latin), meaning tribe–nation or origin–origin. Etymologically, the word genetics means the origin of events. Genetics is the science of inheritance of traits, as well as the variations that may arise therein.

Genetic disorders are deviations from the general or average human nature, and are diseases that arise due to the malfunction of genetic factors that regulate the structure and physiological functions of the human body (McPhee et al., 2005). Genetic diseases are determined genetically, environmentally, or both genetic and environmental.

b. Classification of Genetic Disorders

Genetic material is packaged inside the cell nucleus in a nuclear material called chromatin. When the cell divides, the genetic material in the nucleus condenses into rod-shaped structures known as chromosomes. Total human DNA is packed into 46

chromosomes. These 46 chromosomes include 22 pairs of the same chromosome, or homologous chromosomes called *autosomes* and two *sex* chromosomes, X and Y. Females have two X chromosomes (XX) and males have two Y and X chromosomes (XY).(McPhee et al., 2005). Each chromosome has distinctive size and shape that allows numbering and identification of individual chromosomes.

Chromosomal abnormalities result from an excess or deficiency of an entire chromosome or a portion of a chromosome. There are many documented chromosomal numerical and structural abnormalities in human karyotypes, many of which are associated with down syndrome(Wilkins., 2013).

The following is a classification of genetic disorders that are inherited through autosomal chromosomes and these diseases can affect anyone.

a. Genetic disorders and diseases caused by dominant body chromosome factors
b. Genetic disorders and diseases caused by autosomal recessive factors
c. Genetic disorders and diseases linked to sex chromosomes/gonosomes
d. Genetic disorders and diseases caused by the effect of chromosomal aberrations

1. Genetic disorders and diseases caused by dominant body chromosome factors. Genetic disorders and diseases caused by dominant body chromosome factors are diseases that are inherited through autosomal chromosomes and are independent of gender. Therefore, these diseases can affect anyone. Autosomal dominant inherited diseases, abnormalities will be seen in homozygous dominant or heterozygous dominant states(Kuba & Kubová, 2005). Some types include polydactyly, syndactyly, and huntington.:

a. ***Polydactyly*** is a condition where the number of fingers or toes is more than 10. There are additional fingers on one or both hands/feet. The place of the extra finger is

different, some are found near the thumb and some are found from the little finger. This condition is caused by polydactyly genotypes that are PP or Pp, while the norm is pp.

Figure 25. Polydactyly

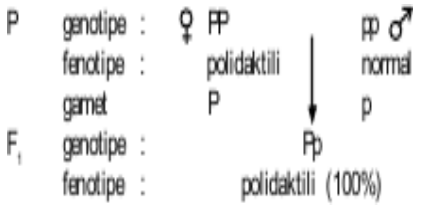


Figure 26. Inheritance of the Polydactyly Trait

b. ***Syndactyly*** is a condition where the fingers stick together because the gene that regulates cell apoptosis is disrupted(Nair, 2009). The syndactyly gene in normal conditions is ss, while the syndactyly gene in patients with attached fingers is SS or Ss.

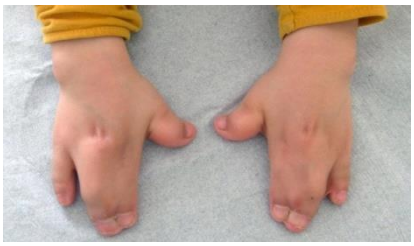


Figure 27. Syndactyly

c. ***Huntington*** disease is a genetic disorder that results in progressive dementia, motor disorders such as chorea, dystonia, and psychiatric disorders(Hammer, 2018). This fatal neurodegenerative disease

This fatal neurodegenerative disease is caused specifically by the expansion of the Cyanine-Adenine-Guanine (CAG) trinucleotide sequence that causes mutations of the Huntingtin gene (HTT) on chromosome 4. The disease is inherited in an autosomal dominant manner that depends on gender. Offspring of an individual with the mutant allele have a 50% risk of developing the disease by as much as 50%. Huntington is a progressive nerve damage that can cause the sufferer's body movements to be disrupted. Patients shake their head in one direction.

2. **Genetic disorders and diseases caused by autosomal recessive factors.** Genetic disorders and diseases caused by autosomal recessive factors is an inherited or hereditary disease linked to a recessive body chromosome(Kuba & Kubová, 2005). Abnormalities will be seen in a recessive state how many types include albino, phenylketonuria, thalassemia, and sickle cell anemia.

   a. **Albino**

   Albino comes from *albus* which means white. Abnormalities occurs because the body is unable to form the enzyme needed to convert the amino acid tyrosine into beta- 3,4- dihydroxyphenylalanine to be converted into melanin pigment. Albinos occur due to a failure in the formation of melanin pigment which serves to protect against UV rays. The albino genotype is aa. Unlike the normal genotype which is AA and the normal genotype with the albino gene is Aa (Huether et al., 2020). Characteristics of Albino sufferers include:

   1) have abnormal skin and hair (milky white/pale white),
   2) have pink or blue iris with red pupils (not all),

3) loss of melanin pigment in the eyes, skin, and hair,
4) Extreme near-sightedness and farsightedness, and
5) they always keep their eyelids half closed by always blinking.

The albino trait is carried by recessive factors contained in the body chromosomes (autosomes). An albino child can be born from a pair of parents who are both heterozygous normal or from a pair of normal and albino. Below is an example of a marriage between an albino and a normal carrier.

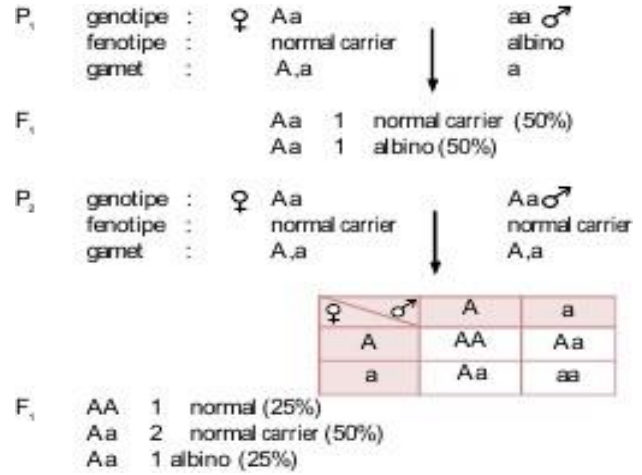


Figure 28. Inheritance of the Albino Trait

b. Phenylketonuria

Phenylketonuria is a deficiency of the enzyme phenylalanine hydroxylase. The enzyme functions to convert the amino acid phenylalanine into tyrosine. This leaves the body with an excess of phenylalanine. Symptoms of the disease are characterized by the accumulation of amino acids in the blood which are mostly wasted through urine, mentally retarded (IQ > 30) white hair, bluish eyes (poor melanin production), a typical body shape like a psychotic person, jerky movements, and musty body odor.

c. ***Thalassemia***

Thalassemia comes from the word *thalasa* which means sea and anemia. Thalassemia is a genetic disorder characterized by reduced or no hemoglobin chain synthesis, so it has little ability to bind oxygen. There is an abnormality in the formation of hemoglobin resulting in a small number of red blood cells. In addition, the blood cells are abnormally shaped and small in size**.**

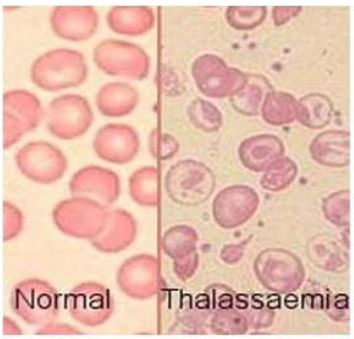


Figure 29. Thalassemia and Inheritance of Thalassemia Traits

d. Sickle cell anemia

Sickle cell anemia is also known as sicklemia. In this type of anemia, the erythrocytes are crescent-shaped so that they cannot circulate oxygen properly to all parts of the body. When the blood oxygen content of the affected individual is low (e.g., at high altitudes or under physical strain), the sickle cell hemoglobin will change the shape of the red blood cells into a crescent shape. Individuals suffering from sickle cell anemia are symbolized by ss. While normal individuals have the SS genotype and sickle cell anemia carriers are symbolized by Ss.

3. **Genetic disorders and diseases linked to sex chromosomes/gonosomes.** The genetic disorders and diseases linked to sex chromosomes/gonosomes has principles of inheritance:

   a. A man with an X chromosome abnormality will not pass it on to his son, only to his daughter.

   b. A woman suffering from an X chromosome related disorder will be passed on to all her children.

   c. A woman is a carrier of a disorder related to the X chromosome, the probability of her sons suffering from the disorder is 50%, while the daughter is 50% normal and 50% carrier.

   Gonosomal abnormalities are also divided into:

   a. Abnormalities caused by being linked to the X chromosome, consists of the following:

      1) Hemophilia

      This disorder causes the body to be unable to make proteins necessary for blood clotting. People with hemophilia can bleed to death from a small cut. Generally, a normal person's wound will close (blood will clot) within 5-7 minutes. But in people with hemophilia, the blood will clot 50 minutes to 2 hours, so it is easy to cause death due to too much blood loss. Females who are homozygous recessive for this gene are the sufferers (XhXh), while females who are heterozygous for this gene are the sufferers (XhXh) his blood coagulation is normal but he only acts as a carrier. A male patient has only one genotype (XhY).

Figure 30. Hemophilia

Hemophilia is divided into 3, namely:

a) Hemophilia A, because the patient does not have anti-hemophilic globulin (factor VIII). This type is found in ± 80% of people with hemophilia. A normal person is able to form anti-hemophili globulin (AHG) in their blood serum because they have the dominant H gene, while the recessive allele cannot form the substance.

b) Hemophilia B (Christmas), because the patient lacks the plasma component thromboplastin (KTP or factor IX) Christmas is named after a boy who was injured when Britain was bombed by Germany during World War II. Present in ± 20% of hemophiliacs.

c) Hemophilia C, because patients are unable to form plasma thromboplastin antecedent (PTA). This disease is not caused by an X-linked recessive gene, but by a recessive gene that is rarely found on autosomes. It occurs in only a small number of patients. No more than 1%. Small, with available factor activity levels of less than 5%.

2) Color blindness

Color blindness is a hereditary disease that causes sufferers to be unable to distinguish

certain colors. There are two types of color blindness, partial color blindness and total color blindness. In partial color blindness, the person is unable to distinguish only a few colors. For example, red-green and blue-green. As for total color blindness, the person cannot distinguish all types of colors. Color blindness is caused by the recessive color blindness (cb) gene on the X chromosome X. Therefore, there are several genotype combinations that can occur.

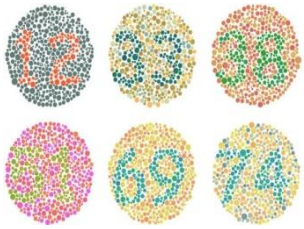


Figure 31. Example of a Color Blindness Test

Normal females have homozygotic dominant BB and heterozygotic Bb genotypes, while those with color blindness are homozygotic recessive bb. Males have only one X-chromosome, so can only be normal XY or color blind XbY. Color blindness genotypes:

Gender	Genotype	Fenotipe
Male	X^BY	Normal
	X^bY	color blindness
Women	X^BX^B	Normal
	X^BX^b	Normal *carrier* (carrier)
	X^bX^b	color blindness

Marriage between a colour-blind carrier woman and a normal man P_1:

♀ X^BX^b X ♂ X^BY

Gamet : X^B X^b X^BY

1 1

♀ ♂	X^B	Y
X^B	X^BX^B (normal)	X^BY (normal)
X^b	X^BX^b (carrier)	X^bY (buta warna)

b. Abnormalities caused by being linked to the X chromosome, consists of hypertrichosis, webbed toes, and hystrix gravior.:

1) Hypertrichosis

Figure 32. Hypertrichosis

Hypertrichosis is a hereditary trait, which is the growth of hair in certain parts of the earlobe. The cause of Hypertrichosis is a recessive gene (h) that is attached to the Y chromosome so that this hereditary trait is only possessed by males(McPhee et al., 2005).

2) Webbed toes

Webbed toes affect the feet-the joining of two or more toes. It is normal in many birds, such as ducks; amphibians, such as frogs; and some mammals, such as kangaroos. In humans, it is rare, and only happened once in about 2,000 to 2,500 live births; generally, the second and third toes are webbed (held together by skin and flexible tissue), which can extend to some or almost all of the toes.

The exact cause of this condition is unknown. In some cases, close family members may develop the condition. In other cases, no one else has the condition. The scientific name for this condition is syndactyly, although the term includes both webbed fingers and webbed toes. Syndactyly occurs when apoptosis or programmed cell death during gestation is absent or incomplete.

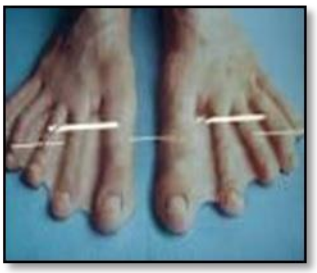


Figure 33. Weebed Toes

3) Hystrix gravior

The term has been used to describe several distinct, rare, and severe keratinizing disorders characterized by massive hyperkeratosis. The term has also been used to describe localized, linear warty epidermal nevi that are sometimes associated with mental retardation, seizures, or bone abnormalities.

- Ichthyosis hystrix gravior–lambert type, a condition characterized by hyperkeratosis covering the entire body except the face, genitals, palms and soles(Nair, 2009). It was first described in the lambert family in England in the early 18th century.
- Ichthyosis hystrix gravior–curth-macklin type, a disorder characterized by hystrix-like changes and keratosis of the palms and soles. the histological findings are different from all other ichthyoses.
- Ichthyosis hystrix gravior–rheydt type, a condition consisting of keratoses mainly on the extremities including the flexor surfaces and to a lesser extent the facial ears. Alopecia and hair and nail abnormalities and inner ear deafness are also seen in these patients.

Figure 34. Hystrix Gravior

4. Genetic disorders and diseases caused by the effects of chromosome aberrations

Chromosomal aberrations (chromosomal mutations) are changes that occur in the number or arrangement of chromosomes in a cell due to loss, rearrangement or duplication of genetic material. These changes can result in hereditary changes in the characteristics of an organism that experiences them (McPhee et al., 2005).

Two types of chromosomal aberrations are a number of aberrations which are changes in one type of chromosome, and arrangement changes which are changes in the structure of chromosome arms. Examples of disorders caused by chromosomal aberrations is Turner syndrome with karyotype (22AA+X0) that has 45 chromosomes due to the loss of 1 sex chromosome (gonosome). Patients with this disorder are female but do not have ovaries, the internal genitals are late in development (infertile) and imperfect, sterile, both nipples are widely spaced, the breasts do not develop, the body tends to be short (approximately 120 cm), the chest is wide, the neck is short, has sagging on the neck, and is mentally retarded. Incidence rate of this disorder is 1 in 2,500 women.

1) **Klinefelter syndrome with karyotype (22 AA+XXY)**

   Klinefelter syndrome with karyotype (22 AA+XXY) has 47 chromosomes due to trisomic sex chromosomes (has 3 sex chromosomes with 2 X chromosomes)(Willis et al., 2014). Patients with this syndrome are male but tend to be like female, with small testicles and barren, enlarged breasts, narrow chest, wide hips, body hair does not grow, their bodies tend to be tall (long arms and legs), mentally retarded.

2) **Jacobs syndrome with karyotype (22AA+XYY)**

   Jacobs syndrome with karyotype (22AA+XYY) has 47 chromosomes due to trisomic in the sex chromosome (has 3 sex chromosomes with 2 Y chromosomes). Patients experience speech delay as a child, delayed motor development, and muscle weakness. As adults, they are below average height and weight, have emotional problems, develop severe acne, and develop autism. Patients generally have a small head with a flat forehead, a wider and rounder nose, abnormal ears, and heart and brain

abnormalities.

3) **Edward syndrome with karyotype (45A+XX/XY)**

Edward syndrome with karyotype (45A+XX/XY) has 47 chromosomes due to trisomic body chromosome number 18. This syndrome causes abnormalities of the head, hands, heart, kidneys, ear defects, and impaired body growth. It generally only reaches the age of 6 months.

4) **Down syndrome with karyotype (47, XX or 47, XY)**

Down syndrome with karyotype (47, XX or 47, XY) has 47 chromosomes due to trisomic body chromosome 21. This syndrome causes short stature, small head, flat nose, and a face that always seems to be smiling. The most common syndrome in Indonesia. All sufferers have a similar face.

c. Test to determine genetic abnormalities

Scientists have developed a number of tests to determine if a fetus is developing normally, i.e., prenatal diagnosis, carrier testing, preimplantation diagnosis, newborn screening, and predictive testing.

1) **Prenatal diagnosis**

Prenatal diagnosis is a measure to look at the health condition of the unborn fetus. Methods used include:

a) Amniocentesis

A prenatal medical procedure by suctioning and testing a sample of amniotic fluid (amniotic fluid) to find whether the fetus has chromosomal or metabolic abnormalities. Amniocentesis is performed between the 12th and 16th week of pregnancy. The earlier it is performed the more useful it is in deciding whether the pregnancy should be terminated.

b) Ultrasound Sonography (USG)

A prenatal medical procedure that directs high-frequency waves to a pregnant woman's abdomen. The echoes are transferred into a visual display of the inner structure of the fetus.

c) Chorionic villus test (CTV)

A prenatal medical procedure that removes a small sample of the placenta between the 8th and 11th week of pregnancy.

d) Maternal blood test

A form of prenatal diagnostics used to measure blood alpha protein levels and associated with neural tract abnormalities.

2) Carrier testing

Carrier testing is a test to determine if a person harbors a gene that carries a genetic disorder. The method used to carry out the test is a simple blood test to see the levels of enzymes related to certain genetic disorders, or by checking the DNA, whether it contains certain abnormalities(Murray et al., 1964).

3) Preimplantation diagnosis

Preimplantation diagnosis is a test that involves in vitro fertilization to determine the levels of genetic abnormalities of the preimplantation embryo. Usually, a woman who will do the test will be given certain drugs to stimulate excessive egg production. The eggs will be retrieved and placed in a dish to be fertilized by donor sperm. After fertilization, the embryo cells formed will be analyzed for genetic abnormalities.

4) Newborn screening

Newborn screening is the examination of babies at the time of new birth. This examination includes genetic, endocrinology, metabolic, and hematology examinations. It is hoped that this examination can determine the future prognosis, so that the appropriate treatment can be pursued.

5) Predictive testing

Predictive testing is a test used to test if someone has a genetic disorder by looking at previous family genetic history. This test is done after birth, and is also commonly referred to as presymptomatic testing.

SUMMARY

Genetics is the study of the inheritance of traits, as well as the variations that may arise in them, while genetic disorders are deviations from common or average human traits. Genetic disorders and diseases can be classified as follows:

1. Abnormalities and diseases caused by dominant body chromosome factors
2. Abnormalities and diseases caused by autosomal recessive factors
3. Genetic disorders and diseases associated with chromosomes/gonosomes
4. Abnormalities and diseases caused by the effects of chromosomal aberrations 4.

Abnormalities and diseases caused by dominant body chromosome factors include: polydactyly, syndactyly and Huntington. Abnormalities and diseases caused by autosomal recessive factors include: albino, phenylketonuria, thalassaemia, and sickle cell anaemia. Kinetic disorders and diseases associated with chromosomes/gonosomes include: Haemophilia, colour blindness, hypertrichosis, webbed toes, and hystrix gravio. Abnormalities and diseases caused by chromosomal abnormalities include: Turner syndrome with karyotype (22AA+X0), Klinefelter syndrome with karyotype (22 AA+XXY), Jacobs syndrome with karyotype (22 AA+XXY), and Klinefelter syndrome.

Jacobs syndrome with a karyotype of (22AA+XYY), Edward syndrome with a karyotype of (45A+XX/XY), Down syndrome with karyotype (47, XX or 47, XY). To find out if there is an abnormality, several tests can be performed, namely Prenatal Diagnosis, Carrier Tests, Preimplantation Diagnosis, Newborn Screening and Predictive Tests.

KEY TERMS

Genetic disorders

Genetic classification of genetic disorders

Genetic disorders and diseases caused by dominant body chromosome factors

Genetic disorders and diseases caused by autosomal recessive factors

Genetic disorders and diseases linked to sex chromosomes/gonosomes

Genetic disorders and diseases caused by the effect of chromosomal aberrations

Test to determine genetic abnormalities

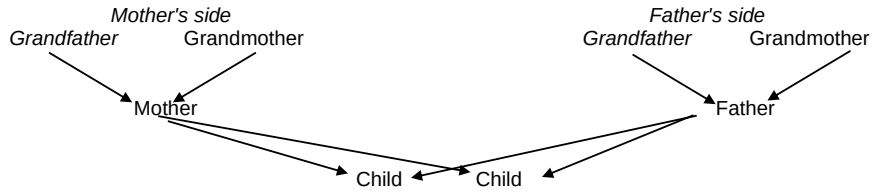
REVIEW QUESTION

FORMATIVE TESTS

Assignment

Have a discussion with your friends about the cases below, then present the cases that have been discussed.

What is the probability of a child receiving allele pairs from both grandparents as shown in the following chart?



Questions:

a. In human sex ratio theory, it is known that colour blindness is more common in males than females, explain the meaning of this statement with a mating diagram!

b. Explain the difference between Mendel's law and Morgan's law!

FORMATIVE TEST

1. What causes Down syndrome?
    a. Mutations in the BRCA1 gene
    b. Deficiency of glucosidase enzyme
    b. Errors in the formation of sex chromosomes

c. Excess chromosome 21

2. What causes haemophilia?
   a. Deficiency of blood clotting factors
   b. Mutation in the p53 gene
   b. Presence of an extra X sex chromosome
   c. Red blood cell deficiency

3. What causes phenylketonuria (PKU)?
   a. Insulin hormone deficiency
   b. Mutation in the BRCA2 gene
   b. Deficiency of phenylalanine hydroxylase enzyme
   c. Presence of an extra chromosome 18

4. What causes Duchenne muscular dystrophy?
   a. Deficiency of dystrophin protein
   b. Mutation in the RB1 gene
   b. Excess Y sex chromosome
   c. Lack of lactase enzyme

5. What causes Turner syndrome?
   a. Growth hormone deficiency
   b. Mutation in the CFTR gene
   b. Presence of an extra Y sex chromosome
   c. Lack of X sex chromosome

6. What causes Klinefelter's syndrome?
   a. Deficiency of thyroid hormone
   b. Mutation in the BRCA1 gene
   b. Presence of an extra Y sex chromosome
   c. Lack of X sex chromosome

7. What causes thalassaemia?
   a. Deficiency of haemoglobin

b. Mutation in BRCA2 gene
b. Excess X sex chromosome
c. Lack of chromosome 21

8. What causes cystic fibrosis?
   a. Mutation in the CFTR gene
   b. Blood clotting factor deficiency
   b. Presence of an extra X sex chromosome
   c. Lack of collagen protein

9. What causes Marfan syndrome?
   a. Insulin hormone deficiency
   b. Mutation in the BRCA1 gene
   b. Excess Y sex chromosome
   c. Deficiency of fibrillin protein

10. What causes Fragile X syndrome?
    a. Growth hormone deficiency
    b. Mutation in the FMR1 gene
    b. Presence of an extra X sex chromosome
    c. Deficiency of keratin protein

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