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Ministry of Labor and Skills

ANIMAL HEALTH

LEVEL II

BASED ON MARCH 2022, VERSION 4 OCCUPATIONAL STANDARD



Module Title: - Identifying Pathological Lesions

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Introduction to the module

This Module covers the knowledge, skills and attitude required to identify gross pathological lesions and used in the diagnosis of wide range of animal health disorders.

LG #4	LO #1- Identify gross pathological lesions and terminologies

Instruction sheet

This learning guide is developed to provide you the necessary information regarding the following content coverage and topics:

- Introduction to general veterinary pathology
- Pathological terminologies
- Indicators of cell damage and types of necrosis
- Gross pathological lesions on ante mortem examination and Post mortem examination

This guide will also assist you to attain the learning outcomes stated in the cover page. Specifically, upon completion of this learning guide, you will be able to:

- Describe Concepts of pathology
- Identify associated technical pathological terminologies clearly.
- Identify Changes indicative of cell damage including degeneration and necrosis.
- Mention and describe Gross pathological lesions that can be detected on ante mortem animals.
- Mention and describe Gross pathological lesions that can be detected on post mortem animals

Learning Instructions:

1. Read the specific objectives of this Learning Guide.
2. Follow the instructions described below.
3. Read the information written in the information Sheets
4. Accomplish the Self-checks

Information Sheet 1

1.1. Introduction to general veterinary pathology

Pathology is the study of the way diseases and illnesses develop or the study of the causes and effects of disease or injury. It investigates the essential nature of disease and is usually summarized as the study of the functional and morphological changes in the tissue and fluids of the body during disease.

- **Disease** is a state in which some part of the body is not functioning properly or it is an altered (deranged) normal physiological activity of the body or is a condition in which an individual shows an anatomical, chemical or physiological deviation from the normal. (Discomfort with environment & body). Pathology gives explanations of a disease by studying the following four aspects of the disease. This means

- the study of the essential nature of diseases and especially of the structural and functional changes produced by them studied animal pathology
- something abnormal:
- The structural and functional deviations from the normal that constitute disease or characterize particular disease the pathology of pneumonia.
- Deviation from propriety or from an assumed normal state of something nonliving or non-material.

Veterinary Pathology is: The study of animal disease in a variety of species, often with human implications. Pathology provides the scientific foundation for the practice of medicine by studying the aetiology and pathogenesis of disease at all levels. It is Crucial in determining cause of animal disease and its risk to human health (at the forefront of the One Health concept). It also Studies range from live animals to specific proteins involved in disease.

Pathology is the study of the anatomical, chemical and physiological alterations from normal as a result of disease in animals. It is a key subject because it forms a vital bridge between preclinical sciences (Anatomy, Physiology, and Biochemistry) and clinical branches of medicine and surgery.

Pathology is derived from a Greek word pathos = disease, logos= study. It has many branches, which are defined as under:

Notes: Health, illness and disease differences are:

- **Health** is a state of an individual living in complete harmony, with his environment; surroundings.
- **Illness** is the reaction of an individual to disease in the form of illness.

1.2. Pathological terminologies

Generally study personnel will find the language that pathologists use perplexing and esoteric. This is not a reflection on the ability of the study personnel! Although difficult for non-pathologists to understand, the complex language of pathology is used to convey precisely the observations made by the pathologist. In general, necrosis, degeneration and vacuolation are given the suffix '-opathy' (a general term indicating a pathologic necrotic or degenerative condition in a specific organ). This is preceded by the organ name (generally in Greek), indicating the tissue or organ affected. An example is 'nephropathy', which indicates necrosis or degeneration in the kidney ('nephros'). Qualifiers such as distribution, duration, severity and type of cell involved are used to 'build a diagnosis'; for example, 'multifocal, chronic, severe nephropathy'. The following are some of the general terms that we convey communication between in the working environmental area of pathology.

- **Pathogenesis** is the progressive development of a disease process. It starts with the entry of cause in body and ends either with recovery or death. It is the mechanism by which the lesions are produced in body.
- **Etiology** is the study of causation of disease.
- **Inflammation:** is a protective response to rid the body of the cause of cell injury and the resultant necrotic cells that cell injury produces. It is the body's mechanism for coping with agents that could damage it.
- **Necrosis**: (from Ancient Greek νέκρωσις (nékrōsis) 'death') is a form of cell injury which results in the premature death of cells in living tissue by autolysis.

- **Oedema**: also spelled oedema, and also known as fluid retention, dropsy, hydropsy and swelling, is the build-up of fluid in the body's tissue. Most commonly, the legs or arms are affected.
- **Cancer** is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body.
- **Jaundice:** also known as icterus, is a yellowish or greenish pigmentation of the skin and sclera due to high bilirubin levels
- **Homeostasis** is the mechanism by which body keeps equilibrium between health and disease. E.g. Adaptation to an altered environment.
- **Diagnosis** is an art of precisely knowing the cause of a particular disease (Dia= thorough, gnosis= knowledge).
- **Symptoms:** any subjective evidence of disease of animal characterized by an indication of altered bodily or mental state as told by owner (Complaints of the patients).
- **Signs:** indication of the existence of something, any objective evidence of disease, perceptible to veterinarian (Observations of the clinicians).
- **Syndrome**: a combination of symptoms caused by altered physiological process.
- **Lesion** is a pathological alteration in structure or function that can be detectable.
- **Incubation period** is the time elapses between the action of a cause and manifestation of disease.
- **Course of disease** is the duration for which the disease process remains till fate either in the form of recovery or death.
- **Prognosis** is an estimate by a clinician of probable severity/outcome of disease.
- **Morbidity rate** is the percentage/ proportions of affected animals out of total population in a particular disease outbreak. E.g. out of 100 animals, 20 are suffering from diarrhoea. The morbidity rate of diarrhoea will be 20%.
- **Mortality rate** is the percentage/ proportions of animals out of total population died due to disease in a particular disease outbreak. e.g. In a population of 100 animals, 20 falls sick and 5 died. The mortality rate will be 5%.
- **Case fatality rate** is the percentage/ proportions of animals died among the affected animals. In a population of 100 animals, 20 falls sick and 5 died. The case fatality rate will be 25%.

- **Biopsy** is the examination of tissues received from living animals.
- **Infection** is the invasion of the tissues of the body by pathogenic organisms resulting in the development of a disease process.
- I**nfestation** is the superficial attack of any parasite/ organisms on the surface of body.
- **Pathogenicity** is the capability of an organism for producing a disease.
- **Virulence** is the degree of invasiveness of pathogenic organism.

- **Morphologic changes** refer to the structural alterations in cells or tissues that occur following the pathogenic mechanisms. The structural changes in the organ can be seen with the naked eye or they may only be seen under the microscope. Those changes that can be seen with the naked eye are called gross morphologic changes & those that are seen under the microscope are called microscopic changes. Some of the morphological changes are listed as follow:
  - ✓ **Contusions or bruises** arise from rupture of blood vessel with disintegration of extra vassated blood.
  - ✓ **Abrasions** are circumscribed areas where epithelium has been removed by injury and it may indicate the direction of force.
  - ✓ **Erosions:** a partial loss of surface epithelium on skin or mucosal surface.
  - ✓ **Laceration:** severance of tissue by excessive stretching and is common over bony surfaces or are produced by cut through a dull instrument.
  - ✓ **Compression injury** is produced as a result of force applied slowly e.g. during parturition.
  - ✓ **Hyperthermia** means increased body temperature due to high environmental temperature e.g. Pets in hot environment without water.
  - ✓ **Hyperpnoea:** increased respiration
  - ✓ **Tachycardia:** rapid heart beat
  - ✓ **Eupnea:** true respiration
  - ✓ **Eucardia:** true heart beat
  - ✓ **Degeneration:** loss of muscle relaxation or decrease work load
  - ✓ **Hypothermia:** decreased body temperature
  - ✓ **Atrophy:** decrease in muscle mass
  - ✓ **Hypertrophy:** increase in muscle mass.

1.3. Indicators of cell damage and types of necrosis

1.3.1. Cell damage

Cell damage (also known as cell injury) is a variety of changes of stress that a cell suffers due to external as well as internal environmental changes. Amongst other causes, this can be due to **physical, chemical, infectious, biological, nutritional or immunological factors**. Cell damage can be **reversible or irreversible**. Depending on the extent of injury, the cellular response may be adaptive and where possible, homeostasis is restored. Cell death occurs when the severity of the injury exceeds the cell's ability to repair itself. Cell death is relative to both the length of exposure to a harmful stimulus and the severity of the damage caused. Cell death may occur by necrosis or apoptosis.

Cellular death due to necrosis does not follow the apoptotic signal transduction pathway, but rather various receptors are activated and result in the loss of cell membrane integrity and an uncontrolled release of products of cell death into the extracellular space. This initiates in the surrounding tissue an inflammatory response, which attracts leukocytes and nearby phagocytes which eliminate the dead cells by phagocytosis. However, microbial damaging substances released by leukocytes would create collateral damage to surrounding tissues. This lead to the first indicator of cell damage which is morphology changes, degeneration, Functional derangements and clinical significance and necrosis.

- **Morphologic changes**

The morphologic changes refer to the structural alterations in cells or tissues that occur following the pathogenic mechanisms. The structural changes in the organ can be seen with the naked eye or they may only be seen under the microscope. Those changes that can be seen with the naked eye are called gross morphologic changes & those that are seen under the microscope are called microscopic changes. Both the gross & the microscopic morphologic changes may only be seen in that disease, i.e. they may be specific to that disease. Therefore, such morphologic changes can be used by the pathologist to identify (i.e. to diagnose) the disease. In addition, the morphologic changes will lead to functional alteration & to the clinical signs & symptoms of the disease.

- **Functional derangements and clinical significance**

The morphologic changes in the organ influence the normal function of the organ. By doing so, they determine the clinical features (symptoms and signs), course, and prognosis of the disease. In summary, pathology studies:- Etiology ⇨ Pathogenesis Morphologic changes ⇨ Clinical features & Prognosis of all diseases.

Understanding of the above core aspects of disease (i.e. understanding pathology) will help one to understand how the clinical features of different diseases occur & how their treatments work. This understanding will, in turn, enable health care workers to handle & help their patients in a better & scientific way. It is for these reasons that the health science student should study pathology. In addition, the pathologist can use the morphologic changes seen in diseases to diagnose different diseases. There are different diagnostic modalities used in pathology. Most of these diagnostic techniques are based on morphologic changes.

- **Degeration**

The normal cell is a highly complex unit in which the various organelles and enzyme systems continuously carry out the metabolic activities that maintain cell viability and support its normal functions. Normal function is dependent on:

- ✓ The immediate environment of the cell
- ✓ A continuous supply of nutrients such as oxygen, glucose, and amino acids; and
- ✓ Constant removal of the products of metabolism, including CO_2.

Degeneration refers to the process by which tissue deteriorates and loses its functional ability due to traumatic injury, aging and wear and tear.While degeneration affects all tissues of the body, the natural degenerative process can particularly affect the vertebral discs and joints of the spine, resulting in chronic back pain. Degeneration is reversible but may progress to necrosis if injury persists. When it is associated with abnormal cell function, cell degeneration may also cause clinical disease.

For example, the failure of the blood supply to an organ (ischaemia) due to thrombosis will cause massive cell death due to lack of oxygen. A large area of cell death caused by ischaemia is

called an infarction. Another example of cell necrosis is seen in severe viral infections with cytopathic viruses (e.g. **rinderpest**).

Notes

- Nonlethal Injury = Degeneration
- Programmed Cell Death = Apoptosis
- Lethal Injury = Necrosis
  - ✓ **Characterizations of Cell degeneration are:**
    - Abnormality of biochemical function,
    - a recognizable structural change, or a combined biochemical and
    - Structural abnormality.

- **Types of necrosis**

Necrosis is caused by factors external to the cell or tissue, such as infection, or trauma which result in the unregulated digestion of cell components. In contrast, apoptosis is a naturally occurring programmed and targeted cause of cellular death. While apoptosis often provides beneficial effects to the organism, necrosis is almost always detrimental and can be fatal. There are different types of necrosis. The most known ones are the following.

- ✓ **Coagulative necrosis**

This is a type of accidental cell death typically caused by ischemia or infarction. In coagulative necrosis, the architectures of dead tissue are preserved for at least a couple of days. It is believed that the injury denatures structural proteins as well as lysosomal enzymes, thus blocking the proteolysis of the damaged cells. The lack of lysosomal enzymes allows it to maintain a "coagulated" morphology for some time. Like most types of necrosis, if enough viable cells are present around the affected area, regeneration will usually occur. Coagulative necrosis occurs in most bodily organs, excluding the brain. Different diseases are associated with coagulative necrosis, including acute tubular necrosis and acute myocardial infarction.

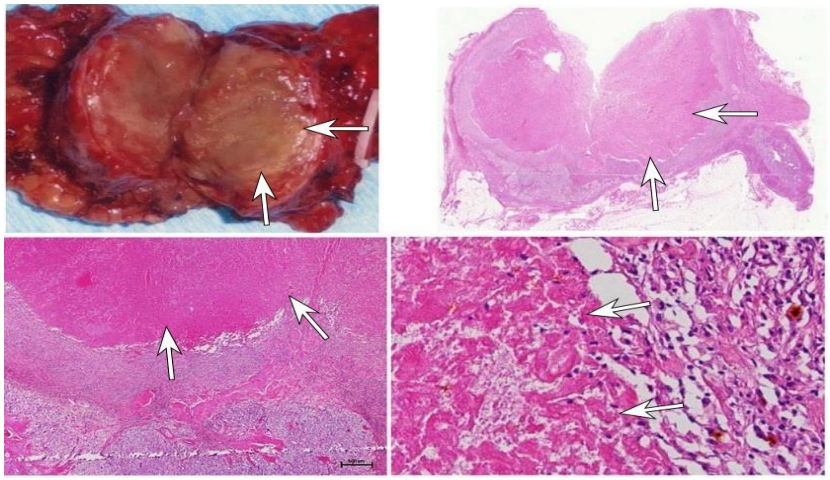


Fig1.1: coagulative necrosis

(https://upload.wikimedia.org/wikipedia/commons/3/3b/Histopathology_of_a_pheochromocytoma_with_coagula) (1/9/2022)

✓ **Caseous necrosis:**

Caseous necrosis or caseous degeneration is a unique form of cell death in which the tissue maintains a cheese-like appearance. It is also a distinctive form of coagulative necrosis. The dead tissue appears as a soft and white proteinaceous dead cell mass.

✓ **Liquefactive necrosis**

Liquefactive necrosis is characterized by digestion of tissue. It shows softening & liquefaction of tissue. It characteristically results from ischemic injury to the CNS. It also occurs in suppurative infections characterized by formation of pus.

✓ **Fat necrosis**

Fat necrosis can be caused by trauma to tissue with high fat content, such as the breast or it can also be caused by acute hemorrhagic pancreatitis in which pancreatic enzymes diffuse into the inflamed pancreatic tissue & digest it. The fatty acids released from the digestion form calcium salts (soap formation or dystrophic calcification). In addition, the elastase enzymes digest the blood vessels & cause the hemorrhage inside the pancreas, hence the name hemorrhagic pancreatitis.

- ✓ **Caseous nerosis**

Caseous necrosis has a cheese-like (caseous, white) appearance to the naked eye. And it appears as an amorphous eosinophilic material on microscopic examination. Caseous necrosis is typical of tuberculosis.

- ✓ **Gangrenous necrosis**

This is due to vascular occlusion & most often affects the lower extremities & the bowel. It is called wet gangrene if it is complicated by bacterial infection which leads to superimposed liquefactive necrosis. Whereas it is called dry gangrene if there is only coagulative necrosis without liquefactive necrosis.

- ✓ **Gangrenous necrosis**

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1.4. Gross pathological lesions

A gross pathological lesion is one that can be seen with the naked eye or any of various pathological or traumatic changes in a bodily organ or tissue, including tumors, ulcers, sores, and wounds. A microscopic or histologic lesion requires the magnification of a microscope to be seen. The basis of sickle cell disease is a molecular lesion, one that is not even visible with a microscope but is only detectable on the molecular (protein or DNA) level.

Gross pathological lesion can be described generally start with an overview of the location and distribution of the lesion, then move on to the fine details of the lesion's size, shape, colour, texture, etc. We usually describe the most important abnormalities first, and describe **arte factual** changes last, if at all.

- **Color**
  - ✓ Red – Hemorrhage, Congestion, Hemoglobin Staining (Imbibition)
  - ✓ White – Mineral, Fat, Fibrous Tissue, Absence of Blood Flow, Necrosis
  - ✓ Green – Bile Staining, Putrefaction, Eosinophilic Inflammation
  - ✓ Yellow – Bilirubin (Icterus), Hematoidin (Erythrocyte Breakdown), Carotenoids (High VitaminA Diet)
  - ✓ Brown – Hemosiderin/Iron Deposition, Methemoglobin, Lipofuscin

- **Consistency**
  - ✓ Soft – Necrosis, adipose tissue, lung
  - ✓ Firm – Inflammation, fibrosis, cartilage
  - ✓ Hard – Mineralization, bone
- **Demarcation**
  - ✓ Well demarcated – vascular insult, benign tumor
  - ✓ Poorly demarcated – inflammation, malignant
- **Contour**
  - ✓ Sessile – having a broad base
  - ✓ Pedunculated or polypoid – having a narrow base
- **Shape**
  - ✓ Round – benign tumor, vascular (some organs), cystic lesion
  - ✓ Rectangular or polygonal – vascular (some organs such as skin)
  - ✓ Irregular – malignant tumor, inflammatory process
- **Distribution**
  - ✓ Focal – primary tumor, traumatic injury, early stage of multifocal process
  - ✓ Multifocal – hematogenous spread of infectious agent or neoplasm
  - ✓ Multifocal to coalescing – Progression of multifocal lesion
  - ✓ Locally extensive – Vascular insult, progression of focal lesion
  - ✓ Diffuse – Metabolic, progression of multifocal or locally extensive lesion, vascular insult.
- **Fluid**
  - ✓ Watery – serum
  - ✓ Viscous – contains mucous or fibrin
  - ✓ Turbid – contains fibrin, inflammatory or neoplastic cells
  - ✓ Opaque – contains cells or lipid droplets

Generally gross pathological lesions or changes that can be encountered during meat inspection are the following

- Fever
- Septicemia
- Pigmentation(melanosis, Icterus (Jaundice),
- Hemorrhage and Hematoma
- Bruises
- Abscess
- Emaciation

- Edema
- Emphysema
- Calcification
- Abnormal odors
- Immaturity
- Swelling
- Shrinkage
- Dislocation
- Breakage
- Discharge

Gross pathological lesions are observed in both ante mortem and post mortem examination.,

1.4.1. Ante mortem examination

Conducting ante mortem procedures at the abattoir on the day of slaughter to identify and condemn animals that are unfit for slaughter and to note clinical signs or lesions of disease that may not be apparent after slaughter.

Diseases lesions or changes detected during **ante mortem examination** are the following.

- **Fever (Pyrexia)**

Fever is an abnormal elevated body temperature. It may be classified as septic and aseptic according to the presence or no presence of an infection. In septic fever the infection is caused by viruses, bacteria, bacterial toxins, protozoa and fungi.

- **Septicemia**

Known at ante mortem examination by Congestion or Petechial hemorrhages of conjunctivae, mouth and vulvar mucosa.

- **Bruises**

Bruises are frequently found on **antemortem and post-mortem examination** in food producing animals and poultry. In cattle bruises caused by transportation or handling are commonly found in the hip, chest and shoulder areas; in pigs within the ham and in sheep in the hind leg. Bruises and hemorrhage in the hip joint are caused by rough handling of animals during shackling. Bruises in poultry can be localized or generalized and are frequently associated with bone fractures or ruptured ligament tendons.

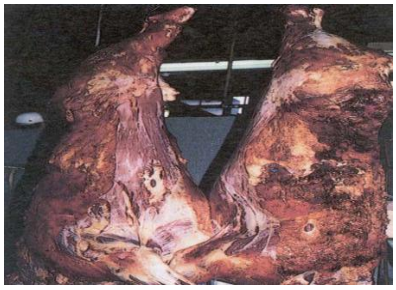


Fig1.2, Extensive bruises of a beef carcass

- Emaciation

Emaciation is a common condition of food animals and is characterized by a loss of fat and flesh following the loss of appetite, starvation and cachexia.

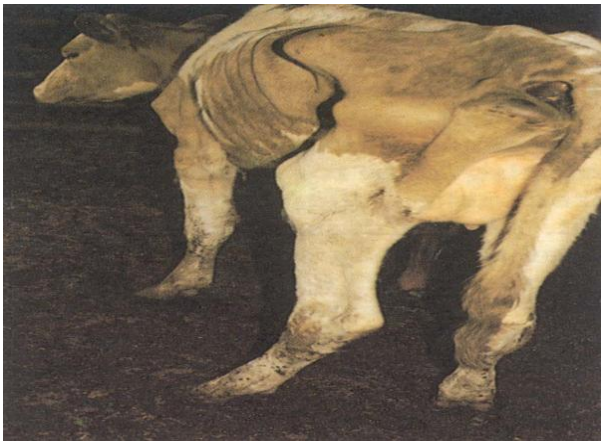


Fig1.3: Emaciated cow showing marked reduction of muscle mass.

- **Edema**

Edema is the accumulation of excess fluid in the intercellular (interstitial) tissue compartments, including body cavities.



Fig.1.4: Ventral edema.

(https://www.researchgate.net/figure/Ventral-edema-and-jugular-venous-distention-in-a-Jersey-cross-bred-cow-with-pericarditis_fig1_51102772) 1/9/2022

- **Immaturity**

Immaturity occurs mainly in calves. The slaughter of calves younger than two weeks of age is prohibited.

1.4.2. Post mortem examination

Post mortem examination are conducted for the purpose of identifying the cause of a disease and for wholesome meat consumption of meat for public. The most encountered gross pathological lesions during post mortem examination are the following.

- **Pigmentations**
  - ✓ Melanosis

Melanosis is is a pigmentation and it is observed in ante mortem and post mortem examination.it is an accumulation of melanin in various organs including the kidneys, heart, lungs and liver and other locations such as brain membranes, spinal cord, connective tissue, periosteum etc. Melanin is an endogenous brown-black pigment randomly distributed in tissue.



Fig1.5: Melanin deposits in the sheep viscera

- ✓ **Icterus (Jaundice)**

Icterus is the result of an abnormal accumulation of bile pigment, bilirubin, or hemoglobin in the blood. Yellow pigmentation is observed in the skin, internal organs, sclera (the white of the eye), tendons, cartilage, arteries, joint surfaces etc.



Fig.1.6: Jaundice of an aged cow caused by liver disease. Note yellow discoloration of body fat, lungs, heart and kidneys (https://www.google.com/search?hl=en&tbm=isch&oq=&aqs=&q=-%09Icterus+%28Jaundice%29} 1/9/2022

- **Hemorrhage and Hematoma**

Hemorrhage is seen at slaughter in various organs, mucous and serous membranes, skin, subcutaneous tissue and muscles. It may be caused by trauma, acute infectious diseases or septicemia.

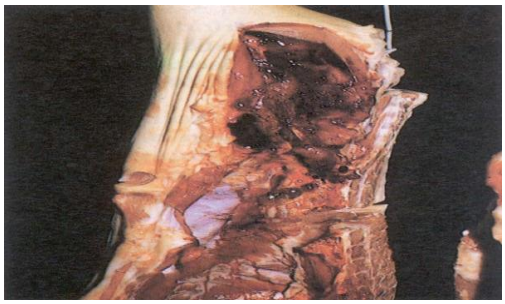


Fig. 1.7: Fractured bone and muscle hemorrhage in a market hog.

- **Abscess**

An abscess is a localized collection of pus separated from the surrounding tissue by a fibrous capsule.

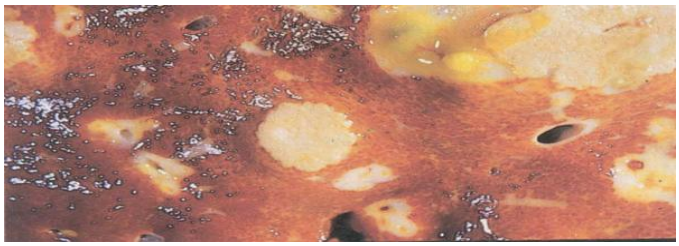


Fig 1.8: Liver abscesses caused by Fusobacterium necrophorum.

- **Emphysema**

Emphysema in animals is associated with some disease conditions and is caused by an obstruction to the outflow of a air or by extensive gasping respiration during slaughter procedures.

- **Calcification**

Calcification is the deposition of calcium salts in dead and degenerating tissue. It may be regarded as a body reaction to immobilize some foreign agents.

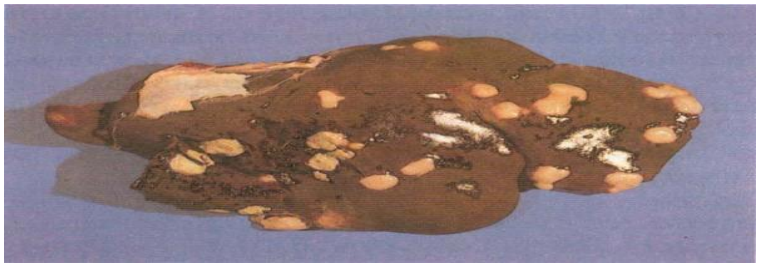


Fig1.9: Parasitic lesions undergoing mineralization in a sheep liver

- **Abnormal odors**

Abnormal odors may result from the ingestion of certain feedstuff, drugs, various pathological conditions, absorption of odors from strong smelling substances and sexual odor from some male animals.

- **Tumor and neoplasm**

A tumour is an abnormal mass of tissue which grows without control and uncoordinated with the tissue or organs of origin or those nearby. Its presence if often cumbersome to the tissue or organ it arose either by pressure or by replacement of normal functional tissue. Tumour cells resemble healthy cells however serve no useful purpose. The term tumour in current medical lexicon is presently limited to neoplastic growths.

- **Wound**

Wounds are cuts, tears, burns, breaks, or other damage to living tissue. Wounds are often classified as clean, contaminated, or infected. Clean wounds are those created under sterile conditions, such as surgical incisions. The number of bacteria present determines the difference between contaminated and infected wounds.

- **Shrinkage**

Tissue shrink is the loss of fluid from body tissues. This occurs when cattle go long periods without feed and water and are then subjected to other types of stress. Stress can be caused by events such as long distance trucking or rough handling. Tissue shrink occurs when cattle experience over 6% weight loss.

- **Breakage**

It is a soft tissue injury at the damage of muscles, ligaments and tendons throughout the body. Common soft tissue injuries usually occur from a sprain, strain, a one-off blow resulting in a contusion or overuse of a particular part of the body.

- **Discharge**

Any pathological fluid come out of the damage tissue or the injured tissue to the extra cellular content or it may liquefy to the external environment.

- **Dislocation**

Dislocation is a condition that happens when the bones of a joint are knocked out of place. A joint can be partially dislocated (subluxation) or fully dislocated. A dislocation can be caused by a trauma (car accident or fall) or the weakening of muscles and tendons. A dislocated joint can be treated through medication, manipulation, rest or surgery.

Dislocations can be very painful and cause the affected joint area to be unsteady or immobile (unable to move). They can also strain or tear the surrounding muscles, nerves, and tendons (tissue that connects the bones at a joint). You should seek medical treatment for a dislocation.

Self-Check 1

Name…… ID…… Date…….

Directions: Answer all the questions listed below. Examples may be necessary to aid some explanations/answers.

Test I: Choose the best answer

1. What is pathology (4 point)?

2. Differentiate health and illness (2pts)?

3. Define diseases in concept of pathology (3pts)?

4. How we can investigate the diseases (2pts)?

Note: **Satisfactory rating – above 5.5 points** **Unsatisfactory - below 5.5 points**

You can ask your teacher the copy of the answer sheet

LG #5	LO#2- Identify inflammatory reactions and exudates

Instruction sheet

This learning guide is developed to provide you the necessary information regarding the following content coverage and topics:

- Inflammatory reactions and cardinal signs
- Mediators and actors of inflammation
- Types and consequences of inflammation
- Clinically important Inflammatory lesions
- Development of oedema, abscess and respiratory discharges

This guide will also assist you to attain the learning outcomes stated in the cover page. Specifically, upon completion of this learning guide, you will be able to:

- describe The definition of inflammation and causes of inflammatory reactions in animal body are
- Mention and describe Mediators and actors of inflammation.
- Identify and describe Cardinal signs of inflammation
- Clinically important inflammatory lesions are mentioned.
- Types and consequences of inflammation are explained.
- Describe the Development of oedema, abscess and respiratory discharges

Learning Instructions:

1) Read the specific objectives of this Learning Guide.
2) Follow the instructions described below.
3) Read the information written in the information Sheets
4) Accomplish the Self-checks

Information Sheet 2

2.1.Inflammatory reactions and cardinal signs

2.1.1. Inflammatory reaction

Inflammatory reaction or response: is a defence mechanism that evolved in higher organisms to protect them from infection and injury. Its purpose is to localize and eliminate the injurious agent and to remove damaged tissue components so that the body can begin to heal. The response consists of changes in blood flow, an increase in permeability of blood vessels, and the migration of fluid, proteins, and white blood cells (leukocytes) from the circulation to the site of tissue damage.

The inflammatory response (inflammation) occurs when tissues are injured by bacteria, trauma, toxins, heat, or any other cause. The damaged cells release chemicals including histamine, bradykinin, and prostaglandins. These chemicals cause blood vessels to leak fluid into the tissues, causing swelling. Inflammation is a complex process of vascular and cellular alterations occurs in body in response to injury. The term inflammation has been derived from a Latin word inflammare, means to ‘set on fire’.

The inflammation is considered as an important event in body for implementation of existing defence mechanisms in circulating blood to dilute, naturalize or kill the irritant causative agent. Thus, it is said that the immunity is the resistance of body, while inflammation is the implementation of that immunity. It is beneficial to body except chronic persistent and immune origin. Inflammation starts with sub- lethal injury and ends with healing**.**

Since the inflammatory reaction are occur when the cells are injured , it is better to explain the cause of cell injury .

2.1.2. Etiology of cell injury:

- **Genetic causes**
  - ✓ Developmental defects: Errors in morphogenesis
  - ✓ Cytogenetic (Karyotypic) defects: chromosomal abnormalities
  - ✓ Single-gene defects: Mendelian disorders

✓ Multifactorial inheritance disorders.

- **Acquired causes**

✓ Hypoxia and ischemia

- Ischemia (loss of blood supply).
- Inadequate oxygenation (cardio respiratory failure).
- Loss of oxygen carrying capacity of the blood (anemia or CO poisoning).

✓ Physical agents

- Trauma
- Heat
- Cold
- Radiation
- Electric shock

✓ Chemical agents and drugs

- Endogenous products: urea, glucose
- Exogenous agents
- Therapeutic drugs: hormones
- Nontherapeutic agents: lead or alcohol

✓ Microbial agents

- Viruses
- Rickettsiae
- Bacteria
- Fungi
- Parasites

✓ Immunologic agents

- The immune process is normally protective but in certain circumstances the reaction may become deranged.
- Hypersensitivity to various substances can lead to anaphylaxis or to more localized lesions such as asthma.
- In other circumstances the immune process may act against the body cells – autoimmunity.

✓ Nutritional derangements

- Protein-calorie deficiencies are the most examples of nutrition deficiencies.
- Vitamins deficiency.

- Excess in nutrition are important causes of morbidity and mortality.
- Excess calories and diet rich in animal fat are now strongly implicated in the development of atherosclerosis.
- Obesity alone leads to an increased vulnerability to certain disorders, such as atherosclerosis, coronary heart disease, diabetes mellitus.

✓ Aging

- Programmed aging whereby after a defined number of divisions the cell undergoes terminal differentiation.
- Development of an increasing population of cells irreversibly committed to senescence and death.

✓ Psychogenic diseases

✓ Iatrogenic factors

✓ Idiopathic diseases.

2.1.3. The cardinal sign

Inflammation is response triggered by damage to living tissue. Inflammation is a **local response to cellular injury** that is marked by capillary dilatation, leukocytic infiltration, redness, heat, and pain and that serves as a mechanism initiating the elimination of noxious agents and of damaged tissue. Based on this pathogenesis mechanism to the initiation of cell injury: There are **five cardinal signs** of inflammation, though it may also cause additional symptoms if severe.

a. **Pain:** An unpleasant sensation that can range from mild, localized discomfort to agony. Pain has both physical and emotional components. The physical part of pain results from nerve stimulation. Pain may be contained to a discrete area, as in an injury, or it can be more diffuse, as in disorders like fibromyalgia.
b. **Redness: Erythema** (from the Greek erythros, meaning red) is redness of the skin or mucous membranes, caused by hyperemia (increased blood flow) in superficial capillaries. It occurs with any skin injury, infection, or inflammation.
c. **Swelling:** is an increase in the size or a change in the shape of an area of the body. Swelling can be caused by collection of body fluid, tissue growth, or abnormal movement or position of tissue.

d. **Hotness**: ischaracterized by high temperature. Being at or exhibiting a temperature that is higher than normal or desirable: a hot forehead.

e. **Loss of function:** A mutation that results in reduced or abolished muscle (protein) function. Muscle function loss is when a muscle does not work or move normally. The medical term for complete loss of muscle function is paralysis.



Fig2.1: The cardinal signs of inflammation include: pain, heat, redness, swelling, and loss of function. Some of these indicators can be seen here due to an allergic reaction (https://en.wikipedia.org/wiki/Inflammation#Causes), (1/92022)

2.2.Mediators and actors of inflammation

The mediators and actors of inflammation are those functional participants of body systems to the protective response involving immune cells, blood vessels, and molecular mediators to eliminate the initial cause of cell injury, clear out necrotic cells and tissues damaged from the original insult and the inflammatory process, and initiate tissue repair. These activator and mediators are involved in the different phase of inflammatory response which includes histamine, cytokines, complements, interleukin (mediators) and, neutrophils, macrophages, monocytes and B-cell as actors of inflammation.

Inflammation can be classified as either acute or chronic. Acute inflammation is the initial response of the body to harmful stimuli, and is achieved by the increased movement of plasma and leukocytes (in particular granulocytes) from the blood into the injured tissues. A series of biochemical events propagates and matures the inflammatory response, involving

the local vascular system, the immune system, and various cells within the injured tissue. Prolonged inflammation, known as chronic inflammation, leads to a progressive shift in the type of cells present at the site of inflammation, such as mononuclear cells, and is characterized by simultaneous destruction and healing of the tissue from the inflammatory process.

2.3.Types and consequence of inflammation

2.3.1. Phase of inflammation

- **Acute phase of inflammation**

Acute inflammation occurs immediately upon injury, lasting only a few days. Cytokines and chemokines promote the migration of neutrophils and macrophages to the site of inflammation. Pathogens, allergens, toxins, burns, and frostbite are some of the typical causes of acute inflammation. Toll-like receptors (TLRs) recognize microbial pathogens. Acute inflammation can be a defensive mechanism to protect tissues against injury. Inflammation lasting 2–6 weeks is designated sub-acute inflammation.

Acute inflammation is the early (almost immediate) response of a tissue to injury. It is nonspecific and may be evoked by any injury short of one that is immediately lethal. Acute inflammation may be regarded as the first line of defense against injury and is characterized by changes in the microcirculation: exudation of fluid and emigration of leukocytes from blood vessels to the area of injury. Acute inflammation is typically of short duration, occurring before the immune response becomes established, and it is aimed primarily at removing the injurious agent.Phases of acute inflammation may include

- ✓ **Vascular phase**

In the vascular phase, small blood vessels adjacent to the injury dilate (vasodilatation) and blood flow to the area increases. The endothelial cells initially swell, then contract to increase the space between them, thereby increasing the permeability of the vascular barrier. This process is regulated by chemical mediators.

Exudation of fluid leads to a net loss of fluid from the vascular space into the interstitial space, resulting in oedema (tumour). The formation of increased tissue fluid acts as a medium for which inflammatory proteins (such as complement and immunoglobulins) can migrate through. It may also help to remove pathogens and cell debris in the area through lymphatic drainage.

✓ **Exudative phase**

Exudative phase indicates significant alteration in the normal permeability of the small blood vessels in the region of injury. The two components of exudate, fluid and protein, serve good purposes.They are attracted to the site of injury by the presence of chemotaxins, the mediators released into the blood immediately after the insult.

- Margination: cells line up against the endothelium
- Rolling: close contact with and roll along the endothelium
- Adhesion: connecting to the endothelial wall
- Emigration: cells move through the vessel wall to the affected area

✓ **Cellular phase**

The cellular stage of acute inflammation is marked by changes in the endothelial cells lining the vasculature and movement of phagocytic leukocytes into the area of injury or infection.The most important feature of inflammation is the accumulation of white blood cells at the site of injury. Most of these cells are phagocytes, certain “cell-eating” leukocytes that ingest bacteria and other foreign particles and also clean up cellular debris caused by the injury. The main phagocytes involved in acute inflammation are the neutrophils, a type of white blood cell that contains granules of cell-destroying enzymes and proteins. Outcomes cellular phase results are:

- Complete resolution – with total repair and destruction of the insult
- Fibrosis and scar formation – occurs in cases of significant inflammation
- Chronic inflammation – from a persisting insult
- Formation of an abscess

- **Inflammatory exudates of acute inflammation**

The main characteristics of acute inflammation are the exudation of fluid and plasma proteins (edema) and the emigration of leukocytes (predominantly neutrophils). Neutrophils and other

motile white cells emigrate or move from the blood vessels to the perivascular tissues and the injury (implant) site.

a. "**Exudate"** is fluid buildup caused by tissue leakage due to inflammation or local cellular damage.

b. "**Transudate**" is fluid buildup caused by systemic conditions that alter the pressure in blood vessels, causing fluid to leave the vascular system.

✓ **The fluid is exudate if one** of the following Light's criteria is present:

- Effusion protein/serum protein ratio greater than 0.5
- Effusion lactate dehydrogenase (LDH)/serum LDH ratio greater than 0.6
- Effusion LDH level greater than two-thirds the upper limit of the laboratory's reference range of serum LDH.

Lactate dehydrogenase (LDH) is an enzyme normally inside of cells in the body. When there is damage to cells, LDH leaks out and becomes part of the effusion. Measuring a high LDH in the effusion is indicative of cell damage, which typically comes from an exudative process. This is why one of Light's criteria measures LDH in the effusion.

✓ **Causes of Transudative cells**

- Partially collapsed lung tissue (atelectasis): Due to increased negative pressure inside the lung cavity
- Cerebrospinal fluid (CSF) leak into lung cavity (pleural space): Thoracic spine injury, ventriculo peritoneal (VP) shunt dysfunction
- Heart failure
- Liver dysfunction
- Lowbloodalbumin (hypoalbuminemia)
- Iatrogenic (misplaced catheter into lung)
- Nephrotic syndrome
- Peritoneal dialysis
- Blockage of urinary system causing urine backup in the body (urinothorax due to obstructive uropathy)

- ✓ **Causes of Oxidative Effusions**
  - **Abdominal fluid**: Abscess in tissues near lung, fluid in the abdomen (ascites), Meigs syndrome, pancreatitis
  - **Connective tissue disease**:churg-strauss disease, lupus, rheumatoid arthritis, Wegener granulomatosis.
  - **Endocrine**: Low thyroid (hypothyroidism), ovarian hyperstimulation.
  - **Iatrogenic**: Drug-induced, esophageal perforation, feeding tube in lung
  - **Infectious**: Abscess in tissues near lung, bacterial pneumonia, fungal disease, parasites, tuberculosis
  - **Inflammatory**: Acute respiratory distress syndrome (ARDS), asbestosis, pancreatitis, radiation, sarcoidosis, high levels of urea in the blood (uremia)
  - **Lymphatic abnormalities**: Chylothorax (fluid around the lungs), cancer in the lymph nodes, lymphangiectasia (over-dilation of lymph vessels)
  - **Malignancy**: Cancer, lymphoma, leukemia, mesothelioma, paraproteinemia

The process of acute inflammation is initiated by resident immune cells already present in the involved tissue, mainly resident macrophages, dendritic cells, histiocytes, Kupffer cells and mast cells. These cells possess surface receptors known as pattern recognition receptors (PRRs), which recognize (i.e., bind) two subclasses of molecules: pathogen-associated molecular patterns (PAMPs) and damage-associated molecular patterns (DAMPs). PAMPs are compounds that are associated with various pathogens, but which are distinguishable from host molecules. DAMPs are compounds that are associated with host-related injury and cell damage.

At the onset of an infection, burn, or other injuries, these cells undergo activation (one of the PRRs recognizes a PAMP or DAMP) and release inflammatory mediators responsible for the clinical signs of inflammation. Vasodilation and its resulting increased blood flow causes the redness (rubor) and increased heat (calor). Increased permeability of the blood vessels results in an exudation (leakage) of plasma proteins and fluid into the tissue (edema), which manifests itself as swelling (tumor). Some of the released mediators such as bradykinin increase the sensitivity to pain (hyperalgesia, dolor). The mediator molecules also alter the blood vessels to permit the migration of leukocytes, mainly neutrophils and macrophages, to flow out of the blood vessels (extravasation) and into the tissue. The neutrophils migrate along a chemotactic

gradient created by the local cells to reach the site of injury. The loss of function (functio laesa) is probably the result of a neurological reflex in response to pain.

In addition to cell-derived mediators, several acellular biochemical cascade systems—consisting of preformed plasma proteins—act in parallel to initiate and propagate the inflammatory response. These include the complement system activated by bacteria and the coagulation and fibrinolysis systems activated by necrosis (e.g., burn, trauma).

Acute inflammation may be regarded as the first line of defense against injury. Acute inflammatory response requires constant stimulation to be sustained. Inflammatory mediators are short-lived and are quickly degraded in the tissue. Hence, acute inflammation begins to cease once the stimulus has been removed.

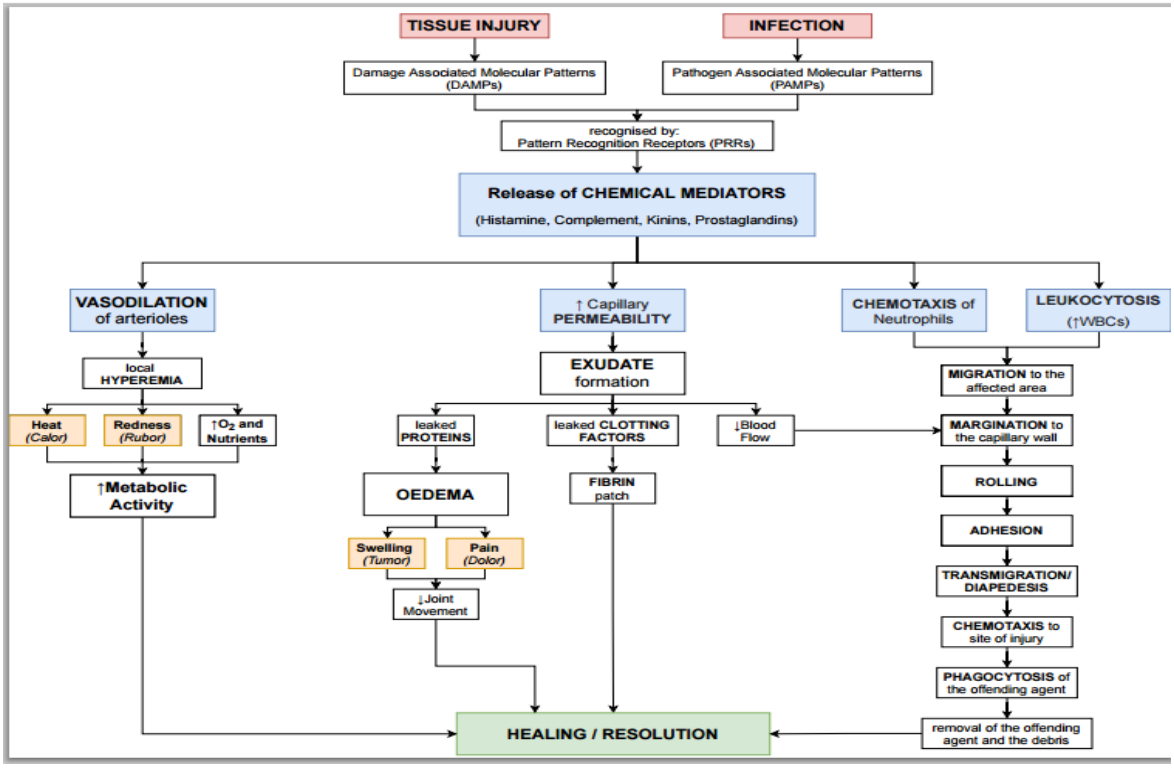


Diagram 2.1: A flowchart depicting the events of acute (inflammation (https://en.wikipedia.org/wiki/Inflammation#Types), (1/92022)

- **Chronic phase of inflammation**

Chronic inflammation is inflammation that lasts for months or years. Macrophages, lymphocytes, and plasma cells predominate in chronic inflammation, in contrast to the neutrophils that predominate in acute inflammation. Diabetes, cardiovascular disease, allergies, and chronic obstructive pulmonary disease (COPD) are examples of diseases mediated by chronic inflammation. Obesity, smoking, stress and insufficient diet are some of the factors that promote chronic inflammation.[9] A 2014 study reported that 60% of Americans had at least one chronic inflammatory condition, and 42% had more than one.

- **Chronic inflammation** is the response of tissue against injurious agent that persists for a long time. The tissue affected by chronic inflammation usually show immune response, phagocytosis, necrosis and repair. Chronic inflammatory process is usually productive or proliferative rather than exudative.

✓ **Causes**

Chronic inflammation usually develops following acute inflammation due to persistence of infection. Chronic inflammation usually follows repeated acute inflammation Moreover, It may be primary develop due to a low grade of tissue response to persist infection with intracellular microorganisms as Mycobacterium tuberculosis, prolonged exposure to non-degradable but potent toxic substance as silicosis and immune reaction as type IV hypersensitivity.

The affected tissue in chronic inflammation usually shows the following characters, Immune response represented by plasma cells, lymphocytes and macrophages. Moreover, phagocytosis, necrosis and repair, which characterized by presence of newly, formed capillary and fibrous tissue proliferation and collagen fiber deposition.

✓ **Microscopic picture**

The characteristic feature of chronic inflammation is infiltration of tissue with mononuclear cells specially macrophages, lymphocytes and plasma cells besides newly develop blood vessels, fibroblast proliferation and collagen fibre deposition.

✓ **Gross appearance**

Chronic inflammation is characterized by absence of cardinal signs of inflammation. The inflammatory area is indurated and grayish white in color. Moreover the inflammation may be not noticed. Granulomatous inflammation Granulomatous inflammation is a special kind of

chronic inflammation, which occurs in the presence of indigestible material and/or cell-mediated immunity. Moreover, granulomatous inflammation is a type of chronic inflammation characterized by presence of granuloma. Granuloma composed of closely packed collection of cells or sheets of predominantly macrophages. Macrophage in granuloma usually activated (epithelioid cells). Besides macrophages, granulomatous inflammation shows lymphocytes, plasma cells, giant cells and sometimes neutrophils. The classic granulomatous diseases include tuberculosis, leprosy, foreign body reactions, including the reactions to everything from sutures to schistosome eggs.

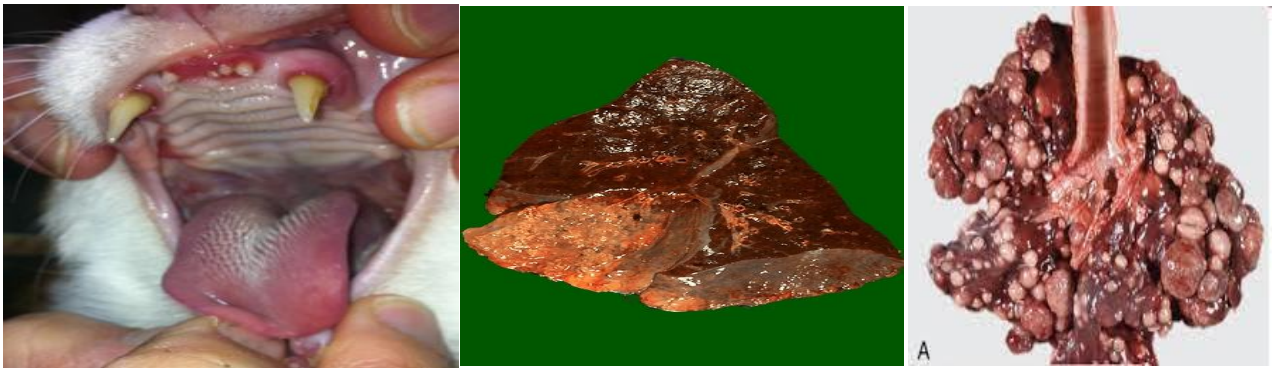


Fig2.2: Chronic inflammation of tongue, liver and lung

(https://www.google.com/search?hl=en&tbm=isch&oq=&aqs=&q=Chronic+inflammation+of+tongue%2C+liver+and+lung%2Canimal) 1/9/2022

2.3.2. Consecounse of inflammation

The consequence of inflammation is ended by the process of tissue repair and wound healing

- **Introduction Tissue Repair and Healing**

Wound Healing: Healing is the body response to injury in an attempt to restore normal structure and function. Two Distinct processes

i. **Regeneration:** - Complete restoration of the original tissues.
ii. **Repair:** - When the healing takes place by proliferation of connective tissue element resulting in fibrosis and scarring.

A. Healing (Tissue Repair)

- **Tissue:** Proliferating potential of cell types

- **Labile cells** - Continuously dividing cells. E.g. epidermis, epithelial cells, bone marrow cells.
- **Stable cells**
  - ✓ Quiescent cells
  - ✓ Undergoes division occasionally
  - ✓ Liver, kidney pancreas, fibroblasts, endothelial cells
- **Permanent cells**
  - ✓ Non–dividing cells
  - ✓ Neurons, muscle cells (cardiac, skeletal)

Hence, healing occurs Depending on the proliferation potential of the cells as described above by

a. Healing by regeneration
b. Healing by substitution

Wound healing is not a separate process and occurs along with the inflammatory reaction. It is a complex but orderly phenomenon involving a number of processes.Namely,

- Acute inflammatory reaction following initial injury.
- Parenchymatous cellular regeneration
- Migration and production of parenchymatous and connective tissue cell
- Extracellular matrix, protein synthesis
- Remodelling of connective tissue

a. Healing by primary union or first intention (regeneration)

- This type of healing occurs in clean surgical approximated incision i.e. limited bleeding and tissue destruction.
- The sequence of events occurring in primary union is given below

0 hrs	Clot filling the incised area
3-24hrs.	Neutrophilic infiltration
48 hrs	Basal cell proliferation and epithelial closure takes place by 24-48 hours
72 hrs	Macrophages replace neutrophils. Granulation tissue begins to appear. Collagen is arranged vertically
120 hrs	Incised space is filled with granulation tissue. Neovascularisation is maximal. Collagen fibre begin to appear and epithelial proliferation is maximal

2 weeks Proliferation of fibroblast with continuous collagen accumulation producing a scar. Type III collagen is deposited early in scar tissue and is replaced by adult type I collagen which accounts for wound strength. Newly formed blood vessels disappear.

8 week Scar tissue consists of granulation tissue which is devoid of inflammation covering intact epidermis.

b. Healing by second intention (substitution)

The wound involved shows extensive loss of cells and tissue. E.g. infarction, ulceration, abscesses, surface wound with large defects. The wound is filled with tissue debris, a few erythrocytes and bacteria. Abundant granulation tissue (soft, pink, granular appearance of wound surfaces) grows in from the margin to fill the defect but at the same time the wound contracts i.e., the defect is marked by depression and decrease from its original size. Microscopically granulation tissue consists of new capillaries, fibroblasts, collagen and proteoglycan rich ground substance. Initially granulation tissue is soft and spongy due to leaky blood vessels

Injury – open wound – excess loss of tissue – infected – necrosis – inflammation

↓

Blood clot

↓

24 hours – neutrophils infiltrate to destroy irritant

↓

48-72 hours – macrophages and lymphocytes infiltrate

↓

Removal of necrotic and cellular debris by liquefaction by macrophages

↓

Red granules from underneath (granulation tissue) represent proliferating capillaries. Fibroblast also proliferate to fill the gap

↓

There is a definite order.

Base - capillaries grow vertically and project towards the surface. Fibroblast grows perpendicular to capillary and parallel to surface – pulling pressure of the wound

↓

Surface – fibroblasts are arranged parallel to capillaries exerting tension towards wound surface for easy closure. This arrangement differentiates granulation tissue from fibrosarcoma which lacks orderly arrangement.

↓

The surface is closed by the epithelium proliferating from the margin

↓

The tissue is devoid of sweat gland, sebaceous gland, hair and hair follicles and pigment. So, the scar appears dry and un pigmented white and puckered as it becomes avascular and shrinkage of collagen.

Exuberant granulation or proud flesh

Sometimes the granulation continues to grow in abnormally large amount due to irritant, movement or trauma which prevents healing. This condition is called proud flesh or excess granulation tissue.

Keloid

- Keloid is another condition. Reason for its development is not known. The connective tissue below the epithelial covering continues to proliferate. This condition may recur after the removal. This is found in horses and black people having some genetic or familial predisposition.

Systemic and local factors influencing wound healing

Systemic factors

- Nutritional
    - ✓ Vitamins – vitamin C is required for collagen synthesis.
    - ✓ Proteins deficiency – starvation.
    - ✓ Sulphur containing amino acids (methionine and cystine) are important and required for intermediate forms of collagen.
    - ✓ Zinc – as metalloenzyme, it is essential for remodelling of extracellular matrix
- Metabolic factors
    - ✓ Diabetes mellitus – delays healing.
    - ✓ Hyperadrenocortism
- Circulatory stasis or adequacy of blood supply

Inadequate blood supply – delays healing

- Hormones: concurrent glucocorticoid therapy hinders inflammatory and reparatory process

Local factors

- Infection can delay healing
- Mechanical – movements directly affect wound healing
- Foreign bodies impede healing
- Size, location and type of wound
- Cold inhibits wound healing

Others

- Old age-Healing is slower than young ones.
- Chemotherapeutic agents
- Radiation
- Immunodeficiency

2.4. Clinically important Inflammatory lesions

Inflammatory cells are a source of cytokines and growth factors that may target the endothelial cells and contribute to the development of structural and functional abnormalities of the vessel wall. Inflammatory lesions in acne include small red bumps (papules), pustules, large red bumps (nodules) and pseudocysts (these are fluctuant nodules). Inflammatory acne lesions are often painful. The most known and clinically important inflammatory lesions are the following.

- **Macule**: Macules are circumscribed alterations in skin color. The skin surface is either elevated or depressed in relation to the surrounding skin. Macules may be of any size or color.
- **Papule**: Papule is a solid, elevated lesion with no visible fluid which may be up to ½ cm. in diameter. The elevation may be accounted for by metabolic deposits, infiltrates, or hyperplasia of cellular elements, etc. A papulosquamous lesion is a papule with desquamation (scaling).
- **Nodules**: Nodules are forms of papules, but are larger and deeper. They may be located in the dermis or subcutaneous tissue, or in the epidermis. Nodules are usually ½ cm. or more in diameter. Ex: Metastatic neoplasm; xanthoma

- **Plaque**: An elevated area of skin 2 cm. or more in diameter. It may be formed by a coalescence of papules or nodules. The surface area is greater than its height. It is a plate-like lesion.
- **Wheal**: A wheal is an evanescent rounded or flat-topped elevation in the skin that is edematous, and often erythematous. They may vary in size from a few mm. to many cm. The shape may change and these lesions are usually pruritic (itchy). These are really variations of papules, nodules or plaques that are evanescent.
- **Vesicles and Bullae**: (Blisters) Vesicles are circumscribed epidermal elevations in the skin containing clear fluid and less than ½ cm. in diameter. If the lesion has a diameter of greater than ½ cm, it is called a bulla. Vesicles and bullae arise from a cleavage at various levels of the skin. The more superficial the location, the more flaccid the bullous lesion. Vesicles and bullae are commonly called blisters. It is the diameter, not the cleavage plane that differentiates vesicles and bullae.
- **Pustule**: A pustule is a circumscribed elevation of the skin that contains a purulent exudate that may be white, yellow, or greenish-yellow in color.
- **Abscess:** A localized collection of pus in a cavity formed by disintegration or necrosis of tissue.
- **Cyst**: A cyst is a closed sac that contains liquid or semisolid material. On palpation a cyst is usually resilient.
- **Atrophy**: Atrophy of the skin may involve the epidermis, or the dermis, or both. It is the thinning process associated with decreased number of cutaneous cells. Sometimes the normal skin markings may be lost. Dermal atrophy may give rise to a depression in the skin. Stria (plural striae) is linear, atrophic, pink, purple, or white lesions of the skin and is sometimes called “stretch marks”.
- **Sclerosis**: Sclerosis refers to a circumscribed, diffuse hardening or induration in the skin. It is usually produced by induration of the dermis and/or subcutaneous tissue. Palpation is often necessary in diagnosing sclerosis.
- **Erosion**: A loss of epidermis.
- **Ulcer**: A loss of epidermis and dermis (and sometimes deeper tissue). If erosions and/or ulcers are produced by scratching, the term excoriation is used.

- **Scar:** Scars occur whenever ulceration has taken place and they reflect the pattern of healing. They may be hypertrophic, atrophic, or cribriform (perforated with multiple small pits).
- **Crusts (scabs):** Crusts result when serum, blood, or purulent exudate dries and it is a hallmark of pyogenic infection. Crusts are yellow when they have arisen from dried serum; green or yellow-green when formed from purulent exudate; and brown or dark red when formed from blood.
- **Lichenification**: A chronic thickening of the epidermis with exaggeration of its normal markings, often as a result of scratching or rubbing.
- **Acne**: presents primarily as papules but can also cause pustules, nodules, or cysts. It is most common on the face, neck, chest, and upper back and can leave scars if not treated
- **Keratitis**: is caused by exposure to sunlight (ultraviolet radiation) and appears as thick, scaly crusts on the skin.
- **Blisters**: a small bubble on the skin filled with serum and caused by friction, burning, or other damage.
- **Cellulitis**: a lesion caused by agents that affected skin appears swollen and red and may be hot and tender. Without treatment with an antibiotic, cellulitis can be life-threatening.
- **Sore:** physically painful or sensitive, as a wound, hurt, or diseased part: a sore arm. Suffering bodily pain from wounds, bruises, etc., as a person: He is sore because of all that exercise. Suffering mental pain; grieved, distressed, or sorrowful: to be sore at heart.
- **Dermatitis**: is a general term that describes a common skin irritation. It has many causes and forms and usually involves itchy, dry skin or a rash. Or it might cause the skin to blister, ooze, and crust or flake off.
- **Enzema:** a particular type of inflammatory reaction of the skin in which there is erythema (reddening), edema (swelling), papules (bumps), and crusting of the skin followed, finally, by lichenification (thickening) and scaling of the skin.
- **Utricaria**: is a unique dermatologic disorder caused by infiltration of mast cells in the skin and has pathology distinct from common urticaria but can present with urticarial lesions associated with blisters.
- **Scabies**: is an itchy skin condition caused by a tiny burrowing mite called Sarcoptesscabiei. Intense itching occurs in the area where the mite burrows.

- **Cyst**: is caused by an infestation of the skin by the human itch mite (Sarcoptesscabiei var. hominis). The microscopic scabies mite burrows into the upper layer of the skin where it lives and lays its eggs. The most common symptoms of scabies are intense itching and a pimple-like skin rash.

The shape, size, color and texture of the primary lesion as well as any symptoms that may or may not be present are important in describing skin lesions. The arrangements of lesions in relation to one another as well as their distribution over the body are also important in fully describing a dermatosis. The following terms may apply to the shape or arrangement of skin lesions: linear, annular, polycyclic; aciform; serpiginous; grouped (herpetiform and zosteriform); agminate (collected together into clusters or masses); reticular (netlike). The following terms are helpful in describing the distribution of skin lesions: generalized; localized; bilateral; unilateral; symmetrical; asymmetrical; sun-exposed; intertriginous.

Miscellaneous:

• Pruritus = itching

• Pruritic = itchy

• Erythema = redness of the skin produced by vascular congestion or increased perfusion.



Figure 2. 3: Cyst, Blister and **Acne** types of lesions

(https://www.google.com/search?hl=en&tbm=isch&oq=&aqs=&q=Cyst%2C+Blister+and+Acne+%2Canimal) , (1/92022)

2.5. Development of oedema, abscess and respiratory discharges

2.5.1. Introduction To Oedema

- Oedema denotes abnormal accumulation of fluid in the interstitial tissue spaces and body cavities.
- There is always certain amount of fluid in these structures, but any excess is removed by the lymphatics as lymph.
- In health condition there is a constant passage of fluid from the capillaries to the tissues and vice versa, and the chief factors concerned in the process are hydrostatic (capillary blood-pressure) and osmotic pressure of the protein.
- At the arterial end of capillaries blood pressure exceeds osmotic pressure of the blood and fluid diffuses to the tissue spaces.
- At the venous end of capillaries osmotic pressure of blood increases owing to increased concentration of colloids, whereas, blood pressure falls hence facilitating re-absorption of fluid.
- If the hydrostatic or osmotic balances in the blood vessels and tissues are impaired or the permeability of capillaries is increased oedema would develop.



Figure 2.4. Oedema of Supra orbital fossa:

((https://www.google.com/search?hl=en&tbm=isch&oq=&aqs=&q=.Oedema+of+Supra+orbital+fossa) 1//9/2022

2.5.2. Factors concerned with production of oedema:

- Increased capillary blood pressure (hydrostatic pressure)
- Decreased colloid osmotic pressure of blood plasma
- Increased permeability of capillary wall
- Increased colloid osmotic pressure of the tissue
- Lymphatic obstruction- only causes local oedema

NB: colloid osmotic balance of blood is controlled by a protein called albumin. Damage to the liver, which is responsible for the synthesis of albumin, would lead to oedema.

2.5.3. Fluid nature of oedema:

- Oedematous fluid is transudate.
- Resembles plasma and has pale or straw-colour
- It is watery, but contains protein and has lower specific gravity
- It does not clot in any way

2.5.4. Structural changes due to oedema:

When subcutaneous tissues are involved:

- Puffy swelling that pits on pressure

- Freely moving fluid that oozes on cutting
- Generalized subcutaneous oedema is called **anasarca.**

In the involvement of serous cavities:

- **Ascites-** fluid in the peritoneum
- **Hydro pericardium-** fluid in the pericardium
- **Hydrothorax-** fluid in the thoracic cavity

2.5.5. Types of oedema

- **Renal oedema-** renal diseases may lead to filtration of protein from glomeruli leading to hypoproteinaemia hence causing oedema.
- **Parasitic oedema** – this develops due to blood sucking parasites like Hemonchus in sheep. In cases of hemonchosis fluid accumulates under the lower jaw known as bottle-jaw/submandibular oedema due to lowering of the neck during grazing.
- **Nutritional oedema-** mal-nutrition leads to hypoproteinaemia.
- **Liver diseases-** albumin and other proteins are synthesised in the liver. Any disease in the liver may interfere with albumin synthesis
- **Cardiac oedema-** this is due to lack of increased hydrostatic pressure. E.g. heart failure (congestion)
- **Inflammatory oedema-** there histamine production in inflammation. Histamine causes dilatation of vessel wall leading to leakage of fluid and colloid.

2.5.6. Outcome of oedema:

- Recovery if the cause is removed
- Inflammation due to bacterial infection
- Death due to:
  - ✓ Pressure of accumulating fluid
  - ✓ Inability of vital organs to function. E.g. oedema of lungs that fills the alveoli with fluid
  - ✓ Asphyxia- oedema of larynx.

2.5.7. Abscess

Abscess is defined as Symptom consisting of a localized collection of pus surrounded by inflamed tissue. It is a tender mass generally surrounded by a colored area from pink to deep red. Abscesses are often easy to feel by touching. The vast majority of them are caused by infections. Inside, they are full of pus, bacteria and debris. It is Painful and warm to touch, abscesses can show up any place on the animal body. The most common sites on the skin, areas around the anus and vagina, feet's, around a tooth (dental abscess), and in groin. Inflammation around a hair follicle can also lead to the formation of an abscess, which is called a boil (furuncle)

- **Abscess Causes**

When normal skin barrier is broken, even from minor trauma, or small tears, or inflammation, bacteria can enter the skin. An abscess can form as the body's defences try to kill these germs with inflammatory response (white blood cells = pus). Obstruction in a sweat or oil (sebaceous) gland, or a hair follicle or a pre-existing cyst can also trigger an abscess. The middle of the abscess liquefies and contains dead cells, bacteria, and other debris. This area begins to grow, creating tension under the skin and further inflammation of the surrounding tissues. Pressure and inflammation cause the pain.

2.5.8. Respiratory discharge

It is a clinical manifestation of respiratory disease expressed in nasal discharge. Nasal discharge may be serous, catarrhal, purulent, or haemorrhagic, depending on the extent of mucosal or turbinate damage. It indicates increased production of normal secretions, sometimes supplemented by neutrophils (purulent) or blood (haemorrhage). It probably also indicates decreased "grooming" of the nostrils with the tongue when animals are ill. Epistaxis (bleeding from the nose) is often caused by vascular rupture, such as in mycotic infection of the guttural pouch or exercise-induced pulmonary hemorrhage in horses, or by intranasal fungal infection or neoplasia, systemic coagulopathy, vasculitis, thrombocytopenia (immune-mediated or a result of rickettsial infection), hyperviscosity syndrome, hypertension, or nasal trauma. Hemoptysis (the coughing up of blood) occurs after rupture of pulmonary aneurysms in the lungs of cattle with chronic lung abscesses. Bleeding may also result from polyps, neoplasms, granulomas, trauma, thrombocytopenia, and bracken fern or sweet clover toxicity.

Self-Check – 2

Name…… ID…… Date…….

Directions: Answer all the questions listed below. Examples may be necessary to aid some explanations/answers.

Test I: Give Short Answer

1. Define what inflammatory response is or reaction means (4pts)?

2. What is the cause of cells inflammatory reactions are (4pts)

Test II: Choice the best answer

1. Which one is the part of physical agents (2pts)?
   A. Urea B. Trauma C. Bacteria D. Rickettsiae
2. Which one is the part of chemicals agents (2pts)?
   A Urea B. Trauma C. Bacteria D. Rickettsiae
3. Which one is not the part of infectious agents (2pts)?
   A. Urea B. Virus C. Bacteria D. Rickettsiae

Note: Satisfactory rating – above 7 points **Unsatisfactory - below 7 points**

You can ask your teacher the copy of the answer sheet

LG #6	LO#3- Identify basic circulatory pathological disorders

Instruction sheet

This learning guide is developed to provide you the necessary information regarding the following content coverage and topics:

- Causes and consequences of impaired blood supply to tissues/ organs
- Pathological lesions in circulatory disturbances
- Aetiology for development of congestion and jaundice/icterus
- Types and causes of shock

This guide will also assist you to attain the learning outcomes stated in the cover page. Specifically, upon completion of this learning guide, you will be able to:

- Identify and describe Causes and consequences of Impaired blood supply to tissues/ organs
- Mention and describe Pathologies associated with circulatory disturbances .
- identified General cause for the development of congestion and jaundice/icterus
- mention Types and causes of shock are

Learning Instructions:

1) Read the specific objectives of this Learning Guide.
2) Follow the instructions described below.
3) Read the information written in the information Sheets
4) Accomplish the Self-checks

Information Sheet 3

3.1. Causes and consequences of impaired blood supply to tissues/ organs

3.1.1. Introduction

Impaired blood supply is the disturbance of blood out of the right direction or impairment of the blood content that reaches to the cell. The known impaired blood supply is ischemia and infarction

3.1.2. Causes of impaired blood supply

A. Thrombosis: is a formation of clotted mass of blood within the cardiovascular system, while **blood clot** is a clump of blood that has changed from a liquid to a gel-like or semisolid state .Differences between thrombus and blood clot

	Formation	Composition	Prognosis
Thrombus	✓ Blood vessels ✓ Platelets ✓ Blood clotting system	✓ Platelets ✓ Fibrin	✓ Life threatening
Blood clot	✓ Blood clotting system	✓ Only fibrin	✓ Life saving

✓ **Causes for thrombosis**

- Trauma : lacerations, contusion, rupture, o/r injection
- Toxins : Streptococci, erysipelothrix (vegetations)
- Degenerations : Atherosclerosis (damage to intima)
- Viruses : Hog cholera virus
- Parasites : Strongylus vulgaris in anterior mesenteric artery in horses
- Tumours : Invading tumours

✓ **Mechanism of thrombus formation**

- **Active**
  - Antithrombotic factors and prothrombotic factors are seen on surface of endothelium

- **Passive**

Endothelium is thrombo-resistant whereas sub-endothelial connective tissue is highly thrombogenic.

- Sub-endothelial connective tissue consists of collagen, elastic, fibrinonectin, laminin glycosoaminoglycans and thrombosporin.
- Damage to endothelium exposes the sub-endothelial connective tissue and activates intrinsic blood clotting pathway and platelet adhesion.

- **Antithrombotic factors (present on endothelial cells) - Inhibit thrombosis**
  - ✓ Anticoagulant properties
    - Thrombo modulin - Protect against action of heparin and thrombin which converts fibrinogen to fibrin
  - ✓ Anti-platelet properties - Inhibit platelet aggregation
    - Prostacyclin (PGI2)
    - Nitric oxide (NO_2)
  - ✓ Fibrinolytic properties
    - Tissue plasminogen activator (tPAs) - Promotes fibrinolytic activity in blood and reacts against blood clots
- **Thrombotic factors**
  - ✓ Tissue factor (Thromboplastin)
    - Present on endothelium in small amounts
    - Activate extrinsic clottingpathway
    - Stimulated by
    - Endotoxins
    - Cytokines (IL – 1)
    - Tumour necrosis factor (TNF)
  - ✓ von Willebrand factor (vWF)
    - Protein helps in platelet adherence thrombus
  - ✓ Platelet Activating Factor (PAF)
    - Helps in platelet aggregation thrombus
  - ✓ Inhibitor of Plasminogen Activator
    - Prevents fibrinolysis thrombus

Notes

- ✓ **Normal homeostasis:** There will be a balance between antithrombotic and prothrombotic factors in normal endothelium.

B. Embolism

An embolus is any foreign body floating in blood. The process is called embolism.

- **Location of embolism**

✓ Artery / venous / capillaries / lymphatics

✓ In domestic animals emboli always occurs in arteries

✓ In human, venous embolism is common

✓ Thrombus in leg vein may form emboli to reach large blood vessel, right side heart and pulmonary artery embolism

- **Types / Causes of emboli**

✓ **Thrombotic emboli** : Thrombo embolism – arteries (Thrombi detach to form emboli)

- Heart – vegetations
- Parasitic; atherosclerotic; bacteria

✓ **Bacterial emboli** : Septicaemia

✓ **Parasitic emboli** : Dirofilariaimmitis - Pulmonary artery – dog

- Schistosomes – Portal; mesenteric; Nasal blood vessels
- Trypanasomes – If tartar emetic is given rapidly, it kills large number of organism and forms emboli on coronary vessels which is fatal.
- Filarial - Lymphatics emboli in brain

✓ **Neoplastic emboli**: Clumps of tumour cells in circulation producing metastatic tumours.

✓ **Fibrin** - In blood transfusion, when blood is improperly defibrinated / inadequate anticoagulants

✓ **Fat embolus** - In fracture of long bones, fat in the marrow cavity gets dislodged and forms emboli. These are lodged in lungs and leads to death.

✓ "**Fat embolism** syndrome" (Acute respiratory symptoms, tachycardia neurological symptoms)

✓ **Air or gas emboli**

C. **Vasoconstriction:** is the narrowing (constriction) of blood vessels by small muscles in their walls.

- ✓ When blood vessels constrict, blood flow is slowed or blocked.Vasoconstriction may be slight or severe. It may result from disease, drugs, or psychological conditions.

D. **Aneurysm:** (dilation or outpouching of a blood vessel wall) are pathologic abnormalities that can occur within the vasculature.

i. Consequence of impaired blood spplay.

Ischemia is decreased blood flow to or from an organ, while infarction is the cellular response to lack of perfusion (blocked blood flow to or from organs).Ischemia can be caused by obstruction of arterial blood flow – the most common cause, or by decreased perfusion of tissues by oxygen-carrying blood as occurs in cardiac failure, hypotension, & shock.

- ✓ **Nature and characteristics of ischemia**

  Ischemia is a restriction in blood supply to tissues, causing a shortage of oxygen that is needed for cellular metabolism (to keep tissue alive). Ischemia is deficiency of arterial blood in any part of an organ. It is also known as local anemia local anemia.

- ✓ **Description**

- Decreased blood supply that cannot meet the oxygen demands of an organ or tissue
- If not corrected, ischemia can lead to cell death due to cellular swelling (orcosis).

- ✓ **Pathogenesis**

- Decreased arterial perfusion (e.g., due to atherosclerosis, thromboembolism) in solid organs with only a single (end-arterial) blood supply (e.g., kidney, heart) → pale infarct
- Decreased venous drainage (e.g., venous occlusion, Budd-Chiari syndrome, testicular torsion, ovarian torsion) in tissues with more than one blood supply (e.g., intestine, lung, liver, testes) or reperfusion (e.g., following angioplasty) → red infarct
- **Shock** with the following variants:
  - Hypovolemic shock(e.g., hemorrhage) → ↓ intravascular volume → ↓ delivery of oxygen to tissue → ischemia

- Cardiogenic shock(e.g., cardiac tamponade) → ↓ left ventricular function → ↓ forward flow of blood → ↓ delivery of oxygen to tissue → ischemia
- Distributive shock (e.g., septic, neurogenic, and anaphylactic shock) → systemic vasodilation → peripheral pooling of blood → ↓ delivery of oxygen to tissue → ischemia.

✓ **Pathophysiology of ischemia**

Ischemia results in tissue damage in a process known as ischemic cascade. The damage is the result of the:

- Build-up of metabolic waste products,
- Inability to maintain cell membranes,
- Mitochondrial damage, and
- Leakage of autolyzing proteolytic enzymes into the cell and surrounding tissues
- Cardiac arrhythmias (irregular heart beat; too fast or slow)
- Cellular self-destruction
- Damage white blood cells

✓ **Etiology**

- Occlusion: The thrombi may dislodge and may travel anywhere in the circulatory system, where they may lead to pulmonary embolus, an acute arterial occlusion causing the oxygen and blood supply distal to the embolus to decrease suddenly.
- Trauma: traumatic injury to an extremity may produce partial or total occlusion of a vessel from compression, shearing, or laceration.
- External pressure on artery
- Narrowing / obliteration of lumen of artery
- Thrombi / emboli

✓ **Notes**

Ischemia: Death of cell by absences of blood supply or lack of oxygenated blood

oncosis: Death of cells with swelling.

Necrosis: Cell death by environmental stimuli with uncontrolled release of inflammatory cellular contents.

Infarction: Cell death by occlusion of blood supply veins or arteries

- **Infarction**

An infract is an area of ischemic necrosis caused by occlusion of either the arterial supply or venous drainage in a particular tissue. Nearly 99% of all infarcts result from thrombotic or embolic events. Other mechanisms include (all of them are arterial in origin): **Local vasospasm, Expansion of atheroma due to hemorrhage in to athermanous plaque, External compression of the vessels. E.g. trauma, Entrapment of vessels at hernial rings etc.**

- ✓ **The development & the size of an infarct are determined by the following factors:**
  - The nature of the vascular supply
  - The rate of development of occlusion
  - Susceptibility of the tissue for hypoxia
  - Oxygen content of the blood
  - The severity and duration of ischemia
- ✓ **The nature of vascular supply**

The following organs have a dual blood supply.

- Lung → pulumonary artery → Bronchial artery
- Liver → hepatic artery → Portal vein
- Hand & forearm → Radial arteries → Ulnar arteries.

The effect of such a dual blood supply is that if there is obstruction of one of the arterial supplies, the other one may offset the rapid occurrence of infarction in these organs unlike the renal & splenic circulations which have end arterial supply. Infarction caused by venous thrombosis is more likely to occur in organs with single venous outflow channels, such as testis &ovary.

- ✓ **Rate of development occlusion**

Slowly developing occlusions are less likely to cause infraction since they provide time for the development of collaterals.

- ✓ **Tissue susceptibility to hypoxia**

The susceptibility of a tissue to hypoxia influences the likelihood of infarction. Neurons undergo irreversible damage when deprived of their blood supply for only 3 to 4 minutes. Myocardial cells die after 20-30 minutes of ischemia. Fibroblasts are more resistant, especially those in the myocardium.

- ✓ **Oxygen content of blood**

  Partial obstruction of the flow of blood in an anaemic or cyanotic patient may lead to tissue infarction.

- ✓ **The severity & duration of ischemia.**

- **Types of infarcts**

Infarcts are classified depending on:

- ✓ The basis of their colour (reflecting the amount of hemorrhage) into:
  - **a. Hemorrhagic (Red) infarcts**
  - **b. Anemic (White) infarcts**
- ✓ The presence or absence of microbial infection into:
  - I. Septic infarcts
  - II. Bland infarcts

a. Red infarcts occur in:

- Venous occlusions as in ovarian torsion
- Loose tissues such as the lung which allow blood to collect in infarct zone.
- Tissues with dual circulations (e.g. the lung), permitting flow of blood from unobstructed vessel in to necrotic zone.
- In tissues that were previously congested because of sluggish outflow of blood.
- When blood flow is reestablished to a site of previous arterial occlusion & necrosis.

b. White infarcts occur in:

- Arterial occlusion in organs with a single arterial blood supply.
- Solid organs such as the heart, spleen, & kidney, where the solidity of the tissue limits the amount of hemorrage that can percolate or seep in to the area of ischemic necrosis from the nearby capillaries.

- **Morphology of infarcts**

Gross: All infarcts are wedge-shaped with the occluded vessel at the apex and the periphery of the organ forming the base of the wedge. The infarction will induce inflammation in the tissue surrounding the area of infarction. Following inflammation, some of the infarcts may show recovery, however, most are ultimately replaced with scars except in the brain.

Microscopy: The dominant histologic feature of infarction is ischemic coagulative necrosis. The brain is an exception to this generalization, where liquefactive necrosis is common.

- **Clinical examples of infarction:**
  - ✓ **Myocardial infarction**
    - Usually results from occlusive thrombosis supervening on ulcerating atheroma of a major coronary artery.
    - Is a white infarct.
    - Can cause sudden death, cardiac failure, etc.

  - ✓ **Cerebral infarcts**

- May appear as pale or hemorrhagic
- A fatal increase in intracranial pressure may occur due to swelling of large cerebral infarction, as recent infarcts are raised above the surface since hypoxic cells lack the ability to maintain ionic gradients & they absorb water & swell.
- Is one type of cerebrovascular accidents (CVA) or stroke which has various clinical manifestations.

  - ✓ **Lung infarcts**

- Are typically dark red & conical (wedge-shaped).
- Can cause chest pain, hemoptysis, etc.

  - ✓ **Splenic infarcts**

- Conical & sub capsular
- Initially dark red later turned to be pale.

3.1.3. Pathological lesions in circulatory disturbances

I. Jaundice/Icterus

Icterus is increased amount of bile pigments in blood circulation and is often called as hyper-bilirubinemia or jaundice. It is of three types.

- **Hemolytic**

Hemolytic jaundice occurs as a result of excessive hemolysis in circulating blood. It is also known as prehepatic jaundice.

✓ **Etiology**

- Piroplasmosis (Babesiabigemina)
- Anaplasmosis (Anaplasma marginale)
- Leptospirosis(Leptospira ictehaemmorrhagae)
- Equine infectious anemia virus
- Anthrax (Bacillus anthracis)
- Clostriduumhemolyticum
- haemolytic streptococci

- **Toxic**

Toxic jaundice occurs as a result of damage in liver leading to increased amount of unconjugated and conjugated bilirubin in blood. It is also known as hepatic jaundice.

✓ **Etiology**

- Toxinj Poisons
- Copper poisoning
- Leptospirosis

- **Obstructive Jaundice:**

Occurs as a result of obstruction in bile duct causing hindrance in normal flow of bile. It is also known as post hepatic jaundice.

✓ **Etiology**

- Blocking of bile canaliculi by swollen hepatocytes
- Obstruction in bile duct (Liver flukes, tapeworms and ascaris)
- Biliary cirrhosis, Cholangitis and Cholelithiasis

- Pressure on bile duct due to abscess, neoplasm.
- Inflammation and swelling at duct opening in duodenum

II. Hyperaemia

Hyperaemia is increased volume of blood in affected tissue or part.

- **Hyperaemia (Active hyperaemia)**
  - ✓ Occurs in arterioles or arteries
  - ✓ Increased blood flow in capillaries
- **Congestion (Passive hyperaemia)**
  - ✓ Occurs due to impaired venous drainage
  - ✓ Stasis of blood in veins
- **Classification of Hyperaemia**
  - ✓ **Active Hyperaemia**
    - Increased blood in arterial side
    - Usually due to inflammation
    - All active hyperaemia are acute
    - Chronic active hyperaemia does not occur
    - Occurs when there is a demand for oxygen and nutrients - increase metabolismIt is beneficial.
  - ✓ **Acute General Active Hyperaemia**
    - Increased blood throughout the body
  - ✓ **Causes**

Various systemic diseases. E.g. Pasteurellosis, erysipelas Rapidly beating heart → increased blood supply

Renal diseases - due to retention of fluids

- ✓ **Macroscopically**

Bright red color organs

- ✓ **Microscopically**

Arteries and capillaries dilated with blood

- ✓ **Result**

Disappears if cause is removed

- ✓ **Acute Local Active Hyperaemia**

- Increased amount of blood in arterial system within a local area (leg, Stomach, lung)
- Most common type of hyperaemia

Causes

- ✓ Physiological
  - Occurs in stomach and intestine following a meal
  - Lactating mammary gland
  - Muscles during exercise
  - Genital tract during oestrus
  - ✓ **Blushing**
- Acute inflammation

Macroscopically

- Enlarged, swollen, heary
- ↑ warmth in Skin
  - ✓ **Microscopically**

✓ In live animals, arteries, arterioles and capillaries are distended with blood

✓ Difficult to detect in dead animals.

III. Congestion :

It is increased blood in the venous end due to improper drainage. .It can be: **genera**l if interference is central (i.e.) lungs, heart or **Loca**l, if vein of an organ or body it can be acute or chronic venous congestion is more common

- **Types of congestion**

A. Acute

This is occurred when Increase in the amount of blood on the venous side of circulatory system Due to sudden obstruction to the flow of blood in heart and lungs.

- **Causes**
- Heart failure
- Degeneration and necrosis of myocardium
- Myocardial infarction
- Pneumonia
- Pulmonary thrombosis or embolism
- Hydropericardium, Haemopericadium, etc.

- Hydrothorax, Haemothorax, etc.

- **Macroscopically**
  - Organs are blue in color (Unoxygenated blood)
  - Veins distended with blood
  - Organs enlarged, heavy
  - Upon incision, blood oozes out

- **Result**
  - Causes are mild → Recovery
  - Causes are severe → Death

B. Chronic

- Increased blood on venous end persisting for long period of time causes Permanent changes (fibrosis, atrophy). Due to central lesions in heart and lungs.

✓ Heart lesions
- Stenosis of valvular openings

✓ Valvular insufficiency
- Failure of cusps of valves to close property
- Inflammatory tissue
- Thrombus

✓ Myocardial failure: Degeneration and necrosis of muscles

✓ Anomalies of heart
- Persistent foramen orale
- Interventricular septal defects
- Constrictive lesons in pericardium
- Traumatic pericarditis in cattle

✓ Lesions of lungs
- Obliteration of capillary bed in lungs
- Prevents free flow of blood through the lungs
- Retards flow through right side of heart
- Blood back flows into Liver

✓ It Causes(results):
- Chronic alveolar pulmonary emphysema in horses (BROKEN WIND)

- Pneumonia
- Hydrothorax, haemothorax
- Compression of major pulmonary vessels
  - Tumours
  - Cysts
  - Abscesses.

C. Acute Local

Increase in blood in the veins of a portion (foot, tail, kidney etc) Due to sudden obstruction to blood flow

- **It Causes (results)**
  - ✓ Malposition of viscera
    - Volvulus, intussusception, torsion
  - ✓ External pressure
    - Ligatures, tourniquets, bandages
- **Pathogenesis**
  - ✓ **Hydrostatic:** Accumulation of blood in ventral portions of the body due to gravity..
- **Causes**(etiology)
  - ✓ Occurs in heart diseases
  - ✓ Recumbency
  - ✓ Inactive animals
  - ✓ Large animals
  - ✓ Heart failure - Agonal congestion

- **Appearances**
  - ✓ Veins in ventral portion or organs distended with blood
  - ✓ Lungs - increase capillary bed
  - ✓ Intestine & kidneys – necrosis and gangrene
  - ✓ Causes pneumonia and gangrene of intestine
- **Significance;** Indicates.
  - the side of animals which was ventral at the time of death
  - Heart was not able to pump properly
  - Location of body in medico–legal cases
- **Grossly and microscopically**

  Veins are engorged with blood ➡ Necrosis of endothelial cells ➡ Haemorrhage

D. Chronic Local; this is due to bIncrease in amount of blood for a long time in veins, results in Permanent tissue changes (atrophy, fibrosis).

- **Causes**
  - ✓ External pressure
  - Tumors, abscesses
  - ✓ Obstruction from within
  - Thrombus (blood clot)
- **Gross and microscopic appearance**
  - ✓ Enlarged initially later undergoes atrophy
  - ✓ Veins - bluish blood
  - ✓ Oedema due to increase permeability of capillaries
  - ✓ Fibrosis

3.2. Aetiology for development of congestion and jaundice/icterus

3.2.1. Aetiology for development of congestion

Congestion is a Passive hyperemia (Venous congestion).it can be an acute or chronic case.

It is increased volume of blood in the venous side of the vascular system due to interference venous return from tissue.

- **Classification of congestion**

Active hyperemia may be classified according to duration and affected area into:

I. General venous congestion.
II. Local venous congestion.

i. General venous congestion

Causes

As mentioned before venous congestion occurs due to interference of blood flow. Moreover acute general venous congestion are resulting from any cause interfere with blood flow through heart and lungs. Degeneration and necrosis of myocardium, in animal put to sever exercise after a prolonged rest or in some infectious diseases, beside interference with flow of blood in lungs, in case of pneumonia where exudates compress the capillaries, are the common causes.

ii. Hypostatic congestion (acute local passive congestion)

It is the gravitation of blood in the lowermost portion of the body. It **is usually caused by cardiac** defect, which fail to maintain sufficient blood pressure to overcome the force of gravity.

Pathogenesis

The defect in heart, or lungs lead to accumulation of blood in venous side with increase of CO2 concentration, which affect on the endothelial lining of capillaries and venules leading to increase its permeability and permits plasma to escape to tissue and serous cavities. Moreover, increase CO2 concentration stimulates fibroblast proliferation. Pressure atrophy results from persist of large amount of blood in venous side.

3.2.2. Aetiology for development jaundice/icterus

Jaundice is a condition in which a yellowish tinge appears on the skin, mucous membranes, and the whites of the eye. Body fluids may also change color.

Jaundice frequently indicates a problem with the liver or bile ducts. When the liver is not working properly, it can cause a waste material called bilirubin to build up in the blood.

With moderate bilirubin levels, the skin, eyes, and mucous membranes can turn yellow. As it progresses, the color can also change from yellow to green. The green color occurs due to biliverdin, the green pigment present in bile.

Jaundice can develop in people of all ages and is normally the result of an underlying condition. Newborns and older adults have the highest likelihood of developing jaundice. Bilirubin levels increase as the red blood cells naturally break down. Typically, the liver filters this waste material out of the bloodstream and turns it into a new form called conjugated bilirubin. The new form then exits the body in a person's stool. If there is too much bilirubin for the liver to process, it can build up in the body. This is known as hyper bilirubinemia, and it causes the yellow color in the skin and eyes.

Jaundice typically occurs due to an underlying disorder that either causes the production of too much bilirubin or prevents the liver from eliminating it.

Some possible underlying conditions and causes of jaundice include:

- side effects of certain medications
- gallstone disease
- excessive alcohol consumption
- gallbladder or pancreatic cancer
- cirrhosis, which is a disease that causes scar tissue to replace healthy tissue in the liver
- hepatitis or other liver infections
- hemolytic anemia

3.3. Types and causes of shock

Shock

Definition: Shock is a state in which there is failure of the circulatory system to maintain adequate cellular perfusion resulting in widespread reduction in delivery of oxygen & other nutrients to tissues. In shock, the mean arterial pressure is less than 60 mmHg or the systolic blood pressure is less than 90 mmHg.Adequate organ perfusion depends on arterial blood pressure (BP) which, in turn, depends on:

- Cardiac output.
- Peripheral vascular resistance.

Cardiac output = stroke volume X heart rate

In turn, stroke volume depends on:

a. Preload i.e. blood volume,
b. Afterload i.e. arterial resistance, &
c. Myocardial contractility.

Therefore, shock (i.e. widespread decreased perfusion of tissues) occurs when the preload (i.e. the blood volume) is decreased, or when the afterload (the peripheral vascular resistance) is decreased, or when the myocardium fails to contract. These basic mechanisms of shock are used to classify it. Next, we will look at the classification of shock.

3.3.1. Types of shock: Shock can be divided into:

I. Hypovolemic shock
II. Cardiogenic shock
III. Distributive shock

I. Hypovolemic shock

Definition: This is shock caused by reduced blood volume. Reduction in circulating blood volume results in the reduction of the preload which leads to inadequate left ventricular filling, reflected as decreased left & right ventricular end diastolic volume and pressure. The reduced preload culminates in decreased cardiac output which leads to widespread tissue perfusion (shock).

- **Causes of hypovolumic shock include**:

✓ Haemorrhage
✓ Diarrhoea and vomiting
✓ Burns
✓ Trauma and etc.

The effect of haemorrhage depends on the rate and amount of blood loss. Hypovolumic shock is the most common type of shock in clinical medicine .A normal healthy adult can lose 550ml (10%of blood volume) without significant symptoms.

II. Cardiogenic shock

Definition: This is shock that results from severe depression of cardiac performance. It primarily results from pump failure (myocardial failure). Causes of cardiogenic shock can be divided into:

A. Myopathic
B. Mechanical

A. Myopathic causes of cardiogenic shock include:

- Acute myocardial infraction. Usually shock occurs in this conditioin if ≥ 40% of the left ventricular mass & more on the right ventricle is involved by infarction.
- Mycocarditis
- Dilated cardiomyopathy/hypertrophic cardiomyopathy
- Myocardial depression in septic shock and etc.

B. Mechanical

- **Intracardiac**
  - ✓ Left ventricle outflow obstruction E.g.Aortic stenosis, hypertrophic cardiomyopathy
  - ✓ Reduction in forward cardiac output E.g. Aortic or mitral regurgitation
  - ✓ Arrhythmia
- **Extracardiac**

This can be called obstructive shock. The extracardiac causes of cardiogenic shock can be caused by:

- ✓ Pericardial tamponade (gross fluid accumulation in the pericardial space) results in a decreased ventricular diastolic filling → ↓CO
- ✓ Tension pneumothorax (gas accumulation in pleural space). This decreases the venous return by creating a positive pressure.
- ✓ Acute massive pulumonary embolism occupying 50-60% of pulumonary vascular bed.
- ✓ Severe pulmonary hypertension (10pulmonary hypertension).

III. Distributive shock

Definition: Distributive shock refers to a group of shock subtypes caused by profound peripheral vasodilatation despite normal or high cardiac output.

Causes of distributive shock:

- Septic shock – the commonest among the group& clinically very important.
- Neurogenic shock
  - ✓ Usually occurs in the setting of anaesthetic procedure [cephalo-caudal migration of anaesthetic agent] or spinal cord injury owing to loss of vascular tone &peripheral pooling of blood.
- Anaphylactic shock
  - ✓ Initiated by generalized IgE – mediated hypersensitivity response, associated with systemic vasodilatation & increased vascular permeability.
- Endocrine shock
  - ✓ This is a type of shock that typically occurs in adrenal insufficiency.

Notes

- **Bactermia:**is the presence of viable bacteria in the blood as evidenced by blood culture.
- **Septicemia:**is systemic infection due the presence of microbes and their toxin the blood.
- **Sepsis:**is a systemic response to severe infection mediated via macrophage-derived cytokines that target end organ receptors in response to infection.

Self-Check – 3	Written test

Name…… ID…… Date…….

Directions: Answer all the questions listed below. Examples may be necessary to aid some explanations/answers.

Test I: Short Answer Questions

1. Define shock (2pts)?
2. List and define the types of shock (4pts)?
3. What is the cause of cardiogenic shock (2pts)?
4. What are the pathological lesion occurred in blood circulation (2pts)?
5. Explain clearly the differences among hyperemia, congestion and icterus neatly (4pts)?

LG #7	LO#4- Recognize Growth disorder

Instruction sheet

This learning guide is developed to provide you the necessary information regarding the following content coverage and topics:

- Congenital defects of body systems
- Adaptive changes in animal cells
- Characteristics and common types of neoplasia

This guide will also assist you to attain the learning outcomes stated in the cover page. Specifically, upon completion of this learning guide, you will be able to:

- clearly seen Congenital defects of the different body systems .
- identify All adaptive changes in cells which help the cell to cope with an alteration in its environment
- identify and describe The common types of neoplasia occurring in animals
- identify and describe The characteristics and classification of most commonly prevalent cases of neoplasia

Learning Instructions:

1) Read the specific objectives of this Learning Guide.
2) Follow the instructions described below.
3) Read the information written in the information Sheets
4) Accomplish the Self-checks

Information Sheet 4

4.1. Congenital defects of body systems

Introduction to congenital defects

Congenital anomalies can be defined as structural or functional anomalies that occur during intrauterine life. Also called birth defects, congenital disorders, or congenital malformations, these conditions develop prenatally and may be identified before or at birth, or later in life.



Figure 4.1 :Congenital defeacts occurred at animals level

4.1.1. Disturbances in Development (Anomalies & Monster)

- Anomaly is developmental defect affecting an organ or part of the body.
- Anomaly is the disturbance of development that involves an organ or a portion of an organ.
- Monster is an animal in which extensive abnormal developments are present.
- A Congenital disease is one in which the patient is born with the disease whereas an inherited disease is one which is due to factors in the genetic materials received from the parents.

4.1.2. Classification of Anomalies

A. Arrest of Development

- **Agenesia** is an incomplete and imperfect development of an organ or part and **aplasia** is absence of an organ or part. There some exaamples of agenesis and aplasia lists:
  - ✓ **Acrania** is absence of most or all of the bones of the cranium.
  - ✓ **Amelia** is absence of one or more limbs.
  - ✓ **Agnathia** is absence of lower jaw.
  - ✓ **Anencephalia** is absence of the brain
  - ✓ **Hypocephalia** is incomplete development of the brain.
  - ✓ **Anophathalmia** is absence of one or both eyes.
  - ✓ **Hemicrania** is absence of half of the head.
  - ✓ **Atresia** is absence of normal opening e.g. Atresia ani is absence of anus opening and Atresia coli is absence of rectum.
  - ✓ **Exencephalia** is defective skull with brain exposed or extruded. If the protruding brain contains a ventricle which is filled with excessive amount of fluid, the malformation is a hydrencephalocele.
  - ✓ **Arhinencephalia** is absence or rudimentary development of the olfactory lobe with corresponding lack of development of the external olfactory organs.
  - ✓ **Agnathia** is absence of the lower jaw.
  - ✓ **Anophthalmia**is absence of one or both eyes.
  - ✓ **Abrachia** is absence of the forelimbs.
  - ✓ **Abrachiocephalia** is absence of forelimbs and head.
  - ✓ **Adactylia** is absence of digits.

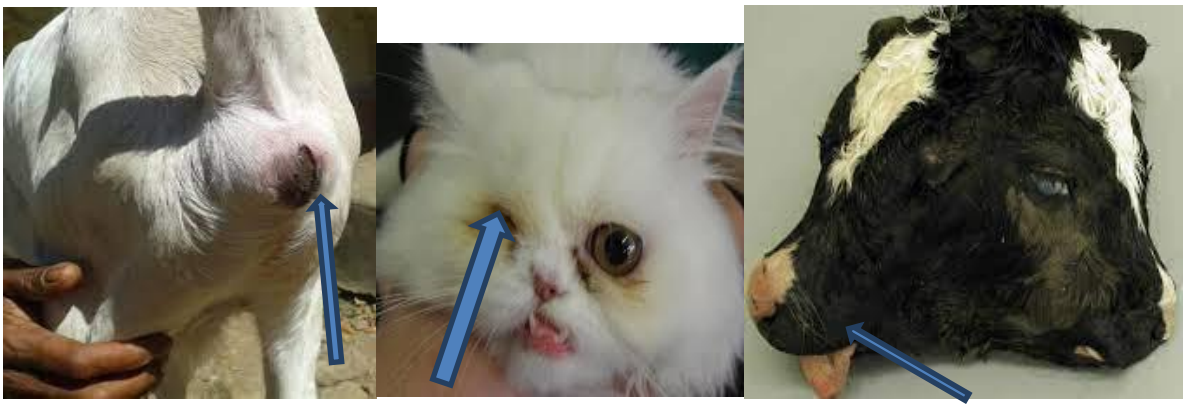


Figure 4.2: Anomalies of Atresia, Anophthalmia and Anencephalia

- **Fissures on the median line of the head, thorax, and abdomen.**
  - ✓ Craniooschisis (skull)
  - ✓ Cheiloschisis (lip), often referred to as harelip.
  - ✓ Palatoschisis (oral) cavity, often called cleft palate. Harelip and cleft palate result from faulty development of the maxillary process derived from the first visceral arch.
  - ✓ Rachischisis (spinal column).
  - ✓ Schistorrachis or spina bifida (spinal column)
  - ✓ Schistothorax (thoraz or sternum).
  - ✓ Schistosomus (abdomen).
  - ✓ Schistocormus (thorax, neck or abdominal wall). Results from arrested development of the amnion.



Figure 4.3 : Organs monasteries indications of some animals

- **Fusion of paired organs**
  - ✓ Cyclopia (eyes)
  - ✓ Ren arcuatus (kidneys), often referred to as horseshoe kidney.

B. Excess of Development

- Congenital hypertrophy
- Hemi hypertrophy (partial)
  - ✓ Increase in the number of a part.
    - Polyotia (ears)
    - Polyodontia(teeth)
    - Polymelia (limbs)
    - Polydactylia(digits)
    - Polymastia (mammary gland)
    - Polythelia(teat

4.1.3. Displacements During Development

I. Displacements of organs

- Dextrocardia is transposition of the heart to the right side.
- Ectopiacordiscervicalis is displacement of the heart into the neck.

II. Displacements of tissues

- Teratoma is inclusion of multiple displaced and also neoplastic tissues within an individual.
- Dermoid is inclusion within an individual of a mass containing skin, hair, feathers, or teeth depending on the species and often arranged as an epidermal cyst (Dermoid cyst).
- Odontoid cyst is inclusion within an individual of a mass of dental enamel and cement.
- Dentigerous cyst is inclusion within an individual of one or more imperfectly formed teeth.
- Fusion of Sexual Characters
- Hermaphrodite is an individual having both testicular and ovarian tissue. Pseudohermaphrodite is an animal having unisexual development of the sex glands

(either testicular or ovarian tissue), but having also either a unisexual or bisexual development of the other parts of the genitalia.

- Freemartin is a female calf having arrested development of the sex organs and being the twin of perfect male.

iii. Monsters

A monster or monstrosity is a disturbance of development that involves several organs and causes great distortion of the individual. For the most part monsters possess a duplication of all or most of the organs and other parts of the body. They develop from a single ovum. They are therefore the product of incomplete twinning.

Classification of the Monsters

a. Twins Entirely Separate

Although separate, these twins are in a single chorion. One twin as a rule is well developed; the other is malformed (acardius). In the malformed foetus there is arrested development of the heart, lungs, and trunk. Such monsters may lack a head (acephalus), limbs and other recognizable features (amorphous), or the trunk (acormus).

b. Twins United; these twins are more or less completely united and are of symmetrical development.

a. Twins United

✓ **Anterior Twinning:** The anterior part of the individual is double, the posterior single.

- Pygopagus – united in the pelvic region with the bodies side by side.
- Ischiopagus – united in the pelvic region with the bodies at an obtuse (not pointed) angle.
- Dicephalus – two separate heads; doubling may also affect the neck, thorax and trunk.
- Diproosopus – doubling in the cephalic region without complete separation of heads; only the face doubled.

✓ **Posterior Twinning:**The posterior part is double, the anterior single.

- Craniopagus – brains usually separated; bodies as a rule at an acute angle.
- Cephalothoracopagus – union of head and thorax.

- Dipygus – doubling of posterior extremities and posterior part of body.



Figure 4.4: twins united anomalies

b. Twinning Almost Complete

Duplication of the whole trunk or the anterioror posterior extremities with parallel, ventral arrangement of the foetuses. The pair is joined in the region of the thorax, and also often in the abdominal region.

- Thoracopagus – united only by the thorax.
- Prosopothoracopagus – besides the union the thorax the abdomen, the head and neck are united.
- Rachipagus – thorax and lumbar portion of the spinal column united.

4.2. Adaptive changes in animal cells

4.2.1. Cellular changes and adaptive responses

Cellular adaptation is the ability of cells to respond to various types of stimuli and adverse environmental changes. Tissues adapt differently depending on the replicative characteristics of the cells that make up the tissue. For example, labile tissue such as the skin can rapidly replicate, and therefore can also regenerate after injury, whereas permanent tissue such as neural and cardiac tissue cannot regenerate after injury. If cells are not able to adapt to the 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 adaptive mechanisms and their different consequences in the human body. Cellular adaptations include:

- Hypertrophy (enlargement of individual cells),
- Hyperplasia (increase in cell number),
- Atrophy (reduction in size and cell number),
- Metaplasia (transformation from one type of epithelium to another), and
- Dysplasia (disordered growth of cells).

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4.2.2. Types of cellular adaptation

I. Hypertrophy

Hypertrophy is increase in the size of cells. Increased workload leads to increased protein synthesis & increased size & number of intracellular organelles which, in turn, leads to increased cell size. The increased cell size leads to increased size of the organ.E.g.: the enlargement of the left ventricle in hypertensive heart disease & the increase in skeletal muscle during sternous exercise.

II. Hyperplasia

Hyperplasia is an increase in the number of cells. It can lead to an increase in the size of the organ. It is usually caused by hormonal stimulation. It can be physiological as in enlargement of the breast during pregnancy or it can pathological as in endometrial hyperplasia.

III. Atrophy

Atrophy is a decrease in the size of a cell. This can lead to decreased size of the organ. The atrophic cell shows autophagic vacuoles which contain cellular debris from degraded organelles. Atrophy can be caused by:

- Disuse
- Undernutrition
- Decreased endocrine stimulation
- denervation
- Old age

IV. Metaplasia

Metaplasia is the replacement of one differentiated tissue by another differentiated tissue. There are different types of metaplasia. Examples include:

a. **Squamous metaplasia**: this is replacement of another type of epithelium by squamous epithelium. For example, the columnar epithelium of the bronchus can be replaced by squamous epithelium in cigarette smokers
b. **Osseous metaplasia:** this replacement of a connective tissue by bone, for example at sites of injury.

V. Dysplasia

A term used to describe the presence of abnormal cells within a tissue or organ. Dysplasia is not cancer, but it may sometimes become cancer. Dysplasia can be mild, moderate, or severe, depending on how abnormal the cells look under a microscope and how much of the tissue or organ is affected.



Figure 4.5: Organs and bovine heart hypertrophy



Figure 4.6: Development of metaplasia in oral cavity of both animals and plant

4.2. Characteristics and common types of neoplasia

4.3.1. Characteristics of neoplasia

Neoplasia

Neoplasia is the abnormal growth of a tissue into a mass that is not responsive to normal control mechanisms and may be benign or malignant. Growth of this mass is not affected when the inciting stimulus is removed.

Overview: The terms **tumor, nodule, and mass** are nonspecific terms that refer to an abnormal proliferation of cells. The term **neoplasm** means new growth and does not imply benign or malignant (i.e., there are benign neoplasms, and there are malignant neoplasms).

A. Nomenclature for general categories of neoplasms

I. Adenoma: Benign neoplasm derived from glandular cells.

Adenoma is **a type of non-cancerous tumor or benign** that may affect various organs. It is derived from the word “adeno” meaning 'pertaining to a gland'. Every cell in the body has a tightly regulated system that dictates when it needs to grow, mature and eventually die off.

II. Carcinoma: Malignant neoplasm derived from epithelial cells.

- Carcinoma refers to a malignant neoplasm of epithelial origin or cancer of the internal or external lining of the body. Carcinomas, malignancies of epithelial tissue, account for 80 to 90 percent of all cancer cases.
- Epithelial tissue is found throughout the body. It is present in the skin, as well as the covering and lining of organs and internal passageways, such as the gastrointestinal tract.
- Carcinomas are divided into two major subtypes: adenocarcinoma, which develops in an organ or gland, and squamous cell carcinoma, which originates in the squamous epithelium.
- Adenocarcinomas generally occur in mucus membranes and are first seen as a thickened plaque-like white mucosa. They often spread easily through the soft tissue where they occur. Squamous cell carcinomas occur in many areas of the body.
- Most carcinomas affect organs or glands capable of secretion, such as the breasts, which produce milk, or the lungs, which secrete mucus, or colon or prostate or bladder.

III. Sarcoma: Malignant neoplasm derived from mesenchymal cells (e.g., fat, muscle).

Sarcoma refers to cancer that originates in supportive and connective tissues such as bones, tendons, cartilage, muscle, and fat. Generally occurring in young adults, the most common sarcoma often develops as a painful mass on the bone. Sarcoma tumors usually resemble the tissue in which they grow. Examples of sarcomas are:

- Osteosarcoma or osteogenic sarcoma (bone)
- Chondrosarcoma (cartilage)
- Leiomyosarcoma (smooth muscle)
- Rhabdomyosarcoma (skeletal muscle)
- Mesothelial sarcoma or mesothelioma (membranous lining of body cavities)

- Fibrosarcoma (fibrous tissue)
- Angiosarcoma or hemangioendothelioma (blood vessels)
- Liposarcoma (adipose tissue)
- Glioma or astrocytoma (neurogenic connective tissue found in the brain)
- Myxosarcoma (primitive embryonic connective tissue)
- Mesenchymous or mixed mesodermal tumor (mixed connective tissue types)

IV. Lymphoma: Malignant neoplasm derived from lymphocytes.

Lymphomas develop in the glands or nodes of the lymphatic system, a network of vessels, nodes, and organs (specifically the spleen, tonsils, and thymus) that purify bodily fluids and produce infection-fighting white blood cells, or lymphocytes. Unlike the leukemia's which are sometimes called "liquid cancers," lymphomas are "solid cancers." Lymphomas may also occur in specific organs such as the stomach, breast or brain. These lymphomas are referred to as extra nodal lymphomas. The lymphomas are sub-classified into two categories: Hodgkin lymphoma and Non-Hodgkin lymphoma. The presence of Reed-Sternberg cells in Hodgkin lymphoma diagnostically distinguishes Hodgkin lymphoma from Non-Hodgkin lymphoma.

V. Melanoma: Malignant neoplasm derived from melanocytes.

Myeloma is cancer that originates in the plasma cells of bone marrow. The plasma cells produce some of the proteins found in blood.

- **Leukemia**

Leukemias ("liquid cancers" or "blood cancers") are cancers of the bone marrow (the site of blood cell production). The word leukemia means "white blood" in Greek. The disease is often associated with the overproduction of immature white blood cells. These immature white blood cells do not perform as well as they should, therefore the patient is often prone to infection. Leukemia also affects red blood cells and can cause poor blood clotting and fatigue due to anemia. Examples of leukemia include:

- Myelogenous or granulocytic leukemia (malignancy of the myeloid and granulocytic white blood cell series)
- Lymphatic, lymphocytic, or lymphoblastic leukemia (malignancy of the lymphoid and lymphocytic blood cell series)
- Polycythemia vera or erythremia (malignancy of various blood cell products, but with red cells predominating).

VI. **Germ cell tumor:** Malignant neoplasm derived from germ cells. The type components may be within one category or from different categories. Some examples are:

- adenosquamous carcinoma
- mixed mesodermal tumor
- carcinosarcoma
- teratocarcinoma

B. Nomenclature for benign neoplasms

In general, the name of a benign neoplasm often ends with - oma.

- **Examples:** Adenoma (benign neoplasm of glandular epithelium), fibroadenoma (benign neoplasm of the breast), and leiomyoma (benign neoplasm of smooth muscle).
- **Some exceptions:** Hepatoma (malignant neoplasm of liver), melanoma (malignant neoplasm of melanocytes), mesothelioma (malignant neoplasm of mesothelial cells), and seminoma (malignant germ cell neoplasm of testis).

C. Nomenclature for malignant neoplasms

In general, the name of a malignant neoplasm often ends with –carcinoma or –sarcoma.

- **Examples:** Adenocarcinoma (malignant neoplasm of glandular tissue), rhabdomyosarcoma (malignant neoplasm of skeletal muscle), and leiomyosarcoma (malignant neoplasm of smooth muscle).

4.3.2. Common types of neoplasia

Definition and Nomenclature

Recently, neoplasiameans new growth and technically,defined as abnormal mass of tissues the growth of which exceeds and persists in the same excessive manner after cessation of the stimulus, evoking the transformation.

Nomenclature: Neoplasms are named based upon two factors:

- On the histologic types → **mesenchymal** and **epithelial**
- On behavioral patterns : **benign** and **malignant** neoplasms



Figure 4.7:Neoplasia of dog eye and eyelid

Neoplasms are classified so that one can:

- Deduce a prognosis
- Investigate the cause
  - ✓ Perhaps with a view to prevention
- Assess the results of treatment.
- It must be remembered that there are several types of proliferative change, and neoplasia must be distinguised from these.
- In addition to neoplasia, hyperplasia and dysplasia are also proliferative changes.
  - ✓ Inflammatory, repair and granuloma lesions may also masquerade as neoplasms.
- However, destructive or necrotic tumours may have inflammation present.
  - ✓ Unlike inflammation, hyperplasia or dysplasia, neoplastic cells show uncontrolled proliferation in the absence of a triggering stimulus.

4.3.3. Types of Classification of neoplasim

Tumours are classified by:

a) **Histogenesis:** by identification of the cells/ tissue of origin.
b) **Anatomical origin**: by site of anatomical growth.
c) **State of differentiation**: by relative development or maturity of the cell type involved.
d) **Behaviour**: by host-tumour growth patterns.e.g. **benign** or **malignant**.

- **Behaviour**

✓ The terms 'benign' and 'malignant' represent two ends of a spectrum of behaviour patterns in tumours.

✓ Certain features exhibited by the neoplastic cells allowtumours to be labelled as benign or malignant.

a. Characteristics of Benign and Malignant Neoplasms

Benign neoplasia: Thus, the suffix -oma denotes a benign neoplasm. Benign mesenchymal neoplasms originating from muscle, bone, fat, blood vessel nerve, fibrous tissue and cartilages are named as Rhabdomyoma, osteoma, lipoma, hemangioma, neuroma, fibroma and chondroma respectively. Benign epithelial neoplasms are classified on the basis of cell of origin for example adenoma is the term for benign epithelial neoplasm that form glandular pattern or on basis of microscopic or macroscopic patterns for example visible finger like or warty projection from epithelial surface are referred to as papillomas.

Malignant neoplasm nomenclature essentially follows the same scheme used for benign neoplasm with certain additions. Malignant neoplasms arising from mesenchymal tissues are called sarcomas (Greed sar =fleshy). Thus, it is a fleshy tumour. These neoplasms are named as fibrosarcoma, liposarcoma, osteosarcoma, hemangiosarcoma etc. Malignant neoplasms of epithelial cell origin derived from any of the three germ layers are called carcinomas.

Eg. Ectodermal origin: skin (epidermis squamous cell carcinoma, basal cell carcinoma) Mesodermal origin: renal tubules (renal cell carcinoma).Endodermal origin: linings of the gastrointestinal tract (colonic carcinoma). The difference in characteristics of these neoplasms can be conveniently discussed under the following:-

i. Differentiation & anaplasia
ii. Rate of growth
iii. Local invasion
iv. Metastasis

i. Differentiation & anaplasia

Differentiation refers to the extent to which parenchymal cells resemble comparable normal cells both morphologically and functionally.Thus, well-differentiated tumourscells resemble mature normal cells of tissue of origin. In general, benign neoplasms are well differentiated. Malignant neoplasms in contrast, range from well differentiated, moderately differentiated to poorly differentiate types. Malignant neoplasm composed of undifferentiated cells are said to be anaplastic, literally anaplasia means to form backward.

- Morphology of anaplastic cell includes large Pleomorphic; hyperchromatic nucleus with high nuclear cytoplasmic ratio 1:1(normally 1:4 to 1:6). The cell usually reveals large nucleoli with high and often abnormal mitoses. Tumour giant cells and frequent loss of polarity of epithelial arrangements are encountered.
- On functional differentiation, the well differentiated the neoplasm, the more completely it retains the functional capabilities found in its normal counterparts thus, endocrine tumours produce hormone (ex. Thyroid, adrenal) so also, well differentiated squamous cell carcinoma and well differentiated hepatocellular carcinomas produce keratine and bile respectively.
- However, highly anaplastic or undifferentiated cells of what cell tissue of origin come to resemble each other functionally and morphologically more than the normal cells which they have arisen this is called chemical convergence.

ii. Rate of growth

- Most benign tumours grow slowly whereas; most malignant tumours grow rapidly sometimes, at erratic pace.
- Some benign tumours for example uterine leiomyoma increase in size during pregnancy due to probably steroidal effects (estrogen) and regress in menopause.

- In general, the growth rate of neoplasms correlate with their level of differentiation and thus, most malignant neoplasms grow more rapidly than do benign neoplasms.
- On occasions, cancers have been observed to decrease in size and even spontaneously disappear. E.g. renal cell carcinoma, malignant melanoma, choriocarcinoma.

iii. Local invasion

- Nearly all benign neoplasms grow as cohesive expansile masses that remains localized to their site of origin and do not have the capacity to invade or metastasize to distant sites, as do malignant neoplasms.
- Rims of fibrous capsules encapsulate most benign neoplasms. However, hemangiomas and neuro fibromas are exceptions. Thus, such encapsulations tend to contain the 193 benign neoplasms as a discrete, rapidly palpable and easily movable mass that can easily surgically enucleated.
- The growth of malignant neoplasms is accompanied by progressive infiltration, invasion and destruction of the surrounding tissue. Generally, they are poorly demarcated from the surrounding normal tissue (and a well-defined cleavage plane is lacking).
- Next to the development of metastasis, invasiveness is the most reliable feature that differentiates malignant from benign neoplasms.
- Even though, malignant neoplasms can invade all tissues in the body, connective tissues are the favoured invasive path for most malignant neoplasms, due to the elaboration of some enzymes such as type IV collagnases& plasmin, which is specific to collagen of basement membrane. Several matrix-degrading enzymes including glycosidase may be associated with tumour invasion.

iv. Metastasis

- It is defined as a transfer of malignant cells from one site to another not directly connected with it (as it is described in the above steps).

- Metastasis is the most reliable sign of malignancy. The invasiveness of cancers permits them to penetrate in to the blood vessel, lymphatic and body cavities providing the opportunity for spread.
- Most malignant neoplasm metastasies except few such as gliomas in the central nervous system, basal cell carcinoma (Rodent ulcer) in the skin and dermato fibrosarcoma in soft tissues.
- Organs least favoured for metastatic spread include striated muscles and spleen.
- Since the pattern of metastasis is unpredictable, no judgment can be made about the possibility of metastasis from pathologic examination of the primary tumour.

b. **Pathways of spread:**

Dissemination of malignant neoplasm may occur through one of the following pathways.

i. Seeding of body cavities and surfaces (transcoelomic spread)

ii. Lymphatic spread: The most common pathway for the initial dissemination of carcinomas

iii. Hematogenous spread

Self-Check – 4	Written test

Name…… ID…… Date…….

Directions: Answer all the questions listed below. Examples may be necessary to aid some explanations/answers.

Test I: Short Answer Questions

1. Compare & contrast the various types of cellular adaptation (4pts).
2. Define cell injury (2pts).
3. Define congenital in pathological concept (4pts).
4. List atleast 5 congenital organs and explain it (3pts).
5. What is aplasia and freemartins' (4pts).
6. Define neoplasia (3pts).
7. Discuss the differences between benign and malignant neoplasms (3pts).

Note: Satisfactory rating – above 7 points **Unsatisfactory - below 7 points**

You can ask your teacher the copy of the answer sheet

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