Course Outline

1. Anatomic Review of Haemopoietic organs: Structure and functions of
   - Bone Marrow
   - Blood Cells
   - Thymus
   - Lymph Nodes
   - Spleen
2. Responses of the heamopoietic organs to injury and causes: General and Specific.
3. Portal of entry of infections agents into the system.
4. Pathology of the organs of the haemopoietic system
5. Specific diseases and tumors of the haemopoietic system

REVIEW OF ANATOMY OF HAEMOPOIETIC ORGANS

INTRODUCTION

The haemopoietic system includes all cells that arise from stem cells in the bone marrow and organs such as peyer's patches, thymus, tonsils, lymph/nodes, spleen, bursa of fabricious and blood cells.

The system consists of 2 major tissues:

I Lympho-reticular (Mucosa associated lymphoid tissue (MALT) – spleen and lymph nodes.

II. Lympho-epithelial tissues – peyer's patches, thymus, tonsils etc.

The cellular component of these organs provide oxygen transport (Erythrocytes) and protective responses to infectious and noninfectious agents (lymphoid cells mononuclear phagocytic cells, granulocytes and supportive tissues).

Organs such as the thymus, lymph nodes and spleen are the places where cells of the system (cellular component) are sequestered for conditioning, proliferation and function.

The bone marrow, spleen and lymph nodes share certain basic anatomic feature e.g. specialized fibroblast-like reticular cells extend long filamentous processes and provide a scaffolding

arrangement to support population of cells. In addition to physical support, these cells also provided microenvironment that attracts the appropriate circulating cells and enables them to multiply or differentiate into cell of a particular lineage.
Within the reticular network of these organs are thin-walled sinuses that control movement of cells and large molecular. These sinuses are located between arterioles and venules in the bone marrow and spleen, but contain lymph within lymph nodes.
Significant insight into diseases of the heamopoeitic system may be gained by simply submitting blood for hematology. A complete haemogram is frequently of greater value than the necropsy in understanding disease mechanisms of the haemopoietic system.
Learning to evaluate blood smears is invaluable addition to the information gained from the physical examination of an animal. Lymph nodes and bone marrow aspirates are also frequently indicated when studying disorders of the haemopoietic system.

Organs of the haemopoietic system.

A) **Bone Marrow and Blood Cells**

Haemopoiesis takes place in the bone marrow and remains active throughout life and constantly produces new cells into the circulation. Haemopoiesis is defined as process through which blood cells are produced. Specific processes include:

- Erythropoiesis
- Myelopoiesis/ granulopoiesis
- Monocytopoiesis
- Thrombopoiesis
- Lymphopoiesis

(b) Thymus

Classified as a component of the lymphatic system, but also been called a lympho-epithelial organ because of the epithelial component. Thymus is essential for the development and function of the immune system especially for the development T-Lymphocytes.
Histologically, two portions are recognized i.e. stromal portion and thymocytes (lymphocyte at different stages of maturation).
Unlike spleen and Lymph node the stroma of thymus consist of epithelial cells as well as macrophages and dentritic cells. The shape and location of the thymus vary among young domestic animals. In ruminants, the thymus has 2 lobes i.e. cervical and thoracic. While dogs do not have the cervical, the thoracic portion is present in all the domestic animals and lies in the cranial mediastinum, ventrally in the horse, pig and dog and dorsally in ruminants. The cervical lobe is large and extends to along the sides of the cervical trachea. However the size varies in cats and horses.
This organ is of greatest importance in the young animals. It begins to regress about the time of puberty and may eventually almost disappear; even when a more sizeable vestige persists, this will be found to consist largely of fat and fibrous elements, with suppression of the thymus tissue

(c) Spleen

The functions of the spleen are analogous to those of the lymph nodes. It is the largest 2^0 lymphoid organ and also acts as reservoir for blood (reserve pool), it is also an organ of extra-medullary haemopoiesis (EMH). Spleen filters blood of foreign materials and microorganisms and removes senescent and altered erythrocytes. Summarily, the spleen has components of three anatomic systems

1. The monocyte – macrophage system.
2. The lymphopoietic system and
3. The vasculature.

Histology: the spleen is divided into Red pulp and White pulp.

The functions include:

- Removal of foreign materials, particularly micro-organism and also senescent and altered erythrocytes.
- Storage of mature erythrocytes in the vascular spaces of the red pulp.
- Haemopoiesis under certain circumstances.
- Immunologic response with production of B–lymphocytes and plasma cells to produce antibody and memory lymphocytes.

(d) Lymph node

Classified as secondary lymphoid organ – defined as the site of production of antibody and cells for cell mediated immunity.

A lymph node includes components of 2 different anatomic systems – monocytes – MQ system and the haematopoietic (lymphopoietic) system.

Its most important functions are filtration of lymph and immune responses. The lymph node is enclosed almost completely by a fibrous capsule and in a cross section of lymph nodes there are 2 main areas viz: cortex (outer) and medullar (inner).

Lymphoid Nodules

This includes the so-called solitary and aggregated lymphoid nodules. Lymphoid are present and in the mucosal – Associated lymphoid tissue (MALT) which include BALT. Bronchus – Associated Lymphoid tissue, GALT (Gut Associated lymph tissue) and lymphoid nodules at other sites. Such as tonsils, mucosa of the nasal cavity, conjunction and urinary bladder. These lymphoid nodules consist of lymph follicles, and some loose lymphoid tissue. The follicles, if antigenically stimulated can have active germical centers.

Haemal Nodes

Although these are often considered to be unique to ruminants, they have also been found in horses and primates. Their architecture resembles that of a lymph node with lymph follicles and sinuses, except that they are filled with blood. Some authors regard them as “Miniature spleen”. It is presumed that haemal nodes can filter blood and remove senescent erythrocytes.

Responses of the haemopoietic organs to injury

Generally the main pattern of responses of these organs includes.

1. Atrophy
2. Hypertrophy
3. Hyperplasia
4. Neoplasia
5. Inflammation
6. Degenerative changes

Atrophy

Atrophy of the bone marrow and haemopoietic cell population follows certain types of injury and result in failure of erythropoiesis granulopoiesis, thrombopoiesis etc. Occasionally injury to stem cells results in complete failure of haemopoiesis with resultant pancytopaenia. Spleen atrophy is uncommon, but does occur in older animals, and is usually of little pathological consequence. Certain viruses and toxins as well as malnutrition can cause thymus and lymph node atrophy, which impairs immune functions. In cachexia, the haemopoietic tissue in the bone marrow can be displaced by gelatinous, almost translucent materials; non-infections agents can induce atrophic changes, either by "exhaustion" of the response capacity of the tissue. High levels of glucocorticoids may cause lymphoid depletion in lymphoid tissues.

Hypertrophy

In animals this is most unlikely in the bone marrow because the tissue is enclosed by bone. In children with congenital baemolytic anaemia, some flat bone may become enlarged as a result of prolonged hyperplasisa. Hypertrophy of the superficial lymph nodes is usually confined to the lymph node receiving lymph from that area if injury or stimulation. Generally lymph node hyperplasia and hypertrophy is uncommon and occurs with systemic infection of some duration.

Hyperplasia

Hyperplasia of the splenic lymphocytes or macrophages population can result from splenic hypertrophy; when this occurs, the spleen is firm and fleshy when incised. Lymph node enlargement secondary to cellular proliferation or hyperplasia occurs in response to stimulation and antigenic stimulation. Hyperplasia of bone marrow haemopoietic tissue occurs following prolonged hemorrhage, haemolysis; and bacterial infections. The haemopoietic tissue expands and replaces adipocytes; yellow marrow becomes red extending from the ends of the long bones along the endosteum.

Neoplasia

Neoplasia of the haemopietic system are relatively common in both companion and production animals and are classified according to their histogenic lineage. The different types of malignant lymphoma and leukemia are the most frequent haemopoietic tumors in domestic animals. Neoplasm of the haemopoietic system in some species, such as the cat has a significant of incidence. The most common neoplasm of the marrow is sarcoma. Sarcomas of the bone

marrow can be derived from erythrocytic, granulocytic, megakaryocytic, lymphocytic and plasma cells.
Lymphosarcomas may arise in and organ and frequently cause lymph node enlargement. Superficial lymph node aspirates for cytology, and biopsies for histology, usually allow differentiation of lymphosarcoma from lymphadenitis or hyperplasia

Inflammation

When characteristic inflammatory changes like suppuration or caseation are visible in lymph nodes or spleen, lymphadenitis and splenitis are respectively used.

Degenerative Changes

Degenerative Changes of erythrocytes, neutrophils and organs of this system may occur.

SPECIFIC RESPONSES OF HAEMOPOIETIC ORGANS TO INJURY

(1) Bone marrow and blood cells

Bone Marrow	**Causes**
Hypoplasia	Increased destruction
Hyperplasia	Haemophthisis
Aplasia	Neoplasm
Neoplasia	Decreased production
Myelophthisis	Abnormal function

Thymus	**Causes**
Atrophy	Infectious agents – viruses
Neoplasia	- Bacteria
	Chemotherapeutic agents
Haemorhage and haemoatoma	Chemical agents and toxins
Inflammation – very rare	Ionizing radiation
Lymphoid hyperplasia – very rare	Malnutrition, cachexia, Aging

Spleen

- Acute inflammation
- Hyperplasia of monocyte- mQ system
- Lymphoid atrophy/hyperplasia
- Splenomegaly
- Spleen contraction/torsion
- Neoplasia

Lymph Node

- Hyperplastic change involving cells of monocyte-macrophage system as seen in swine histocytosis.
- Lymphoid tissue – Hyperplasia with production of antibody,
- Atrophic changes – Lymphoid atrophy
- Inflammation: Acute – micro abscesses and abscess formation.
  Chronic – abscesses and granulomas

PORTAL OF ENTRY OF INFECTIOUS ORGANISMS INTO HEAMOPOIETIC SYSTEM

* Bone Marrow
  Haematogenously
  Direct penetration (trauma)

* Thymus
  Haematogenously

* Spleen
  Haematogenously
  Direct penetration (rare)

* Lymphoid Nodules
  Via Afferent Lymphatics
  Haematogenously

* Lymphoid Nodules
  Haematogenously

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Bone Marrow

- Haematogenous
- Direct penetration (trauma)

Invading cells or microorganisms gain access to bone marrow haematogenously or by trauma. Trauma may be as obvious as a gaping wound or a subtle as the bite of an insect.

Thymus

Haematogenous route is the most significant. Toxic agents, such as aflatoxins as well as viruses, enter the thymus through the blood.

Spleen

1. Haematogenously
2. Direct Penetration (rare)

Noxious agents such as bacterial enter the spleen by 2 routes, haematogenously or by direct penetration. The spleen has no afferent lymphatics, so this is not a possible route of entry of infection. Direct penetration is extremely rate. The capsule is thick, and thus inflammation from an adjacent peritonitis is extremely rare. However, foreign bodies occasionally do. This is seen sequel to traumatic reticulitis in cattle, where foreign bodies such a nail or wire is extruded through the left caudal reticulum wall by its contraction and enters the visceral surface of ventral extremity of the spleen which often cause splenic abscess. Most of the extruded foreign bodies usually travel cranially to penetrate the diaphgram and pericardium causing traumatiac reticulo-pericarditis. In horses, on rare occasion, splenic abscess can develop secondary to perforation of

the gastric wall caused by *Gastrophilus intestinalis* or extension of granulomatous inflammation around *Habronema spp* in wall of the stomach.

Lymph Node

1. Via Afferent lymphatic
2. Haematogenously

Agents such as bacteria and viruses are that not removed by any of the lymph node in the process of transportation of lymph to regional lymph nodes may be eventually transported via lymphatic to the circulation blood. In most cases, pathogens arrive at lymph node via afferent lymphatic. However, agents may enter haematogenously in septicaemia and bacteraemia.

Lymphoid nodules

Haematogenously: In the intestine, via M cells and dentritic cells to Payer's patches. Lymphoid nodules respond to antigens arriving haemotogenously, but in many cases the agents or antigens will cross the M/membrane e.g. in chronic inflammations of nasal, oral, bronchial, gastrointestinal and conjunctival mucous membranes.

SPECIFIC PATHOLOGY OF HAEMOPOIETIC ORGANS

THYMUS

Congenital anomaly: The most important disorder is equine combine immunodeficiency. This will be discussed under specific diseases.

1 Atrophy

Because thymus involutes after sexual maturity, evaluating whether it is smaller than normal is difficult unless the change extreme or age – matched and control animals are available. The thymus is easily identified as a lobular organ white – gray with a thin capsule. An extremely small thymus in a neonatal animal should be considered abnormal and an indicator of a possible underlying primary or acquired immunodeficiency. Enlargement of the thymus is almost always due to tumour. The cut surface should therefore be examined for tumours and hematomas.

2. Thymic cysts can be found within the developing and mature thymus and I thymic remnants in the anterior mediastium.These cysts represent developmental remnants of branchial arch epithelium and are usually of no significance.

3. Neoplastic Disorders of the thymus

Since the thymus has both lymphoid and epithelial components. It is possible for either or both to be neoplastically transformed. Thymic lymphosarcoma is a T- lymphocyte neoplasm of young animals, particularly cats, with a much lower incidence in dogs.

3a. Bovine thymic lymphosarcoma most often occurs in beef cattle 6 to 24 months of age and is characterized by massive thymic enlargement. The etiology is unknown.

3b. **Thymomas** are primary neoplasms of thymic epithelial cells and are accompanied by varying proportions of nenneoplasticlymphocytes (thymocytes). They grow slowly and are uncommon but occur in dogs, cats, cattle and sheep

BONE MARROW

HYPERPLASIA OF BONE MARROW

This is an increase in the amount of the red marrow with a decrease in the yellow marrow for a given age of an individual. This usual takes place in the long bones and other bones of the adult where the red marrow is not normal found in large amounts. In the femur and humerus, it may extend from the proximal to the distal ends. There are two types of myeloid hyperplasia.

Erythroblastic hyperplasia: Characterized microscopically by red erythrocytes like pronormoblast, normoblast and reticulocytes. This is a reaction to most anaemias except tonic a plastic anaemia which is due in –ability of as the marrow to function.

Leukoblastic hyperplasia: Characterized microscopically by a predominance of the precursors of leukocytes, for examples the myeloblasts, programulocytes and others.This occurs in the infections accompanied by leucocytosis and a pus forming reaction.

Hypoplasia of bone marrow: A decrease in the red marrow, even in the areas where it should normally be found in large amounts. It occurs in connection with toxic aplastic anaemia.

Agranulocytosisi: Refers to a more or less complete absence of granulocytes from circulating blood due to complete aplasia of the leukoblastic cel,ls of the bone marrow. It is related to apastic anaemia.

Osteomyelitis: Is the inflammation of the bone marrow due to an infection that gains access to the marrow through a local wound or by way of the blood.

SPLEEN PATHOLOGY

Splenomegaly

Spleen can be enlarged, normal or small. 2 types of splenomegaly are described.

(a) Congestive and non - congestive.
(a) Congestive: - The cut surface of severely congested spleen may be red to bluish-black and exudates blow (bloody spleen).
(b) **Non-Congestive:-** Firm and often called meaty because of the firmness and texture. Little blood oozes out from the cut surface and colour of the surface depends on how much of the normal red pulp has been replaced by stored materials, neoplastic cells and inflammation.
Splenomegaly can result from (1) Circulatory disturbances

(2) Inflammatory diseases

(3) Metabolic diseases

(4) Neoplastic diseases

(A) Acute splenic congestion are caused by

- Acute myocardial failure.
- Euthanasia with Newbutal & barbiturates
- Torsion of the spleen which also leads to infarction.

(b) Chronic passive splenic congestion: Enlarged spleen is filled with blood, but is firm because of an increase in fibrous tissue.

Microscopocally:

Distention of sinusoids and cords with blood

- Appreciable hyperplasia of the endothelium of the sinusoids so that lining cells resembles cuboidal epithelium.
- Marked diffuse fibrosis throughout the pulp.
- Thickening of trebeculae
- Accumulation of phagocytized haemosiderin from erythrocytes which have been entrapped in the nearly static blood and haemolyzed in excessive numbers

Splenic Atrophy

Causes include:
Developmental Disorders
Aging
Wasting/Cachextic Disease
Starvation, malabsoption syndrome
Systemic neoplasm
Splenic Contraction – controlled by autonomic nervous system and cotecholamine release which can occur in fight or flight situation and in heart failure and cardiogenic hypovolaemic and septic shock. It is also present in acute splenic rupture that results in heamorrhage.

Nodular Hyperplasia- Nodular hyperplasia of the spleen occurs with or without enlargement. Nodular disorders are characterized by nodules that are randomly distributed, may be discrete or and are raised above the spleen surface, budge from the cut surface, and have a variety appearance and colours based on the cause of the lesion.
Many of the disease processes causing a nodular splenomegaly are similar to those causing a uniform splenomegarly. Nodules can be abscesses granulomas, haemotomas, foci of lymphocytes, haemopoietic cells are primary or metastatic neoplasms. Nodudlar hyperplasia is most commonly seen in as the spleen of older dogs and is often as accidental finding. This lesion has been called canine nodular hyperplasia and splenoma. Nodules are formed by lymphoid cells or mixed accumulation of hyperplastic erythroid myeloid and megakaryocytic cell with lymphoid cells. Lesion may appear single discrete or multiple coalescing firm nodules protruding from the surface cut covered by the capsule.

Torsion of the spleen
Usually occurs mainly in pigs and dogs. Torsion of the spleen and stomach together occurs in dogs, usually deep-chested ones. In contrast to ruminants, in which the spleen is firmly attached to the rumen, the spleen of dogs and pigs is attached loosely to the stomach by gastrosplenic ligament. It is the twisting of the spleen on the ligament that result initially in occlusion of the veins, causing splenic congestion, and later occlusion of the artery results in splenic infarction and later necrosis sets in. Torsion of the spleen occurs commonly in dogs in association with torsion of the stomach; however it can occur alone especially in pigs. One usually finds severe congestion and haemorrhagic infarction due to occlusion of the vein. If the artery is also occluded, necrosis sets in.
Gross: Spleen is uniformly and markedly enlarged and blue black from cyanosis.
It is often folded back on itself – RX – Splenectomy. Removal will make the individual to be susceptible to certain microorganism such as haemotropic microorganisms e.g. Haemobatonella and Eperythrozon in dogs and Babesiosis and Theleriosis in cattle in endemic areas.

Congenital anomalies
These are rare in our domestic animals. There may be an accessory spleen in the omentum or a duplication of the spleen may occur in swine.

Atrophy: This is often seen in old dogs and horses in cases of chronic inanition and wasting diseases.

Amyloidosis: occurs usually as part of a generalized syndrome. It is usually detectable only by means of special stains in histopathology. Amyloid gives an increased size and grayish translucence to the corpuscles so that they protrude on out surface.

Pigmentation: Haemosiderosis which is a storage form of iron is the only important pigment. It is usually present in reticular macrophages but in long standing hemosiderosis may be encrusted in the fibres of connective tissue. It is important in haemolytic anaemias.

Rupture of the spleen: This is common in dogs and cats. It is usually as a result of trauma, for example, car accidents or it can be spontaneous if the spleen becomes much enlarged (splenomegaly). A spleen can either be fully divided into two or merely ruptured at the edges and healing may then occur. Rupture of an enlarged spleen leads to internal haemorrhage.

Circulatory Disturbances: These include acute hyperaemia seen in acute bacterial infection as a result of systemic and portal disturbances and also in barbiturate anaesthesia. Thrombi and emboli of splenic vessels are common too. Multiple thrombi along spleen margins are seen in hog cholera/ASF. Cysts are uncommon in the spleen but hydratid cysts may be found from time to time.

Splenitis: Inflammation of the spleen. Specific diseases like anthrax, swine erysipelas, anaplasmosis of cattle and acute infectious anaemia and salmonellosis cause acute splenitis. The spleen is enlarged and soft. Microscopically there is marked hyperaemia with collections of neutrophils, lymphocytes and plasma cells. Chronic splenitis and suppurative splenitis occur in association with specific pyogenic organism. Abscesses are not usually common but could result from traumatic reticulopertonitis in cattle.

Tumors of the spleen: Fibrosarcomas and leiomyosarcoma are rare. More commonly, we find hemangiosarcomas which metastasize mostly to muscles. Secondary tumors are very common e.g. lymphosarcomas can metastasize to the spleen.

Lymph Node

Causes of atrophy include:-

- Developmental disorders resulting into hypoplasia and immunodeficiency syndrome.
- Lack of antigenic stimulation.
- Cachexia and malnutrition.
- Aging
- Viral infection.

Enlargement of Lymph Node

- Follicular and diffuse hyperplasia.
- Lymphadenitis – acute and chronic.
- Primary Neoplasms and metastatic
- Hyperplasia of monocyte – macrophage syste

Hypoplasia of Lymph Nodes is caused (together with degenerative changes) by infection and toxic agents or hormonal mechanism. in “Alarm reaction” of stress. Diffuse dissolution of lymphocytes is seen.

Necrosis: Necrosis of the whole or a part of a lymph node may occur when infections agents grow locally, in anthrax and erysipelas, necrosis of the lymph node draining the affected area occurs.

Macroscopically, the necrotic areas are dry, and circumscribed. In some infections, gas bubbles may be present.

Amyloid degeneration: In general amyloidosis, amyloid may be found in the lymph nodes. Deposition of amyloid starts in the germinal centre and spreads outwards.

Hyperplasia of the lymph nodes is an usual reaction to sub acute or chronic type of irritants and is met with either as a general or a local phenomeon in such diseases like canine distemper, chronic enteritis or chronic pneumonia**.**

Macroscopically, the affected nodes are enlarged, whitish-gray and firm but not fibrosed or calcified. Follicles are prominent.

Macroscopically there is great enlargement of the germinal centres with a zone of mature lymphocytes surrounding them. If the underlying disease is removed, hyperplasia subsides.

Lymph Node Pigmentation

Exogenous

Exogenous pigmentation of the lymph nodes is most common in the pulmonary and mesenteric lymph nodes. Examples include:

Anthracosis: Coal dust in the bronchial nodes is common in animals especially dogs that live in indendial area. The coal particles are found in the macrophage of the medullary cords. In ruminants mesantanic and other lymph nodes develop a grey exogenous pigmentation of the medulla proprable due to some pigments ingested with feed. In tattooed anomals, the granucles of the pigment used for it tattooing are found in the regional. Lymph nodes: These exogenous pigmentations are not of clinical importance.

Endogenous Pigmentation: Examples include:

(i) Haemosiderosis. This is the most common, found in the lymph nodes training area where haemorrhage has occurred. Grossly, such nodes are brownish in colour. Microscopically, brown amorphous cr ystals of haemosiderin are found in the reticular and sinusoid macrophages.

(ii) Bile Pigment

This occurs in the portal/hepatic L/nodes nodes as a result of obstructive jaundice.

(iii) Melanin – This is particularly conspicosis in the superficial lymph nodes of old grey horses

(vi) Helminth Pigment

A melanin – like blank pigment usually present in the hepatic nodes of sheep and cattle which have or have had hepatic distomiasis. The same pigment occurs in the bile ducts infection by *Fasciola hepatica*, and in the case of *F. magna*, whenever, the fluke has wondered.

Emphysema

In emphysema of lymph nodes, the gas is confined in the sinuses; it affects the mesenteric nodes of swine in association with intestinal emphysema. In cattle emphysema of the bronchial nodes is common with interstitial pulmonary emphysema.

Grossly: The Lymph nodes are enlarged, puffy, light and soft with surface appeared like sponge

Histology: Sinuses are the distended with vesicles, endothelial cell become large, mobilized into large MQs and even giant cells. These cells occur in small clusters of spotty distribution on the wall of the sinusoids

Circulatory disturbances: Hemorrhages are seen in lymph nodes in severe infections disease, hemorrhagic diathesis, local trauma and passive venous congestion.

Macroscopically, reddened areas are noticed, which may be diffuse, local or even petechial. Haema lymph nodes must not be confused with hemorrhagic lesions.