Lecture 2: Myeloproliferative diseases
Lymph nodes
Primary Hematopoietic Neoplasia

Hematopoietic Neoplasia

Lymphoproliferative Disease

Lymphoma

Lymphoid leukemia

Plasma cell tumours

Myeloproliferative Disease

Histiocytic Neoplasia

Myeloid leukemia

Myelodysplastic Syndrome

Mast cell tumour?
Histiocytic proliferative / neoplastic disorders

1. Cutaneous histiocytoma
   - common benign skin mass
   - young dogs
   - spontaneously regress

2. Reactive histiocytosis
   - immunoregulatory disease
   - proliferation of dermal/interstitial dendritic cells
   - waxing & waning / slowly progressive

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<thead>
<tr>
<th>Cutaneous reactive histiocytosis</th>
<th>Systemic reactive histiocytosis</th>
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<td>• multiple skin masses</td>
<td>• skin, lymph nodes &amp; viscera</td>
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3. Histiocytic Sarcoma

- malignant neoplasia of histiocytes (macrophages or dendritic cells)

- breed predispositions
  - Bernese Mountain dog, Rottweiler, Flat-coated retriever

- solitary lesions
  - periarticular, skin / subcutis, lymph nodes, spleen or liver

- multisystemic lesions
  - disseminated histiocytic sarcoma
    = malignant histiocytosis
Histiocytic proliferative / neoplastic disorders

Disseminated histiocytic sarcoma (= malignant histiocytosis)

• aggressive multisystemic disease
  - tumor masses in many organs, eg spleen, liver, lung, BM, LN’s, CNS, (rarely skin)

Histioytic sarcoma, hilar & mesenteric lymph nodes

Courtesy of Dr A Lopez, AVC
Histiocytic proliferative / neoplastic disorders

Disseminated histiocytic sarcoma (= malignant histiocytosis)

- histology: - diffuse infiltrates of atypical histiocytes
  - may be avidly hemophagocytic → non-regenerative anemia.
Mast cell neoplasia

Mast cells are widely distributed in connective tissues - but originate in BM

Cutaneous mast cell tumours

- common skin tumors of dogs

Systemic mastocytosis*

- rare, mostly cats.
- two main forms: splenic and intestinal
**Mast cell neoplasia**

**Systemic mastocytosis (visceral mast cell tumors)**

- **Gross:** splenomegaly +/- nodular surface
- can metastasize to liver, BM, lung, etc

Note, with the splenic form of systemic mastocytosis, see diffuse &/or nodular splenomegaly

Can also see diffuse hepatic enlargement

For information only
Mast cell neoplasia

Systemic mastocytosis (visceral mast cell tumors)

Histology: sheets of neoplastic mast cells efface the parenchyma
Secondary bone marrow neoplasia

- result of **metastasis** of a tumor from a distant site to the bone marrow
- can be a carcinoma or a sarcoma

Arrows show the interface between the tumor (upper right) and the bone marrow of the rib (lower left)

Image Courtesy of Dr A Lopez

Metastasis of a malignant pheochromocytoma to the rib, dog
Myelophthisis = replacement of hematopoietic tissue within the bone marrow by abnormal tissue

- fibrosis → myelofibrosis
- neoplastic cells → leukemia, lymphoma, histiocytic sarcoma, etc

- may result in pancytopenia due to competition for space / nutrients

Dog: Replacement of bone marrow by lymphoma
Monocyte-macrophage system (MMS)

- blood monocytes & fixed macrophages

Discussion of diseases affecting the monocyte-macrophage system are discussed in the various organ systems.
Lymphoid Tissue: Lymph nodes

Normal lymph node, cow
Lymph node

Function:
- filtration of lymph
- immune response

Structure:
- outer cortex → follicles
  (mostly B cells)
- inner cortex → paracortex
  (mostly T cells)
- medulla → mostly B cells

Lymph circulation: Afferent lymphatics → subcapsular sinuses → trabecular sinuses → medullary sinuses → efferent lymphatics → thoracic duct

Modified from Pathologic Basis of Veterinary Disease
Lymph node

Function:
- filtration of lymph
- immune response

Structure:
- outer cortex → follicles
  (mostly B cells)
- inner cortex → paracortex
  (mostly T cells)
- medulla → mostly B cells
Lymph node: Miscellaneous changes

Lymph node: Hemorrhage

- can originate within the lymph node or in the tissues drained by the node
- red discolouration of the lymph nodes

Lymph node: Anthracosis

- black discoloration due to carbon within phagocytes
Lymph node: General response to injury

Two basic responses: decrease in size or increase in size

Small lymph nodes
- atrophy / degeneration
- hypoplasia

Enlarged lymph nodes
- Lymphoid hyperplasia
- Lymphadenitis
- Primary neoplasia
- Secondary neoplasia
## Small lymph nodes

### Lymph node atrophy / degeneration

- **Senile atrophy (aging)**

- **Cachexia / malnutrition**

- **Viral infection**
  - BVD
  - FIV
  - CDV
  - FPV / CPV

- **Toxins / Drugs / Irradiation**

### Lesions:

- **Gross:** small lymph nodes
- **Histo:** lymphoid depletion / degeneration
Lymphadenopathy (lymphadenomegaly)

- enlargement of the lymph nodes, of unknown or unspecified cause
- can be localized or generalized

Markedly enlarged supramammary lymph nodes (ie marked lymphadenopathy) from cow with mastitis. It is called lymphadenopathy (ie enlarge lymph nodes of unknown cause) until diagnostic testing (eg histopathology) is done to determine the cause of the enlargement.
Benign reactive hyperplasia:

- Immunological reaction = response to antigen or circulating interleukins
  - Lymph nodes draining site of local infection or vaccination
  - Also occurs during early stages of lymphadenitis
- Can be localized or generalized

Gross:

- Enlargement of node(s)
- May bulge on cut section

Peripheral lymph nodes from a cow with localized dermatitis. The normal node above is from an area where the overlying skin was normal. The enlarged (hyperplastic) lymph node below was draining an area with dermatitis due to *Dermatophilus congolensis*. 
**Lymph Node Hyperplasia**

**Histology:**
- proliferation of lymphoid follicles with prominent germinal centers
- increased T cells in the paracortex
- +/- increased plasma cells in the medullary cords

*Note,* the number of lymphoid follicles has increased (hyperplasia), and all have germinal centers (secondary follicles) indicating active proliferation of B lymphocytes to form plasma cells in response to an antigenic stimulus.
Enlarged lymph nodes

Lymphadenitis

- an inflammatory response to an infectious agent within the node
  (*vs reactive hyperplasia which is an antigen driven immunologic response*

Acute lymphadenitis

- esp regional lymph node draining a site of inflammation & becoming infected
- with sepsis – multiple nodes involved

Cervical & mediastinal lymphadenitis with sepsis
Gross lesions:
- enlarged, soft, wet, red lymph nodes
- often bulging & hyperemic on cut surface
- exudates are usually serous

Figure 13-71 (Zachary) Acute lymphadenitis, tracheobronchial lymph nodes, pig. The nodes are enlarged and reddened from draining the pneumonic cranial lung lobes. Note the red consolidation of the dorsal portion of the cranial lung lobes.

Mesenteric lymphadenitis
Chronic lymphadenitis

- with chronicity, inflamed lymph nodes become irregular and firm due to fibrosis
- chronic suppurative lymphadenitis vs chronic granulomatous lymphadenitis

Note tracheobronchial lymphadenitis in a foal with pneumonia due to *Rhodococcus equi*
Chronic Suppurative Lymphadenitis

- swollen lymph node with pus-filled area surrounded by fibrous capsule = lymph node abscess
- response to pyogenic bacteria
- can fistulate to the skin surface
Chronic Suppurative Lymphadenitis

Equine Strangles

- *Streptococcus equi* subsp *equi*
- inflammation of the URT → abscesses in the mandibular, retropharyngeal & parotid LN’s
- may fistulate to the surface
- can spread to the viscera → “Bastard Strangles”

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Fig. 13-74 (Zachary) Acute suppurative lymphadenitis, equine strangles (*Streptococcus equi* ssp. *equi*), dorsal view of larynx, left and right retropharyngeal lymph nodes, horse. The lymph nodes are grossly distended with pus.
Caseous lymphadenitis: *Corynebacterium pseudotuberculosis*

- chronic suppurative lymphadenitis in sheep & goats
- ulcerative lymphangitis in horses and cattle
- pectoral abscesses in horses

**Pathogenesis:**
- usually enters via contamination of shear wounds; rarely by inhalation
- drains to regional lymph nodes
- superficial nodes > internal nodes
  - prescapular LN
  - prefemoral LN
Chronic Suppurative Lymphadenitis

Caseous lymphadenitis: *Corynebacterium pseudotuberculosis*

- chronic suppurative inflammation and caseous necrosis
- as lesion progresses → characteristic concentric laminations

Fig. 13-71 (Zachary) Caseous lymphadenitis, *Corynebacterium pseudotuberculosis*, lymph node, sheep. The whole lymph node has been replaced by an abscess containing mostly semifluid yellowish pus. This is an early stage of caseous lymphadenitis, before the pus has become inspissated and caseous.

Note, the concentric laminations often seen in the abscesses of “caseous lymphadenitis” are considered characteristic of the disease.
Chronic Suppurative Lymphadenitis

Caseous lymphadenitis: *Corynebacterium pseudotuberculosis*

- some cases have systemic involvement with abscesses in the internal organs

Goat, caudal mediastinal lymph nodes: lymph node abscesses
Chronic Granulomatous Lymphadenitis

Nodular granulomatous lymphadenitis
- Mycobacterium bovis
- Mycobacterium avium subsp. paratuberculosis
- Actinobacillus lignieresii
- Migrating parasitic larva

- focal or multifocal, white-yellow nodules
- +/- caseous necrosis / mineralization

Diffuse granulomatous lymphadenitis
- Porcine Circovirus type 2
- Histoplasma capsulatum
- Blastomyces dermatitidis
- Cryptococcus neoformans

- enlarged, pale, dry, firm lymph nodes
- diffuse loss of architecture
Nodular Granulomatous Lymphadenitis

Bovine tuberculosis: *Mycobacterium bovis*

**Gross:** - enlargement of the lymph node with single to multiple pale caseous nodules, often with gritty (mineralized) centers

- confluence of multiple lesions may produce locally extensive to generalized (diffuse) involvement of the node

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**Fig. 1-19 (Zachary) Tuberculosis (*Mycobacterium bovis*), lymph node, ox.** The normal architecture of the lymph node has been completely obliterated by multiple caseating granulomas, typical of *Mycobacterium bovis* lesions. Note the caseous necrosis characterized by a pale yellow, crumbly exudate.

Note, in some cases of tuberculosis (such as the one above) there is coalescing of multiple lesions which results in generalized (diffuse) distribution of the inflammation.
Nodular Granulomatous Lymphadenitis

Bovine tuberculosis: *Mycobacterium bovis*

**Histology:** granulomas with central necrosis and mineralization surrounded by epithelioid macrophages and multinucleated giant cells
Nodular Granulomatous Lymphadenitis

Bovine tuberculosis: *Mycobacterium bovis*

**Histology:** granulomas with central necrosis and mineralization surrounded by epithelioid macrophages and multinucleated giant cells.

Acid fast staining shows numerous acid-fast positive bacilli within the macrophages and giant cells. (note, mycobacteria are readily seen on acid-fast stains, but not on routine H&E staining).

Histolopathology of lymph node, showing part of a large granuloma with caseous necrosis (right) surrounded by a zone of inflammatory cells (left), ie epithelioid (large epithelial looking), macrophages, inflammatory giant cells (ie from fused macrophages), lymphocytes & plasma cells.
Diffuse Granulomatous Lymphadenitis

Postweaning multisystemic wasting syndrome (PMWS): Porcine Circovirus type 2

**Gross:** enlargement of the lymph nodes (esp mesentric lymph nodes)

Pig on the left with PMWS is the same age as the pig on the right.
Diffuse Granulomatous Lymphadenitis

Postweaning multisystemic wasting syndrome (PMWS): Porcine Circovirus type 2

- **histo**: granulomatous inflammation of the node with large botryoid (grape-like) intracytoplasmic viral inclusions
Neoplastic Diseases of the Lymph Nodes

Primary Neoplasia  lymph node neoplasia

* covered in primary hematopoietic neoplasia
Lymph node metastasis:

- common with carcinomas, melanomas, mast cell tumors, etc
- lymph nodes may be enlarged
- variable effacement of normal architecture
Metastasis of mammary carcinoma to a lymph node