Pathology of the Hematopoietic System

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
### Myeloproliferative disease: Histiocytic neoplasia/proliferative disorders

1. **Cutaneous histiocytoma**
   - Common benign skin mass
   - Young dogs
   - Spontaneously regress

2. **Reactive histiocytosis**
   - Immunoregulatory disease
   - Waxing and waning, progressive
   - **Cutaneous histiocytosis**
     - Affects the skin
   - **Systemic histiocytosis**
     - Affects skin and viscera

[http://vetmedicine.about.com/od/diseasesandconditions/tp/Lumps-Bumps.htm](http://vetmedicine.about.com/od/diseasesandconditions/tp/Lumps-Bumps.htm)
Myeloproliferative disease: Histiocytic neoplasia/proliferative disorders

3. Histiocytic sarcoma

- Malignant neoplasia of macrophage or dendritic cells
- Breed predispositions
  - Bernese Mountain dog
  - Rottweiler
- Can be solitary or multiple
  - Solitary lesions
    - Surrounding joints, subcutis
    - Lymph nodes, spleen or liver
  - Multiple lesions
    - Disseminated histiocytic sarcoma = malignant histiocytosis
Myeloproliferative disease: Histiocytic sarcoma

3. Disseminated histiocytic sarcoma (= malignant histiocytosis)

- Aggressive multisystemic disease
  - Tumour masses in several organs: spleen*, bone marrow*, lymph nodes*, lung, skin
  - Splenomegaly, hepatomegaly
3. Disseminated histiocytic sarcoma (= malignant histiocytois)

- **Histology**: Masses / diffuse infiltrates composed of atypical histiocytes
  - May be avidly hemophagocytic causing a non-regenerative anemia
Myeloproliferative disease: Mast cell neoplasia

Mast cells are widely distributed in the connective tissues - however they originate in bone marrow

Cutaneous mast cell tumours
- Common skin tumours of dogs

Alimentary mast cell tumour
- Intestinal or gastric masses

Systemic mastocytosis
- Involves primarily the hematopoietic organs
Systemic mastocytosis

- Primarily involves the hematopoietic system
  - Spleen, bone marrow
- Rare in animals: cats
- **Gross**: Splenomegaly +/- nodular surface
Myeloproliferative disease: Mast cell neoplasia

Systemic mastocytosis

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- **Gross**: Splenomegaly +/- nodular surface
Myeloproliferative disease: Mast cell neoplasia

Systemic mastocytosis

Histology:
Cords and sheets of mast cells efface the parenchyma

Toluidine Blue
Secondary bone marrow neoplasia

- Results of **metastasis** of a tumour from a distant site to the bone marrow
- Can be a carcinoma or a sarcoma

Metastasis of a malignant pheochromocytoma to the rib, dog

Courtesy of Dr Alfonso Lopez
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
Lymphoid Tissue: Lymph nodes
Lymph nodes

**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 nodes

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**Lymph nodes**

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# Lymph node: General response to injury

## Two basic responses: Decrease in size or increase in size

<table>
<thead>
<tr>
<th><strong>Enlarged lymph nodes</strong></th>
<th><strong>Small lymph nodes</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphadenitis</td>
<td>Lymphoid atrophy</td>
</tr>
<tr>
<td>Lymphoid hyperplasia</td>
<td>Lymph node degeneration</td>
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<tr>
<td>Hyperplasia of the</td>
<td>Lymph node hypoplasia</td>
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<tr>
<td>monocyte/macrophage</td>
<td></td>
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<tr>
<td>system</td>
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</tr>
<tr>
<td>Primary neoplasia</td>
<td></td>
</tr>
<tr>
<td>Secondary neoplasia</td>
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</table>
### Lymph node: Decrease in size

#### Small lymph nodes

<table>
<thead>
<tr>
<th>Lymphoid atrophy</th>
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<tbody>
<tr>
<td>• Aging</td>
</tr>
<tr>
<td>• Cachexia/malnutrition</td>
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<table>
<thead>
<tr>
<th>Lymph node degeneration</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Toxins</td>
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<tr>
<td>• Chemotherapy</td>
</tr>
<tr>
<td>• Viral infections</td>
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<th>Lymph node hypoplasia</th>
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</table>

#### Lesions:

- **Gross:**
  - Small lymph nodes

- **Histology**
  - Lymphoid depletion / degeneration

- Bovine Viral Diarrhea Virus
- Feline Immunodeficiency Virus
- Canine Distemper Virus
- Feline and Canine Parvovirus
Lymph node: Hemorrhage
- Originate within the lymph node or in the tissues drained by the node

Lymph node: Anthracosis
- Carbon within phagocytes

Red discolouration

Black discolouration
Lymph node: Lymphadenopathy (lymphadenomegaly)

**Lymphadenopathy**
- Enlargement of the lymph node(s) of unknown cause
- Can be localized or generalized

**Enlarged lymph nodes**

- Lymphadenitis
- Lymphoid hyperplasia
- Hyperplasia of the monocyte/macrophage system
- Primary neoplasia
- Secondary neoplasia

Enlargement of the right retropharyngeal LN sheep
As opposed to reactive hyperplasia which is an antigen driven immunologic response. Lymph node: Inflammation

Lymphadenitis

• An inflammatory response to an infectious agent within the node

Acute Lymphadenitis

• Usually the result of a regional lymph node draining a site of inflammation and becoming infected
Lymph node: Acute lymphadenitis

Gross lesions:
- Enlarged, soft, wet, red lymph nodes
- Often bulging & hyperemic on cut surface
- Exudates are usually serous

Dr McGavin, College of Veterinary Medicine
University of Tennessee
Lymph node: Chronic suppurative lymphadenitis

- Gross lesions:
  - Swollen lymph node with pus-filled center = Lymph node abscess
- Response to pyogenic bacteria
- Can fistulate to the skin surface
Equine Strangles

- *Streptococcus equi* subsp *equi*
- Inflammation of the URT → abscesses in the mandibular, retropharyngeal and parotid Lnn
- May fistulate to the surface
- Can spread to the viscera → “Bastard Strangles”
Porcine jowl abscess

- *Streptococcus porcinus*
- Colonizes oral cavity/tonsils and spreads to the mandibular lymph nodes

Lymph node: Chronic suppurative lymphadenitis

(Courtesy Dr. J.M. King, College of Veterinary Medicine, Cornell University)
Pathogenesis:
• Usually enters via contamination of shear wounds; rarely by inhalation
• Drains to regional lymph nodes
  – Superficial nodes more often affected than internal nodes
    • Prescapular LN
    • Prefemoral LN

Caseous lymphadenitis: *Corynebacterium pseudotuberculosis*

• Chronic suppurative lymphadenitis in sheep & goats
• Ulcerative lymphangitis in horses and cattle
• Pectoral abscesses in horses

Lymph node: Chronic suppurative lymphadenitis
Goat, caudal mediastinal lymph nodes: lymph node abscesses

Lymph node: Chronic suppurative lymphadenitis

Caseous lymphadenitis: Corynebacterium pseudotuberculosis
Chronic suppurative inflammation, caseous necrosis & fibrosis

As lesion progresses → characteristic concentric laminations

In some cases there is systemic involvement with abscesses in the organs: especially the lungs

Caseous lymphadenitis: *Corynebacterium pseudotuberculosis*
# Lymph node: Granulomatous lymphadenitis

## Nodular granulomatous lymphadenitis

<table>
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<th>Pathogen</th>
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<tbody>
<tr>
<td><em>Mycobacterium bovis</em></td>
</tr>
<tr>
<td><em>Mycobacterium avium</em> subsp. <em>paratuberculosis</em></td>
</tr>
<tr>
<td><em>Actinobacillus lignieresii</em></td>
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<tr>
<td>Migrating parasitic larva</td>
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</table>

- Focal or multifocal
- Often white-yellow nodules
- +/- caseous necrosis/mineralization

## Diffuse granulomatous lymphadenitis

<table>
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<th>Pathogen</th>
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<tbody>
<tr>
<td>Porcine Circovirus type 2</td>
</tr>
<tr>
<td><em>Histoplasma capsulatum</em></td>
</tr>
<tr>
<td><em>Blastomyces dermatitidis</em></td>
</tr>
<tr>
<td><em>Cryptococcus neoformans</em></td>
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</tbody>
</table>

- Enlarged, pale, dry, firm lymph nodes
- Loss of architecture
Bovine Tuberculosis: *Mycobacterium bovis*

**Gross:** Enlargement of the lymph node with multiple discrete yellow-tan gritty (caseated) nodules
**Lymph node: Nodular granulomatous lymphadenitis**

**Bovine Tuberculosis: Mycobacterium bovis**

- **Histology:** Granulomas with central necrotic debris surrounded by epithelioid macrophages and multinucleated giant cells

*Image: Noah’s Arkive*
Lymph node: Nodular granulomatous lymphadenitis

Bovine Tuberculosis: *Mycobacterium bovis*

- **Histology**: Granulomas with central necrotic debris surrounded by epithelioid macrophages and multinucleated giant cells

Image: Noah’s Arkive

Acid fast bacilli within macrophages and MNGCs
Lymph node: Diffuse granulomatous lymphadenitis

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

- **Gross:** Diffuse enlargement of the mesenteric lymph nodes
Histology:
Granulomatous infiltration of the node with large botryoid intracytoplasmic viral inclusions

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

• Can be localized or generalized
• Immunological reaction = response to antigen presentation or circulating interleukin levels
  – Lymph nodes draining site of local infection or vaccination
  – Also occurs during early stages of lymphadenitis

Gross:
• Enlargement of the node(s)
  = Lymphadenopathy
• May bulge on cut section
Histology:
- Proliferation of lymphoid follicles with prominent germinal centers*
- Increased T cells in the paracortex
- +/- Increased plasma cells in the medullary cords
Lymph node: Neoplasia

Primary lymph node neoplasia = Lymphoma

Covered in primary hematopoietic neoplasia*
• Lymph node metastasis:
  • Common with carcinomas, melanomas, mast cell tumors, etc.
  • May see lymph node enlargement
  • Variable effacement of normal architecture

• One basis of staging tumor malignancy
  • Stage 0: regional node normal
  • Stage 1: regional node enlarged but still freely moveable
  • Stage 2: regional node enlarged and fixed
Metastasis of mammary carcinoma to a lymph node

Lymph node: Secondary neoplasia
Questions?