Pathology of the Hematopoietic System

Lecture 3: Spleen and Thymus
Spleen – Structure and Function

- present in the left cranial part of the abdomen
- attached to the greater curvature of the stomach by the gastrosplenic ligament
- covered by a fibromuscular capsule and dissected by fibromuscular trabeculae
- varies in size and shape among species

Normal spleen from a cat
### Spleen – Structure and Function

<table>
<thead>
<tr>
<th>Structure</th>
<th>Function</th>
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<tbody>
<tr>
<td><strong>Red Pulp</strong></td>
<td></td>
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<tr>
<td>• splenic sinusoids (vascular spaces)</td>
<td>• filters blood - removal of foreign material (phagocytosis)</td>
</tr>
<tr>
<td>• splenic cords</td>
<td>• RBC storage</td>
</tr>
<tr>
<td></td>
<td>• hematopoiesis (EMH)</td>
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<tr>
<td><strong>White Pulp</strong></td>
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<tr>
<td>• PALS - periarteriolar lymphatic sheaths (T-cells)</td>
<td>• immune response</td>
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<tr>
<td>• lymphoid nodules (B-cells)</td>
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<tr>
<td>• marginal zone (macrophages)</td>
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</table>
Diseases of the spleen

- Miscellaneous Diseases
- Circulatory diseases of the spleen
- Inflammation of the spleen (splenitis)
- Adaptations of growth
- Primary and secondary splenic neoplasia
## Misc. Diseases

<table>
<thead>
<tr>
<th>Disease</th>
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<tr>
<td>Siderofibrosis (Gamna-gandy bodies)</td>
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<tr>
<td>Splenic amyloidosis</td>
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<tr>
<td>Splenic contraction</td>
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<tr>
<td>Splenic lymphoid necrosis</td>
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<tr>
<td>Hemosiderin deposition / hemosiderosis</td>
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</table>

Dog spleens. Normal spleen (right) vs spleen with large numbers of siderofibrotic plaques / nodules in the capsule.
Spleen: Miscellaneous Diseases

1. Siderofibrosis = Gamna-Gandy bodies
   - incidental finding / senile change
   - likely sequela of prior hemorrhage

**Gross:** Granular white-yellow deposits in the splenic capsule
1. Siderofibrosis = Gamna-Gandy bodies
   - incidental finding / senile change
   - likely sequela of prior hemorrhage

Web Fig. 13-6B (Zachary) Sidero-calcific plaque, spleen, dog. The sidero-calcific plaque lies in the fibrous connective tissue of the capsule and consists chiefly of calcium (blue) and hemosiderin (brown) in fibrous connective tissue. The yellow material is bilirubin (hematoidin), resulting from the breakdown of erythrocytes in a capsular hemorrhage. H&E stain.
2. **Splenic amyloidosis**

- especially 2°amyloidosis – chronic inflammation
- **Gross:** splenomegaly, beige to orange
- **Histology:** deposition of amyloid around the splenic arteries (Congo red stain)

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**Fig. 13-57 (Zachary) Amyloid spleen, dog.** The spleen is pale beige, firm and waxy, and uniformly distended in this advanced case of amyloidosis.
Spleen: Miscellaneous Diseases

3. Splenic contraction

- contraction of the smooth muscle in the capsule / trabeculae
- occurs with catecholamine release, shock, acute splenic rupture
- **Gross**: small dry spleen with wrinkling of the capsule

If contraction is incomplete it can look similar to splenic infarction.
## 4. Splenic lymphoid necrosis

**Viral infections**
- Panleukopenia virus
- Canine parvovirus
- Bovine viral diarrhea virus
- Equine viral rhinotracheitis

**Stress**

**Toxins**

**Aging**

## 5. Hemosiderin deposition / Hemosiderosis

- small amount of hemosiderin in splenic macrophages → normal rbc turnover
- hemosiderosis = increased amount due to increased erythrocyte destruction.
# Spleen: Circulatory Disturbances

<table>
<thead>
<tr>
<th>Circulatory disturbances</th>
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<td>Active hyperemia</td>
</tr>
<tr>
<td>Passive congestion</td>
</tr>
<tr>
<td>Splenic infarction</td>
</tr>
<tr>
<td>Splenic rupture</td>
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<tr>
<td>Splenic hematoma</td>
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<tr>
<td>Splenic torsion</td>
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</tbody>
</table>
Spleen: Circulatory Disturbances

1. Active hyperemia
   - acute systemic infection

2. Passive congestion
   - vascular pooling (shock)
   - barbiturate administration**
   - hemolytic anemia

Similar grossly:
- splenomegaly
- red to purple
- oozes blood on cut surface

Congested vs normal spleen
Spleen: Circulatory Disturbances

1. Active hyperemia
   - acute systemic infection

2. Passive congestion
   - vascular pooling (shock)
   - barbiturate administration**
   - hemolytic anemia

Similar grossly:
- splenomegaly
- red to purple
- oozes blood on cut surface

note, blood oozing from cut surface
Histology: with splenic congestion the red pulp vascular spaces are marked distended with blood; the white pulp areas are widely separated.
3. Splenic infarction

Thrombosis and infarction occurs with:
- diseases causing vascular damage
- hypercoagulable states
- splenomegaly of any cause
- septic thromboemboli

Gross Lesions:
- acutely: infarcts are discrete, raised & dark red – at the margins of the organ
- with time: pale and firm (fibrosis)
4. Splenic rupture

- fairly common
- primary - trauma
- 2° to splenomegaly, splenic neoplasia
- sequelae: hemoabdomen and splenosis

Splenic rupture 2° to hemangiosarcoma in a dog

Splenic rupture and hemoabdomen 2° to splenomegaly (lymphoma) in a pig
4. Splenic rupture - splenosis

- seeding of splenic explants on peritoneal surfaces ("splenosis")

**Gross:** small red nodules within the omentum

**Histology:** looks like normal spleen

Grossly can be mistaken for hemangiosarcoma metastases
Spleen: Circulatory Disturbances

5. Splenic hematoma

- common in dogs
- trauma
- \(2^o\) to nodular hyperplasia or vascular tumors

Need histology to rule out underlying neoplasia!

Gross: red nodular mass; often large, soft & dark red on cut surface
Spleen: Circulatory Disturbances

6. Splenic torsion

- dogs and pigs
- with or without volvulus of the stomach (GDV)
- twists around the gastrosplenic ligament

**Gross:** splenomegaly, blue to black, often folded back on itself
**Spleen: Inflammation**

**Acute splenitis - Multifocal necrosuppurative splenitis**

- Tularemia (*Francisella tularensis*)
- Yersiniosis (*Yersinia pseudotuberculosis*)

**Gross:**
- multifocal miliary white foci within the spleen
- older lesions resemble granulomas/abscesses
- can see similar lesions in the lymph nodes & liver

*Image courtesy of Dr. Daoust*

Tularemia, multifocal hepatitis and splenitis in a beaver
**Acute splenitis – Septicemic (diffuse) splenitis**

- African swine fever
- Erysipelas
- Anthrax**

**Gross Findings**

- splenomegaly
- soft, dark, engorged with viscous blood

*Spleen: Inflammation*
Acute splenitis – Septicemic (diffuse) splenitis

**Anthrax**

- zoonosis caused by a gram-positive, spore-forming bacillus: *Bacillus anthracis*
- in ruminants – septicemic disease
- in horses, pigs & dogs – pharyngeal and enteric disease
Anthrax – Pathogenesis in ruminants:

- ingestion / wound contamination / inhalation of spores
- lymphangitis and localized lymphadenitis
- massive bacteremia (sepsis) and toxemia
- increased vascular permeability and impaired coagulation
- Sudden Death

• with sepsis, huge numbers of vegetative organisms in blood
• become spores when exposed to air:
  - spores very resistant:
    - survive decades in soil
    - infections often follow soil excavation
Anthrax - Lesions in ruminants

Characteristic Findings:

• bloated autolysed carcass with blood oozing from the orifices
Characteristic Findings:

- bloated autolysed carcass with blood oozing from the orifices
- **Do Not Necropsy Suspect Cases!**

- take a blood smear from the ear!
- methylene blue stain: see short chains of large bacilli with distinct pink capsule and square ends

Anthrax - Lesions in ruminants
Anthrax – Lesions:

Gross:

- marked splenomegaly: dark red to black, soft to semi-fluid spleen
- multifocal hemorrhage & edema
- thick tarry blood; fails to clot
Spleen: Inflammation

2. Chronic splenitis: Granulomatous splenitis

Nodular granulomatous splenitis:
- avian & bovine tuberculosis

Diffuse granulomatous splenitis:
- Histoplasmosis, Blastomycosis

Fig. 13-50 Histoplasmosis, spleen, dog. A, There is uniform splenomegaly and the surface of the spleen is mottled from the diffuse granulomatous infiltrate. B, Cross section of spleen. The red pulp has been almost completely replaced by diffuse noncaseous granulomatous inflammation.
3. Chronic splenitis: Splenic abscesses

- rarely following sepsis with pyogenic bacteria (esp *T. pyogenes*)
<table>
<thead>
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<th>Growth disturbances</th>
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<tbody>
<tr>
<td>Aplasia</td>
</tr>
<tr>
<td>Atrophy</td>
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<tr>
<td>Benign nodular hyperplasia</td>
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<tr>
<td>Lymphoid hyperplasia</td>
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<tr>
<td>Hyperplasia of the monocyte-macrophage system</td>
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<tr>
<td>Extramedullary hematopoiesis</td>
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</table>
Spleen: Disturbances of Growth

Benign nodular hyperplasia

- common finding in old dogs
- usually incidental
- may predispose to splenic hematomas

Gross: gray to red nodular mass(es), composed of lymphoid tissue and red pulp

Importance → rule-out neoplasia

Fig. 13-59 (Zachary) Nodular hyperplasia, spleen, dog.
A, A hemispherical 4-cm diameter nodule is protruding from the capsular surface.
B, Cross section of the nodular mass showing intermixed red and white areas composed of red blood cells & proliferating leukocytes.
Lymphoid hyperplasia

- hyperplasia of the white pulp
- response to blood-borne antigen / chronic antigenic stimulation

Gross: Lymphoid follicles visible as 1-3 mm foci

Fig. 13-54 (Zachary) Lymphoid hyperplasia, cross section of spleen, dog. Each of the 1- to 3-mm pale foci consists of hyperplastic periarteriolar lymphoid sheaths and splenic follicles. These structures are not visible in the normal spleen but become enlarged and visible from marked lymphoid hyperplasia or from lymphoma.
# Spleen: Neoplasia

## Primary splenic neoplasia

<table>
<thead>
<tr>
<th>Neoplasm Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphoma/Leukemia*</td>
<td>Primary hematopoietic neoplasia</td>
</tr>
<tr>
<td>Myeloproliferative diseases</td>
<td>(e.g., histiocytic sarcoma)*</td>
</tr>
<tr>
<td>Mastocytosis*</td>
<td></td>
</tr>
<tr>
<td>Hemangioma</td>
<td></td>
</tr>
<tr>
<td>Hemangiosarcoma</td>
<td></td>
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<tr>
<td>Others: Fibrosarcoma, Fibrohistiocytic nodules, etc</td>
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</tr>
</tbody>
</table>

* covered in primary hematopoietic neoplasia
Splenic hemangioma
• benign tumor of endothelial origin

Gross: single, soft, dark red nodular mass
   can look like hematoma  or heangiosarcoma
   (requires histopathology)

Histology: cavernous blood-filled spaces lined by a well-differentiated endothelium
Splenic hemangiosarcoma

- most common malignant tumour of the canine spleen

Gross:
- single to multiple, discrete to coalescing dark red masses
- +/- metastases
Splenic hemangiosarcoma

- most common malignant tumour of the canine spleen

**Fig. 13-61B (Zachary)**

**Hemangiosarcoma, spleen, dog.** The ventral mass has been incised to reveal the stroma of the hemangiosarcoma.
Splenic Hemangiosarcoma

**Histology:** blood-filled vascular spaces lined by anaplastic endothelial cells

*Figure 13-57. Hemangiosarcoma, spleen, dog.* Note the haphazardly arranged vascular channels lined by anaplastic endothelial cells.
**Sequelae:** rupture with resultant hemoabdomen

+/- peritoneal seeding or concurrent masses in the right auricle &/or liver
Spleen: Metastatic Neoplasia

- metastases to the spleen doesn’t occur as frequently as expected

Metastatic splenic tumours: dogs with pancreatic carcinoma (top) and mammary gland carcinoma (bottom)
# Splenic Nodules – important differentials

## Splenic nodules with a bloody consistency
- Hematoma
- Hemangioma
- Hemangiosarcoma
- Splenic infarcts
- Incompletely contracted areas of the spleen

## Splenic nodules with a firm consistency
- Nodular hyperplasia
- Primary Neoplasia (eg lymphoma, histiocytic sarcoma)
- Metastatic (secondary) Neoplasia
- Abscess
- Granuloma
### Diffuse Splenomegaly – important differentials

#### Diffuse splenomegaly with a bloody consistency = Bloody Spleens
- Acute septicemia
- Acute hemolytic anemia
- Splenic torsion
- Barbiturate anesthesia/euthanasia
- Vascular pooling

#### Diffuse splenomegaly with a firm consistency = Meaty Spleens
- Septicemia
  - Salmonella
- Hemolytic anemia
- Neoplasia
  - eg lymphoma, mast cell tumor, histiocytic sarcoma
- Granulomatous disease
- Amyloidosis
Thymus: structure and function

- white to tan lobulated organ within the anterior mediastinum
- ruminants & pigs have a large cervical lobe that extends along the cervical trachea
Thymus: structure and function

Structure
• composed of epithelial tissue and lymphoid tissue

Function
• proliferation & maturation of T cells

Fig. 13-36 (Zachary) Schematic illustration of the organization of the thymus. The thymus consists of several incomplete lobules. Each lobule contains an independent outer cortical region, but the central medullary region is shared by adjacent lobules. Trabeculae, extensions of the capsule down to the corticomedullary region, form the boundary of each lobule. The cortex consists of stromal cells and developing T lymphocytes (thymocytes), macrophages, and cortical epithelial cells. Major histocompatibility complex class I and II molecules are present on the surface of the cortical epithelial cells. The characteristic deep blue nucleus staining of the cortex in histological preparation reflects the predominant population of T lymphocytes as compared with the less basophilic medulla, which contains a lower number of thymocytes. Hassall's corpuscles are a characteristic component of the medulla. Hassall's corpuscles are not seen in the cortex.
<table>
<thead>
<tr>
<th>Thymus – Misc. diseases</th>
<th></th>
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<tbody>
<tr>
<td>Lymphocytolysis / thymic atrophy</td>
<td>Can lead to acquired immunodeficiency</td>
</tr>
<tr>
<td>Thymic aplasia / hypoplasia</td>
<td>Congenital immunodeficiency</td>
</tr>
<tr>
<td>Thymic hemorrhage / hematoma</td>
<td></td>
</tr>
</tbody>
</table>

*Severe combined immunodeficiency* (SCID): Foals, mice, dogs (jack Russell terriers & Basset hounds)

Both congenital & acquired immunodeficiency make animals more susceptible to opportunistic pathogens & more severe infections
Thymic hemorrhage:

- in dogs, can occasionally see sudden death due to hypovolemic shock resulting from massive thymic / mediastinal hemorrhage.
- several implicated causes: trauma, ruptured aorta, anticoagulant rodenticide.
Thymus: Primary Neoplasia

Thymoma, goat. Note, it would require histology to differentiate this from a thymic lymphoma.
**Thymus: Primary Neoplasia**

- **Thymoma**
  - Neoplastic proliferation of thymic epithelial cells
  - Less common (dogs, sheep, goats)
  - Slow growing, encapsulated, rarely metastasize

- **Thymic (mediastinal) Lymphoma**
  - Neoplastic proliferation of T-cells
  - Often younger animals
  - Malignant behavior
Accessory lymphoid organs

- tonsils
- mucosal-associated lymphoid tissue (MALT)
  - bronchial-associated lymphoid tissue (BALT)
  - peyer’s patches / GALT
- subjected to similar pathologic processes as the lymph node

Lymphoma in the tonsils of a dog

Necrotizing tonsillitis in a pig