PATHOLOGY OF THE SPLEEN

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PATHOLOGY OF THE SPLEEN

• Structure and function

• Specific splenic pathology
  • Malformations / Developmental lesions
  • Torsion of the spleen
  • Rupture of the spleen
  • Circulatory diseases of the spleen
  • Degenerative lesions of the spleen
  • Inflammatory diseases of the spleen (splenitis)
  • Hyperplasia (benign) of the spleen
  • Neoplastic lesions of the spleen

• Summary

Structure and function

■ Red pulp:
  ■ Filtration and phagocytosis of blood constituents*
  ■ Storage (red blood cells, platelets)
  ■ Hematopoiesis (in fetal age and in response to anemia)

* about 1% of the total number of red blood cells removed per day
  \[ 1 \times 10^{11} \text{ cells normally removed daily in a 25 kg dog} \]
Structure and function: White pulp:

- Immune response to blood borne antigens
- Periarticular sheaths (T cells)
- Lymphoid follicles (B-cells) with germinal centers and corona ("Malpighian nodules")
- Marginal zone: at the periphery of follicles, with intense vascularisation, port of entry for recirculating lymphocytes, B- and T-cells

![Image of white pulp and red pulp](image_url)

![Diagram of lymphoid system](diagram_url)
Vessels / blood circulation:

- Trabecular arteries → arterioles → penicillary arterioles → capillaries (→ splenic cords → venous sinuses) → venules → trabecular veins

- "open circuit (slow): blood flow through splenic cords ("Biliot sphere area" into sinuses (13% of the splenic blood circulation)

- "closed circuit (rapid): direct blood flow from capillaries to sinuses (4.97% of the splenic blood circulation)

Source: Junqueira/Carneiro, Basic Histology
Vessels / blood circulation:

- Arteries are „end arteries“ (without anastomoses) → predisposing for infarcts
- Splenic veins enter into the portal vein → Retrograde tumour metastasis
- Sheath-like ellipsoid structures in the capillary walls, predominant in piglets → „Schweiger-Beiker sheath“, contractile, phagocytic

Species differences:

- **Storage type**: in dogs, cats, horses, ruminants, pigs → red pulp > white pulp
  red pulp rich in intermediate filaments and in adrenergic nerves
- **Defense type**: in rabbit, guinea pig, chicken, man → white pulp > red pulp
- „Sinusoideal spleen“: dogs, rabbits and man
- „Nonsinusoideal spleen“: horse, ruminants, cats, pigs

Age dependent differences:

- **Juveniles**:
  - hematopoiesis
  - abundant lymphatic tissue (foals!)
  - number of lymphocytes and other mononuclear cells decreasing with age (leading to atrophy in senescence)
Innervation of the spleen

- Sympathetic nervous system (SNS) (noradrenergic)
  - Enter PALS and marginal zone
  - Diminished with age (rats, mice)
  - Diminished in murine AIDS (SNS-destruction)

(Lit: Follen DL et al., U.of California, Irvine College of Medicine)

Splenectomy: Risk?

- Risk of acute fatal infection, leading to rapid septicemia ("Overwhelming post-splenectomy infection").
- Human patients are at risk from Pneumococcus and Meningococcus infections, but also from Haemophilus influenzae
- Liver may substitute phagocytic functions of the spleen

Simplified View of splenic lesions:

- Small spleen (Atrophy)
- Enlarged spleen (Splenomegaly)
- Nodular lesions
Specific splenic pathology

- Malformations / Developmental lesions
  - Torsion of the spleen
  - Rupture of the spleen
  - Circulatory diseases of the spleen
  - Degenerative lesions of the spleen
  - Inflammatory diseases of the spleen (splenitis)
  - Hyperplasia (benign) of the spleen
  - Neoplastic lesions of the spleen

Malformations / Developmental lesions

- Aplasia, Hypoplasia:
  - very rare (in conjunction with other multiple anomalies)

- Hypoplasia of the white pulp:
  - in conjunction with primary immunodeficiencies (i.e. nude mice, severe combined immunodeficiencies...)

Malformations / Developmental lesions

- Double spleens, accessory spleens:
  - located in the omentum (to be differentiated from acquired accessory spleens following trauma).

- Ectopic spleen:
  - associated with congenital herniations of the diaphragm

- Minor shape abnormalities, i.e. notches at the edge of the spleen are frequently seen, to be differentiated from acquired lesions (scars).
**Torsion of the spleen:**
- Torsion of stomach and spleen (Lig. gastrolienale!)
- Torsion of the spleen (pig, > dog, man > rarely in horses)
  - Complete torsion (180 - 240°)
    - results in hemorrhagic infarction of the whole organ,
  - Partial torsion (mainly distal portion) results in local infarction
    - isolated torsion of the splenic pedicle in dogs*: acute or chronic abdominal pain, mean duration 1 wk
    - mainly large breeds (German Shepherd, Great Dane...)
      - age 3-11 yrs

*Hartl F, Mikula P, Blumlein B. Stadler’s HS. Radiographic analysis of 70 cases of isolated torsion of the splenic pedicle in dogs.

**Spleenic Torsion:**
- Often results in sudden death (??) <> Slaughterhouse
  - Sometimes animals (mainly pigs) may survive
    - > severe splenic necrosis
  - Twisted spleens may be a risk of infection by organisms usually controlled by the spleen (i.e. blood parasites).
  - Hematological findings after torsion of the spleen resemble those after splenectomy (i.e. Howell-Jolly bodies, red cell pils...).

**Rupture of the spleen**

  => HEMABDOMEN
  - due to trauma, or
  - severe swelling in all animal species (i.e. lymphosarcoma, anthrax, amyloidosis),
  - or due to local tumours, mainly hemangiosarcomas
    - (dog)
  - Incomplete rupture may cause subcapsular hematoma; > complete rupture
  - Complete traumatic rupture (severing) can results in two isolated spleen fragments.
Circulatory diseases of the spleen

- Congestion
  - Acute congestion: splenomegaly
  - Chronic congestion: fibrosis
- Splenic infarcts

Congestion

- Acute congestion: occurs in association with acute septicemia, toxemia, splenic torsion, but also with euthanasia.
- Chronic congestion: leads to a firm spleen with thickening of the capsule and trabeculae.
  - It is mostly due to systemic, portal or splenic venous hypertension.
  - In man (but rarely in animals) severe liver cirrhosis may be the primary cause.

Splenic infarcts

- Severely swollen spleens are generally prone to thrombosis of arteries and veins. The same applies for diseases with hypercoagulation (i.e. canine autoimmune hemolytic anemia, acute pancreatitis).
- Typically, splenic infarcts along the margin of the spleen are seen in hog cholera, related to fibrinoid thrombosis and endothelial damage.
- Splenic vein thrombosis often occurs in association with traumatic reticulitis, splenic abscesses, and portal vein thrombosis. Arterial embolism may be caused by valvular endocarditis.
Splenic infarction in 16 dogs, associated with:
- Liver disease
- Renal disease
- Cushing
- Uniform splenomegaly (congestion, leukemia, EMH...)
- Neoplasia
- Cardiovascular disease > thrombosis

Splenic infarction as a sign of altered blood flow, rather than primary disease!

Degenerative lesions of the spleen

- Atrophy
- Hemosiderosis
- Siderotic nodules
- Amyloidosis
- Hyalinosis

Atrophy of the spleen

**Atrophy:** occurs in association with
- Old age.
- Starvation, emaciation
- Irradiation injury
- Chronic stress, viral disease, corticosteroids
  - Destruction of lymphocytes → **lymphoid depletion**

Atrophic spleens are shrunken, firm with shriveled surface.

Histological signs of atrophy include lymphoid atrophy and fibrous induration of the red pulp, often associated with accumulation of hemosiderin.
Hemosiderosis of the spleen

- Hemosiderin present in normal animals in splenic macrophages (storage form of iron). The amount is varying depending on species and age: equines > ruminants > carnivores; old > young.
- Severe hemosiderosis occurs in hemolytic anemias, often associated with fibrosis of the sinusoidal tissue.
  
  Accumulation of hemosiderin can also be seen in other types of anemia, due to increased resorption of iron.

Siderotic nodules:

- Focal deposition of iron and calcium in the trabeculae and capsule. These lesions are particularly common in old dogs, representing remnants of local hemorrhage:
  
  → „Gandy-Gamma bodies“, siderofibrosis, siderotic nodules

Amyloidosis

- Occurs in association with generalized amyloidosis, in horses, dogs, cats and bovines, beech martens (Martes foina), certain mouse strains
- Spleens with amyloidosis may be enlarged, but often no gross lesions are visible.
- Two forms:
  - Amyloid deposition in lymph follicles → „sago spleen“
  - Amyloid deposition in the red pulp → „lardaceous spleen“
  
  This type is rare in animals, i.e. in horses after hyperimmunization. Splenomegaly and high fragility → risk for spontaneous rupture!

Pathogenetic differences of the two forms unknown!
Hyalinosis

- Centrofollicular and arteriolar wall hyalinosis is frequently seen in the spleen of old dogs and cats, possibly related to age dependent depletion of lymphoid tissue.
- Occurs also in man
- Significance uncertain

Splenitis: main types

- Purulent splenitis can be caused by hematogenous bacterial spread, i.e. thromboembolic endocarditis valvularis, multiple abscesses, or in association with reticuloperitonitis in bovines.
- Necrotic/necropurulent splenitis
- Granulomatous splenitis: bacterial infections such as necrobacillosis, tuberculosis, pseudotuberculosis, as well as fungal infections can be the cause of multifocal.
- Hyperplastic splenitis, viral, protozoal

Inflammatory diseases of the spleen (splenitis): Pathogenesis

Early splenitis, i.e. following experimental injection of endotoxin or bacterial antigens:
- Accumulation of neutrophils in the mantle zone
  - Migration of macrophages with antigen fragments towards germinal center within 10-12 hrs.

Overwhelming infections result in destruction of lymphocytes in the follicular center
  - Lympholysis
  - Depletion
  - Epitheloid germinal centers, intrafollicular hyalinosis
The Spleen in Septicemia ("Septicemic splenitis")

- **Acute**: characterized by splenic enlargement, acute congestion, degeneration of follicles and PALS, hypercellularity of sinuses.

- **Subacute**: Hyperplastic changes in the sinuses and in the white pulp in bacterial infections (hyperplastic splenitis) (i.e., pneumococcal septicemia), in protozoal infections (i.e., trypanosomiasis, leishmaniasis, babesiosis) and viral infections (i.e., EHV, Equine Infectious Anemia, PCV type-2).

![Fig. 11. ESM over intravacuolar. In the infected spleen, the domi-nant elements of the red pulp is the pafs strike. In case of thiosuccinyl, a protein of thermostable and a hyperplasia of histiocytes can be seen clearly. Bar = 3 μm.](image)


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Hyperplasia (benign) of the spleen

- Diffuse hyperplasia of the white pulp,
- Immune reactions against blood borne microbial agents. (See hyperplastic splenitis)

- Diffuse hyperplasia of the red pulp > splenomegaly
  - Extramedullary hematopoiesis
  - Myeloid metaplasia /hyperplasia in dogs with splenomegaly

- Nodular hyperplasia
  - "fibrohistiocytic nodules"
  - Myelolipomas
Spangler WL, Kass PH. Splenic myeloid metaplasia, histiocytosis, and hypersplenism in the dog (65 cases). Vet Pathol. 1999 Nov;36(6):583-93

- 65 canine spleens with myeloid metaplasia/hyperplasia:
  - Typical history: vomiting, lethargy, fever, anemia, cytopenia
  - Typical gross lesion: splenomegaly, possibly infarction
  - Histology:
    - Diffuse hematopoiesis ("myeloid metaplasia")
    - Vascular thrombosis
    - Hyperplasia of reticular network
    - Excessive erythropoiesis in bone marrow and spleen
  - Comparison with human syndromes:
    - Acute myeloid metaplasia
    - Hemophagocytic syndrome
    - Hypersplenism

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- Analysis of 1,480 canine spleens:
  - Group 1: nonselected diagnostic survey material (n=1372)
  - Group 2: surgical splenectomy specimens (n=50)
  - Group 3: beagle colony (n=108)
- Most frequent findings:
  - Hemangiosarcomas
  - Hyperplastic nodules
  - Hematomas
  - Hyperplastic nodules/ Hemanatomas
  - Myeloid metaplasia
  - Lymphosarcoma

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<tr>
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<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
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<tbody>
<tr>
<td>Hemangiosarcomas</td>
<td>10%</td>
<td>24%</td>
<td>9%</td>
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<tr>
<td>Hyperplastic nodules</td>
<td>23%</td>
<td>5%</td>
<td>48%</td>
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<tr>
<td>Hematomas</td>
<td>10%</td>
<td>19%</td>
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<tr>
<td>Hyperplastic nodules/ Hemanatomas</td>
<td>10%</td>
<td>19%</td>
<td>6%</td>
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<tr>
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<tr>
<td>Lymphosarcoma</td>
<td>3%</td>
<td>3%</td>
<td>6%</td>
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Fibrohistiocytic nodules (canine)

- Characterized by a mixed population of histiocytoid and/or spindle cells, intermixed with hematopoietic, lymphoid and plasma cells.
- All breeds, but German Shepherds, Labrador and Golden R. are predisposed.

Fibrohistiocytic nodules (canine)

- Nodular lymphoid hyperplasia (grade I): Nodular hyperplasia of lymphoid tissue, consisting of monomorphous medium or large lymphocytes without germinal centers. Occurs often in old dogs.
- Benign fibrous histiocytoma (grade II): equal proportions of lymphoid and fibrohistiocytic cells
- Malignant fibrous histiocytoma (grade III): pleomorphic sarcoma, low proportion of lymphoid cells, with karyomegallic or multinucleated cells

Myelolipomas

- Myelolipomas are rare nodular structures containing fat cells and active bone marrow.
- They occur mainly in the adrenal gland, but also in spleen and liver of various animal species.

References:
Neoplasia of the spleen

- Primary neoplasia of the spleen:
  - Lymphoma
  - Myeloma
  - Mast cell tumours, mast cell leukemia (cat)
  - Hemangioma, Hemangiosarcoma
  - Leiomyosarcoma
  - Fibrosarcoma
  - Osteosarcoma
  - Chondrosarcoma
  - (Fibrohistiocytic nodules)
  - Metastatic neoplasia (rather uncommon)

Lymphoma

- Splenic involvement is reported in
- 57% of dogs with lymphoma
- 43% of cats with lymphoma
- 30% of bovines with lymphoma

Spangler WL, Culbertson MR.
J Am Vet Med Assoc. 1992 Sep 1;201(5):773-6

- Analysis of 455 feline spleens:
  - 37% neoplastic (lymphosarcoma, mastocytoma, myeloproliferative disease, hemangiosarcoma)
  - 4% Hyperplastic nodules, hematomas
Summary: Small spleen (Atrophy)

- Old age
- Wasting, chronic congestion, hemosiderosis
- Corticosteroids...
- Radiation...
- Viral diseases (i.e. Parvo-V)

Summary: Large spleen: SPLENOMEGALY

- Any blood borne infection, i.e. Anthrax, Salmonellosis...
- Other bacteria
- African war
- other viruses
- Babesiosis...
- Leishmaniasis...

Summary: Nodular lesions

- Hematomas
- Fibrohistiocytic nodules
- Hemangiosarcoma, other Neoplasias