Patterns of hepatocellular necrosis

### Zonal
- **Centrilobular** – Toxic and hypoxic conditions
- Paracentral
- Midzonal – Aflatoxicosis sometimes
- **Periportal** – Infectious diseases, cholangitis, etc
- Bridging – Extensive (P-P, C-C, C-P)
- Massive – Hepatosis dietetica, algae poisoning parasitic migration, iron-dextran poisoning

What can you tell about the gross appearance of this liver?

**Answer:**
- It has an **enhanced lobular pattern**
- Possible **zonal pattern** of liver damage (degeneration, necrosis, infiltration)
Which pattern of hepatic necrosis do you see in these livers?

**Answer: Multifocal** hepatic necrosis, (Multiple, randomly distributed, white foci disseminated throughout the liver parenchyma)

Possible etiologies?

**Answer: Bacterial septicemias** (Salmonellosis, listeriosis, actinobacillosis, Tyzzer’s disease, etc.), **Herpesvirus infections**
Liver from a 2 week old puppy. Give a morphologic diagnosis and possible etiology

**Answer**: Multifocal hepatic necrosis and hemorrhage

**Etiology**: Canine herpesvirus 1
What causes the disruption of the entire hepatic architecture in liver cirrhosis?

**Answer:** The central pathogenic processes in cirrhosis are death of hepatocytes, nodular regeneration, extracellular matrix deposition, and vascular reorganization.
Liver from a calf. Give a morphologic diagnosis and most likely etiology

**Answer:** Hepatic cyst; congenital

Liver from a pig. Give a morphologic diagnosis and most likely etiology

**Answer:** Hepatic cysts; Parasitic (hydatid)
Liver from a lion with multiple clusters of cysts scattered throughout the parenchyma

Congenital cysts vs neoplastic cysts (biliary cystadenoma)
Liver from a dog. Give a morphologic diagnosis

Dx: Liver rupture, multiple

Predisposing conditions?

**Answer:** Severe congestion acute hepatitis, amyloidosis neoplastic infiltrations (Leukemia), hepatic steatosis
Liver from a cow, give two morphologic diagnoses

**Focal hepatic lipidosis and multifocal telangiectasis** (tension lipidosis commonly seen near mesenteric attachments). Incidental finding. Note the area of fatty infiltration ($F$), the ligamentous attachment adjacent to the affected portion (arrowhead), and the areas of telangiectasis (arrows).
1. **What microscopic changes are usually associated with congenital portosystemic shunts in dogs?**

**1. Answer:** The portal area is abnormal because it lacks a portal vein or it is too small (pv), and contains numerous (more than 3) arterioles (arrows).

2. **Which other congenital anomaly has similar microscopic findings?**

**2. Answer:** Portal vein hypoplasia (microvascular dysplasia) but this condition is associated with portal hypertension.

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*Pathologic Basis of Veterinary Disease (2006), 4th ed., Mosby-Elsevier*
Examples of chronic passive congestion in dogs (top and bottom left) and a cat (bottom right). Note the rounded edges (liver expansion) and extensive areas of subcapsular fibrosis due to chronic exudation of lymph.

Dog. Describe the changes and give a morphologic diagnosis.
Livers from cats with similar findings. Describe the changes and give a morphologic diagnosis

**Answer:** Multifocal areas of dark-red discoloration (there is also diffuse pale discoloration and enhanced lobular pattern)

Dx: 1. Liver: **Telangiectasis**, multifocal
2. Diffuse, moderate, hepatic lipidosis.

What is the significance of these changes?

**Answer:** Telangiectasis is an incidental finding (no clinical significance)
Telangiectasis, liver, cat. Cavernous dilation of blood filled sinusoids (T) with loss of hepatocytes. Courtesy: Dr Legge.
Livers from pigs and mesocolon. Give a morphologic diagnosis and etiology

**Dx:** Liver: massive necrosis

**Etiology:** Vitamin E/Selenium deficiency (hepatosis dietetica)

Other possible etiologies: Iron dextran poisoning, Cresols
What microscopic changes are seen in acute toxic-induced liver disease?

*Hydropic degeneration, steatosis & necrosis of hepatocytes, often centrilobular*

What morphologic changes are seen in chronic toxic-induced liver disease?

*Fibrosis, biliary hyperplasia and regeneration (nodular)*

What toxic agents are most commonly associated with acute toxic-induced liver disease?

*Amanita phalloides, blue-green algae (microcystin), phosphorus, cresols, CCl₄, Cu in sheep, Fe in piglets*

What toxic agents are most commonly associated with chronic toxic-induced liver disease?

*Pyrrolizidine alkaloids, cycads (cycasin), alsike clover, aflatoxins, sporidesmin, phomopsin, anticonvulsant drugs*
Quiz (hepatotoxins)

Which toxic agents produce small (fibrotic), finely nodular livers and megalocytosis?
*Pyrrolizidine alkaloids, cycads (cycasin), aflatoxins, phomopsin*

Which toxic agents (or conditions) produce massive necrosis?
*Amanita phalloides, blue-green algae (microcystin), cresols, Fe in piglets, Hepatosis dietetica*

Which toxic agents produce periportal necrosis?
*Phosphorus, aflatoxins (only in ducklings), Alsike clover (colangiohepatitis & fibrosis)*

Which toxic agents produce photosensitization?
*Alsike clover, sporidesmin (facial eczema), phomopsin, Lantana camara*

Which toxic agents produce cholestasis?
*Sporidesmin (necrosis of biliary epithelium / cholangiohepatitis), Alsike clover, Lantana camara*
**Hepatic nodular hyperplasia vs. regenerative nodules**

**Nodular hyperplasia:** Usually focal, no fibrosis, no previous necrosis or inflammation.

**Regenerative nodules:** A diffuse change, areas of retraction (fibrosis), necrosis and/or inflammation.
**Hepatocellular nodular hyperplasia:** No fibrous capsule, vacuolar change is common

**Regenerative nodules:** Nodule surrounded by thick bands of fibrous tissue
Liver from an old dog. Give a morphologic diagnosis

**Dx:** Cholangiocellular carcinoma

Multiple, firm, nodules often showing central areas of depression/necrosis (arrow)
Gallbladder distension

- Common result of fasting
- *Lantana camara* toxicosis
  - Toxic metabolite: Lantadene A
  - Cholestasis, icterus, photosensitization
- Secondary to biliary obstruction

Gallbladder distension (*top*) due to *Lantana camara* (*bottom*) toxicosis, liver, sheep.

The colors of some flowers of *Lantana camara* recall the flag of which country?

Answer: Spain
Cystic hyperplasia of the gall bladder mucosa. The gallbladder is opened. Note multiple green and pale yellow cystic nodules / polyps in the mucosa.

**Dx:** Cystic mucinous hyperplasia of the gall bladder  
**Sequela:** Mucocele
Tissues from a dog. Describe the changes, give a morphologic diagnosis and possible sequelae

**Description:** The gall bladder is markedly dilated with bile-tinged mucoid material.

**Dx:** Gall bladder mucocele

**Sequelae:** Extrahepatic biliary obstruction; Ischemic necrosis, rupture and chemical or septic peritonitis