Lecture 23 Recap + Learning Objectives

Learning Objective 1: Hepatic lipidosis

Intracellular accumulations are generally accomplished via 2 ways:

Overload of cells (metabolic alterations)

Decreased function of cells (especially lysosomes)

Hepatic lipidosis: Energy imbalance overwhelms the liver's ability to metabolize and clear fatty acids. This leads to a buildup of triglycerides within hepatocytes.

Hepatocytes become enlarged resulting in a big liver

Accumulation of Cytoplasmic Material

Cell injury and metabolic conditions (the big 2)

Overload (too much ——— to handle)

- Fatty liver in peri-parturient cows: negative energy imbalance
  - ↳ So much energy is mobilized to the liver → hepatic lipidosis
- Feline fatty liver: anorexic fat cat → fat mobilized to liver → hepatic lipidosis
  - ↗ accidently locked in closet

Altered Cell or Metabolic function (improper handling of ———)

Cell injury: decreased ATP, decreased oxygen, decreased protein (enzyme) Synthesis → decreased lysosomal function → build up of intracellular metabolites

- Diabetes: insufficient carbohydrate processing, preferential use of fatty acids → hepatic lipidosis
- Miniature horses, donkeys: "Unique" metabolism predisposes them to fatty liver

Learning Objective 2: Intra- and extravascular hemolysis

Extravascular: Hgb is released into a phagocytic cell (macrophage)

Breakdown occurs in **macrophages**

- Hgb → Hemosiderin yellow/brown pigment like a bruise

Icterus (jaundice) is a major Clinical Sign

Example: Immune mediated hemolitic anemia, trauma

Intravascular: HgB is released directly into the blood

Breakdown occurs in circulation

- HgB → filtered out in kidneys before macrophages can see it

Hemoglobinuria is a major clinical sign

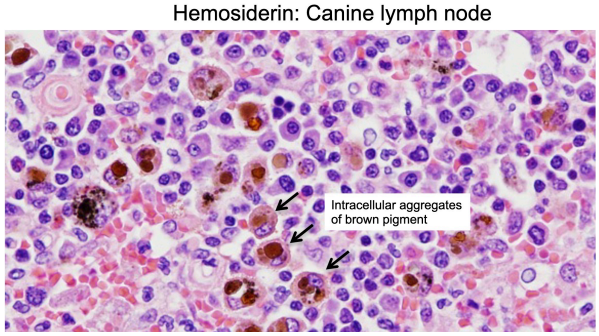
Example: Copper toxicity in small ruminants, bacterial toxemia, sepsis

Time Course - think about bruises red → yellow → blue/black

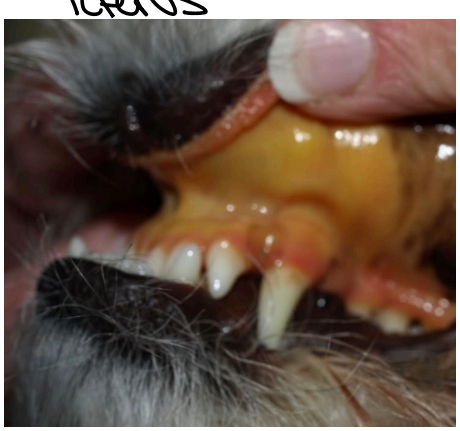
Hemosiderin takes time: implies chronicity to hemorrhage (days, weeks, months)

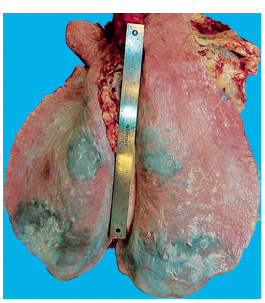
Extravascular Hemolysis

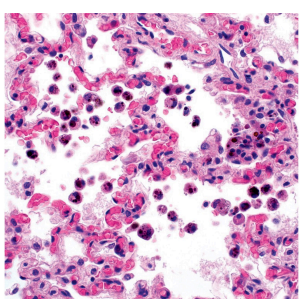
Hemosiderin: Canine lymph node



Icterus

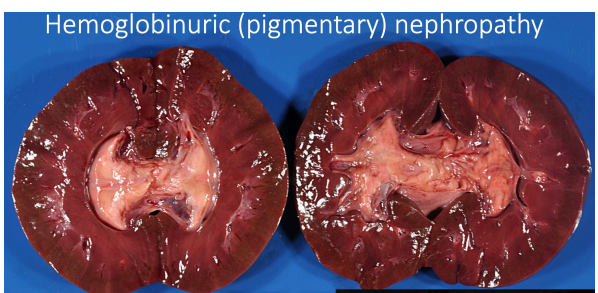






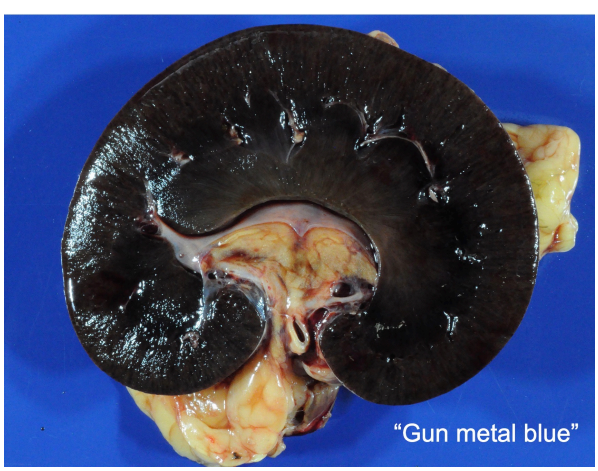
Intravascular Hemolysis

Hemoglobinuric (pigmentary) nephropathy



Normal kidney →

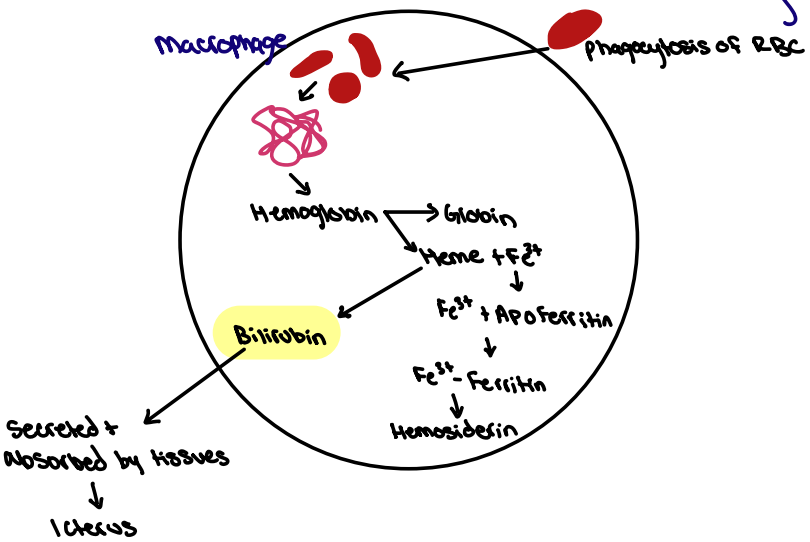
Massive Hemoglobinuria



Learning Objective 3: Icterus formation

Icterus implies severe extravascular hemolysis

Bilirubin taken, excreted and metabolized by tissues



Learning Objective 4: Lysosomal storage disease

Lysosomal storage disease (LSD)

↳ Inherited enzyme deficiencies → lysosomes incapable of breaking down protein, lipid or carbs leading to a buildup of partially digested metabolites in cells → cell death

Tissues affected: Brain, Liver, Muscles

Why? These tissues have rapid turnover of organelles and high energy demands

Buildup of material eventually interferes w/ cell function

Lysosome function depends on

↳ Enzyme synthesis + Fidelity

↳ Trafficking

↳ Fusion

Any disruption (mutation) in a protein involved in any step can interrupt the process

Lysosomes are involved in breaking things down

Cells affected by specific disease depends on expression / activity of enzyme + substrate

Brain has a lot of the substrate as does the liver which is why they are targeted

Learning Objectives 5/6: Amyloidosis and the Liver

Amyloidosis: Deposition of misfolded protein in tissue

Main types of amyloid:

Primary amyloidosis: Overproduction of light chain of immunoglobulins

- Defect in plasma cell production - "Plasma cell dyscrasia"

Secondary amyloidosis: serum amyloid A (SAA) produced in liver (overproduction)

- SAA is upregulated by the liver during inflammation
- **Chronic inflammation** → Chronic overproduction of SAA
- Deposited systemically but most severe in kidney + liver

Hepatic Amyloidosis

Amyloid in the liver blocks the hepatocytes from being able to "filter" the blood

Hepatocytes become atrophied leading to liver failure

Entire liver grossly looks big because of the amyloid accumulation

Islet cell amyloid: IAPP produced by pancreatic B-cells
↓
Islet amyloid polypeptide

Learning Objective 7: Dystrophic vs Metastatic Mineralization

*Deposition of hydroxyapatite calcium mineral

Dystrophic Calcification

Local deposition of calcium in injured, dying and dead tissue; unrelated to serum Ca:PO4 balance

Location: anywhere - dead cells/tissues, old abscesses/granulomas, dead parasites

Metastatic Calcification

Systemic deposition of calcium in connective tissue and basement membranes when there is hypercalcemia or hyperphosphatemia and the solubility product of calcium-phosphate is exceeded

Etiologies: kidney disease, Vit. D toxicosis, Parathyroid disorders, Neoplasia

Location: Stomach, lungs, heart, kidney, parietal pleura