Lab 1 Instructor Notes

Objectives:

No need to go over the approaching pathologic specimens in lab

Keywords:

Hydropic Change
Cellular swelling occurs when ischemia causes ATP depletion and the loss of membrane ion pumps, resulting in the movement of water into cells. It is a form of reversible injury.
Adaptation
Reversible changes in the size, number, phenotype, or function of cells in response to stimuli (e.g. hormonal or neural) or injury.
Hypertrophy
Increase in the size of cells
Hyperplasia
Increase in the number of cells
Atrophy
Decrease in the size or number of cells
Metaplasia
Reversible change from on differentiated cell to to another.
Barrett esophagus
I ntestinal metaplasia of the esophageal squamous epithelium in response to gastric (acid) reflux.
Steatosis
A reversible accumulation of triglycerides in cells (particularly hepatocytes) as a result metabolic dysfunction.
Hemosiderin
A hemoglobin derived pigment that is deposited when red blood cells are digested by macrophages.
Dystrophic calcification
The deposition of calcium phosphate in areas of necrosis or chronic cellular injury.
Pyknosis
Irreversible condensation of chromatin in the nucleus
Karyorrhexis
The irreversible destructive fragmentation of the nucleus of a necrotic cell.
Karyolysis
The complete dissolution of the nucleus of a cell (irreversible).
Apoptosis
"Programmed" cell death induced by the activation of a suicide pathway. In contrast to necrosis, it usually occurs with single cells that are ultimately resorbed, and does not elicit an inflammatory response.
Intrinsic apoptosis
Self-induced apoptosis occurring via the Bcl-2 and mitochondrial suicide pathways.
Extrinsic apoptosis
Induction of apoptosis by the activation of membrane bound death receptors.
Acidophil body
An eosinophilic apoptotic hepatocyte frequently seen in viral hepatitis.
Mallory Body
An eosinophilic, intracytoplasmic inclusion containing cytokeratin and ubiquitin frequently seen in alcoholic liver disease
Necrosis
The death of cells resulting from, for example, loss of blood supply, bacterial toxins, or physical or chemical agents. Subdivided into caseous, coagulative, liquefactive, gangrenous, fat, and fibrinoid (we define these in subsequent labs).
Gangrenous necrosis
Necrotic tissue acted upon by bacteria. "wet" and "dry" types.
Edema
The abnormal accumulation of interstitial (extravascular) fluid.
Transudate
Fluid that escapes the vasculature because of disturbances of hydrostatic or colloid osmotic pressure.
Exudate
Fluid that that escapes the vasculature because of inflammation.

Folio 1: Dystrophic Calcification & Ventricular Hypertrophy

Aortic valve stenosis
- Chronic injury
- age-related "wear and tear," pts 70-90 years old
- dystrophic calcification, a pathologic adaptation
- Restricted blood flow through aortic valve
- X-ray: calcification appears dense white like bone

Left Ventricular Hypertrophy
- increase in the size of the myofibers
- More common cause:
- hypertension (vascular resistance in peripheral circulation)

Folio 2: Congestive heart failure – lungs

- "Heavy lungs" due to the buildup of fluid
- Progressive aortic stenosis, LVH adaptation can't compensate leading to failure
- Early CHF: perivascular and interstitial edema thickens the alveolar septae.
- Later CHF: Alveolar spaces fill with transudative fluid.
- RBCs are too big to passively move with the transudate, the fluid is clear.
- Eventually thin walled alveolar capillaries to burst releasing RBCs into alveoli
- Heart Failure Cells
- Macrophages phagocytose the RBCs: hemoglobin iron -> hemosiderin
- Tissue processing: transudate washes away, RBCs and macrophages remain

Folio 3: Ischemic injury, Kidney

Chronic kidney changes
- Granular surface.
- Small vessel disease: diabetes or hypertension
- Cortical Thinning: atrophy due to chronic ischemia (heart failure in this patient)

Reversible Ischemic change
- Chronic mononuclear infiltrate, interstitial fibrosis
- Hydropic change (ballooning degeneration) of tubular epithelium
- Acute injury resulting from really low blood flow right before death.

Irreversible Ischemic change
- Acute tubular necrosis
- Grossly swollen: lack of tubular filtration causes fluid backup - interstitial edema
- Histology: range of necrosis:
  - Hypereosinophilic cytoplasm
    - lysosomal enzymes denatures proteins exposes basic amino acids
  - Nuclear disruption
    - pyknosis, karyorrhexis, karyolysis
  - Advance necrosis
    - Complete cellular disruption
- Not seen yet: inflammation, fibrosis

Folio 4: Alcoholic Steatosis

Gross: slightly yellow & greasy texture
Microscopic:
- Droplets of lipid (triglycerides) in hepatocytes
- Some fibrosis (but not cirrhosis, yet) and mild monocytic inflammation.
- Mallory bodies: eosinophilic (red/pink) inclusions
  - Tangles of cytokeratin and ubiquitin
  - Non-specific but seen in alcoholic liver
- Steatosis is reversible, fibrosis (and cirrhosis) is not

Causes of steatosis:
- Occurs when fatty acid oxidation is impaired
- Direct toxic injury to the hepatocytes
  - (e.g. mitochondrial damage that inhibits oxidative phosphorylation)
- Shunting of energy stores to another task (e.g. the detoxification of ethanol)
- Obesity

Folio 5: Apoptosis, Hepatitis C

Virtual microscope
- Core needle liver biopsy (note the shape)
- Apoptotic hepatocytes a.k.a. acidophil bodies) – not specific for Hepatitis

Apoptotic cascade
- Activation of caspases (cysteine proteases)
- Enzymatic degradation of structural proteins
- Activation of DNAses: characteristic "ladder" cleavage pattern of the cells DNA

Extrinsic apoptosis (Death Receptor Initiated)
- Virally-infected hepatocytes undergo apoptosis
- Response to cytotoxic T lymphocytes (CTLs)
- CTLs release perforin & granzymes
- CTL Fas-ligand binds to hepatocyte inducing apoptotic cascade
- Also seen in Graft-versus-host disease

Intrinsic apoptosis (Mitochondrial)
- Physiologic
  - The involution of hormone-dependent tissues
  - Cell loss in proliferating cell populations (germinal centers, lymphomas)
  - Elimination of self-reactive lymphocytes
- Pathologic
  - Radiation damage to DNA
  - Free-radical damage
  - Genetic (e.g. accumulation of misfolded protein in ER)
  - Tumors (BCL-2 inhibits apoptosis and is mutated (switched off) in lymphoma)

Folio 6: Intestinal metaplasia (Barrett esophagus)

Gross: islands of ("salmon pink") mucosa surrounded by squamous mucosa ("pearly white") above the GEJ.

Micro:

- Replacement by intestinal-like columnar cells (well-formed goblet cells)
- In response to the reflux of gastric acid into the esophagus.
- Mucinous epithelium which is more resistant to damage by gastric enzymes
- Mucin stain shows mucin in goblet cells

Reversible injury (with elimination of the reflux).
Associated with a higher risk of cancer, typically adenocarcinoma
Considered pre-malignant (but not dysplastic).
Results from reprogramming of stem cells

Other example:

- Squamous metaplasia in bronchi
  - Ciliated respiratory mucosa to squamous epithelium in response to tobacco smoke.
  - "Smokers cough" results from this loss of ciliated epithelium (the mucociliary escalator).

Folio 7: Atrophy & Gangrenous Necrosis

Cortical Atrophy

- Compensatory enlargement of the lateral ventricles
- Seen in Alzheimer Disease and multi-infarct dementia
- Cognitive impairment

Gangrene - necrotic tissue that has been digested by bacteria

- Dry gangrene (shown)
  - mummified flesh
  - chronic ischemia (diabetics, peripheral arterial disease).
  - Hemoglobin reacts with hydrogen sulfide (produced by bacteria), and
    - forms a black iron sulfide pigment.
- Wet gangrene
  - venous stasis (e.g. bed sores) or rapid complete blood loss
  - tissue remains wet and can become a medium for significant bacterial growth
  - malodorous.