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Case 1. Tissue from a mouse.

MICROSCOPIC DESCRIPTION: Liver: There is diffuse and discrete coagulative necrosis **(2 pt)** of centrilobular **(2 pt)** hepatocytes which extends outward 5-8 layers of hepatocytes outward from the central vein itself. The necrosis is characterized by the maintenance of cellular architecture; cytoplasm is brightly eosinophilic and granular and nuclei are either shrunken and hyperchromatic, or lost **(2 pt)**. There is mild congestion and hemorrhage multifocally surrounding central veins **(1 pt)**. Within these areas, Kupffer cells and sinusoidal endothelial cells are hypertrophic **(1 pt)**, and there is infiltration of low numbers of neutrophils and rare histiocytes **(1 pt)**. Diffusely, hepatocytes are mildly swollen with accumulation of numerous coalescing cytoplasmic vacuoles **(1 pt)** (glycogenosis) **(2 pt)**. There is multifocal small amounts of extramedullary hematopoiesis scattered throughout the section **(1 pt)**.

MORPHOLOGIC DIAGNOSIS: Liver, centrilobular hepatocytes: Necrosis, coagulative, diffuse. **(3 pt)**

CAUSE: Acetominophen toxicity (hypoxia, CCl_4 ok) **(3 pt)**

O/C: (1 pt)

(Note: While many toxicologic pathologists will understandably quantify necrosis with the modifiers "mild", "moderate", or "severe", this terminology is not traditionally used in diagnostic pathology at the AFIP/JPC, as we don't believe that you can have mild or severe necrosis.

However, as the extent of necrosis in toxicities such as this one IS important, we utilize an objective measurement in terms of the number of cells that are necrotic; i.e., acetaminophen is an excellent example of a dose-related response; in this case a small dose may result in only a rim of 1-2 necrotic hepatocytes, while the one you are looking at is a fairly hefty dose. Bhw)

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Case 2. Tissue from a mouse.

MICROSCOPIC DESCRIPTION: Brain, multiple sections at the level of hippocampus (caudal diencephalon) and rostral cerebellum **(1 pt for not just saying "Brain")**: Diffusely, primarily within the grey matter **(2 pt)** neuropil of the cerebral cortex, hippocampus, amygdaloid nucleus, and the brainstem **(2 pt for multiple locations)** (but to a lesser extent in the white matter also), there are numerous randomly **(1 pt)** arranged round to oval plaques **(2 pt)** of pale eosinophilic **(1 pt)** protein filaments (neuritic plaques) **(2 pt)** which often have an amphophilic to basophilic cast **(1 pt)**. Areas with high concentrations of plaques often have increased numbers of glial cells **(1 pt)**, occasionally surrounding plaques in close proximity **(1 pt)**. The cerebellum appears to be clear of these plaques. Within the brainstem nuclei **(1 pt)**, neuronal cell bodies are often expanded up to 75um with dissolution of Nissl substance **(1 pt)**; axons are also large, pale, and swollen (spheroids). Ther is mild diffuse neuronal loss within the cerebrum, most noticeably in the area of the hippocampus.

MORPHOLOGIC DIAGNOSIS: 1. Cerebrum, hippocampus, amygdaloid nucleus, brainstem: Neuritic plaques, multifocal, moderate to severe, with gliosis **(3pt)**.

2. Brainstem nuclei, neurons: Chromatolysis, multifocal, moderate to severe with spheroid formation. **(1 pt)**

3. Cerebrum, hippocampus: Neuronal loss, diffuse, mild to moderate.

O/C: **(1pt)**

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Case 3. Tissue from a dog.

MICROSCOPIC DESCRIPTION: Cerebrum: Within the cerebrum, extending into the ventricle **(1pt)** and multifocally along Virchow-Robins spaces and beneath the overlying meninges and compressing the cerebral cortex is an unencapsulated, expansile, densely cellular, well demarcated neoplasm **(2pt)**. The neoplasm is composed of sheets **(1pt)** and lobules of neoplastic cells which are subdivided by a moderate fibrous to fibrovascular stroma **(1pt)**. Throughout most of the neoplasm, neoplastic cells are irregularly round with a moderate amount of a finely granular amphophilic to eosinophilic cytoplasm and indistinct cell borders **(1pt)**. Nuclei are round, often eccentrically placed, with coarsely stippled chromatin and one to three small basophilic nucleoli **(1pt)**. There is marked anisokaryosis **(1pt)**. The mitotic rate averages 5-8 per 400X hpf**(1pt)**, and are often atypical **(1pt)**. In some areas, neoplastic cells form dense trabeculae of cohesive cells **(1pt)**, in which cytoplasm is more densely eosinophilic and cytoplasm often contains single large discrete vacuoles **(1pt)** which peripheralize and compress the nucleus. There is extensive necrosis **(1pt)** throughout the neoplasm, both of single and large groups of cells (often within the center of lobules) , and multifocally, variably-sized vessels contain fibrin thrombi **(1pt)**. There are small aggregates of lymphocytes and plasma cells surrounding large vessels within the neoplasm **(1pt)**.

MORPHOLOGIC DIAGNOSIS: Cerebrum: Suprasellar germ cell tumor **(4pt)**

O/C: (1pt)

Note: As is the case with most of these tumors, there is significant variations between sections, both in the anatomy (some sections have pituitary gland or pyriform lobe), as well as the distribution of cell type in this neoplasm which is well known for its phenotypic variation.

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Case 4. Tissue from a ferret.

MICROSCOPIC DESCRIPTION: Lung: Approximately 50% of alveolar lumina **(1pt)** and occasional bronchioles are filled with flocculent eosinophilic exudate **(1pt)** containing innumerable ill-defined, 3-4 um **(1pt)**, round to oval structures (fungal cysts) **(1pt)** with small basophilic nuclei. Fungal cysts are both extracellular and also contained within the cytoplasm **(1pt)** of epithelioid macrophages **(1pt)**, foamy alveolar macrophages, and rare multinucleated foreign body-type macrophages **(1pt)**, admixed with low numbers of neutrophils **(1pt)**. Throughout the section, alveolar septa are thickened **(1pt)** up to two to three times normal by foamy macrophages **(1pt)**, congestion, fibrin, edema, and in areas in which the alveoli are expanded by fungi, fibroblasts and fibrous connective tissue **(1pt)**. In lesser affected areas, alveolar walls multifocally contain necrotic cellular debris and are lined by polymerized fibrin (hyaline membranes) **(1pt.)**. There is rare type 2 pneumocyte hyperplasia. Blood vessels are often surrounded by large numbers of foamy macrophages **(1pt)**, as well as fewer lymphocytes and plasma cells **(1pt)**.

MORPHOLOGIC DIAGNOSIS: Lung: Pneumonia, interstitial, histiocytic and necrotizing, diffuse, marked, with many intra-alveolar fungal cysts. **(3pt)**

CAUSE: Pneumocystis carinii **(2pt)**

O/C: (1pt)