

Case 1 – Tissue from an ox.

MICROSCOPIC DESCRIPTION: Small intestine: Diffusely expanding **(1pt)** the multifocally ulcerated mucosa, and separating, surrounding, and replacing crypts **(1pt)** is an inflammatory infiltrate composed of large numbers of lymphocytes **(1pt)** and macrophages **(1pt)** with fewer admixed plasma cells, neutrophils, and eosinophils (the latter two in areas of ulceration). **(1pt)** Macrophages are polygonal and range up to 25um in diameter with abundant granular eosinophilic cytoplasm **(1pt)**. Villi are diffusely shortened and blunted **(1pt)**, and numerous crypts are lost **(1pt)**. Multifocally, crypts are dilated up to 750um in diameter **(1pt)**, lined by attenuated epithelium, and contain numerous viable and degenerate neutrophils and eosinophils admixed with sloughed epithelium and cell debris (crypt abscesses) **(1pt)**. Hyperplastic, occasionally abscessed crypts extend downward into mildly hyperplastic Peyer's patches. **(1pt)** The infiltrate extends through the muscularis into the underlying edematous and congested submucosa, where inflammatory cells are fewer in number but also admixed with large multinucleated Langhan's type **(1pt)** multinucleated macrophages. Dilated lymphatics are often surrounded by similar cells (lymphangitis) **(1pt)**, as well as in the muscularis and serosa. There is mild fat atrophy within the adjacent mesentery and multifocal mesothelial hyperplasia.

MORPHOLOGIC DIAGNOSIS: Intestine: Enteritis, lymphohistiocytic **(1pt)**, diffuse, marked, with marked villar blunting, crypt abscessation and loss **(1pt)**, and moderate lymphohistiocytic lymphangitis **(1pt)**.

CAUSE: Mycobacterium paratuberculosis **(3pt)**

O/C - (1pt)

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Case 2 – Tissue from a cat.

MICROSCOPIC DESCRIPTION: Kidney: Diffusely, extending from the capsular surface into the medulla, the epithelium of proximal convoluted tubules **(1pt.)** shows evidence of degeneration **(1pt.)** (vacuolation, hypereosinophilia, swelling, and granularity) **(1pt.)**, necrosis **(1pt.)** (pyknosis, fragmentation, and lifting off of the basement membrane) **(1pt.)**, and loss and the lumina of affected tubules is expanded by abundant granular to vacuolated eosinophilic cellular debris **(1pt.)**. Remaining epithelium of affected tubules is flattened and attenuated **(1pt.)**. The basement membrane of affected tubules remains intact **(1pt.)**. Deeper into the cortex, and within the medulla, numerous tubules contain dull pink protein or brightly eosinophilic granular casts. **(1pt.)** Remaining tubules are lined by cuboidal, basophilic epithelium which has occasional mitotic figures **(1pt.)** and rare large nuclei (regeneration) **(1pt.)**. Rare tubules contain lamellated crystalline mineral within their lumina **(1pt.)**, and rare tubules are lined by epithelial cells which are mineralized (dystrophic mineralization)**(1pt.)**. Other tubules contain aggregated bluish protein.

MORPHOLOGIC DIAGNOSIS: Kidney, proximal convoluted tubules: Necrosis and regeneration, diffuse, with granular cast formation. **(4pt)**.

CAUSE: Any toxin affecting PCT: Lily (this case), raisin, acetaminophen, aminoglycoside **(2pt)**

O/C: (1pt)

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Case 3 – Tissue from a dog.

MICROSCOPIC DESCRIPTION: Liver: There is diffuse fibrosis **(1pt)** which separates and surrounds proliferating nodules of hepatocytes **(1pt)**. Areas of fibrosis are hypercellular with an infiltrate of large numbers of neutrophils and lymphocytes admixed with fewer macrophages and plasma cells amongst plump fibroblast nuclei and congested capillaries. **(1pt)** Macrophages are present both individually and in clusters **(1pt)** and often contain large amounts of a brown granular pigment **(1pt)**. There is moderate biliary hyperplasia **(1pt)** and biliary epithelium is plump. The fibrous connective tissue and biliary hyperplasia often extends past the limiting plates, encompassing and occasionally replacing hepatocytes **(1pt)** (piecemeal necrosis) **(1pt)**. Entrapped hepatocytes are either shrunken or swollen with abundant intracellular edema as well as moderate amounts of brown granular pigment. **(1pt)** In some areas, portal hepatocytes are compressed and sinusoids are dilated and lined with plump endothelium (sinusoidal capillarization). Canaliculi between portal hepatocytes are often swollen (cholestasis) **(1pt)**. There are scattered aggregates of macrophages **(1pt)** and neutrophils diffusely throughout the section in midzonal and centrilobular areas, as well as shrunken, hypereosinophilic hepatocytes (apoptosis) **(1pt)**. Approximately 50% of hepatocytes within all areas of the lobule contain numerous discrete intracytoplasmic lipid vacuoles. **(1pt)** There is widely scattered extramedullary hematopoiesis. **(1pt)**.

MORPHOLOGIC DIAGNOSIS: Liver: Fibrosis, bridging and portal **(1pt)**, diffuse, severe, with macronodular hepatocellular regeneration **(1pt)**, piecemeal necrosis, cholestasis, siderosis, and sinusoidal capillarization. **(1pt)**.

NAME 3 POSSIBLE CAUSES: Copper toxicosis, chronic active hepatitis of Dobermans, chronic administration of anticonvulsants, aflatoxicosis, extrahepatic cholestasis, severe cardiac disease **(1pt)**

O/C: (1pt)

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Case 4 – Tissue from an ox.

MICROSCOPIC DESCRIPTION: Lymph node. There is diffuse reactive hyperplasia **(1pt.)**, with numerous well-formed follicles distributed throughout the node. Follicular centers are often mildly hypocellular **(1pt.)** and contain low numbers of macrophages whose cytoplasm is distended by a golden brown pigment **(1pt.)**, as well as aggregates of hyaline protein **(1pt.)**. Medullary sinuses **(1pt.)** are expanded by numerous macrophages **(1pt.)**, the majority of which contain light brown to green strongly birefringent **(1pt.)** granular pigment **(1pt.)**. There is multifocal scattered hyalinosis of vessels within medullary sinuses. **(1pt)**

Liver: Diffusely, portal areas **(1pt.)** are mildly expanded by largely individualized macrophages containing a brownish-green strongly birefringent pigment **(1pt.)** – small aggregates are scattered throughout the rest of the section in other areas of the lobule. Portal areas contain small numbers of lymphocytes and plasma cells. Hepatocytes are diffusely swollen by large numbers of intracytoplasmic vacuoles (glycogen) **(1pt.)** and they compress sinusoids **(1pt.)**. Kupffer cells are diffusely activated throughout the section **(1pt.)**. There is minimal biliary hyperplasia. **(1pt.)**

MORPHOLOGIC DIAGNOSIS: 1. Lymph node: Sinus histiocytosis, diffuse, severe, with abundant anisotropic intracytoplasmic pigment **(1pt.)**

2. Lymph node: Rective hyperplasia, diffuse, moderate.

2. Liver, portal areas: Abundant intrahistiocytic pigment. **(1pt.)**

CAUSE: 2-8 dihydroadenine accumulation due to purine catabolic deficiency **(1pt.)**

O/C: (1pt.)