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Case 1. Tissue from a hamster.

MICROSCOPIC DESCRIPTION: Liver: Expanding sinusoids and perivascular areas, largely replacing the hepatic parenchyma, and compressing remaining moderately atrophic hepatocytes (1pt.), there is an unencapsulated, densely cellular, poorly demarcated neoplasm. (1pt.) The neoplasm is composed of sheets (1pt.) of neoplastic lymphocytes (1pt.) on a pre-existent stroma. Neoplastic lymphocytes are large averaging 2-3 times the size of an erythrocyte (1pt.) with a moderate n:c ratio, moderate amounts of a granular amphophilic cytoplasm (1pt.) and indistinct cell borders. Nuclei are round with coarsely stippled chromatin and 1-2 eosinophilic nucleoli. (1pt.) Mitoses average 5 per 400X field or 25-30 per 2.37mm<sup>2</sup> (1pt.) There is mild anisokaryosis and anisocytosis, and scattered throughout the infiltrate are low numbers of an individual apoptotic cells. Diffusely, sinusoidal architecture is obscured, and remaining hepatocytes are either shrunken with hypereosinophilic cytoplasm and a moderately hyperchromatic nucleus (atrophic) (1pt.) or are swollen with numbers of overlapping discrete vacuoles in their cytoplasm (lipidosis) (1pt.). Neoplastic cells also infiltrate and markedly expand the wall of the gallbladder. (1pt.) Similar neoplastic lymphocytes infiltrate and largely efface the omentum, and there are scattered areas of lytic and or coagulative necrosis (1pt.) measuring up to 1mm in diameter throughout. One omental/mesenteric mass is contiguous with the ventral aspect of the spleen, and neoplastic cells directly invade the splenic capsule. Neoplastic cells fill and expand splenic sinusoids (1pt.), occasionally replacing splenic white pulp. Neoplastic lymphocytes expand the pancreatic interstitium, separating, surrounding and replacing exocrine acini and islets. (1pt.) The lobules of the pancreas is additional expanded by edema and neoplastic lymphocytes in the pancreatic interstitial tissue. Rarely macrophages within each section of tissue contain moderate numbers of 2-3 um amastigotes (1pt.) within their cytoplasm. Amastigotes have a basophilic nucleus and a small rod-shaped kinetoplasm. (1pt.)

MORPHOLOGIC DIAGNOSIS: 1. Liver, spleen, omentum, pancreas: Lymphoma. (1pt.)
2. Liver, spleen, omentum, pancreas, macrophages: Intracytoplasmic amastigotes, rare. (1pt.)

CAUSE: Hamster polyomavirus (1pt.), Leishmania sp. (1pt.)

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Case 2. Tissue from a rhesus macaque.

MICROSCOPIC DESCRIPTION: Lung: Affecting approximately 50% of the section (1pt.) alveoli are filled with various combinations and concentrations of macrophages (1pt.), neutrophils (1pt.), abundant homogenous to flocculent (1pt.) protein, rare polymerized fibrin, hemorrhage, and cellular debris, and scattered colonies of bacteria. Multifocally within alveolar spaces, there are numerous syncytial giant cells (1pt.) up to 90um in diameter (1pt.), with moderate amounts of granular, eosinophilic cytoplasm and up to 40 nuclei arrayed in a semi- or full circle (1pt.). Multifocally, there are areas of septal necrosis (1pt.) in which remnant coalescing alveoli contains numerous neutrophils, abundant cellular debris, and proliferating fibroblasts. (1pt.). Alveolar septa are expanded by low to moderate numbers of macrophages(1pt.), neutrophils, fewer lymphocytes, congestion and edema and occasionally contain plump fibroblasts. There is multifocal Type II pneumocyte hyperplasia (1pt.) and smooth muscle hyperplasia (1pt.) within the affected area. There is diffuse expansion of alveolar septa by low numbers of macrophages, neutrophils, edema and rare fibrin diffusely (1pt.) throughout the section. Airways within the affected area contain refluxed neutrophils, macrophages and cellular debris in a mix of edema fluid and mucus. (1pt.) Airway walls show a range of severity of damage, from necrosis and loss of bronchiolar epithelium and replacement by inflammatory exudate, to mild bronchiolar epithelial hyperplasia and few lymphocytes or neutrophils within the epithelium. Within the affected area, several large arterioles contain large masses of polymerized fibrin.

MORPHOLOGIC DIAGNOSIS: Lung: Pneumonia, interstitial (1pt.) histiocytic (1pt.), with abundant fungal cysts (1pt.), neutrophils, and numerous viral syncytia. (1pt.).

CAUSE: Simian lentivirus (simian immunodeficiency virus) (2pt.), Pneumocystis carinii (1pt.)

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Case 3. Tissue from a rat.

MICROSCOPIC DESCRIPTION: Kidney: There are changes at all levels of the nephron. Bowman's space is often moderately dilated and the Bowman's space contains variable amounts of eosinophilic proteinaceous material. (1pt) Diffusely, glomeruli exhibit one or more of the following changes: variation in size, marked expansion of the glomerular capillaries by abundant granular, lamellated or homogenous eosinophilic material, (1pt) adhesions of the glomerular tuft to Bowman's capsule (synechia) (1pt), hypertrophy of parietal epithelium, marked thickening of Bowman's capsule (1pt), and periglomerular fibrosis Manyglomeruli are shrunken and sclerotic (1pt). Diffusely, tubules show marked variation in size diameter, with ectatic tubules ranging up to 1mm in diameter (1pt). Ectatic tubules are lined by attenuated epithelium whose height is inversely proportional to the cross-sectional area of the tubule (1pt), and contain large amounts of pale to brightly eosinophilic granular to homogenous protein and occasionally sloughed epithelial cells, cellular and karyorrhectic debris, degenerate neutrophils, and rare erythrocytes. (1pt) Less affected tubules are lined by cuboidal cells with abundant eosinophilic granules within their cytoplasm. Occasional tubules are lined by multiple layers of basophilic cuboidal epithelium (1pt) which encroach upon or fill the lumen (regeneration) (1pt). In areas of dense interstitial fibrosis, tubules are atrophic, with shrunken epithelial cells and inapparent lumens (1pt). Rarely tubular epithelium and basement membranes contain crystalline mineral. Diffusely, the interstitium is markedly and irregularly expanded by edema, (1pt) fibrosis, (1pt) and low to moderate numbers of aggregated lymphocytes and plasma cells which often form aggregates (1pt) Small to medium numbers of neutrophils and macrophages containing a brown to black pigment (digested tubular protein) are also present within the interstitium. The pelvis is mildly dilated, pelvic epithelium is vacuolated and there multifocal papillary hyperplasia of the lining epithelium. (1pt) The peripelvic fat contains multifocal hemorrhage and low numbers of neutrophils and lymphocytes. The capsular surface is irregular.

MORPHOLOGIC DIAGNOSIS: Kidney: Nephritis, interstitial, chronic, diffuse, severe, with membranous glomerulonephritis, synechiae, tubular loss, degeneration, necrosis, and regeneration, and marked interstitial fibrosis. (3pt)

NAME THE CONDITION: Chronic progressive nephropathy of rats (1pt)

NAME A LIKELY STRAIN: Fischer 344, Sprague-Dawley (1pt)

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Case 4. Tissue from a rabbit.

(There is marked slide variation, so not all slides will have all features.)

MORPHOLOGIC DESCRIPTION: Haired skin and bone/joint: Expanding the deep dermis and subcutis, elevating the overlying epidermis, and abutting but not infiltrating the periosteum and joint capsule (1pt), are numerous coalescing well-formed pyogranulomas (2pt) measuring up to 5mm in diameter (1pt). The pyogranulomas are centered on colonies of bacteria (1pt) which are in turn surrounded by club-shaped to spicular aggregates of crystalline eosinophilic protein (1pt) (Splendore-Hoeppli material) (1pt). This material is in turn surrounded by innumerable viable and degenerate heterophils (1pt) and abundant cellular debris, and centrifugally, multiple layers of epithelioid macrophages (1pt), and ultimately, moderate numbers of macrophages, lymphocytes (1pt) and plasma cells enmeshed in lamellae of collagen and plump fibroblasts. (1pt) Inflammation and fibrosis effaces skeletal muscle and underlying tendon sheath (1pt), and there is mild fibrosis within the tendon itself. The fibrous connective tissue effaces the subcutis and in some areas extends to the epidermis, entrapping adnexa; there are several cystic hair follicles containing abundant keratin debris. (1pt) There are moderate lymphocyte and plasma cells scattered throughout the superficial dermis and small amounts of edema. (1pt) In some sections, there are pyogranulomas within the superficial dermis which extend into the overlying markedly hyperplastic epidermis (transepidermal elimination). (1pt) There is mild orthokeratotic hyperkeratosis overlying areas of hyperplastic epidermis. In some slides, there is growth of periosteal new bone (woven bone) adjacent to pyogranulomas. (1pt)

MORPHOLOGIC DIAGNOSIS: Partial cross section of leg: Dermatitis and cellulitis, pyogranulomatous (1pt), multifocal to coalescing, severe, with Splendore-Hoeppli material (1pt) and numerous bacilli. (1pt)

NAME THE CONDITION: Botryomycosis (1pt)