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Case 1. Tissue from a dog.

MICROSCOPIC DESCRIPTION: Kidney: There are changes at all levels of the nephron. Diffusely, glomeruli vary in size, some measuring up to 250 um in diameter **(1pt)**, and glomeruli often appear enlarged **(1pt)**. (Sectioning of these cystic Bowman's spaces may result in some glomeruli being partially sectioned, but these should not be interpreted as atrophic or sclerotic.) Multifocally, glomeruli exhibit one or more of the following change in a global fashion: hypercellularity **(1pt)** with the presence of few neutrophils and scattered karyorrhectic cellular debris (necrosis) **(1pt)**; thickening of glomerular capillary loops **(1pt)** up to three times normal by a granular eosinophilic material; expansion of glomerular mesangium by variable amounts of collagen. Additional glomerular changes include adhesions between glomerular tufts and Bowman's capsule (synechiae) **(1pt)** occasionally with associated fibrin or fibrous connective tissue (crescent formation) **(1pt)**, marked periglomerular fibrosis, hypertrophy of the parietal epithelium along Bowman's capsule, and reflux of tubular contents to include protein cases and hemorrhage. Occasional glomeruli are shrunken and effaced by collagen. (sclerosis). Tubules are diffusely ectatic **(1pt)**, with some tubules up to 50 um in diameter, are occasionally (degeneration) or by attenuated epithelium, and may contain brightly eosinophilic protein as well as rare hemorrhage. Low numbers of tubules are lined either by swollen vesicular epithelium (degeneration) or epithelial cells with shrunken hypereosinophilic granular cytoplasm and pyknotic nuclei (necrosis) **(1pt)**. Rare tubules contained sloughed necrotic cells and granular debris, or low numbers of anisotropic crystals (oxalates), or mineral (more common in the medulla). Rare mitotic figures are seen within tubular epithelium **(1pt)**. In areas of increased interstitial collagen and inflammation, tubules are often atrophic **(1pt)** with markedly decreased lumina and a thickened basement membrane. Within the medulla, tubule basement membranes are often outlined by granular to crystalline mineral **(1pt)**, with occasionally form subepithelial plaques or in some cases, effaces the tubule entirely. Multifocal, the interstitium is expanded by moderate amounts of mature collagen **(1pt)** and contains moderate numbers of lymphocytes and plasma cells **(1pt)**, often in aggregates. There is also fibrosis of the medulla, but no inflammation. **(1pt)** The walls of approximately 20% of the glomerular vascular poles are effaced by brightly eosinophilic protein and cellular debris, and lumina occasionally contain occlusive fibrin thrombi (fibrinoid necrosis).

MORPHOLOGIC DIAGNOSIS: Kidney: Glomerulonephritis, membranoproliferative **(1pt)**, diffuse and global, severe, with synechia and crescent formation **(1pt)** formation, tubular epithelial necrosis **(1pt)**, thrombtoci microangiopathy of vascular poles, and moderate lymphoplasmacytic interstitial nephritis.

CAUSE: *Borrelia burgdorferi* **(1pt)** or other chronic infections agents (any that result in immune-mediated cause.

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Case 2. Tissue from a cynomolgus macaque.

ULTRASTRUCTURAL DESCRIPTION: Kidney, glomerulus **(1pt.)**. The photomicrograph contains cross-sections of two glomerular capillaries and the intervening uriniferous space. **(1pt.)** One capillary contains cross-sections of three erythrocytes **(1pt)**and is lined by fenestrated endothelium on a basement membrane. **(1pt.)** The other capillary contains a cross-section of a macrophage within the lumen and is lined by fenestrated endothelium. **(1pt.)**

The basement membrane **(1pt.)** of both capillaries multifocally contains subepithelial **(2pt.)** electron-dense deposits **(2pt.)** which are oval to oblong and have a variegated appearance with both light and dense parts, are covered by a layer of podocyte-derived basement membrane, and protrude into the uriniferous space. **(1pt.)** There is diffuse effacement of podocyte foot processes **(2pt.)** especially overlying areas were dense deposits have expanded the basement membrane. Multifocally, there is a granular electron dense material (actin polymerization) in the podocyte cytoplasm in proximity to dense deposits. Foot processes which are not fused often project filiform appendages into the uriniferous space ("villar transformation") **(1pt.)** The endothelium of one capillary is poorly fenestrated and endothelial cytoplasm bulges multifocally into the lumen. **(1pt.)** Numerous organelles are visible and there is a focal electron dense protein droplet within the endothelial cell at one edge of the picture.

ULTRASTRUCTURAL DIAGNOSIS: Kidney: Glomerulonephritis, **(1pt.)** membranous, **(1pt.)** diffuse, marked, with subepithelial dense deposits **(1pt.)** effacement of podocyte foot processes, and podocyte villar hypertrophy. **(1pt.)**

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

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Case 3. Tissue from a horse.

MICROSCOPIC DESCRIPTION: Kidney: Approximately 90% of the renal cortex is infarcted **(1pt)**. Areas of cortical infarction indiscriminately involve glomeruli, tubules, and interstitium, **(1pt)** which exhibit a diffuse loss of differential staining **(1pt)** (to include extravasated erythrocytes) within these areas and pyknosis **(1pt)** of tubular epithelial cells as well as glomerular endothelium and mesangial cells. At the borders of the infarcted tissue, there are viable areas of hemorrhage **(1pt)** admixed multifocally with low numbers of degenerate neutrophils **(1pt)**, cellular debris, and edema. Within these (slightly better preserved areas), glomeruli are diffusely hemorrhagic **(1pt)** and the tunica intima and media of afferent arterioles **(1pt)** is replaced by a brightly eosinophilic extruded protein and fibrin (fibrinoid necrosis) **(2pt)**. Similar changes are multifocally present within the glomerular capillaries, radial and interlobular arteries **(1pt)** and multifocally these vessels are partially to completely occluded by fibrin thrombi **(2pt)**. There are small numbers of lymphocytes and plasma cell scattered throughout the interstitium, often at the corticomedullary junction in perivascular locations. Crystalline mineral is multifocally present within the endothelium of segmental arteries (asteroid bodies)

MORPHOLOGIC DIAGNOSIS: Kidney, cortex: Necrosis **(1pt)** and hemorrhage **(1pt)**, diffuse, severe with fibrinoid vasculitis **(1pt)** and numerous fibrin thrombi **(1pt)**.

NAME THE CONDITION: Hemolytic-uremic syndrome **(1pt)**

CAUSE: Shiga toxin-producing *E. coli* **(1pt)**

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

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Case 4. Tissue from a dog.

MICROSCOPIC DESCRIPTION: Kidney: There is diffuse cystic dilation of Bowman's spaces **(1pt**.), with atrophy of the tufts contained within. **(2pt)** In proximity to the renal capsule **(1pt.)**, glomeruli are fetal **(2pt.)** in appearance, characterized by small volume, lack of capillary loops, and a peripheral rim of podocyte precursors **(1pt.)** There is multifocal periglomerular fibrosis, thickening of the basement membrane of Bowman's capsule, and mild parietal cell hyperplasia. **(1pt.)** Within the cortex, tubules vary markedly in size, are decreased in number **(1pt.)**, and often markedly ectatic **(1pt.)**. Lining epithelium ranges from columnar, highly vacuolated eosinophilic epithelium, which is attenuated in ectatic tubules. **(1pt.)** Multifocally, tubules contain granular eosinophilic protein, cellular debris, and occasional hemorrhage. Throughout the cortex, tubules are often separated by edematous fibrous connective tissue, which, when in contact with the overlying cortex, results in capsular depressions. **(1pt.)** There are scattered low numbers of lymphocytes and plasma cells, often in aggregates throughout the areas of interstitial fibrosis **(1pt.)** There is severe loss of medullary tubules and marked expansion of the interstitium by mature collagen. **(1pt.)** Medullary tubules often contain eosinophilic protein, sloughed epithelium, and rare hemorrhage.

MORPHOLOGIC DIAGNOSIS: 1. Kidney: Asynchronous maturation **(1pt.)**, diffuse, marked with glomerulocystic atrophy **(1pt.)**, fetal glomeruli **(1pt.)**, marked tubular ectasia and moderate chronic interstitial nephritis. **(1pt.)**

2. Kidney: Tubular loss, diffuse, marked, mild to moderate with granular cast formation and rare epithelial necrosis. (**1pt.)**

O/C – **(1pt.)**