Diagnostic Exercise

From The Davis-Thompson Foundation*

Case #: 112 Month: January Year: 2019

Answer Sheet

Title: Ethylene glycol toxicity in a cat

Contributors: Tatiane Terumi Negrão Watanabe,[1,2] DVM, MS, PhD; Peter Jowett,[2] BS, PhD, Ashley Hegler,[3] DVM, Amy Grooters,[3] DVM, DACVIM, Ingeborg M. Langohr,[1,2] BS, DVM, MS, PhD, DACVP. [1]Louisiana State University School of Veterinary Medicine, Department of Pathobiological Sciences, Skip Bertman Drive, Baton Rouge, LA 70803; [2]Louisiana Animal Disease Diagnostic Laboratory, River Road 1043, Baton Rouge, LA 70803; [3]Louisiana State University School of Veterinary Medicine, Department of Veterinary Clinical Sciences, Skip Bertman Drive, Baton Rouge, LA 70803

Microscopic Findings:

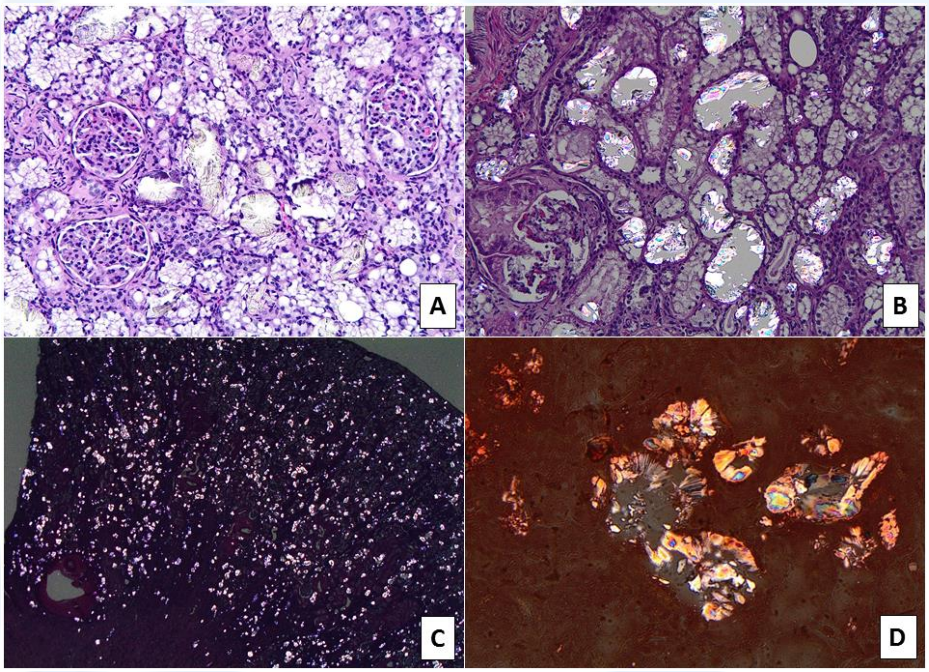

Figure 2. Ethylene glycol intoxication in a cat; kidney. **A.** The renal tubular epithelium, primarily within the cortex and outer medulla, is variably degenerate and atrophied associated with numerous intraluminal sheaves or rosettes of pale yellow, translucent, birefringent crystals (oxalate crystals). Mild to moderate interstitial fibrosis is present in affected areas (H&E; 20x). **B.** As in A, with polarized light to better demonstrate the intratubular retractile calcium oxalate crystals (H&E; 40x). **C.** As in B, highlighting the numerous cortical intraluminal calcium oxalate crystals (H&E; subgross microphotograph). **D.** The calcium deposits are highlighted in orange and red (Alizarin red stain, 40x).

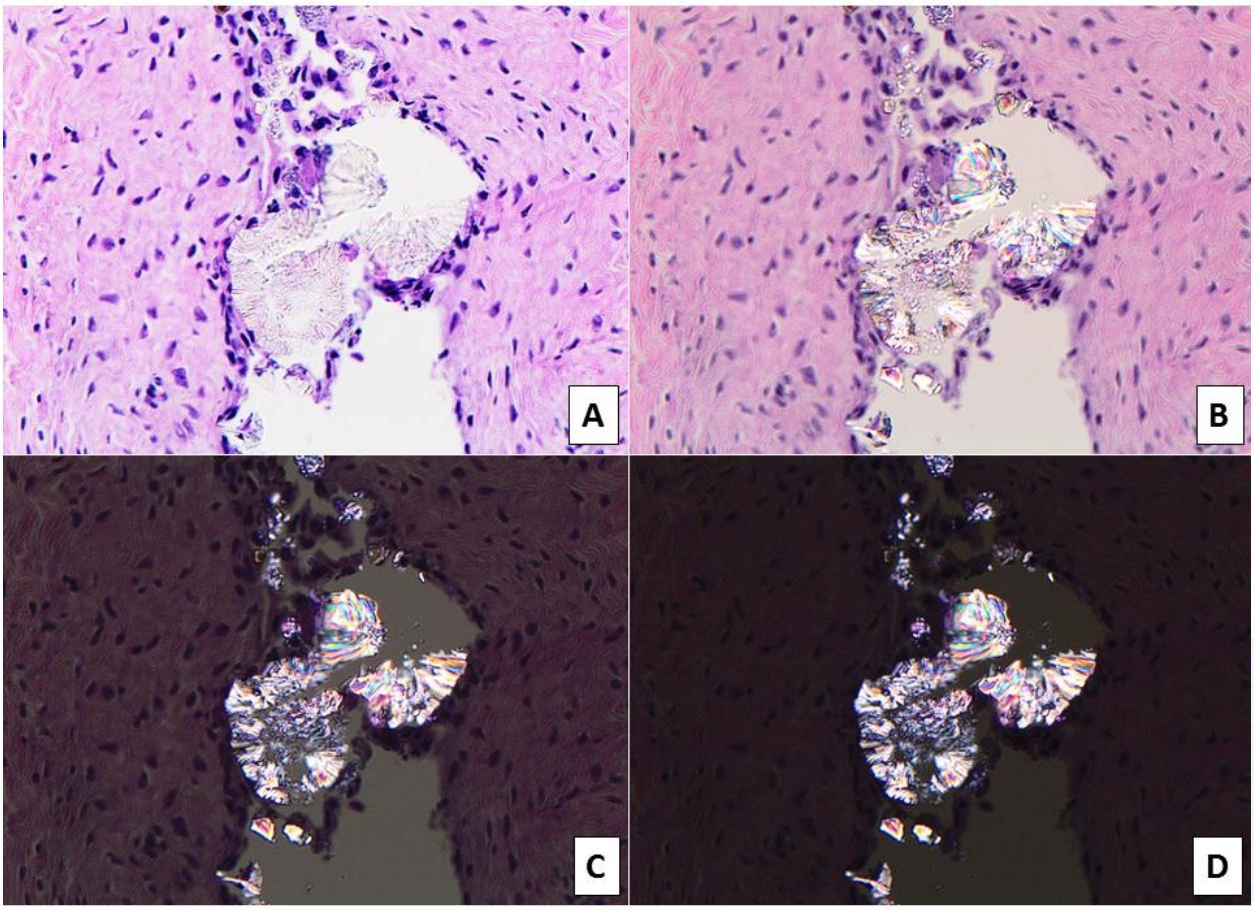

Figure 3. Ethylene glycol intoxication in a cat; urinary bladder. **A.** Numerous birefringent crystals with similar morphology as those observed within the renal tubules are embedded in the urothelial lining and mixed with sloughed urothelial cells, accompanied by a layer of dense fibrous stroma in the superficial propria submucosa. No inflammatory reaction is evident (H&E, 40x). **B-D.** As in A, with polarized light to better demonstrate the retractile calcium oxalate crystals (H&E, 40x).

Morphologic Diagnoses:
Kidneys: Tubular degeneration and atrophy, multifocal to coalescing, moderate to marked, with numerous
intratubular oxalate crystals, interstitial fibrosis, and mild unilateral (left) nephrolithiasis;
Urinary bladder: Superficial propria submucosal fibrosis, diffuse, mild to moderate, with numerous urothelial oxalate
crystals;
Liver: Lipidosis, macro- and microvesicular, diffuse, moderate to marked (not shown)

Ancillary Testing: Ethylene glycol was detected in the kidney by gas chromatography/mass spectrometry (GC/MS) at a concentration of ~500 ppm.

Discussion: Based on the young age of this cat, a congenital renal disease had been suspected prior to necropsy; however, there was no histologic evidence of renal dysplasia.[1] Instead, there were large numbers of crystals morphologically consistent with calcium oxalate in renal tubules and in the urinary bladder. In small animals, this is considered virtually pathognomonic of ethylene glycol poisoning.[2] Semi-quantitative toxicological testing for ethylene glycol of the kidney allowed for confirmation of the presumptive etiologic diagnosis. Ethylene glycol, a sweet-tasting liquid, is the major constituent of antifreeze solutions (95% concentration). It causes acute nephrotoxicity due to a small percentage being oxidized after ingestion by alcohol dehydrogenase in the liver into glycoaldehyde and glyoxylate. These are considered the primary nephrotoxic metabolites, causing ATP depletion and damage to membrane phospholipids and enzymes in the renal tubular epithelium. The minimum lethal dose (undiluted) is 1.5 ml/kg body weight in cats and 6.6 ml/kg in dogs.[2] Calcium oxalate crystalluria is seen as early as 3 hours (cat) and 6 hours (dog) after ingestion.

This cat survived the acute toxic insult, in which case the presence of the calcium oxalate crystals eventually leads to chronic renal failure. Few crystals may be left in the chronic stage. In this cat, the large number of intralesional crystals even a month after initial clinical signs suggests the possibility of repeated exposure to antifreeze solution. The chronic renal disease was further complicated by concurrent hepatic lipidosis, a common finding in anorectic cats. The ethylene glycol toxicity was confirmed by semi-quantitative toxicological testing. Differential diagnoses for nephrotoxins in cats should include aminoglycoside antibiotics (e.g., gentamicin), melamine and cyanuric acid, heavy metals (e.g., lead, arsenic, mercury), and certain plants (e.g., *Lilium* spp.).[2]

References and Recommended Literature:

1. Brown CA, Elliott J, Schmiedt CW, Brown SA. Chronic Kidney Disease in Aged Cats: Clinical Features, Morphology, and Proposed Pathogeneses. Veterinary Pathology. 2016; 53(2):309-326.

2. Cianciolo RE, Mohr FC. Urinary System: Acute Tubular Injury. In: Jubb, Kennedy, and Palmer's Pathology of Domestic Animals. Maxie MG (Ed.), 6th ed., v. 2, St. Louis, MO: Elsevier, 2016; 422-428.

*The Diagnostic Exercises are an initiative of the **Latin Comparative Pathology Group (LCPG)**, the Latin American subdivision of The Davis-Thompson Foundation. These exercises are contributed by members and non-members from any country of residence. Consider submitting an exercise! A final document containing this material with answers and a brief discussion will be posted on the CL Davis website (http://www.cldavis.org/diagnostic_exercises.html).

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