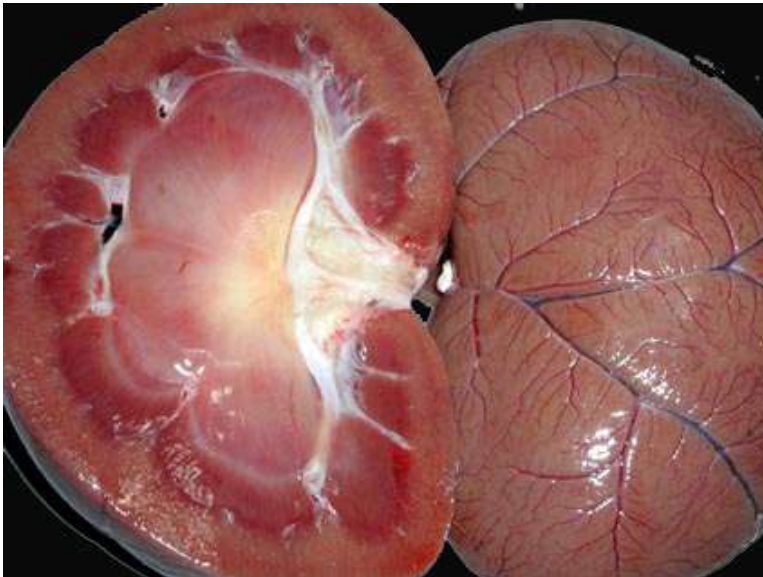


Pathology of renal disease in cheetahs

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Captive cheetahs suffer from a variety of renal diseases including amyloidosis, glomerulosclerosis and oxalate nephrosis and more than one disease may be present in the same cheetah. Chronic renal failure in cheetahs is associated with prominent uraemic gastropathy and pneumopathy, parathyroid hyperplasia and metastatic mineralisation of the stomach, lungs and elastic tissue of arterioles.

Figure 1: Normal kidney from a healthy young adult cheetah



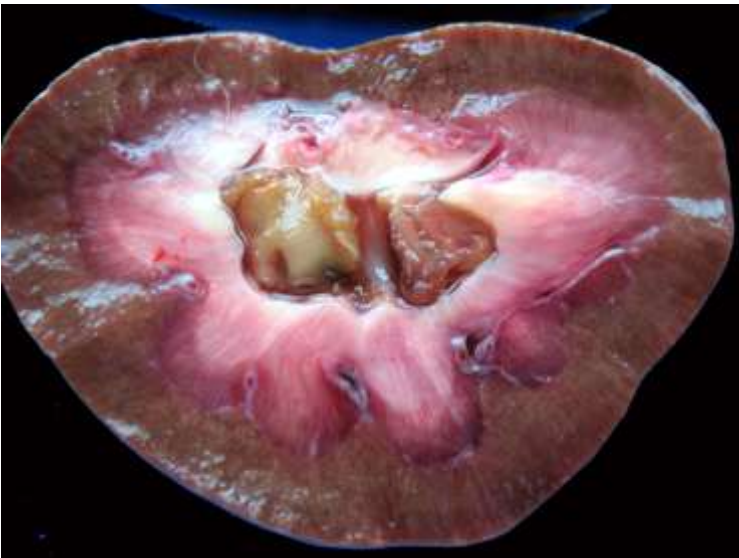
Systemic AA amyloidosis in cheetahs is reactive, or secondary to chronic inflammation¹. Deposition of often antibody-derived protein fibrils occurs in the renal medulla, hepatic sinusoids, intestinal lamina propria, thyroid and parathyroid, spleen, adrenal medulla as well as other tissues including lymph nodes. Medullary interstitial deposition of amyloid may result in renal papillary necrosis, pyelonephritis and/or infarction due to obstruction of thin-walled medullary blood vessels, resulting in ischaemia and susceptibility to opportunistic ascending bacterial infection. In cheetahs the most common source of inflammation is often lymphoplasmacytic gastritis, but inflammation of the maxillary palatine cleft, peritonitis, enteritis, and hepatic abscesses have also been seen with amyloidosis. Chronic lymphoplasmacytic atrophic gastritis is extremely common in

captive cheetahs and is an interstitial lymphoplasmacytic inflammatory response, possibly an immune-mediated reaction to *Helicobacter* infection. Up-regulated pro-inflammatory (or down-regulated anti-inflammatory) cytokines are recorded over time in captive cheetahs². Amyloid deposits in the intestine and liver can contribute to the weight loss seen in chronic renal failure due to malabsorption and hepatocellular atrophy. Amyloid fibrils isolated from cheetah faeces caused amyloidosis when injected into mice; raising the possibility that amyloidosis may be transmissible in a prion-like manner similar to transmissible spongiform encephalopathies such as scrapie and chronic wasting disease of deer and elk³.

Figure 2: Renal amyloidosis in a cheetah



Figure 3: Renal papillary necrosis in a cheetah



Glomerulosclerosis in cheetahs is the progressive obliteration by fibrosis of renal glomeruli and subsequent loss of the renal tubule, and although the aetiology is not confirmed, the lesions resemble those of diabetic nephropathy⁴. Possible causes of

persistently raised blood glucose include adrenocortical hyperplasia due to chronic stress, frequency of feeding, high protein or sugar diets (such as horse meat) and genetic predisposition⁴. Cheetah physiology resembles that of cats, and therefore, like cats, they may be inefficient in dealing with fluctuating blood glucose levels. Adrenocortical hyperplasia is a very common finding in captive cheetahs. Other lesions found in cheetahs thought to be related to stress include lymphoid depletion, myocardial perivascular fibrosis, gastric and duodenal ulcers, hepatic veno-occlusive disease and splenic myelolipomas⁵.

Oxalate nephrosis has been recorded sporadically in captive cheetahs in the United States and was attributed to ethylene glycol toxicosis. However, cases are seen in captive cheetahs from different institutions in South Africa in conditions where ethylene glycol toxicosis seems unlikely. Ante mortem diagnosis is difficult, as oxalate crystals in urine are rare, but critical as this is a potentially more treatable form of renal disease than amyloidosis and glomerulosclerosis. Despite exhaustive investigation the source of oxalate has not been determined. Exposure to ethylene glycol has not been documented and meat products do not fluoresce under UV light (done by Prof. W Meltzer) was negative, although oxalate and glycolic acid levels were raised in urine. Propylene glycol fed to feedlot cattle has been considered but thought unlikely and its secondary toxic propensity is uncertain. No refrigerant spills were noted. Limited samples have tested negative for melamine and the crystals are not typical of melamine (and do not bind calcium (Von Kossa stain)). Vitamin C toxicosis and Vitamin B6 deficiency cause oxalate nephrosis. The only source of these would be vitamin/mineral supplements and renal disease in other felids fed similar supplements has not been reported. Some cheetahs consume grass, occasionally in very large quantities, including *Panicum* spp., but toxicosis through this route seems unlikely. Similarly, no mouldy food material containing oxalate rich *Aspergillus* products have been located. Comprehensive water analysis in one institution has revealed potential exposure to a number of renal toxins but none specifically resulting in oxalate crystal deposition. Since environmental factors alone do not seem sufficient to account for these cases, primary oxaluria as is described in domestic cats is a possibility⁶. Dr A Tordiffe of the National Zoological Gardens of South Africa plans to characterize the metabolic profiles of cheetahs, with Professors Reyers and Mienie, which may shed some light on this and other cheetah diseases. Characterization of the epidemiology and histological lesions of oxalate nephrosis in cheetahs is also underway by pathologists in several countries.

Figure 4: Oxalate nephrosis in a cheetah



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