THE FELINE CENTRE UNIVERSITY OF BRISTOL
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feline UPDATE
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SPRING 2009

Management of Chronic Kidney Disease in Cats

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Fig 1: Cat suffering from CKD

Chronic renal failure is one of the most common illnesses of geriatric cats *(Lulich et al., 1992)*, and in one study the incidence was reported to have increased from 4.5% to 9.6% between 1990 and 2000 *(Plotnick, 2007)*. It is typically a progressive disease resulting in significant morbidity and mortality in cats. The prevalence increases with age and up to 31% of cats over 15 years are affected.

It is presumed that most cats develop chronic kidney disease (CKD) after an earlier renal insult (e.g. infectious, immune-mediated, congenital, metabolic, neoplastic, traumatic, obstructive event) which may have gone unnoticed without causing clinical signs. CKD is an irreversible condition as nephrons cannot be regenerated. Fortunately the kidney has considerable reserves and in early stages nephron loss may pass unnoticed. However, once a critical level of renal damage has occurred, chronic renal failure develops. This can be self-perpetuating and may progress from an asymptomatic non-azotaemic period to end-stage uraemia.

Acute renal failure (ARF) can be reversible if diagnosed promptly and treated effectively however recurrence (e.g. urethral obstruction) or prolonged ARF can progress to CKD.

Polyuria and polydipsia as a result of inadequate urine concentrating ability (normal urine specific gravity >1.035) are usually the first clinical signs noticed by the owners and occur when renal function is only about one-third of normal. Azotaemia only develops when 75% of nephrons are non-functional, thus early detection is crucial in order to implement measures that support renal function and protect against complications (e.g. hypertension, renal secondary hyperparathyroidism) associated with the disease.

Depending on the stage of CRF clinical signs can be variable.

Clinical Signs

- PU/PD
- Anorexia
- Vomiting
- Weight loss and loss of body condition
- Pallor
- Oral ulceration
- Acute blindness secondary to hypertension

Laboratory abnormalities

Blood

- Azotaemia
- Hyperphosphataemia
- Hypokalaemia
- Hypercalcaemia
- Metabolic acidosis
- Non-regenerative anaemia

Urine

- Isosthenuric urine
- Proteinuria
- Urinary Tract Infections

IRIS classification (www.iris-kidney.com)

Accurate staging of chronic kidney disease allows the clinician to choose the most appropriate therapies, monitor the patient and assess prognosis. The "International Renal Interest Society" (IRIS) has produced a set of guidelines which help to stage chronic kidney disease based on serum creatinine values (Table 1), and substage based on proteinuria (Table 2) and systolic blood pressure (Table 3). The creatinine values of stage 1 may be considered within the normal reference range for many labs, however the IRIS staging system takes into account that significant renal disease can be present in the absence of azotaemia. Recent studies have highlighted the importance of proteinuria in renal disease. It is now understood that even low levels (i.e. UPC >0.4) of

Stage	Plasma creatinine µmol/l mg/dl	Comments:
1	<140 <1.6	Non-azotaemic Some other renal abnormality present e.g inadequate concentrating ability without identifiable cause: abnormal renal palpation and/or abnormal renal imaging findings; proteinuria of renal origin; abnormal renal biopsy results
2	140 - 249 1.6 -2.8	Mild renal azotaemia Clinical signs usually mild or absent
3	250 - 439 2.9 - 5.0	Moderate renal azotaemia Many systemic clinical signs may be present
4	>440 >5.0	Severe renal azotaemia Many extra-renal clinical signs present

Table 1: IRIS staging system based on plasma creatinine

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proteinuria are significant whereas previously 0.5-1.0 was used as a cut-off. In a healthy cat the UPC should however not exceed 0.2. However, proteinuria can have many other causes (see below).

UPC value	Substage
<0.2	Non-proteinuric
0.2 - 0.4	Borderline proteinuric
>0.4	Proteinuric

Table 2: IRIS substaging on urine protein: creatinine ration (UPC).

Systolic BP mmHg	Diastolic BP mmHg	Substage
<150	<95	Minimal risk
150-159	95-99	Low risk
160-179	100-119	Moderate risk
>180	>120	High risk

Table 3: IRIS substaging on blood pressure (BP)

Markers of Renal Function

Creatinine and urea

Although commonly used, creatinine is not the most sensitive indicator of renal clearance, and in early kidney disease, small changes in creatinine may represent large changes in glomerular filtration rate (GRF). As GFR has to be compromised significantly (>75% nephrons non-functional) before plasma creatinine leads to accumulation in the bloodstream exceeding the upper limit of normal there is significant overlap in the creatinine levels of healthy cats and those with early renal disease. Sequential samples may be of greater use than a single value to identify trends. Despite staying in the reference range, sequential increases of plasma creatinine may still be indicative of a progression of the renal disease.

A number of factors can influence urea concentrations in addition to GFR. The most important is dehydration which is a common feature in cats with CKD. The ingestion of protein meals (e.g. food, GI haemorrhage, catabolic state) and – to a lesser extent - its production by the liver can also have an impact on urea measurements. Creatinine measurement is not influenced by diet and is a better marker of GFR than urea. However, poorly muscled, thin cats can have reduced creatinine due to the reduced muscle turnover. Hence, some cats with CKD have normal creatinine and elevated urea.

Proteinuria

A small amount of protein can be found in the urine of healthy cats and may be physiological and transient associated with strenuous exercise, stress or pyrexia. Post-renal causes for proteinuria include trauma, neoplasia, urinary tract infection (UTI), or haemorrhage. Urine dipsticks are most sensitive to albumin but can yield false positive results in concentrated or alkaline urine or false negative results in dilute urine. For example, a trace of protein in a very concentrated sample is less likely to be significant than if the same amount is present in dilute urine.

Proteinuria is not as common in cats with chronic kidney disease as in dogs but if it is present it is a predictor for progressive renal damage. Persistent proteinuria should always be quantified with the means of urine protein: creatinine (UPC) ratio which is an accurate measurement unaffected by the urine concentration or daily fluctuations. The severity of proteinuria has been found to be associated with survival time: A UPC >0.4 has been linked with a four fold higher risk of death or euthanasia (Syme et al., 2006). Haematuria and pyuria may lead to increases of the UPC, but in these cases an active sediment would be expected. Before substaging according to the IRIS system, pre-renal (e.g. haemolysis, hyperglobulinaemia, functional renal proteinuria) and post-renal (e.g. lower urinary tract infection) proteinuria as well as concurrent inflammation/infection should be excluded. Large amounts of protein with inactive sediment can also occur in association with glomerular disease (e.g. glomerulonephritis). If persistent proteinuria with the absence of inflammatory urinary sediment is detected, it may be suspicious of early renal injury and warrant intervention.

An even earlier marker to detect proteinuria is microalbuminuria which is defined as the presence of a very small quantity of urine albumin (<30mg/dl) below the limit of detection for a dipstick. However, various disease processes (e.g. inflammation, infections) and drugs (e.g. prednisolone) may lead to a positive result and the significance of microalbuminuria is therefore currently not fully understood.

Urine concentrating ability

The urine concentrating ability is the earliest marker of tubular renal disease and any patient suspected of kidney disease should undergo sequential measurements. In azotaemic patients determining the specific gravity (SG) further allows differentiating between renal and pre-renal causes. Ideally, urine should be collected at the same time as blood samples and before fluid therapy or administration of drugs (e.g. diuretics, steroids) that could affect the urine concentration.

Phosphate

Hyperphosphataemia occurs commonly in approximately 60% of cases of CKD due to renal secondary hyperparathyroidism. The prevalence rises with progression of disease and declining renal function (DiBartola *et al.*, 1987). In a very recent study carried out by Boyd *et al* (2008), phosphate was the only clinicopathologic variable to be predictive of an increased risk of death in the multivariate analysis. With impaired kidney function, phosphate accumulates in the blood stream and perpetuates kidney disease. It was shown that for each 1U (mg/dl) increase of phosphate levels in the blood, there is an 11.8% higher risk of death, thus tackling hyperphosphataemia is crucial in prolonging survival.

Common complications and consequences of chronic kidney disease

Hypertension

One study found that hypertension occurs in almost 20% of cats with chronic renal failure in first opinion practice (Syme *et al.*, 2002). However in cats seen at referral hospitals an incidence of as high as 65% has been reported (Stiles *et al.*, 1994). Persistent hypertension increases not only the risk of vascular injury of end-on-organs (e.g. eyes, brain, kidneys) but also predisposes to uraemic crises and death associated with renal disease. Even though hypertension itself is not significantly associated with survival time, management of hypertension offers indirect benefits to longevity by decreasing the level of proteinuria which is directly correlated to hypertension (Jepson *et al.*, 2007). The complications associated with it can also be serious including e.g. hyphaema, seizures, left ventricular hypertrophy, etc. hence blood pressure should be monitored in all cats with chronic kidney disease. About 70% of hypertensive cats with chronic renal disease were found to have lesions compatible with hypertensive retinopathy (Syme *et al.*, 2002). The same study found that 50% of hypertensive cats had more serious complications such as hyphaema or vision loss. Sudden onset blindness is the first sign to alert the clinician of the condition.

Hypertension in cats is defined as an indirect systolic blood pressure greater than 160 or 170 mmHg. Doppler or oscillometric methods have been used to monitor blood pressure. Stress induced hypertension and a "white coat effect" are well recognised in human, canine and feline patients requiring consideration in obtaining measurements: For an accurate assessment it is crucial to allow the cat to settle down before taking multiple measurements in a calm environment.

If significant hypertension is detected, antihypertensive treatment is warranted: the drug of choice is amlodipine *(Isten®, Pfizer)*, a calcium channel blocker which is highly effective and well tolerated at a dose of 0.625-1.25mg PO once daily. ACE inhibitors *(e.g. ForteKor®, Novartis; Enacard®, Merial)* only have relatively weak anti-hypertensive properties (reducing the BP only by 5-15 mmHg) but may offer additional intra-renal protection. The aim of treatment is to maintain the systolic blood pressure below 160 mmHg.

Renal secondary hyperparathyroidism

Renal secondary hyperparathyroidism occurs commonly in cats as a result of increased phosphate retention and an impaired ability to produce calcitriol (active vitamin D) (Barber & Elliot, 1998). With declining kidney function, phosphate which is usually filtered and reabsorbed on the proximal renal tubule, accumulates in the blood stream, leading to hyperphosphataemia. This results in a reduction of the ionised calcium which subsequently stimulates the production of parathyroid hormone (PTH).

Further, the decrease of renal functional mass also affects the production of calcitriol (active Vitamin D). In turn lower than normal levels of calcitriol result in a decrease of intestinal calcium uptake, the mobilisation of calcium from the mineralised reserves (bone) and an increase of the PTH level.

Dietary phosphate restriction and the use of phosphate binders help to resolve hyperphosphataemia and control renal secondary hyperparathyroidism (Barber *et al.*, 1999).

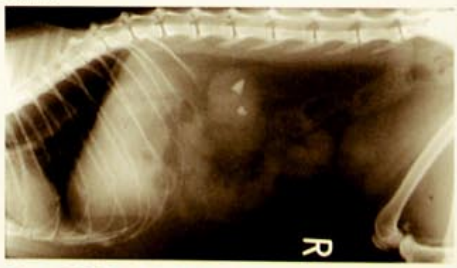
Even though calcitriol given orally would be expected to reduce PTH levels, in a recent study (Hostutler *et al.*, 2006) calcitriol failed to normalise the PTH in 10 cats with chronic renal failure. However calcitriol may still be of clinical benefit when managing renal secondary hyperparathyroidism in cats with CKD (Nagode *et al.*, 1996) as long as neither hyperphosphataemia nor hypercalcaemia are present. The current evidence is however insufficient to support for/against routine therapy with calcitriol and studies are ongoing to elucidate its role in feline patients.

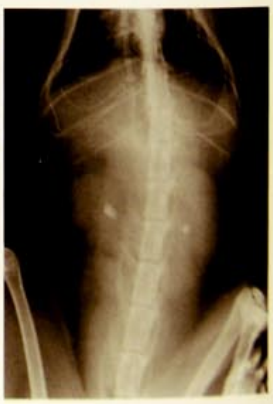
Hypokalaemia

Increased urinary losses as a consequence of CKD commonly result in hypokalaemia. In general, hypertensive cats tend to have a significantly lower plasma potassium concentration than normotensive cats (Syme *et al.*, 2002). The degree of hypokalaemia and severity of associated clinical signs is highly variable: Classically hypokalaemia presents as ventroflexion of the neck, but signs of generalised muscle weakness may occur. It has been speculated that hypokalaemia may contribute to the progression of kidney failure (Polzin *et al.*, 2000). Prescription diets contain increased potassium concentrations to combat this problem. However, in more severe cases, potassium supplementation in the form of potassium gluconate is required to maintain levels within reference range.

Anaemia

With the progression of CKD renal production of erythropoietin reduces. In conjunction with a shortened





X-rays (DV & lateral) of a cat with Chronic Renal Disease: Two increased triangular mineral opacities can be seen bilaterally in the area of the renal pelvises which were confirmed on ultra-sound to represent renal calculi. Increased opacity in the region of the bladder could be indicative of crystals or calculi.

erythrocyte life span and possible uraemia induced gastrointestinal haemorrhage many patients develop anaemia, typically non-regenerative in nature. Clinical signs may become apparent once the haematocrit falls below 20% and intestinal protectants (e.g. sucralfate *Antepsin®, Chugai;* H2 blockers, omeprazole), blood transfusions or administration of recombinant human erythropoietin have been suggested. The use of EPO should be reserved until the patient develops clinical signs associated with anaemia, due to the risk of development of EPO antibodies and aplastic anaemia (occurring in up to 30% of treated cats). Anabolic steroids to boost appetite and red blood cell mass are sometimes prescribed in practice, however there is no evidence of effectiveness and they are not recommended in the management of CKD.

Gastrointestinal signs

Nausea, vomiting and anorexia occur frequently in cats with CKD. In particular, the inability of the failing kidneys to excrete excess gastrin, a digestive hormone, results in increased gastric acidity and possibly gastric ulceration which is reflected in the presenting clinical signs (Goldstein *et al.,* 1998). The accumulation of uraemic toxins further contributes to the development of gastroenteritis. The use of anti-emetics, antacids and gastric protectants may prove beneficial in the management of these cases.

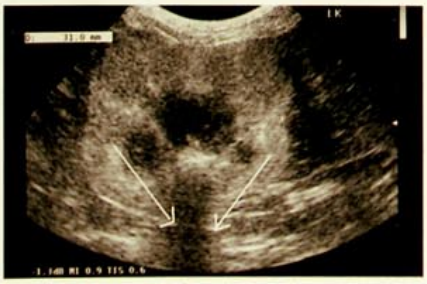
Metabolic acidosis

Chronic acidosis is a common feature of chronic kidney disease due to the decreased renal ability to excrete acid. This may exacerbate renal injury and hypokalaemia, thus most prescription diets are alkaline in nature to address this problem. The assessment of blood gases to determine carbon dioxide, bicarbonate levels and blood pH may help in quantifying the acidaemia accurately. However, blood-gas machines are rarely readily available in practice. Hence the use of alkalising agents (potassium citrate or sodium bicarbonate) is not recommended without adequate monitoring facilities.

Long-term management

Hydration

For cats hospitalised with renal failure, fluid therapy remains the cornerstone of treatment. However, adequate hydration is crucial in the management of chronic cases.Cats should have free access to water at all times. Feeding wet food, additional water bowls or flavoured water (e.g. tuna or prawns) may encourage increasing their water intake further. Some cats prefer drinking from dripping water taps and water intake may be encouraged by water fountains. In some cases, the possibility of administering subcutaneous fluids at home can be considered. Subcutanous fluids (10-20ml/kg) are given typically by placing a needle in the intrascapular region every 2-3 days. New SQ devices have become available using either a permanent SQ catheter *(Endo-Sof Subcutaneous Catheter Set, Dechra; GIF-tub, Practivet)* or a permanent "button" *(Norfolk Vet Products)* through which fluids can be injected. This is generally well tolerated by cats and may provide a useful way to prevent dehydration in the more advanced stages. Guidelines for clients are available from the FAB website (www.fabcats.org). There is also an excellent book "Caring for the Cat with Kidney Failure" which offers valuable advice and guidance to clients (available from www.catprofessional.com).



Ultrasound of a cat with Chronic Renal Disease: The left kidney appears small and irregularly marginated with varying opacity of the cortices. Shadowing (highlighted by white arrows) consistent with a nephrolith can be observed.

Dietary Modification

Dietary modification has been advocated for a long time, and remains the single most important factor in preventing deterioration in this disease. The use of prescription renal diets even if not fed exclusively has been proven to significantly increase longevity (median survival: 16 months vs 7 months (Plantinga *et al.,* 2005); 633 days vs 264 days (Ross *et al.,* 2005)) and reduce the risk of uraemic crises (Ross *et al.,* 2005). Renal prescription diets are moderately protein restricted, have higher levels of water-soluble vitamins (e.g. vitamin B complex, vitamin C), potassium & omega-3 fatty acids and lower levels of phosphate & sodium.

Table 4: Survival (in days) of cats based on stage of CKD determined after correction of prerenal azotemia (Boyd *et al.,* 2008).

Stage at Diagnosis	Number of cats	Percentage of cats	Survival Median (95% CI)
IIb	82	39.4	1.151* 1.014-1.565)
III	84	40.3	679* (445-910)
IV	42	20.2	35* (21-99)

* P<0.001

Table 5: Survival time (Boyd *et al.,* 2008)

Criteria	Number of Cats	Survival Median (95% CI)
Diagnosis	211	771 (651-910)
Weight loss	142	401 (233-601)
Start of SC fluids	142	273 (175-424)
Creatinine >4.0mg/dl	145	123 (81-193)
Anaemia (PCV<25%)	124	100 (35-186)
>25% weight loss	81	83 (56-194)
Creatinine > 5.0mg/dl	98	44 (32-97)
Clinical decompensation	135	40 (31-64)
Anaemia intervention	42	25 (6-74)

Survival was calculated from the time of diagnosis of CKD, the point of consistent weight loss, the initiation of SC fluids (whether before or following any hospital admission), the 1st time that the creatinine was consistently >4.0 mg/dL, the time that anemia was 1st present, the time that >25% of the initial weight was lost, the 1st time that creatinine was consistently >5.0 mg/dL, the point of clinical decompensation, and the time of intervention for anaemia.

Even though dietary modification is very valuable, the most important priority is intake of adequate energy and protein. It is much more important that the cat eats something even if this is not the ideal diet. Diets can easily be modified by adding an intestinal phosphate binder (IPB) and supplementation of potassium to "recreate" a kidney diet.

Phosphate restriction

Phosphate restriction plays a vital role in preventing renal secondary hyperparathyroidism which can promote chronic kidney disease and soft tissue and renal mineralisation (Barber *et al.,* 1999; Chew D., 2008). Phosphate and protein restricted diets have been shown to slow down the progression of disease (Elliot *et al.,* 2000) and their use is considered to be the first step in addressing hyperphosphataemia. If hyperphosphataemia fails to improve within 4-6 weeks despite having instigated dietary modification, an additional intestinal phosphate binder (IPB) should be added in. These must be administered with food to be effective and work by binding phosphate in the intestinal lumen, reducing intestinal absorption. IPB are aluminium, calcium and lanthanum based. In the past aluminium salts (aluminium hydroxide) have been used as a first choice treatment, however toxicity in human patients have lead to difficulties in sourcing these drugs. A study by Wagner *et al,* 2004 confirmed the beneficial effects in decreasing intestinal phosphate absorption when using a phosphate binder containing calcium and chitosan *(Ipakitine®, Vetoquinol)* which is available in the UK; Calcium IPB are however contra-indicated in the face of hypercalcaemia. Lanthanum salts have been developed for use in human CKD as an alternative for calcium and aluminium based products. A new product containing lanthanum carbonate *(Renalzin®, Bayer)* has recently been marketed. Although limited trials (Schmidt *et al.,* 2006) have been carried out and its long term use requires further investigations, it appears to have a dose-dependent effect and successfully reduces phosphorus absorption in combination with maintenance and phosphate restricted diets.

Omega-3 fatty acid supplementation

Recent studies (Brown *et al.,* 1998 & 2000) suggest that diets high in omega-3 unsaturated fatty acids may help to preserve renal function in dogs. The underlying mechanism is contributed to a reduction in intra-glomerular pressure and renal inflammation. However, there are currently no studies in cats confirming these findings in this species.

ACE inhibitors

The benefits of ACE inhibitors in proteinuric patients have been well documented (King *et al.,* 2006; Mizutani *et al.,* 2006) and result from the decrease in efferent arteriolar resistance in the glomerulus. ACE-inhibitors are recommended in cats with a UPC over 0.4 and/or confirmed hypertension. Although the value of therapy in non-proteinuric, non-hypertensive patients is currently unknown there are some studies that indicate that treatment may lead to an improved appetite.

Prognosis and survival times

The management of a cat with chronic kidney disease requires a considerable amount of financial and emotional commitment from the owners. Thus accurate prognostic information is essential to educate owners and help them making decisions based on realistic expectations. A study published in 2008 (Boyd *et al.,* 2008) looked specifically at survival times in cats with chronic kidney disease. This study found a median survival time of 2.1 years (771 days) regardless of the time of diagnosis, but it also indicated that cats diagnosed early (Stage IIb) were documented to live up to 5.8 years, with a median of 3.15 years (1.151 days) (See Table 4 & 5).

The association of laboratory variables and survival were also investigated and only phosphate (P=0.0043) was found to be a prognostic factors in the final multivariate model. An increase of 1U mg/dl was associated with a 12% higher risk of death. Hypertension has also been associated with decreased survival. Age of diagnosis, albumin, urea, creatinine, calcium, bicarbonate, potassium, and haematocrit were not found to be predictive of survival.

Summary

Early diagnosis of chronic kidney disease gives us veterinarians the opportunity to promptly implement treatment that may successfully slow the rate of renal damage. Evaluation and monitoring of laboratory parameters (blood and urine) along with identification and management of associated complications (e.g. hypertension, renal secondary hyperparathyroidism, anaemia) are important in order to formulate an individual management plan. With judicious care, the prognosis of a patient diagnosed early may be favourable and result in a prolonged survival time.

References are available on request.

On occasion, reference may be made to drugs which are not licensed for use in animals. The Editor does not take any responsibility for the safety and efficacy of such products. Anyone using these products does so entirely at their own risk.

Background

Tiggy is a five year old female, neutered Siamese who had been obtained from a breeder as a kitten. She had been vaccinated annually (FHV, FCV, FPV and FeLV) and wormed at vaccination consultations with a veterinary licensed product. She had received intermittent prophylactic flea treatment with a POM spot on. She was housed with an unrelated Siamese who had not exhibited any clinical signs. Tiggy was an indoor/outdoor cat fed on a varied diet of wet and dry cat food and frequent treats. She had received veterinary attention on one previous occasion for an episode of hypersalivation which had resolved without treatment. A cause was not established.

Clinical History

Tiggy presented with a one week history of anorexia and lethargy with occasional vomiting and one episode of diarrhoea. A cat bite wound in the region of the ventral neck had occurred prior to the presenting clinical signs. The referring vet had treated Tiggy with intravenous fluid therapy, amoxicillin clavulanate (50mg po bid), prednisolone 5mg po sid and ursodeoxycholic acid (75mg po sid) but Tiggy had remained profoundly anorexic and had become jaundiced in the days prior to referral.

Clinical Examination

Tiggy had jaundiced mucous membranes, third eyelid protrusion, mild submandibular and prescapular lymph node enlargement and hepatomegaly. A small, healing bite wound was present over the ventral neck. There was mild hypotension, systolic BP (Doppler) 110mmHg (120-180). Parameters were otherwise within normal limits, HR 180bpm, RR 28, T 38.7°C.

Problem List
1. Anorexia
2. Lethargy
3. Jaundice

Differential Diagnoses

Anorexia and lethargy are very vague clinical signs seen in a variety of conditions. Jaundice can be considered as pre-hepatic, hepatic or post-hepatic.

In pre-hepatic jaundice, increased bilirubin occurs as a result of septicaemia or haemolysis. This can be caused by a variety of inciting factors including *Mycoplasma haemofelis* infection, Heinz body haemolysis secondary to toxicity, most commonly onion or paracetamol, FeLV infection or primary immune mediated haemolytic anaemia.

Hepatic jaundice is caused by decreased uptake of bilirubin by the liver and in the cat this can be caused by neutrophilic cholangitis, lymphocytic cholangitis, FIP, hepatic lipidosis, amyloidosis or due to drug induced hepatopathy.

In post-hepatic jaundice there is decreased excretion of bilirubin due to either intrahepatic or extrahepatic biliary compression. The former is caused by hepatocyte swelling or cholangitis whilst extrahepatic biliary obstruction occurs due to pancreatic disease (pancreatitis, pancreatic cyst, abscess or nodule), neoplasia, traumatic rupture of the gall bladder or bile duct (usually following a road traffic accident) or, less commonly, cholelithiasis.

Investigations

Blood was collected for biochemistry, haematology, feline Pancreatic Lipase Immunoreactivity (fPLI) and FIV/FeLV ELISA. A urine sample was obtained for routine urinalysis, sediment examination and urine protein: creatinine ratio. Thoracic radiographs and abdominal ultrasound were obtained following sedation with ACP (0.02mg/kg im) and Buprenorphine (0.02mg/kg im).

Haematology demonstrated a normal leukocyte count but the presence of adherence on the smear examination is likely to have given a falsely low count. A left shift in the neutrophils in conjunction with toxic changes is consistent with severe inflammatory disease or sepsis. The mild lymphopenia and eosinopenia were not thought to be clinically significant. The thrombocytosis was likely to be artefactual, given the normal platelet count on smear examination.

Results

Haematology			Reference Range
Hb	9.70	g/dl	8-15
HCT	28.5	%	25-45
RBC	6.03	x10^12/l	5.5-10
MCV	47.2	fl	40-55
MCH	16.1	Pg	12.5-17
MCHC	34	g/dl	30-35
Plt	**1073**	**x10^9/l**	**200-700**
WBC	6.6	x10^9/l	4.9-19
Band Neutrophils	**0.53**	**x10^9/l**	**0-0.3**
Neutrophils	4.36	x10^9/l	2.4-12.5
Lymphocytes	**0.99**	**x10^9/l**	**1.4-6**
Monocytes	0.66	x10^9/l	0.1-0.7
Eosinophils	**0.07**	**x10^9/l**	**0.1-1.6**
Basophils	0.00	x10^9/l	0-0.1

- Smear examination revealed a normal number of platelets
- The leukocytes showed adherence which affects the WBC and differential. There was marked toxic change in the neutrophils (cytoplasmic basophilia, vacuolation, Doehle bodies).

Biochemistry			Reference Range
Urea	**5.8**	**mmol/l**	**6.5-10.5**
Creatinine	**64**	**µmol/l**	**133-175**
Total Protein	**56.4**	**g/l**	**77-91**
Albumin	**19.8**	**g/l**	**24-35**
Globulin	36.6	g/l	21-51
ALT	**72**	**IU/l**	**15-45**
ALP	21	IU/l	15-60
GGT	**11**	**IU/l**	**0-2**
Bilirubin	**173.7**	**µmol/l**	**0-10**
Sodium	153.1	mmol/l	149-157
Potassium	**2.33**	**mmol/l**	**4-5**
Chloride	115	mmol/l	115-130
Calcium	**2.08**	**mmol/l**	**2.3-2.5**
Phosphate	0.97	mmol/l	0.95-1.55

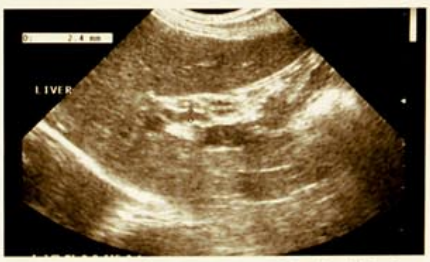


Fig.1: Ultrasound of the liver with a mildly dilated bile duct.

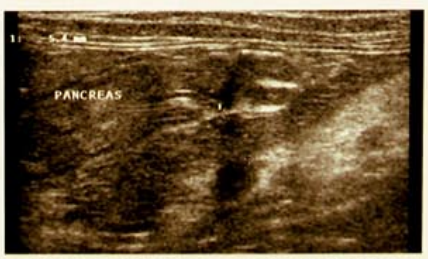


Fig. 2: Ultrasound image showing an enlarged and slightly hypoechoic pancreas with surrounding hyperechoic mesentery.

Further Laboratory Testing

- Ionised Calcium 1.08mmol/l (1.12-1.4)
- fPLI 101µg/l (2-7)

Virology
- FIV and FeLV ELISA negative

Diagnostic Imaging
- Thoracic radiographs were unremarkable
- Abdominal ultrasound demonstrated a markedly enlarged and hypoechoic pancreas with increased echogenicity of surrounding mesentery. No other abnormalities were identified.

Diagnosis

Vague presenting signs, jaundice, ultrasound changes and hypocalcaemia were consistent with pancreatitis and this was confirmed later by an elevated fPLI result. Hypocalcaemia occurs in pancreatitis due to saponification of fat.

Serum biochemistry demonstrated mildly low urea which may have been consistent with liver disease. The hypoproteinaemia and hypoalbuminaemia with normal globulin may reflect liver disease or protein losing nephropathy. The mild elevation in ALT may not be significant but may reflect early/mild hepatocyte damage.

The elevation in GGT is indicative of cholestatic disease. The hyperbilirubinaemia is indicative of pre-, hepatic or post-hepatic disease but in conjunction with the normal haematocrit would not reflect haemolysis. The marked hypokalaemia may be due to anorexia or losses via the gastrointestinal tract although these are not reported to be significant. It may also be due to diuresis from fluid therapy prior to referral. The low total calcium could be artefactual due to the hypoalbuminaemia, and assessing ionised calcium is required to evaluate this further.

Urinalysis was unremarkable apart from marked proteinuria, urine protein:creatinine ratio 1.88 (<0.4).

Treatment

Tiggy was treated with potassium supplemented intravenous fluid therapy (5.5mmol KCl/100ml Hartmanns) administered at twice maintenance (4ml/kg/h) given the mild hypotension and normal hydration status. IV Calcium supplementation was not given as the hypocalcaemia was very mild, asymptomatic and expected to improve with nutritional support.

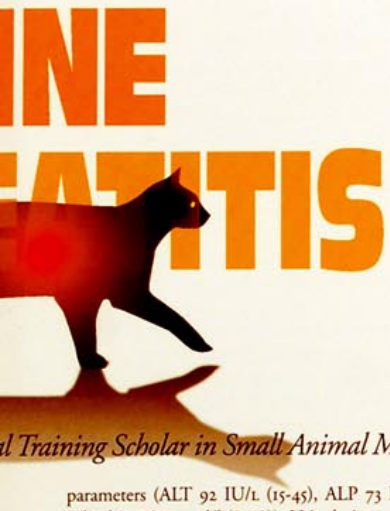
The serum potassium and calcium concentrations were re-evaluated eight hours later and were both within the reference range; potassium 4.0mmol/l (4-5) and ionised calcium 1.13mmol/l (1.12-1.4). Oral calcium supplementation was continued over the next couple of days and monitored daily. Potassium supplementation was continued at maintenance (15mmol KCl /1000ml Hartmanns).

Analgesia was given in the form of buprenorphine *(Vetergesic)* 20µg/kg iv tid.

Natasha Hetzel BSc BVSc MRCVS Senior Clin

Tiggy initially ate quite well and a naso-oesophageal tube was therefore not required for nutritional support. Unfortunately, Tiggy's appetite decreased after the first 24 hours of hospitalisation and she was thus given an appetite stimulant (Mirtazipine, 3.75mg po q 3days), to which she responded well.

As there was evidence of toxic changes and a neutrophilic left shift, treatment with intravenous broad spectrum antibiotics, amoxicillin clavulanate *(Augmentin™)* 20mg/kg iv tid and metronidazole 10mg/kg iv bid was instigated. Repeat haematology two days later revealed a resolution of the haematological changes and a change to oral antibiotics was thus instigated; Amoxicillin clavulanate *(Synulox™)* 75mg po bid and Metronidazole 40mg po bid. Unfortunately there was a clinical deterioration in association with the change to oral antibiotics with recurrence of leukocyte adherence on haematology and an increase in liver enzymes ALT 212 IU/L (15-45), ALP 121 IU/L (15-60), AST 74 IU/L (0-20) and GGT 16 IU/L (0-2). This was suspected to represent neutrophilic cholangitis which is often seen in conjunction with pancreatitis in cats. Abdominal ultrasound demonstrated mild dilation of the common bile duct. Intravenous antibiotics were re-instigated and Tiggy improved from this point. Repeat haematology was normal and biochemistry revealed an improvement in all



l Training Scholar in Small Animal Medicine

parameters (ALT 92 IU/L (15-45), ALP 73 IU/L (15-60), Bilirubin 15.2µmol/l (0-10)). Urinalysis was normal and the urine protein:creatinine ratio had returned to normal. Repeat abdominal ultrasound demonstrated a normal appearance of the liver and pancreas and the diameter of the common bile duct had returned to within normal limits. Tiggy was discharged with a four week course of oral antibiotics and antioxidant therapy, S-Adenosylmethionine *(Zentonil™)* 100mg po sid.

Outcome

Tiggy made a full recovery and has not had any repeat episodes of pancreatitis or cholangitis, nor shown any clinical evidence of inflammatory bowel disease. Repeat haematology and biochemistry performed at the end of the four week course of antibiotics were normal.

Discussion

Prevalence

Pancreatitis is the most common disease of the exocrine pancreas in cats[1]. Necropsy studies initially reported a prevalence of 0.6-2.4%[1]. Pancreatitis is thought to be under-diagnosed and in a recent necropsy study of 115 cats, including apparently healthy animals, an overall prevalence of 67% was recorded. Of the healthy cats, 45% had changes consistent with mild pancreatitis[2]. This perhaps questions the clinical significance of mild histopathological changes in the pancreas, particularly when there is little suspicion of pancreatic disease.

Histopathology

A classification system for pancreatitis has been adapted from the human field. Cases are defined as acute or chronic. Permanent histopathological changes occur in the chronic form but are reversible in acute cases. Cases can be further classified as suppurative (neutrophilic inflammation) or lymphocytic (lymphocytic inflammation). Disease may vary from mild to severe in either acute or chronic forms[1].

Lesions in chronic feline pancreatitis are similar to histopathological findings in humans where fibrosis is more prominent than inflammation. In acute pancreatitis, neutrophilic inflammation, interstitial oedema and mesenteric fat necrosis predominate[2]. Chronic pancreatitis is reported to be more common in cats whilst the acute form is more frequently seen in dogs[1,2,14].

Pathophysiology and Aetiology

Pancreatitis is thought to occur due to a failure of the protective mechanisms of the pancreas. These mechanisms ensure that auto-digestion does not occur by four main mechanisms. Firstly, pancreatic enzymes are kept in an inactive form (zymogens) until they enter the duodenum. Secondly, the lysosomal enzymes (which could activate the zymogens) are kept separate from the zymogens by intracytoplasmic membranes. Thirdly, a tryspin inhibitor is present in pancreatic juice to counteract any premature activation of trypsin within the acinar cells and ducts. Finally, antiproteases are present in the plasma to protect against pancreatic enzymes that may inadvertently reach the circulation[3].

The ways in which these protective mechanisms may be overcome are not well understood but there is general agreement that trypsinogen activation occurs within the pancreas, forming trypsin, which is subsequently capable of activating other zymogens. The pathophysiology of pancreatitis in cats has not yet been determined at a cellular level however, trypsinogen activation may occur when zymogen granules and lysosomal hydrolases coalesce in cytoplasmic vacuoles. This has been demonstrated experimentally but vacuoles have also been observed in healthy rats with no signs of pancreatitis. Chronic hereditary pancreatitis in humans is caused by a mutation of the trypsinogen gene at a trypsin sensitive site. Its loss may thus permit autoactivation of trypsinogen causing pancreatitis[3].

Once pancreatic proteases have been activated, they enter the pancreatic interstitium and peritoneal cavity, causing tissue damage. Circulating proteases also activate the complement, fibrinogen, coagulation and kinin cascades leading to systemic complications[3].

Presenting Signs

Presenting signs are vague and summarized in the table below.

Clinical Sign	Percentage of Cats Affected *(Total 40 cats)*
Lethargy	100
Anorexia	97
Dehydration	92
Hypothermia	68
Vomiting	35
Abdominal pain	25
Abdominal mass effect	23
Dyspnoea	20
Diarrhoea	15
Ataxia	15

Table 3: Clinical Signs in Pancreatitis, taken from Feline Pancreatitis, Steiner *et al.*, 1997

The cause of pancreatitis is often unknown but it has been associated with Toxoplasma, virulent calici virus and FIP infection, as well as trauma (high rise syndrome and road traffic accidents)[4]. Pancreatitis is frequently seen in association with neutrophilic cholangitis and inflammatory bowel disease. This is thought to be due to the unique anatomy of this region in the cat, although this is unlikely to be the sole mechanism. 80% of cats have only one pancreatic duct which enters the duodenum with the bile duct via a single papilla. Gastrointestinal infections can thus ascend via this papilla into both the bile and pancreatic ducts[5]. "Triaditis" is a term that has been used to describe co-existing inflammatory changes in the pancreas, liver and gastrointestinal tract. An association between hepatic lipidosis and pancreatitis has also been reported, and concurrent acute pancreatitis has been demonstrated in approximately 40% of cats with hepatic lipidosis[6], and is associated with a worse prognosis.

Signalment

Pancreatitis has been documented in cats aged from 4 weeks to 16 years with no sex predilection[3]. Siamese and domestic shorthaired cats may be predisposed[3,1].

Clinical Examination

The most common findings on clinical examination are dehydration, pallor, and icterus. Tachypnoea, abdominal pain, hypersalivation, hepatomegaly, intestinal thickening and abdominal mass are less frequently reported[8]. It is not possible to differentiate acute from chronic disease on the basis of history and clinical examination although weight loss is more commonly seen in acute cases[8].

Haematology and Biochemistry

The most commonly identified haematological parameters are mild, non-regenerative anaemia and leukopenia[8]. Haemoconcentration and leukocytosis have also been reported[1]. The most frequent biochemical abnormalities are mild to moderate elevations in ALT, ALP and bilirubin. Azotaemia may be present secondary to dehydration. Hypokalaemia is seen commonly and hypocalcaemia may occur due to saponification of peripancreatic fat[15]. It may also be related to acid-base balance, resistance to or decreased production of parathyroid hormone or increased calcitonin concentrations[17].

ALP is more likely to be elevated in chronic pancreatitis and hypoalbuminaemia is more likely to occur in acute cases. ALT and ALP are likely to be higher in chronic pancreatitis than in the acute form[8].

Specific Biochemical Tests

Amylase and lipase are of no clinical value in the diagnosis of feline pancreatitis[3]. The Trypsin-like immunoreactivity (TLI) assay has poor specificity because high TLI concentrations can also be seen in gastrointestinal disease (IBD, GI lymphoma)[1]. The sensitivity is low (28-40%) due to its short half life[1]. The feline pancreatic lipase immunoreactivity assay (fPLI) specifically measures pancreatic lipase, in contrast to other lipase assays which measure lipase from the stomach and duodenum as well. It has been demonstrated to be 100% specific in healthy cats and 100% sensitive in cats with moderate to severe pancreatitis, although the sensitivity in mild cases was only 54%.

Imaging

The most consistent radiographic finding in pancreatitis is a loss of peritoneal detail in the cranial abdomen, but this was only found in 50% of cases in a study of fourteen cats with chronic disease[8]. Abdominal radiography provides a good survey diagnostic tool but has poor sensitivity and specificity for pancreatitis[1,8].

The sensitivity of abdominal ultrasonography has been reported at 24 to 35%[9,10] but Forman *et al.*, (2004) reported a sensitivity of 80% in moderate to severe cases and 62% in mild cases. The specificity was reported as 73%. Unfortunately, ultrasonography relies heavily on operator skill and machine technology.

Computed tomography (CT) is a valuable diagnostic tool for human pancreatitis but no significant difference was detected between the healthy and diseased feline pancreas[11,9].

Histopathology

This remains the only diagnostic tool that offers a definitive diagnosis of pancreatitis[1]. It is performed fairly infrequently due to its invasive nature. It can be performed safely but the disease is often patchy and localized and thus biopsy may not be diagnostic. It should be performed only if anaesthesia is indicated for another reason such as biopsy of other abdominal organs or placement of a feeding tube. Samples should be submitted for histopathology and culture[17].

/Continued overleaf

Feline Pancreatitis (continued)

Treatment

- Intravenous fluid therapy (Saline 0.9% or Hartmanns) is vital to correct dehydration, acid base and electrolyte disturbances. Colloid administration may be required in hypotensive patients.
- Opioid analgesia is vital even if there is no evidence of abdominal pain on clinical examination. Buprenorphine (i/v, i/m or sublingually) usually provides adequate analgesia.
- Broad spectrum antibiotic therapy should be instigated only when there is evidence of sepsis (toxic neutrophils, pyrexia) or in cases with neutrophilic cholangitis.
- Historically, "pancreatic rest" by withholding food has been advised but studies in humans have suggested that nutritional support is essential[1]. The risk of hepatic lipidosis as a complication of anorexia in cats makes this more pertinent. Liquid food *(Fortol™)* via a naso-oesophageal or oesophagostomy tube is generally well tolerated.
- Anti-emetic treatment should be instigated when vomiting is severe or protracted. Maropitant *(Cerenia™)* should be administered first according to the prescription cascade. However if this is insufficient an infusion of metoclopramide at 1-2mg/kg/24h is usually effective.
- Inappetant cats may benefit from an appetite stimulant. Mirtazapine, a tetracyclic antidepressant used in human medicine also has anti-emetic and appetite stimulating effects by increasing serotonin levels in the CNS but antagonizing serotonin activity in the gastrointestinal tract. A dose of 2.5-3.75mg (1/6 to 1/4 of a 15mg tablet) po every 3 days is recommended. Caution should be exercised in using this drug in patients with compromised hepatic function and a reduced dose should certainly be given.
- Concurrent disease such as IBD and diabetes should also be treated. Treatment for IBD with corticosteroids is not contraindicated in pancreatitis cases as there is no evidence that corticosteroids aggravate pancreatitis[1].

Prognosis

The prognosis with mild disease is excellent. Severe cases or frequent episodes carry a guarded prognosis. Hypocalcaemia and hepatic lipidosis have been associated with a poor prognosis in acute pancreatitis[12, 4].

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Launch of Langford Veterinary Services

Langford
VETERINARY SERVICES

The University of Bristol Vet School has launched a new company, LVS, at the beginning of March 2009 which incorporates the original clinical services & diagnostic laboratories. The company is a wholly owned subsidiary of the UoB. Its aim will be to provide the very best care for animals in its care as well as excellent customer service. Bristol University is the first Vet School to run its clinical services in this way.

Lynne Hill, Chief Executive, commenting on the new company, said: "No other UK university has put all of its facilities into a subsidiary company like this.

A new hospital, surgery and diagnostic imaging centre are currently being planned, with facilities including an MRI scanner and a CT scanner."

The range of veterinary clinics includes first opinion small animal and equine practices, referral services for equine, small animals and exotics, a farm animal practice and diagnostic laboratories. These clinics are supported by highly specialised clinicians, diagnostic imagers, anaesthetists, nurses and other support staff.

Bristol prides itself on providing a premier clinical service for cat patients as well as support for practitioners through providing specialist feline diagnostic services and advice to practitioners in management of cases.

This is an exciting development which will enhance the excellent clinical service we provide whilst emphasising customer services.

Real-time PCR for the detection of Tritrichomonas foetus in cats

The protozoal parasite Tritrichomonas foetus (TF) is now well recognised as a cause of chronic diarrhoea in cats. It is a particular problem in multicat households, notably pedigree breeding catteries and rescue shelters, where one or more cats within the group are usually affected. TF-associated diarrhoea is most often seen in cats under 1 year of age, but it has also been reported in older cats. The parasite targets the large bowel causing colitis, with frequent passage of small quantities of liquid to semi-formed faeces often with blood, mucus and straining. Some affected cats develop faecal incontinence.

The motile TF trophozoites can be identified in fresh faeces (ideally <2 hours old) by direct microscopic examination, but the sensitivity of this method is very low. Infection can also be diagnosed by culturing the organism using the commercially available *InPouch*™ TF kit, which has been marketed for the diagnosis of TF infection in cattle. However, the *InPouch*™ method is laborious and time consuming since pouch contents need to be examined daily by microscopy and results can only be considered negative after 12 days. Additionally the specificity of the *InPouch*™ system is unknown as a positive result does not preclude the possibility of infection with trichomonads other than TF. More recently faecal PCR has been recommended as the diagnostic test of choice for TF infection, being more sensitive than both direct examination and culture by the *InPouch*™ method. However, PCR on faeces can be problematic due to the PCR-inhibitory effect of many substances that are co-purified with the DNA during extraction.

A real-time quantitative (Q)PCR has recently been developed by the Diagnostic PCR Laboratory, Langford Veterinary Services for the detection and quantification of TF in faecal samples. This new multiplex assay is the first to use an internal amplification control PCR alongside the TF PCR, enabling detection of any inhibitory substances present in the extracted DNA, which could cause false negative TF results. The use of QPCR in this new assay also allows us to report the relative amount of TF present in the faeces. The assay can be performed on a small volume of faeces (2-5ml) at a cost of £35 (+VAT).

The treatment of choice appears to be ronidazole, which is related to metronidazole and is used to treat tritrichomoniasis in pigeons. It is not licensed for cats and experience of its use is currently limited, although it appears to be effective. A dosage of 30 mg/kg orally once daily for two weeks has been suggested. The drug does have a narrow safety margin, so cats should be monitored carefully for side effects which usually involve neurotoxicosis. There is a comprehensive information sheet which can be found on the FAB website (www.fabcats.org).

The diarrhoea will usually resolve spontaneously in untreated cats although this may take some time; months or more. Cats in which clinical signs (diarrhoea) have resolved seem to continue to excrete the organism for periods of up to two years.

Welcome to Jim Littlewood *the new FAB scholar*

Jim graduated from the Royal Veterinary College, University of London, in 2004. Upon graduating he worked as a first opinion small animal vet at a practice in Colchester. It was here that his interest in feline medicine was first ignited. He joined the FAB/ESFM shortly after starting in practice. After 18 months he moved to busy 3-centre practice in Hertfordshire and Bedfordshire.

During his time he saw a wide range of feline cardiology and medicine cases and this drove him to pursue a career in all things feline. He was fortunate enough to be awarded the FAB Scholarship in feline medicine at Bristol University in April 2009.

Jim has a broad interest in feline medicine but has particular interests in anaesthesia, feline cardiology and endocrinology. He hopes to sit his examinations for the RCVS certificate in Anaesthesia next year.

Three years ago Jim and his cat 'Kit' were joined by 'Sooty', a local stray, after he walked through the cat flap and decided to set up home. Presently he shows little, if any, intention of leaving as both Jim and 'Kit' suspect he knows when he is on to a good thing.

Applications are invited for the

Fort Dodge Feline Fellowship

based at the University of Bristol School of Veterinary Science

This post offers an opportunity for veterinary surgeons with a particular interest in feline medicine to gain specialist experience and expertise in this field. It has been funded by Fort Dodge Animal Health since 1987 and is based at the Bristol University Veterinary School at Langford.

The successful applicant will join a strong team working in the field of feline medicine involving both clinical and research activity. Current areas of particular interest are infectious diseases, feline immunology, endocrinology and gastroenterology. The major objectives of the Fort Dodge Fellowship are to provide a link between feline clinical and research work in the department, assist in the development of feline projects and to assist in supporting the busy specialist feline diagnostic service. The Fort Dodge Fellow works very closely with the Feline Advisory Bureau Residents who have responsibility for most of the feline referrals but there is some opportunity for clinical work and there is encouragement to develop a particular aspect of feline medicine. Previous Fort Dodge Fellows have developed a particular interest in FIV, FIP, endocrine diseases (mainly diabetes mellitus) and allergic skin disease.

Newly qualified veterinary surgeons will be considered for this post but some experience is an advantage. The post is ideal for veterinary surgeons wishing to pursue an interest in feline medicine. It provides an insight into an academic /research career and is particularly suitable for the graduate who wishes to consider this without making a long term commitment. The Fort Dodge Feline Fellowship provides an excellent basis for a subsequent academic or research career and previous Fellows have subsequently undertaken PhD projects arising from their year.

This position normally starts in October and is for one year although reappointment at the end of the first year may be considered.

Further details of the post are available from:

Prof. T.J. Gruffydd-Jones, The Feline Centre
Department of Clinical Veterinary Science
Division of Companion Animals, University of Bristol
Langford House, Langford, BRISTOL BS40 5DU
Telephone: 0117 928 9558

Prospective applicants are invited to visit Langford and to talk to the current Fort Dodge Feline Fellow.

ABSTRACTS

Evaluation of Urine Specific Gravity and Urine Sediment as Risk Factors for Urinary Tract Infections in Cats

*Nathan L. Basiff, Jodi L. Westropp, Richard W Nelson et al., Vet Clin Pathol 2008;37(3):**317-322.***

Bacterial urinary tract infection is relatively uncommon in younger cats; however, the incidence of UTIs has not been studied in older cats. It has been speculated that isosthenuric urine as a result of common metabolic diseases such as chronic kidney disease (CKD), diabetes mellitus (DM), and hyperthyroidism (HT) predisposes to UTIs. Previous studies reported a prevalence of UTIs of 22% and 12%, but yielded conflicting results about the association between low urine specific gravity (USG) and UTIs in DM whilst other conditions such as lower urinary tract disease (LUTD), HT and CKD had not been studied at all.

Medical records of all cats with a positive aerobic urine culture performed at the University of Davies between 1995 and 2002 were reviewed. Cats that were diagnosed with CKD, DM, HT, or clinical signs of LUTD were included. Exclusion criteria included concurrent disease, except urolithiasis, antimicrobial treatment, urinary tract catheterisation, urinary tract surgery in the preceding 2 weeks, previous urethrostomy, and the presence of anuria or urethral obstruction. Urinalysis including pH, USG, microscopic examination of urine sediment, bacterial and fungal culture and antimicrobial sensitivity was carried out.

Six hundred and fourteen cats met the inclusion criteria. Ninety-three were purebreds, but only Persians were found to be at increased risk (P=0.018) for UTIs irrespective of the disease category. The median age was 10 years. Female cats were four times more likely to have a positive urine culture (P=0.001). Increasing age increased the risk of a positive urine culture (P=0.042). The risk of a positive urine culture was also significantly associated with lower bodyweights.

Three hundred and fourteen cats had urine cultures performed and 14.3% were positive. Among all cats, decreasing USG was not associated with an increased risk of positive urine culture.

Of all cats that met the inclusion criteria, 344 cats had CKD, 121 cats had DM, 46 cats had uncontrolled HT, and 103 cats had signs of LUTD. Positive urine cultures were identified in 16.9% cats with CKD, 13.2% cats with DM, 21.7% cats with uncontrolled HT, and 4.9% cats with LUTD. It is likely that the increase of UTIs in CKD results from an impairment of normal host defence mechanisms that allows colonisation of bacteria in the urinary tract. The reason for a much larger percentage of cats with HT and positive urine culture is unclear as there appears to be no correlation between thyroid hormone and urine culture results. However, the fact that the risk of a UTI increased with decreasing body weight and possible masked renal disease may contribute to this finding. Bacterial UTIs in cats with LUTD are still uncommon.

Each disease was evaluated for the effect of USG on urine culture outcome, but no differences were detected. There were also no associations between the serum creatinine & urea concentrations or the urine pH and the presence of a UTI irrespective of the disease category. However, pyuria, bacteriuria, and haematuria were significantly correlated with a positive urine culture. Of 66 cats that presented with LUTD and had abdominal imaging, 19.7% had bladder stones, but none had a positive urine culture. Of the 253 cats with CKD that had abdominal imaging, 2 had bladder stones, 38 upper tract stones (kidney or ureter or both) and 1 had upper and lower tract stones. Five (out of 41) positive urine cultures were reported and they were all traced back to cats with upper tract stones. Concurrent signs of LUTD with CKD, DM, or HT were only infrequently reported.

Overall 88 of 314 (14.3%) cats had positive urine cultures with a total of 101 isolates. Eleven cats had more than one isolate (9 cats with CKD; 1 cat with DM; 1 cat with HT). Organisms isolated included: *Escherichia coli* (60 isolates), *Enterococcus* (14 isolates), *Staphylococcus sp.* (8 isolates), *Proteus* (4), *Klebsiella sp.* (3 isolates), *Pasteurella* (2 isolates) and *Enterobacter sp.*, *Pseudomonas*, and *Mycoplasma* (1 each). While *E. coli* was the most common isolate among cats with CKD, DM, or HT, *E. coli* was not isolated from any cats presenting with LUTD. More than 85% of isolates were sensitive to commonly used antibiotics such as amoxicillin/clavulanic acid, enrofloxacin, trimethoprim sulfa, cephalexin, and ampicillin. Multiresistance was encountered with *Enterococcus sp.* (3 isolates), *E. coli*, *Enterobacter sp.*, and *Pseudomonas* (1 each), although each isolate was susceptible to at least one of the commonly available oral antibiotics.

This study showed that decreased USG independent of disease status was not associated with an increased risk of a positive urine culture. The severity of haematuria, pyuria, and bacteriuria correlated with positive urine culture outcome, thus emphasising the importance of microscopic examination of the urine sediment as useful predictor of UTIs. Active urine sediment may be an important criteria for deciding whether bacterial culture is warranted.

Survival in Cats with Naturally Occurring Chronic Kidney Disease (2000-2002)

*L.M. Boyd, C. Langston, K. Thompson, et al. J Vet Int Med 2008(22):**1111-1117.***

Chronic kidney disease is one of the most common illnesses in geriatric cats. Its prevalence increases with age and up to 31% of cats over 15 years are affected. CKD can progress unpredictably and there are variable presentations of the disease. Few studies have been performed evaluating long term survival in these cats. This study aimed to determine the average survival time and identify whether commonly measured haematological and clinical parameters would be accurate predictors of survival time.

Medical records were reviewed of all cats with a serum creatinine (SCr) >2.3mg/dL (>209 µmol/L) and a urine specific gravity of <1.035 between 200-2002. Cats with acute renal failure, postrenal causes of azotaemia, hyperthyroidism, diabetes mellitus, any disease known to affect renal function, congestive heart failure, or evidence of malignancy were excluded. Cats with azotaemia persisting after resolution of the post-renal causes were included. The staging system for classifying cats with CKD proposed by the IRIS was used with slight modifications, to categorise cats. Cats were divided into the following groups based on their baseline SCr: Stage IIb = SCr >2.3-2.8 mg/dL (209-249 µmol/L); Stage III = SCr 2.9-5.0 mg/dL (250-439 µmol/L); Stage IV = SCr >5.0 mg/dL (>440 µmol/L). Cats with a SCr <2.3 mg/dL (<209 µmol/L) were not included in the analysis.

Of the 9446 serum chemistry panels performed, 733 records were available from cats that had a SCr >2.3 mg/dL. Cats were excluded for having incomplete records (311 cats), prerenal azotaemia (81 cats), postrenal azotaemia (34 cats), acute renal failure (35 cats), or another undetermined cause of azotaemia that was not consistent with CKD (61 cats). Two-hundred and eleven cats met the inclusion criteria. The most common breed was domestic shorthair (68%), followed by Siamese (10%), Persians (6.6%), Abyssinians (4%), and Himalayans (3%). The mean age at the time of diagnosis was 12.8 years (SD 4.4). At the time of diagnosis, 37% cats (n=78) were identified as having stage IIb kidney disease, 33% (n=69) stage III kidney disease, and 30% (n=64) stage IV kidney disease. Thirty per cent of cats in stage IV at the time of diagnosis were categorised in a lower category after the prerenal component of azotaemia had been corrected. One cat in stage IIb, 8 cats in stage III and 30 cats in stage IV were hospitalised for an average of 5 days in order to correct prerenal azotaemia. After this intervention, cats were re-classified as stage IIb (n=82; 39.4%) with a median survival time of 1.151 days (1.014-1.565), stage III (n=84; 40.3%) with a median survival time of 679 days (445-910), and stage IV (n=42; 20.2%) with a median survival time of 35 days (21-99).

One hundred and twenty-one cats developed anaemia (PCV<25%) before death. Median survival time from the point of anaemia development to death was 100 days (65-186). Cats (n=42) that underwent intervention for anaemia (e.g. blood transfusion, erythropoietin administration) had a median survival time of 25 days (6-74) from the point of intervention. Sustained weight loss was present in 142 cats before death, and had a median survival time of 401 days (233-601) from the point when weight loss was first noted. Eighty-one cats lost more than 25% of their baseline body weight and had a median survival time of 83 days (56-194) from the point that 25% weight loss was first reported.

Median survival from the point of SC fluid administration (n=142) was 273 days (175-424). One hundred and forty-five cats had a documented SCr value of >4.0 mg/dL (363 µmol/L). Median survival from the point that SCr became >4.0 mg/dL (363 µmol/L) was 123 days (81-193) and from the point of a documented SCr >5.0 mg/dL (>440 µmol/L) (n=98) was 44 days (32-97).

Each clinicopathologic parameter was evaluated to determine if it was predictive for survival. Age at diagnosis, albumin, blood urea nitrogen, creatinine, calcium, bicarbonate, potassium, and haematocrit were not found to be predictive of survival in the multivariate model. The only laboratory variable that was predictive of survival was serum phosphorus (P=0.0043). For each 1Umg/dl increase in the blood level of phosphorus, there is an 11.8% increase in the risk of death.

The results of this study indicate that the IRIS stage of kidney disease based on the SCr at the time of diagnosis and more importantly at baseline after correction of prerenal azotaemia, is strongly associated with survival time in cats. Phosphorus has been found to be the most valuable predictor of survival. These data on prognostic factors and survival time will be of great help in educating owners and in helping them to make decisions based on realistic expectations of the outcome of chronic kidney disease.

Remission of Diabetes Mellitus in cats with Diabetic Ketoacidosis

*N.S. Sieber-Ruckstuhl, S. Kley, F. Tschuor et al., J Vet Intern Med 2008, 22;**1326-1332.***

Diabetes Mellitus (DM) is one of the most frequently encountered endocrine disorders in cats. The spontaneous form is very similar to type II diabetes in humans; obesity is strongly correlated with insulin resistance and remission of diabetes can often be achieved with insulin therapy. Diabetic ketoacidosis (DKA) is the most serious hyperglycaemic emergency in patients with DM. The use of diabetogenic medication, underlying clinical disorders or inadequate dosage of insulin can be precipitating events leading to this complication. In veterinary medicine, remission has been reported in up to 50% of cats with DM. This study investigated medical records of *(1)* cats with DKA with diabetic remission to *(2)* cats with DKA without diabetic remission and to *(3)* cats with uncomplicated DM and diabetic remission.

During the study period (2003-2007) 24 cats with DKA were presented and 12 fulfilled the inclusion criteria and were enrolled in this study. Seven of these cats had remission from diabetes *(group 1)*, whereas the remaining 5 cats did not experience remission *(group 2)*. Of 52 cats that presented for uncomplicated DM only 7 cats met the inclusion criteria experiencing remission *(group 3)*. There were no significant differences between the three groups with respect to age, sex, and body weight. Five of the cats (5/12) developing DKA were pre-treated with glucocorticoids, but statistically the number of pre-treated cats was not different among the 3 groups. Cats of group 1 had significantly higher leukocyte and segmented neutrophil counts and significantly fewer eosinophils than cats in group 3. In comparison to cats with uncomplicated DM *(group 3)*, cats presenting with DKA *(group 1 & 2)* had a significantly higher bilirubin, aspartate aminotransferase, and alanine aminotransferase levels, significantly lower potassium and calcium concentrations. Urinalysis revealed significantly more ketone bodies and a higher urine protein:creatinine ratio in cats with DKA *(group 1 & 2)*.

Suspected concurrent disease included: pancreatic disease *(group 1: n=5 cats, group 2: n=2)*, bacterial cystitis *(group 1: n=2; group 2: n=2; group 3: n=1)*, and hypertrophic cardiomyopathy *(group 2: n=1)*. Cats in group 1 suffered significantly more often from pancreatic disease than cats in group 3.

For cats in group 1 and group 2 median hospitalisation time was 9 days and 8 days respectively. Three of 7 cats in group 1 went into diabetic remission and are still alive. Insulin was withdrawn between 10 days and 4 weeks and remission had lasted between 10 and 24 months at the study endpoint. In the other 4 cats in group 1 insulin therapy had been discontinued after 1-4 weeks. However, these cats came out of remission that lasted between 5 weeks and 6 months. All cats were euthanised after 2-2.5 years for reasons unrelated to DM (decompensated renal failure, intestinal lymphoma, brain tumour, geriatric reason).

Cats in group 2 required insulin therapy ranging from 1.5-3U/cat twice daily and 4/5 cats were well controlled *(alive at endpoint: n=2; euthanasia for geriatric reasons: n=1; euthanasia after another episode of DKA: n=1)*. Only one cat was poorly controlled requiring steadily increasing insulin, but a somogy overswing was suspected. However, this cat was lost to follow-up.

Three of seven cats in group 3 were still alive and in remission at the endpoint. Insulin was withdrawn after 2-13 weeks and remission lasted between 9-36 months. Two cats stayed in remission until euthanasia 2-3 years after discontinuation of insulin therapy. Two of the seven cats came out of remission. In one of these cats weight loss resulted in a second episode of remission lasting to the endpoint of this study. The other cat was treated for vestibular syndrome with corticosteroids 7.5 months after insulin cessation which led to clinical signs of diabetes requiring insulin therapy. This cat was euthanised after a pulmonary mass was detected 3 weeks after re-initiation of insulin treatment.

In conclusion this study found that in line with reports from human medicine, complete or partial diabetic remission in cats with DKA was possible, especially if pancreatic disease was suspected to precipitate the disease. Coexisting acute pancreatitis and DKA seemed to be one of the most prevalent concurrent disorders in this study. These findings may help to influence the willingness of owners to treat for DKA.

Feline Update is published as a co-operative venture between Langford House and Fort Dodge Animal Health. Any correspondence should be addressed to Prof. T. Gruffydd-Jones, The Feline Centre, Department of Clinical Veterinary Science, University of Bristol, Langford House, Langford, BS40 5DU, or to Matthew Rowe BSc (Hons) at Fort Dodge Animal Health, Southampton, SO30 4QH.