

ISFM Consensus Guidelines on the Diagnosis and Management of Feline Chronic Kidney Disease



Practical relevance: Chronic kidney disease (CKD) is one of the most commonly diagnosed diseases in older cats. In most cats, CKD is also a progressive disease and can be accompanied by a wide range of clinical and clinicopathological changes. These ISFM Consensus Guidelines have been developed by an independent panel of clinicians and academics to provide practical advice on the diagnosis and management of this complex disease.

Clinical challenges: Although CKD is a common clinical problem in cats, the manifestations of disease vary between individuals. Thus there is a need for careful and repeat evaluation of cats with CKD and adjustment of therapy according to individual needs. In addition to addressing problems arising from CKD and improving quality of life (QoL) for the patient, therapy may also target slowing the underlying progression of disease and hence prolonging life. While maintaining QoL is of paramount importance in our patients, this can be challenging when multiple therapies are indicated. In some cases it is necessary to prioritise therapy, given an understanding of what is likely to most benefit the individual patient.

Evidence base: In preparing these Guidelines, the Panel has carefully reviewed the existing published literature, and has also graded the quality of evidence for different interventions to help to provide practical recommendations on the therapeutic options for feline CKD. This is a field of veterinary medicine that has benefited from some excellent published clinical research and further research findings will undoubtedly modify the recommendations contained in these Guidelines in the future.

INTRODUCTION

Chronic kidney disease (CKD) is a common feline disease. Its prevalence will vary between populations, but a large UK study estimated that the prevalence of feline renal disease in first opinion practices was ~4% (CKD was the seventh most common specific diagnosis made).¹ CKD is more common in older cats,^{2–4} and may affect ≥30–40% of cats over 10 years of age.⁴ Renal disease was the most common cause of mortality in cats ≥5 years of age in a UK study, being the cause of death of >13% of cats at a median age of 15 years.⁵

The underlying aetiology of CKD often remains obscure. Most cats investigated have chronic tubulointerstitial nephritis and renal fibrosis on histology (Figure 1)^{6,7} – lesions thought to be the end phase of a variety of potential underlying aetiologies that may include toxic insults, hypoxia, chronic glomerulonephritis, chronic pyelonephritis,

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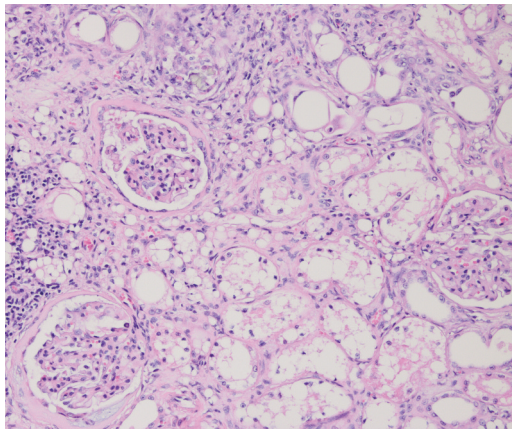
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Figure 1 Typical histopathology of a kidney from a cat with chronic kidney disease (CKD), characterised by inflammatory infiltrate, tubular loss, increase in extracellular matrix and fibrosis x 20. Courtesy of Shannon McLeland



A good relationship and good communication between the clinic and the cat's owner is vital for successful management of CKD.



upper urinary tract obstructions, and potentially viral infections involving retroviruses as well as a recently recognised morbillivirus.^{8–12} Other specific causes of CKD sometimes recognised include amyloidosis, polycystic kidney disease, renal lymphoma, hypercalcaemic nephropathy and congenital disorders – some of these have breed associations.^{4,8,13}

Other than age, clear risk factors for development of CKD have not been identified in cats,^{14–17} but weight loss or poor body condition, polyuria/polydipsia (PU/PD), higher creatinine concentrations, dehydration and potentially lower urine specific gravity (USG) may indicate the presence, or predict development, of CKD.^{14–17}

The purpose of these Guidelines is to give practitioners an up-to-date, critically assessed overview of the current diagnostic and treatment options to guide in the practical management of CKD.

Quality of evidence as an intervention

The Panel has provided guidance on the current quality of evidence for different therapeutic interventions based on peer-reviewed published data – summarising (as 'GOOD', 'POOR' or 'NONE') any evidence that a therapy improves longevity, and also that a therapy improves quality of life (QoL). However, it should be noted that many interventions have not yet been adequately evaluated.



Figure 2 Blood pressure measurement should be part of the routine evaluation of all cats with proven or suspected CKD. Courtesy of Sarah Caney



Figure 3 Ocular examination (in this case distant indirect ophthalmoscopy) performed in a dark room is valuable, given the strong association between CKD and hypertension. Courtesy of Sarah Caney

DIAGNOSIS AND ASSESSMENT OF CKD IN CATS

Routine diagnosis of CKD in cats

CKD in humans is defined as a sustained (≥ 3 months) reduction in glomerular filtration rate (GFR, $< 60 \text{ ml/min/1.73 m}^2$) or evidence of sustained (≥ 3 months) kidney damage (eg, structural damage, proteinuria).¹⁸ Although CKD has not been clearly defined in cats, similar principles should apply; notably there should be evidence of sustained functional or structural kidney damage (eg, ≥ 3 months' duration).

As CKD is more common in older cats, these patients should be targeted for more detailed and frequent health assessments. Recommendations from International Cat Care/International Society of Feline Medicine, the American Association of Feline Practitioners and the American Animal Hospital Association suggest health checks every 6 months for cats > 7 years of age (including evaluation of body weight, body condition score and blood pressure), together with selected diagnostic testing (including haematology, serum biochemistry screening and routine urinalysis) at least annually.^{19,20}

Historical and clinical findings suggestive of CKD, such as weight loss, altered kidney size, unexplained dehydration, PU/PD, systemic hypertension or an unexplained low USG (< 1.035 – 1.040), also justify further investigation.

A simple, accurate biomarker to assess renal function does not currently exist. Thus in clinical practice the combination of azotaemia (increased serum creatinine and/or urea) and an inappropriately low USG are routinely used to diagnose CKD. However, their interpretation is not always straightforward.^{21,22}

✦ Although often measured together, creatinine is preferred over urea as a marker of GFR as its concentration is inversely related to GFR, and is affected by fewer non-renal factors.

✦ Creatinine is an imprecise marker of GFR though; it lacks specificity if reference intervals are set low enough to detect early stage disease, but lacks sensitivity if reference intervals are set higher.

✦ Creatinine concentration is affected by lean tissue mass and hydration.

✦ Creatinine concentrations (and reference intervals) vary between different assays, analysers and laboratories.

✦ The exponential relationship between GFR and creatinine means that substantial early declines in GFR may be accompanied by only small changes in creatinine, while in the latter stages of disease large changes in creatinine may reflect only small changes in GFR.

Bearing in mind these limitations, in clinical practice feline CKD is often diagnosed on the basis of:

- ✦ An increased serum creatinine concentration $>140 \mu\text{mol/l}$ ($>1.6 \text{ mg/dl}$); *together with*
- ✦ An inappropriately low USG (<1.035); *and*
- ✦ Evidence that these changes are sustained (over several weeks or months) or with a history suggesting sustained clinical signs consistent with CKD.

However, not all cats with CKD will meet these criteria:

- ✦ Chronic kidney damage evidenced by structural changes to the kidney recognised on diagnostic imaging or persistent renal-origin elevated proteinuria may be present in the absence of azotaemia or an inappropriate USG.
- ✦ While relatively few healthy cats will

produce a USG <1.035 , this can be affected by diet,²³ and occasionally some cats with azotaemic CKD will produce a USG ≥ 1.035 .^{24,25}

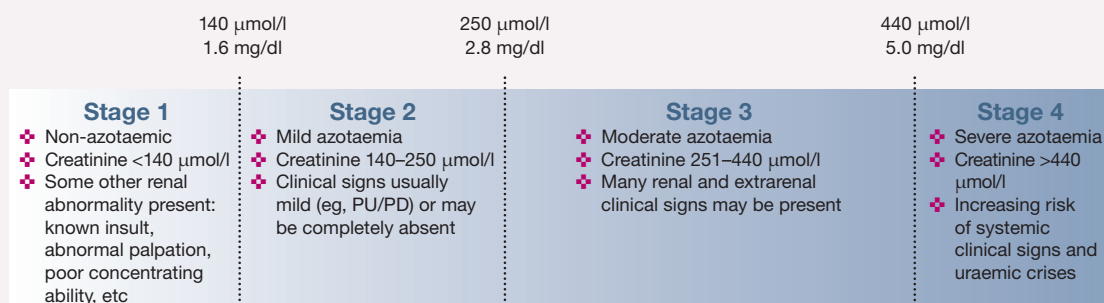
- ✦ Some cats have reduced urine concentrating ability before they develop overt azotaemia.
- ✦ A persistent and substantial ($>15\%$) increase in serum creatinine from previously determined baseline values in a cat is also likely to indicate reduced renal function.

For these reasons, serial (eg, annual or bi-annual) assessment of serum creatinine or symmetric dimethylarginine (SDMA – see later) and USG may be helpful in older cats (>7 years of age) to determine changes over time, as this may facilitate earlier or more certain diagnosis of CKD.^{22,26} Additionally, if there is doubt over the diagnosis, additional testing (see page 222) may be desirable.

Staging of feline CKD

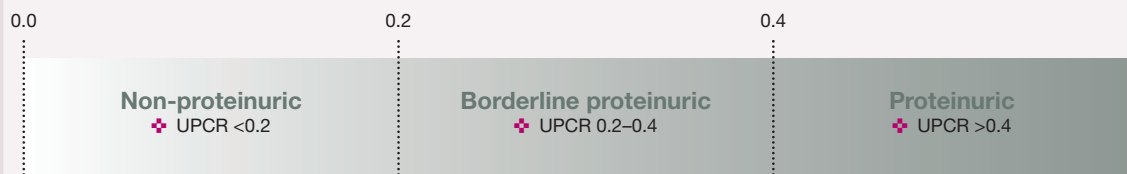
IRIS staging of feline CKD:

Based on fasting blood creatinine concentration, in a stable patient, measured twice



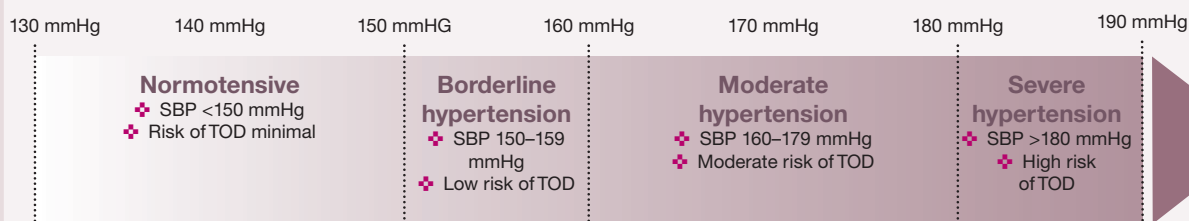
IRIS substaging of feline CKD:

Based on proteinuria (urine protein:creatinine ratio [UPCR])



IRIS substaging of feline CKD:

Based on measurement of systolic blood pressure (SBP)



Adapted from www.iris-kidney.com.²⁷ IRIS = International Renal Interest Society; PU/PD = polyuria/polydipsia; TOD = target organ damage

Routine investigation and staging of CKD in cats

Where CKD is suspected, a minimum routine database should ideally include:

- ✦ Full history and physical examination;
- ✦ Routine urinalysis (to include USG, 'dipstick' analysis, urine sediment analysis, urine protein:creatinine ratio [UPCR], and culture where indicated);
- ✦ Routine serum biochemistry, to include a minimum of proteins, urea, creatinine, electrolytes (Na^+ , K^+ , Ca^{2+} , Cl^- , PO_4^-), and other analytes (eg, thyroxine in an older cat) as relevant;
- ✦ Routine haematology;
- ✦ Systolic blood pressure (SBP);
- ✦ Diagnostic imaging (renal ultrasonography is generally more valuable than radiography);
- ✦ In some situations (eg, unexplained renomegaly) a kidney biopsy or fine-needle aspiration may be desirable.

These investigations are aimed at:

- ✦ Identifying potential underlying aetiologies of the CKD (which may require specific therapy);
- ✦ Identifying complications that are arising from the CKD;
- ✦ Identifying concomitant disease that may affect management (eg, hyperthyroidism).

The International Renal Interest Society (IRIS) has established a CKD staging system²⁷ based on the cat's fasting creatinine concentration (see box on page 221). This is valuable as the stage (severity) of disease is related to the prognosis for the patient (see later) and can help to focus attention on appropriate treatments. Staging is applicable in cats with confirmed, stable CKD that are well hydrated, and IRIS substaging is based on UPCR and SBP, two important prognostic and therapeutic parameters.

Advanced and emerging tests for feline CKD

Estimation of GFR

The gold standard in renal function testing is direct determination of GFR. Limited- and single-sample plasma clearance methods (eg, using iohexol, inulin, exogenous creatinine or radiolabelled markers) have made GFR assessment easier to undertake in clinical practice, but the reduced numbers of blood samples may yield greater inaccuracy.^{21,28} Clinical measurement of GFR is mainly used to confirm suspected CKD in non-azotaemic cats.

Symmetric dimethylarginine (SDMA)

SDMA has become available in the veterinary marketplace as a surrogate marker of GFR and, like creatinine, its reciprocal has a linear relationship with GFR.²⁹ It appears to offer greater sensitivity than creatinine for detection of early CKD³⁰ and does not appear to be affected by muscle mass. However, further studies are required to fully evaluate its accuracy in clinical patients as SDMA may also be affected by non-renal factors.³¹ Although it cannot currently be recommended as a single screening test for CKD, its measurement may be helpful in supporting a diagnosis of CKD or in staging CKD, especially in cats with marked loss of muscle mass.²⁷

Serum cystatin C

Serum cystatin C is a useful surrogate marker of GFR in human patients. However, in cats its diagnostic value appears compromised by overlap in values between healthy cats and cats with CKD, and the interference of non-renal factors.^{32,33}

Microalbuminuria

Detection of microalbuminuria is important in the diagnosis of CKD in human patients where there is a high prevalence of glomerular disease, but its clinical significance in cats remains unclear. It is measured using a species-specific assay but a benefit of measuring urine albumin:creatinine ratio (UACR) over UPCR in predicting which cats will develop azotaemia has not been demonstrated.¹⁷

Other assays

Studies have demonstrated that development of renal secondary hyperparathyroidism³⁴ and increased fibroblast growth

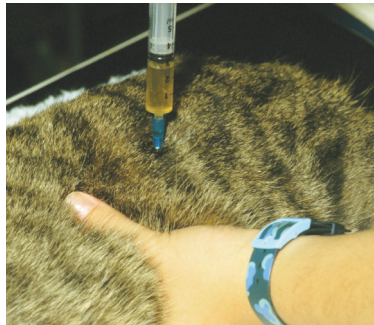


Figure 4 Collection of a urine sample by lateral cystocentesis for routine monitoring of CKD. Courtesy of Sarah Caney



Figure 5 Collection of blood for routine monitoring of CKD (note the no restraint technique). Courtesy of Jessica Quimby

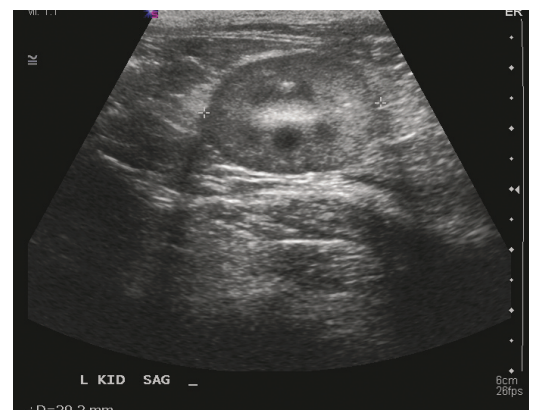


Figure 6 A small kidney and loss of corticomedullary distinction are ultrasound findings consistent with feline CKD. Courtesy of Jessica Quimby

Recommended monitoring of cats with CKD

Optimal monitoring strategies for cats with CKD have not been systematically evaluated and the extent of monitoring will vary depending on the owner, the patient, the disease stability, the number and severity of secondary complications, and the presence of concomitant disease(s). However, in addition to monitoring the clinical signs and clinical condition of the patient, regular assessment for the occurrence of hypertension,³⁶ proteinuria,³⁷ hypokalaemia,³⁸ hyperphosphataemia,³⁸ urinary tract infections (UTIs),³⁹ anaemia and CKD-associated mineral bone disorder^{34,40} is important, given that these complications are common and

often associated with disease progression or a poor QoL. Suggested routine evaluations are outlined in Table 1.

Following diagnosis (and stabilisation, if necessary), initial re-evaluations should typically be undertaken every 1–4 weeks, according to clinical needs. Full monitoring (Table 1) will not be necessary at each visit (and not all evaluations are needed in all cats and at all times), but should be performed sufficiently frequently to allow good patient management. Even in cases of early and apparently stable CKD, initial monthly revisits can be helpful in supporting the

diagnosis, providing support to the owner, and in monitoring progression and therapy. In the long term, even if stable, cats should be re-evaluated at least every 3–6 months. Particular attention should be paid to appropriate monitoring of the efficacy of interventions to ensure that therapeutic targets are being met. In advanced disease, care may be needed to avoid exacerbating anaemia by too frequent blood collection.

Routine monitoring of cats also permits assessment of disease progression and repeat IRIS staging. Deterioration of disease (progression from one IRIS stage to the next, a substantial

increase in serum creatinine or a consistent rise in serial blood samples, a substantial increase in UPCr, a consistent reduction in body weight and body condition, etc) changes the prognosis for the patient and should prompt more detailed re-evaluation.

Veterinary nurses and technicians can play a very valuable role in the ongoing assessment of CKD patients and in supporting owners.

Table 1 Routine evaluation of feline CKD patients

Assessment	To include:
Full history	Evaluation of progress, complications and owner concerns Evaluation of changes since last assessment
Full clinical examination	Body weight, % change in body weight and body condition score Hydration status
Blood pressure assessment	Systolic blood pressure (Figure 2) and ocular examination (Figure 3)
Urinalysis	USG, UPCr, 'dipstick' and sediment analysis Bacterial culture if indicated (Figure 4)
Routine haematology	Full haematology may not always be required but haematocrit or PCV should be regularly assessed (Figure 5)
Serum biochemistry	Proteins, urea, creatinine and electrolytes (Na ⁺ , K ⁺ , Ca ²⁺ , Cl ⁻ , PO ₄ ⁻) Other analytes should be measured as necessary, including thyroxine, liver enzymes and acid-base status
Diagnostic imaging	Ultrasonography or radiography (Figures 6 and 7) – to assess for structural changes, obstructions or other lesions – should be part of the initial investigation and may be worth repeating, especially with unexpected deterioration

USG = urine specific gravity; UPCr = urine protein:creatinine ratio; PCV = packed cell volume

factor-23 (FGF-23)³⁵ may precede azotaemia in feline CKD. However, whether there is any diagnostic utility in these assays remains to be determined.



Figure 7 Radiographs are helpful for identifying abnormalities such as stones within the urinary tract. Courtesy of Jessica Quimby

Prognosis

The prognosis for cats with CKD at the time of diagnosis depends on the severity of the disease, which can be determined according to their IRIS stage²⁷ (Table 2).

Additional clinical variables associated with a significantly worse prognosis include:^{37,41–45}

- ✦ The level of proteinuria
- ✦ The level of hyperphosphataemia
- ✦ The FGF-23 concentration
- ✦ The presence of progression of CKD
- ✦ A lower PCV

Table 2 Studies evaluating IRIS stage and prognosis

Study	Reported median survival time (days)		
	IRIS stage 2	IRIS stage 3	IRIS stage 4
Boyd et al ⁴¹	1151	778	103
King et al ⁴²	Not reached	~500	~70
Syme et al ³⁷	504	154	57
Geddes et al ⁴³	490	263	20

Management of CKD is largely focused on supportive and symptomatic therapy.

APPROACH TO MANAGEMENT

Management of CKD is largely focused on supportive and symptomatic therapy with the aim of improving the quality of life (QoL) of affected cats (especially those in CKD stages 3 and 4) and, where possible, slowing the progression of disease (especially in CKD stages 2 and 3). Although beyond the scope of these Guidelines, careful evaluation of cats (as outlined earlier) should also allow identification of certain underlying aetiologies that permit specific intervention such as renal lymphoma, UTIs, nephroliths and ureteroliths.

Because of the chronic nature of the disease, the need for regular monitoring and the potential for various interventions, establishing a good relationship and good communication between the clinic and the cat's owner is vital. This will facilitate individualised management plans to be created that take into consideration the wishes and ability of the owner, as well as the needs of the cat.

Issues that should be considered are outlined in the box below.



General considerations

- ❖ **Full evaluation of the patient** – often when CKD is diagnosed the disease has actually been present for a long time and thus careful and full patient evaluation is important
- ❖ **Initial stabilisation of the cat** – eg, hospitalisation for investigations and for initial fluid therapy to correct dehydration
- ❖ **Detection and management of concomitant diseases** – this may also help CKD management, especially if concurrent disease is associated with persistent fluid loss or reduced appetite
- ❖ **Assessment of the IRIS stage, substage and complications of CKD (when the cat is stable)** – this allows a more meaningful prognosis to be given, and may identify therapeutic interventions that are required
- ❖ **Therapeutic priorities** – administering multiple medications, potentially several times a day, can be a daunting prospect for many owners and stressful for many cats. Importantly, palatable and easy to administer medications make this easier, and it may be possible to combine medications (eg, placing small tablets together in a single gelatine capsule). However, in some cases optimum therapy may not be achievable, in which case it is important to assess carefully what treatments are practical and likely to have the most impact on improving QoL
- ❖ **Potential for 'acute on chronic' CKD** – cats may present with acute exacerbations of CKD due to concomitant disease, dehydration, etc. Careful assessment and management of these patients is required (including fluid therapy and management of complications)
- ❖ **Progression of CKD** – this often occurs in a stepwise rather than a linear manner. The patient should be thoroughly re-evaluated each time significant progression has occurred to ensure treatable complications are not being overlooked

MANAGEMENT OF CKD PATIENTS

Managing hydration in CKD^{46,47}

Quality of evidence as an intervention

- ❖ Increased longevity: No data
- ❖ Improved QoL: No data, but Panel considers the impact of preventing dehydration is likely GOOD

CKD is associated with variable obligatory diuresis, and affected cats may be predisposed to dehydration, especially in CKD stages 3 and 4.

Panel recommendations: hydration

Although studies confirming the clinical benefit of maintaining hydration in CKD are lacking, the Panel considers it a crucial part of management. It is likely to be important for maintaining QoL, and could affect progression, as dehydration may compromise renal blood flow. In addition to maintaining hydration, fluid therapy may be beneficial in addressing electrolyte and acid–base disturbances, and diluting uraemic toxins.

Correcting dehydration^{46,47}

Cats with unstable or decompensated CKD may require hospitalisation and intravenous fluid therapy, typically with lactated Ringer's solution or Hartmann's. Consideration should also be given to concomitant electrolyte and acid–base disturbances that may need addressing.

The fluid required to correct dehydration (in ml) is calculated from: body weight (kg) × estimated dehydration (%) × 1000, and this (along with maintenance fluids, eg, 50 ml/kg/24 h) is typically provided over 24–48 h, although some cats may tolerate more rapid rehydration.

After rehydration, maintenance fluids can be administered but cats should be monitored carefully to avoid fluid overload. When azotaemia is stable, fluids should be tapered over 2–3 days before the patient is discharged.

Long-term maintenance of hydration

- ❖ **Voluntary water intake** Free access to good quality water should be provided at all times (Figure 8), and owners should be advised to offer a variety of water sources (including flavoured waters and running water – eg, a 'pet fountain') to encourage drinking. Feeding a wet diet rather than dry diet where possible is important, as it will also increase water intake.⁴⁸ Additional water can be added to the food where



Figure 8 Multiple sources of fresh water are important for maintaining hydration. *Courtesy of Jessica Quimby*

dehydration is a concern, but it is important to ensure intake of other nutrients is maintained.⁴⁹

✦ **Use of feeding tubes** Water can also be administered via a feeding tube, and this may be preferable to subcutaneous fluids (see below) in many cases. A feeding tube is suitable for long-term maintenance of hydration and is a more physiological approach. It also allows for nutritional support when needed.

✦ **Subcutaneous fluid therapy** Repeated subcutaneous fluid therapy (75–150 ml every 1–3 days) can be used on an outpatient basis (Figure 9) or by owners at home to maintain hydration. This is most commonly employed in cats with advanced (stages 3 and 4) CKD, but should be considered on a case-by-case basis. Cats should be carefully monitored to ensure there is clinical benefit and to avoid overhydration.

Although a balanced electrolyte solution such as lactated Ringer's solution is often used, a hypotonic solution (half-strength lactated Ringer's or 0.45% saline, with added potassium as needed) may be preferable to reduce the sodium load. Fluids can be administered via a needle and giving set, or through an indwelling subcutaneous catheter, although there is the risk of the latter becoming blocked or infected.

Managing diet and mineral/bone disease in CKD

Dietary manipulation is a mainstay of CKD therapy in human⁵⁰ and veterinary patients. Renal formulated diets are restricted in both protein and phosphorus, but other features include an increased calorie density, sodium restriction, potassium supplementation, alkalisation, and supplementation with B vitamins, antioxidants and omega-3 fatty acids.

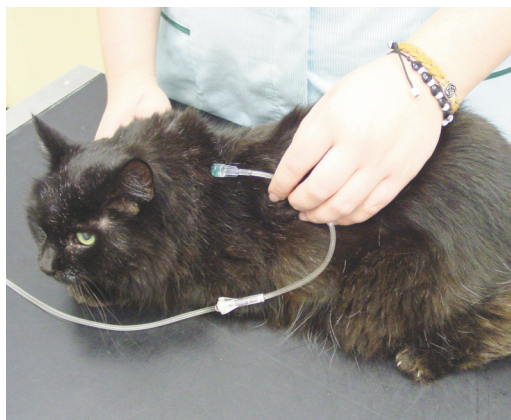


Figure 9 Subcutaneous fluid therapy can be used on an outpatient basis or by owners at home. *Courtesy of Sarah Caney*

Renal diets have been shown to significantly prolong longevity of cats with CKD.



Figure 10 Muscle wasting and dehydration in a cat with CKD. Careful attention to body condition, muscle mass and caloric intake is important. *Courtesy of Jessica Quimby*

Protein and phosphate restriction

Quality of evidence as an intervention

- ✦ Increased longevity: GOOD
- ✦ Improved QoL: GOOD

Protein restriction and phosphate restriction are considered together as they are the main features of commercial renal diets, and are thought to confer the major benefits seen. Feline renal diets typically contain 6–7 g of protein per 100 kcal (above the 5 g/100 kcal recommended allowance for adult cats,⁵¹ but below the 9–10 g/100 kcal commonly seen in maintenance diets). Energy requirements of older (>13 years) cats may increase and severe protein restriction may lead to loss of lean tissue;⁵² thus moderate protein restriction is recommended in CKD, together with monitoring of lean body mass, weight and caloric intake (Figure 10). In addition to protein restriction, renal diets contain much less phosphate compared with typical maintenance diets.^{53,54}

In cats with CKD, renal diets have been shown to reduce clinical signs of uraemia,^{55–57} and to significantly prolong longevity (see Table 3), providing a strong rationale for their use.

Table 3 Studies evaluating effect of renal diets on longevity

Study	Reported median survival time (days, all-cause mortality)	
	Normal diet	Renal diet
Elliott et al ⁵⁵	264	633
Plantinga et al ⁵⁴	210	480
Ross et al ⁵⁶	~730	Not reached

Differentiating the effects of protein and phosphate restriction is complex and not always possible, but while moderate protein restriction is thought to help reduce signs of uraemia, there is little evidence that this alone has a major effect on progression of CKD.^{58–60} Conversely, hyperphosphataemia is known to be associated with progression of CKD,^{42,44,45} and phosphate restriction may reduce the severity of renal pathology in CKD,^{53,61} thus phosphate restriction is thought to be mainly responsible for the improved longevity seen. Furthermore, renal secondary hyperparathyroidism (which may contribute to uraemia and disease progression) can be seen prior to the development of overt hyperphosphataemia or azotaemia,³⁴ and phosphorus-restricted diets reduce hyperphosphataemia, hyperparathyroidism and FGF-23 (which may indirectly promote hyperparathyroidism).^{55–57,62,63}

Panel recommendations: dietary intervention

The Panel strongly recommends the feeding of a commercial renal diet in all cats with azotaemic (stages 2–4) CKD. Where possible, this diet should be fed exclusively but the overall nutrition of the cat should not be compromised. Feeding a wet rather than dry diet to increase water intake is also recommended. Appropriate home-prepared diets⁶⁴ (see box below) may be an alternative if a commercial diet is not accepted.

Changing and transitioning diets

Renal diets are generally less palatable than maintenance diets (probably at least partially due to their lower protein content). This can lead to poor acceptance of these diets,^{24,65} a problem that may be exacerbated by inappetence in cats with more advanced CKD.

Panel recommendations: transitioning cats to a renal diet

- ✦ Although the point at which dietary intervention produces benefits has not been determined, the diet should be introduced as early as possible in stage 2 CKD (before the cat's appetite is affected by the disease)
- ✦ Gradual transition to the new diet will increase its acceptance – this may be achieved by providing the new diet in the same bowl, side by side, next to the old food,⁶⁶ or by mixing the old and new food together. The amount of the old food is then gradually decreased while the new food is increased over several (eg, 4–8) weeks
- ✦ To avoid food aversion, medications should be administered via an alternative, palatable food
- ✦ Feeding home-prepared diets can improve palatability, but these must be balanced for the desired nutrient requirements by a veterinary nutritionist⁶⁴
- ✦ A diet change should not be introduced to the cat while it is hospitalised or clinically unwell (eg, nauseous), to avoid development of food aversion
- ✦ Maintaining caloric intake is the highest priority in CKD and the preferred choice of diet is generally in the following order: wet renal > dry renal > home-prepared renal diet > wet senior > dry senior > wet maintenance > dry maintenance. Senior diets generally have lower protein (and phosphate) than adult maintenance diets but, in the absence of a renal diet, earlier intervention with a phosphate binder may be necessary (see Table 4).
- ✦ Feeding tubes (oesophagostomy or gastrostomy) can be valuable in both short- and long-term maintenance of nutrition and hydration in some cats with CKD

Table 4 Some common oral phosphate binders used in cats

Medication	Initial total daily dose*	Possible adverse effects
Aluminium hydroxide/carbonate	90 mg/kg	Constipation
Calcium carbonate	90 mg/kg	Hypercalcaemia
Calcium acetate	60–90 mg/kg	Hypercalcaemia
Iron, starch, sucrose complex	0.25–0.5 g/day	Little data available
Sevelamer	90–160 mg/kg	Constipation, impaired vitamin absorption, metabolic acidosis
Lanthanum	30–90 mg/kg	Vomiting

*For all phosphate binders, it is important to split the daily dose and give it mixed with food or at the same time that the cat eats. Doses may have to be increased to achieve the desired effect

Use of phosphate binders

Quality of evidence as an intervention

- ✦ Increased longevity: No data, but likely to be GOOD, based on dietary phosphate restriction
- ✦ Improved QoL: No data

As CKD progresses, serum phosphate tends to increase and may become more refractory to control with dietary phosphate restriction. Where diet alone is insufficient, the use of intestinal phosphate binders is important. Several agents can be used for this purpose (see Table 4).^{53,67–69} There are no studies comparing different phosphate binders in cats with CKD, but all are likely to be efficacious.⁵³ Offering alternative binders when needed may be appropriate, as palatability of the phosphate binders varies.^{69,70} If calcium-containing phosphate binders are used, monitoring of serum calcium (ideally ionised) is recommended, as hypercalcaemia is occasionally seen as an adverse event.⁵³

Where cats cannot be transitioned to a commercial or home-prepared renal diet with restricted phosphate, phosphate binders can be used with a maintenance diet, but their efficacy is likely to be compromised by the quantity of phosphate in the diet.

Panel recommendations: phosphate binders

Serum phosphate should be monitored in cats with CKD, and a phosphate-restricted diet should be used in all cats with azotaemic CKD (stages 2–4). If a commercial or home-prepared renal diet cannot be used, or is insufficient to control serum phosphate, phosphate binders should be used (given with food), the response monitored (eg, 1 month after medication change), and the dose adjusted accordingly. Although not subjected to clinical testing, the Panel suggests adopting the target serum phosphate concentrations recommended by IRIS:⁷¹

- ❖ Stage 2 disease: 0.9–1.45 mmol/l (3–4.5 mg/dl)
- ❖ Stage 3 disease: 0.9–1.6 mmol/l (3–5 mg/dl)
- ❖ Stage 4 disease: 0.9–1.9 mmol/l (3–6 mg/dl)

Managing serum calcium

Hypercalcaemia is a recognised cause of renal injury, but CKD can also cause changes in serum calcium, although these are generally mild. Ionised hypocalcaemia appears to be most common, and tends to be seen in advanced CKD.⁷² An increased calcium–phosphorus product has been linked with disease severity in cats.⁷³

Panel recommendations: serum calcium

An increased calcium–phosphorus product in CKD is usually caused by hyperphosphataemia, but cats at risk of hypercalcaemia (eg, those receiving calcium-containing phosphate binders or calcitriol) should have serum calcium monitored, ideally by measuring ionised calcium. If ionised hypercalcaemia develops, maintaining hydration is important and it may be necessary to reduce the dose of any phosphate binder.

Calcitriol therapy

Quality of evidence as an intervention

- ❖ Increased longevity: No evidence of benefit
- ❖ Improved QoL: No evidence of benefit

Calcitriol (active vitamin D) deficiency may occur with CKD due to various mechanisms including hyperphosphataemia-mediated

Dietary intervention is a mainstay therapy, and should be introduced early in stage 2 CKD.



inhibition of hydroxylation and loss of renal tissue. Calcitriol supplementation can potentially help suppress renal secondary hyperparathyroidism and has been shown to be beneficial in dogs and humans;⁷⁴ but despite anecdotal reports of improved QoL, low dose calcitriol has not been shown to have the same benefits in feline CKD.⁷⁵ Additionally, formulations of calcitriol can make accurate dosing difficult in cats. Hyperphosphataemia should also be carefully controlled when using this therapy to avoid increasing the serum calcium–phosphate product.

Panel recommendations: calcitriol

Based on current evidence (a single published study⁷⁵), calcitriol therapy cannot be recommended for cats with CKD, but further studies are needed as therapy has been shown to be helpful in other species.

Managing potassium

Quality of evidence as an intervention

- ❖ Increased longevity: No data
- ❖ Improved QoL: GOOD, if symptomatic with hypokalaemia

Feline CKD can lead to excessive kaliuresis, which may be compounded by reduced potassium intake, vomiting and transcellular shifts.^{55,76} Hypokalaemia may cause or contribute to clinical signs such as lethargy, inappetence, constipation and muscle weakness, and may contribute to development of acidosis, but has not been identified as a risk factor for disease progression or outcome.^{42,44,45}

Although renal diets are typically supplemented with potassium, hypokalaemia may still be seen in some cats. Conversely, hyperkalaemia may occasionally be seen in advanced CKD.

Panel recommendations – potassium

Serum potassium (K) should be routinely monitored in cats with CKD. Supplementation with potassium gluconate (or citrate) is recommended if serum K is <3.5 mmol/l (<3.5 mEq/l), at a typical starting dose of 1–4 mmol (1–4 mEq) K per cat q12h, adjusted according to response. Supplementation may be started earlier, when serum K is 3.5–3.9 mmol/l (3.5–3.9 mEq/l), but the clinical benefits of this are uncertain.

Managing acid–base balance

Quality of evidence as an intervention

✦ Increased longevity:

No data

✦ Improved QoL:

No data

Metabolic acidosis is multifactorial in CKD⁷⁷ and bicarbonate therapy has been shown to improve nutrition (calorie and protein intake, lean body mass) and slow progression in humans with CKD.⁷⁸ Metabolic acidosis has been reported to occur in over half of cats with advanced (stage 4) CKD.^{79,80} However, cats fed commercial renal diets may have higher serum bicarbonate concentrations.⁵⁶

Panel recommendations: acid–base balance

Feeding a renal diet formulated to minimise acidosis, and maintaining good hydration, are likely to be beneficial in preventing clinically significant metabolic acidosis in cats with CKD. Additional therapy is rarely needed, but if clinical concerns exist and blood bicarbonate or total CO₂ concentrations are <16 mmol/l, oral supplementation with potassium citrate (40–75 mg/kg q12h as a starting dose) may be used, aiming to maintain a blood bicarbonate or total CO₂ in the range of 16–24 mmol/l.

Other nutrients

Quality of evidence as an intervention

✦ Increased longevity:

No data

✦ Improved QoL:

No data

One retrospective study suggested that renal diets with the highest omega-3 fatty acid content were associated with the longest survival times.⁵⁴ However, a causal relationship could not be established, and feeding a renal diet may not alter fatty acid profiles.⁸¹

Dietary sodium restriction is recommended for people with CKD to mitigate hypertension and other effects,⁸² but evidence for a beneficial effect in older cats, with and without CKD, is generally lacking, and very restricted sodium intake may be deleterious.^{83–86}

Cats with CKD have evidence of increased oxidative stress compared with healthy cats,^{87,88} and dietary antioxidant therapy (with vitamins E, C and beta-carotene) may reduce this.⁸⁹ Whether this results in any renoprotective effect remains to be determined.

Other dietary supplements, including Chinese rhubarb (*Rheum officinale*) and a prebiotic/probiotic combination, have not shown any beneficial effects.^{90,91}

Panel recommendations: other nutrients

The feeding of commercial renal diets to cats with CKD may have benefits beyond protein and phosphate restriction including minimising risks of hypokalaemia, acidosis and oxidative stress, and increasing essential fatty acid and water-soluble vitamin intake. The potential benefits of some of these effects in CKD have not been critically assessed.

Managing hypertension in CKD

Quality of evidence as an intervention

✦ Increased longevity:

No evidence of benefit

✦ Improved QoL:

GOOD, if symptomatic with hypertension

Systemic hypertension associated with CKD has a reported prevalence of 19–40% in primary care practices,^{36,92} and as high as 65% in referral populations.⁹³ The pathogenesis is not entirely clear, with some cats demonstrating activation of the renin–angiotensin–aldosterone system (RAAS),^{94–96} and some having apparent autonomous hyperaldosteronism.^{96,97} Doppler and high-definition oscillometry are the most reliable non-invasive blood pressure measurement techniques in conscious cats.^{98–105} However, even when cats are calm, and a standardised protocol is followed,¹⁰⁵ measurements will vary with the equipment, the operator, the cat and the circumstances.^{36,106–111} Current non-invasive techniques are inaccurate for assessing diastolic blood pressure in cats.^{101,104} Within these limitations, hypertension is usually defined as an SBP persistently >160–180 mmHg,^{36,112} but has also been defined according to the perceived risk of target organ damage (TOD) (see box on page 221 and Table 5).^{27,105} Target organs are those particularly susceptible to hypertensive damage – the eyes,^{93,107,113} heart,^{114–116} cerebrovascular tissue^{113,117} and kidneys. While hypertension is an independent risk factor for progressive CKD in dogs and people,^{118,119} this has not been proven in cats.^{37,116,117,120} However,

Table 5 Blood pressure categories according to risk of target organ damage (TOD) ^{27,105}		
SBP (mmHg)	Risk of TOD	Treatment
<150	Minimal	No treatment advised
150–159	Mild	No treatment advised
160–179	Moderate	Treatment advised if TOD is present Cats with CKD are assumed to have TOD
≥180	Severe	Treatment indicated
SBP = systolic blood pressure		

Table 6 Suggested oral therapy for systemic hypertension

Drug	Dose	Comments
Amlodipine (calcium channel blocker)	0.0625–0.25 mg/kg q24h	Licensed for feline use in some countries. Good efficacy in several studies. Licensed dose in Europe is 0.125–0.25 mg/kg q24h; dose can be doubled (up to 0.5 mg/kg q24h) if needed ¹²⁷
Telmisartan (ARB)	1–3 mg/kg q24h	Licensed for feline use in some countries as an antiproteinuric agent at 1 mg/kg. Clinical efficacy as antihypertensive uncertain, but higher doses appear to have some efficacy in experimental studies
Benazepril (ACEI)	0.25–0.5 mg/kg q24h	Limited effect on blood pressure used alone; best considered as adjuvant therapy in refractory cases. Dose can be doubled to 0.5–1.0 mg/kg q24h if needed
Propranolol Atenolol (beta-blockers)	2.5–5.0 mg/cat q8h 6.25–12.5 mg/cat q12h	Limited effect on blood pressure used alone; best considered as adjuvant therapy in refractory cases

ARB = angiotensin receptor blocker; ACEI = angiotensin-converting enzyme inhibitor

hypertension is associated with the severity of proteinuria (as in people and dogs),^{37,120–122} which can be reduced with successful antihypertensive therapy.^{37,120,123}

Management of hypertension is aimed at preventing TOD, although the current perceived risk categories (Table 5) are imprecise as data are lacking, risks may vary between individuals and may, for example, depend on how rapidly blood pressure rises. In general, treatment aims to reduce SBP to <150–160 mmHg.^{27,105}

Monotherapy with angiotensin-converting enzyme inhibitors (ACEIs) or atenolol is not effective in most hypertensive cats.^{95,105,112,124,125} There is some experimental data to suggest the ARB telmisartan at 3 mg/kg q24h may be more effective than benazepril as an anti-hypertensive agent,¹²⁶ but further clinical studies are needed. Conversely, the calcium channel blocker amlodipine is an effective monotherapy for most (but not all) cats,^{97,112,113,115,120,127,128} and may be combined with other drugs if adjuvant therapy is needed (Table 6).

Panel recommendations: hypertension

There is a strong association between CKD and hypertension, and cats diagnosed with CKD may subsequently develop hypertension.³⁶ As hypertension has important clinical implications, blood pressure assessment should be part of the routine evaluation of all cats with suspected or proven CKD. Currently amlodipine is the treatment of choice in cats, but other drugs may be helpful, especially in cats refractory to amlodipine therapy. Cats with hypertension (eg, sustained SBP >160 mmHg) should be treated and monitored, with the aim of reducing SBP to <150–160 mmHg.



Complications such as hypertension, anaemia and proteinuria are common and often associated with disease progression or a poor quality of life.



Figure 11 Anaemia is a recognised risk factor for progression of CKD. Courtesy of Cathy Langston

Managing anaemia in CKD

Quality of evidence as an intervention

✦ Increased longevity:	POOR
✦ Improved QoL:	GOOD, if symptomatic with anaemia

Anaemia of varying severity is seen in 30–65% of cats with CKD³⁸ (Figure 11). A relative lack of erythropoietin (EPO) in CKD produces a non- or poorly-regenerative anaemia, which may be exacerbated by blood loss and/or shortened red blood cell (RBC) survival.¹²⁹ Anaemia has been identified as a dependent or independent risk factor for progression of CKD,^{42–45} and there is evidence that treatment with erythrocyte-stimulating agents (ESAs) may improve QoL and potentially survival in some cats with CKD.¹²⁹

Blood transfusions and haemoglobin-based oxygen carrying solutions (eg, Oxyglobin; Dechra Veterinary Products) have limited value for the chronic anaemia associated with CKD,^{130,131} and the use of anabolic steroids is not recommended due to lack of evidence of efficacy and potential adverse events.^{132,133} In contrast, the use of ESAs (EPO or EPO analogues) has become the standard of care in human medicine.

ESA therapy is designed to elevate the packed cell volume (PCV) to around the lower limit of the reference interval – sufficient to meet tissue oxygen demand. Iron supplementation alone is not effective in managing CKD-associated anaemia, but it enhances the efficacy of ESA therapy in humans,¹³⁴ and anecdotal evidence suggests the same is true in cats.

Table 7 Clinical use of human epoetin alfa or darbepoetin alfa in cats with CKD

Drug	Initial therapy	Maintenance therapy	Efficacy studies in CKD anaemia	Adverse events ^{135,136}
Epoetin alfa	100 U/kg SC 3 x weekly Until PCV $\geq$ 25%	50–100 U/kg SC 1–2 x weekly Based on PCV	Effective for cats and dogs ¹³⁷	Systemic hypertension (40–50%) Seizures (2–10%) Polycythemia (unlikely) Injection site discomfort Skin reactions (redness) PRCA (25–40%)*
Darbepoetin alfa	1 μ g/kg SC 1 x weekly Until PCV $\geq$ 25%	1 μ g/kg SC q2–3 weeks; or Lower dose (eg, 0.5 μ g/kg) weekly Based on PCV	Effective in cats Response tends to occur in 2–3 weeks ¹³⁵	Similar adverse event profile to EA but lower incidence of PRCA (<10%)*, so a better choice for therapy in cats

*Anti-erythropoietin antibodies are produced and PRCA manifests as worsening anaemia, lack of erythrocytosis, and no response to ESA therapy. Diagnosis is supported by a bone marrow aspirate/core and cats become transfusion-dependent for months.¹³⁷ SC = subcutaneously; PCV = packed cell volume; PRCA = pure red cell aplasia

The two ESAs most widely used in cats are recombinant human epoetin alfa (EA, ~80% homology to feline EPO) and darbepoetin alfa (DA, a hyperglycosylated recombinant human EPO analogue). Although often successful, in one study, >40% of cats with CKD-associated anaemia failed to respond or failed to develop a sustained response to ESA therapy.¹³⁵ Potential reasons for this include:^{129,135}

- ❖ Concurrent illnesses (present in most cats that fail to respond to ESA);
- ❖ Infections or inflammation;
- ❖ Gastrointestinal bleeding;
- ❖ Iron deficiency;
- ❖ Pure red cell aplasia (PRCA) from production of anti-EPO antibodies (Table 7).

Hypertension is also recognised as an adverse effect of ESA therapy, affecting up to 50% of treated cats.^{129,135}

Panel recommendations – anaemia

ESA therapy should be considered in cats:

- ❖ With persistent CKD-associated anaemia that is symptomatic; or
- ❖ If the PCV is persistently <20%.

The use of DA is preferred over EA as it appears significantly less likely to induce PRCA.¹³⁵ The target for therapy should be a PCV of $\geq$ 25%. Irrespective of the ESA used, iron supplementation is generally recommended to ensure iron deficiency does not contribute to the anaemia:

- ❖ Iron dextran: 50 mg IM per cat at the start of ESA therapy, repeated monthly as needed; or
- ❖ Oral iron supplements (ferrous sulfate): 50–100 mg/cat per day (less ideal)

For cats receiving ESA therapy, PCV, reticulocyte count and blood pressure should be routinely monitored:

- ❖ Weekly until target PCV is reached;
- ❖ At every tapering of ESA dosage;
- ❖ Every 1–3 months once lowest effective dosage is reached¹²⁹

If response to therapy is poor, iron status (serum iron, ferritin and total iron binding capacity) should be verified and the patient reassessed for concomitant disease.^{129,135}

Treatment with erythrocyte-stimulating agents may improve quality of life and potentially survival.



Managing proteinuria in CKD

Quality of evidence as an intervention

- ❖ Increased longevity: No evidence of benefit, although magnitude of proteinuria linked to survival
- ❖ Improved QoL: POOR

In human medicine, regardless of the cause of CKD, the severity of proteinuria at the time of diagnosis is an important prognostic indicator, and controlling proteinuria results in slower progression of CKD, largely irrespective of the underlying cause of the CKD.¹³⁸ CKD is generally associated with increased intraglomerular capillary pressure and other changes that impair glomerular permselectivity, leading to increased loss of albumin (and other proteins) into tubular fluid; this appears to directly contribute to disease progression by promoting tubular inflammation and fibrosis.¹³⁸

Although there may be species differences in pathophysiology, increased proteinuria in cats with CKD (assessed with UPCr and not routine dipsticks, which are inappropriate for assessment of feline proteinuria^{139,140}) is also known to carry a poorer prognosis.^{37,42,44,120,123} In one study,³⁷ cats with a UPCr <0.2 were reported to have a median survival time of ~1000 days compared with ~500 days for those with a UPCr of 0.2–0.4, and ~400 days for those with a UPCr >0.4. Very similar findings have also been reported elsewhere.¹²⁰ Currently, there is no evidence that measurement of UACr rather than UPCr offers any benefits in cats,^{37,141} but the urinary proteome in healthy cats and cats with CKD is complex and more studies are needed.^{142–146}

In humans, treatment with angiotensin receptor blockers (ARBs) or ACEIs is effective in blocking RAAS activation, decreasing glomerular capillary pressure, restoring glomerular permselectivity, reducing proteinuria and slow-

ing the progression of CKD.^{138,147–149} These effects are partly as a result of haemodynamic changes and partly through modifying non-haemodynamic remodelling in the kidney.¹⁵⁰

The existing IRIS²⁷ CKD (see box on page 221) and American College of Veterinary Internal Medicine (ACVIM) proteinuria¹⁵¹ guidelines suggest cats should be classified as:

- ❖ Overtly proteinuric: UPCR >0.4
- ❖ Borderline proteinuric: UPCR 0.2–0.4
- ❖ Non-proteinuric: UPCR <0.2

Using these criteria, around 50–66% of cats with CKD are likely to be non-proteinuric and around 20% overtly proteinuric.^{37,42}

In cats with CKD, RAAS inhibition with the ACEI benazepril has been shown to significantly reduce the severity of proteinuria.^{152–154} More recently, the ARB telmisartan has been licensed in some countries for the management of proteinuric feline CKD. In a large multicentre European study of telmisartan in cats with naturally occurring CKD it was shown to significantly decrease proteinuria at all time points during the 6 months of the study.¹⁵⁵ However, a survival benefit from RAAS blockade in cats has not been demonstrated.^{152,153} The reasons for the lack of effect on survival are uncertain but may include:

- ❖ Underpowered clinical trials;
- ❖ Inadequate duration of clinical trials;
- ❖ Differences in the pathophysiology between humans and cats with CKD (eg, proteinuria could be a marker of tubular dysfunction in cats rather than a cause of progressive disease);
- ❖ Differences in the prevalence or severity of proteinuria between humans and cats with CKD;
- ❖ Inadequate control of proteinuria and/or inappropriate targets for antiproteinuric therapy (while benazepril therapy significantly reduced UPCR in CKD cats compared with placebo in clinical trials, these studies also showed little overall reduction in the UPCR from baseline values within the treatment group^{152,153}).

Further investigations are needed to assess the role of RAAS inhibition in feline CKD and to determine optimal therapy, but currently both ARBs and ACEIs are available and used in cats, and are licensed in some countries (Table 8). There is some (weak) evidence that RAAS blockade may have more beneficial

Panel recommendations: proteinuria

Based on their ability to significantly reduce proteinuria in feline CKD, their modification of renal haemodynamics¹²⁵ and the potential (though yet unproven) beneficial effect this may have, the Panel suggests RAAS inhibition should be considered in non-dehydrated cats with stable CKD where the UPCR is persistently >0.4. Note that:

- ❖ As CKD cats with a UPCR of 0.2–0.4 have a much poorer prognosis than those with a UPCR <0.2, there is also a logical rationale in the decision of some clinicians to institute therapy where UPCR is persistently >0.2;
- ❖ Because the benefits of RAAS blockade have not yet been proven in cats, currently other treatments with proven benefits should have a higher priority if treatment choices need to be made.

As treatment of hypertension can reduce proteinuria,¹²⁰ the need for additional antiproteinuric therapy should be assessed after appropriate antihypertensive therapy in cats with high blood pressure.

Adverse effects of RAAS inhibition are uncommon in cats with stable, well-compensated CKD, but greater care should be taken in patients with more advanced (eg, stage 4) CKD. Potential complications include worsening of azotaemia, reduced blood pressure and (rarely) hyperkalaemia.¹²⁵ The Panel recommends that in addition to clinical signs, urea, creatinine and blood pressure should be monitored 5–7 days after starting therapy or following dose adjustments, and any increase in creatinine of >15–20% should prompt further evaluation and/or cessation of or reduction in therapy. Additionally, the higher risks of acute kidney injury with the concomitant use of both an ACEI or ARB and a non-steroidal anti-inflammatory drug (NSAID) means this combination should be used with caution or avoided in cats with CKD based on a risk:benefit analysis.

effects (possibly on survival, QoL and appetite) in CKD cats with more severe proteinuria (eg, UPCR ≥1.0),¹⁵² and currently IRIS and ACVIM guidelines^{71,151} suggest antiproteinuric therapy should be instituted in CKD cats with a UPCR >0.4.

Managing inappetence, nausea and vomiting in CKD

Quality of evidence as an intervention

- ❖ Increased longevity: No data
- ❖ Improved QoL: Likely to be GOOD if cat is symptomatic

Cats with CKD can suffer from nausea, vomiting and inappetence as a result of uraemic toxins affecting the central chemoreceptor trigger zone. Inappetence is a significant QoL concern for owners,¹⁵⁶ and in the CKD patient could result in protein and calorie malnutrition with its many adverse consequences.¹⁵⁷ A reduced appetite should therefore be actively managed, along with complications of CKD that can contribute to inappetence, such as dehydration, hypokalaemia, acidosis and anaemia. Centrally acting antiemetics such as

Table 8 Suggested oral therapy for managing proteinuria

Drug	Dose
Telmisartan (ARB)	1 mg/kg q24h
Benazepril (ACEI)	0.25–0.5 mg/kg q12h

ARB = angiotensin receptor blocker;
ACEI = angiotensin-converting enzyme inhibitor

Table 9 Suggested therapy for managing inappetence, nausea and vomiting

Drug	Dose
Maropitant (neurokinin-1 receptor antagonist)	1 mg/kg q24h SC/IV 2 mg/kg q24h PO
Mirtazapine (tetracyclic antidepressant, alpha-2 antagonist)	~0.5 mg/kg (or 1.88 mg/cat) q48h PO
Ondansetron (5-HT ₃ receptor antagonist)	0.5–1.0 mg/kg q6–8h SC
Dolasetron (5-HT ₃ receptor antagonist)	1.0 mg/kg q24h SC
Famotidine (H ₂ blocker)	0.5–1 mg/kg q12–24h PO
Omeprazole (proton pump inhibitor)	0.5–1 mg/kg q12–24h PO

SC = subcutaneously; IV = intravenously; PO = orally

maropitant, mirtazapine, ondansetron and dolasetron^{158–160} should be considered for management (Table 9). In placebo-controlled trials of cats with stage 2 or 3 CKD, maropitant (given orally for 2 weeks) was shown to reduce vomiting,¹⁶⁰ and mirtazapine (given orally for 3 weeks) reduced vomiting and also increased appetite and weight.¹⁵⁸ Mirtazapine may therefore be a useful adjunct to the nutritional management of cats with CKD.

There are anecdotal reports of H₂ blockers or proton pump inhibitors alleviating inappetence in some feline CKD patients, but the presence and degree of gastric hyperacidity and efficacy of these medications remain unproven. Additionally, although hypergastrinaemia has been reported in feline CKD,¹⁶¹ gastric ulceration has generally not been observed or reported.^{73,162} If therapy for hyperacidity in cats is considered, omeprazole appears to be superior to famotidine.¹⁶³

Panel recommendations: inappetence, nausea and vomiting

Vomiting should be actively managed in cats with CKD and nausea should always be considered as a potential contributory cause in cats with inappetence. Based on available evidence, centrally acting antiemetics are likely to be most valuable, and the use of mirtazapine may have additional benefits.

If cats remain too nauseous or unwell to maintain sufficient voluntary food intake despite appropriate treatment, placement of an enteral feeding tube (eg, oesophagostomy [Figure 12] or gastrostomy) should be considered, and anecdotal reports suggest these can be valuable in maintaining food and fluid intake in some cats with CKD.



Figure 12 Enteral (oesophagostomy) tube in place to support food and fluid intake. Courtesy of Isuru Gajanayake

Managing UTIs in CKD

Quality of evidence as an intervention

✦ Increased longevity:	No evidence of efficacy
✦ Improved QoL:	Likely to be GOOD if cat is symptomatic

Bacterial UTIs in cats with CKD occur at a reported frequency of around 15–30%,^{39,164–166} with older female cats having an increased risk.³⁹

Most (>70%) of these UTIs appear to be subclinical (ie, without lower urinary tract signs [LUTS]), although >85% show changes on urine sediment analysis (>5 white blood cells [WBCs]/hpf, and/or >5 RBCs/hpf, and/or microscopic bacteriuria).³⁹ *Escherichia coli* represents 60–75% of isolates, while other organisms include *Enterococcus*, *Streptococcus*, *Staphylococcus*, *Enterobacter*, *Pseudomonas* and *Klebsiella* species.

The presence of LUTS or detection of pyuria (≥5 WBCs/hpf) in routine urinalysis of CKD patients are indications for bacterial culture of a cystocentesis sample, but whether routine culture of all urine samples should be recommended is controversial, as the significance of subclinical bacteriuria is uncertain. While some clinicians advocate routine treatment of all CKD-associated UTIs (as cats may be at risk for pyelonephritis and deterioration of CKD), recurrent or recrudescing UTIs are common after treatment,³⁹ the presence of subclinical UTIs has not been associated with disease severity or apparent survival,³⁹ and unnecessary treatment may risk development of bacterial resistance.

When treated, UTIs should be managed according to international guidelines,¹⁶⁷ selecting antibacterials based on sensitivity testing (note that boric acid tubes should be avoided for urine cultures¹⁶⁸) that are excreted unchanged in urine and have a wide therapeutic index (Table 10). If initial empirical therapy is needed, amoxicillin (11–15 mg/kg PO q8h)¹⁶⁷ or potentiated amoxicillin¹⁶⁹ are appropriate choices; 2–4 weeks' therapy has

Panel recommendations: UTIs

Treatment of UTIs in cats with CKD should be considered when there is a positive urine culture and where:

- ✦ LUTS are present; and/or
- ✦ Systemic signs are present (eg, pyrexia, neutrophilia, left shift, abdominal pain); and/or
- ✦ Pyuria is present (>5 WBCs/hpf); and/or
- ✦ When there is an unexplained deterioration in renal function.

Whether other subclinical UTIs should be treated remains controversial and requires further investigation, but it may be more appropriate to monitor cats than intervene at initial diagnosis.

Table 10 Considerations when selecting an antibacterial to treat urinary tract infections in cats with CKD

Consideration	Action	Antibacterials
Probably safe	No dose adjustment required, due to wide therapeutic index or excretion via extrarenal routes	Chloramphenicol Penicillins (including clavulanate)
Consider dosage adjustment	Adjust dose in moderate or severe CKD (IRIS stages 3 and 4)	Cephalosporins (most)* Fluoroquinolones† Sulphonamides (± trimethoprim)
Hazardous, avoid if possible	Accumulation of drug or its metabolites in CKD can increase risk of adverse events	Nalidixic acid Nitrofurantoin Tetracyclines‡ (except doxycycline)
Nephrotoxic	Avoid – high-risk drugs will exacerbate CKD	Aminoglycosides Polymyxins

*Some cephalosporins accumulate in renal tubular cells and can cause damage
†Avoid enrofloxacin in cats with CKD due to increased risk of retinopathy at standard therapeutic doses
‡Water soluble tetracyclines (eg, oxytetracycline) depend partly on renal excretion. Tetracyclines also increase protein catabolism, and breakdown products of oxytetracycline have been shown to be nephrotoxic
IRIS = International Renal Interest Society

been recommended,¹⁶⁷ although optimum duration of therapy for CKD-associated UTIs is uncertain.¹⁷⁰ Response to treatment should be monitored with repeat culture 7 days after cessation of treatment.

Other treatments

Anabolic steroids

Information regarding the efficacy of anabolic steroids for cats with CKD is lacking and, as hepatotoxicity has been reported,¹³³ their use is not currently recommended.

Stem cell therapy

Pilot studies investigating stem cell therapy for feline CKD have not to date demonstrated beneficial effects; and with some techniques adverse effects occur.^{171,172}

Consequently, this treatment is not currently recommended.

Renal transplantation

Kidney transplants from living donors may be available to treat cats with CKD at specialist centres in some regions. This procedure has numerous implications including ethical, financial, welfare and monitoring considerations.^{173–176} While it may be viable in some patients, kidney transplantation is beyond the scope of these Guidelines.

Dialysis therapy

Haemodialysis or peritoneal dialysis are techniques that can be successfully applied to cats, although complications may arise. Their main indications are for management of acute kidney injury or acute on chronic kidney disease.^{177,178}

Specific therapeutic issues in cats with CKD

Adverse drug effects

Nephrotoxic drugs (eg, aminoglycosides, NSAIDs, antineoplastic agents) should be used with great care in cats with CKD and, depending on the drug and the stage of CKD, their use may be contraindicated. Decisions on therapy should be made on a case-by-case basis, assessing risks and benefits. There is, however, evidence that low dose (0.01–0.03 mg/kg) meloxicam, for example, is well tolerated long term for the management of osteoarthritis and pain in cats with stages 1–3 CKD.^{179–181}

Drugs that are primarily excreted in urine may accumulate in patients with CKD, leading to higher risks of adverse events; thus drugs primarily biotransformed by the liver or excreted by extrarenal routes (eg, benazepril,¹⁸² telmisartan¹⁸³) are preferred where possible. Nevertheless, the risk:benefit ratio of each treatment should be assessed,¹⁸⁴ and dose adjustments may help to mitigate risks.

Hyperthyroidism

Hyperthyroidism may contribute to the progression of CKD, and can also mask coexisting CKD as GFR increases in cats with hyperthy-

roidism.¹⁸⁵ Mild to moderate renal azotaemia becomes apparent after treatment of hyperthyroidism in ~15–40% of cats,¹⁸⁵ and hyperthyroid cats with pre-existing CKD have a much higher risk of renal decompensation than non-azotaemic cats.^{185,186} Hyperthyroidism is also frequently associated with significantly elevated parathyroid hormone concentrations that may potentially complicate existing CKD.¹⁸⁷ Conversely, iatrogenic hypothyroidism is also associated with a higher risk of azotaemia and reduced survival times.^{188,189}

In cats with pre-existing CKD, or where there are significant concerns over renal function, a thioureylene (methimazole, carbimazole) is the preferred initial treatment for hyperthyroidism, as its effects can be titrated and are reversible. Close monitoring of the cat's clinical condition, serum creatinine and thyroxine is required to tailor the dose for each patient. Starting doses can be titrated upward if the initial control of hyperthyroidism is inadequate, or downward if there is worsening of clinical signs of CKD or marked worsening of azotaemia.¹⁸⁶ In cats that can be successfully stabilised, definitive treatment for hyperthyroidism may be undertaken (eg, radioiodine therapy).

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CONFLICT OF INTEREST

Jonathan Elliott has acted as a paid consultant for CEVA Animal Health, Boehringer Ingelheim, Pfizer (now Zoetis), Bayer, Idexx, Novartis Animal Health, Waltham Centre for



Pet Nutrition and Royal Canin; he has research grant funding and contracts to work on kidney disease in cats from CEVA Animal Health, Orion, Zoetis, Royal Canin and Novartis Animal Health (now Elanco Animal Health).

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REFERENCES

- O'Neill DG, Church DB, McGreevy PD, et al. **Prevalence of disorders recorded in cats attending primary-care veterinary practices in England.** *Vet J* 2014; 202: 286–291.
- White JD, Norris JM, Baral RM, et al. **Naturally-occurring chronic renal disease in Australian cats: a prospective study of 184 cases.** *Aust Vet J* 2006; 84: 188–194.
- Marino CL, Lascelles BD, Vaden SL, et al. **Prevalence and classification of chronic kidney disease in cats randomly selected from four age groups and in cats recruited for degenerative joint disease studies.** *J Feline Med Surg* 2014; 16: 465–472.
- Lulich JP, Osborne CA, O'Brien TD, et al. **Feline renal failure: questions, answers, questions.** *Compen Contin Educ Pract Vet* 1992; 14: 127–152.
- O'Neill DG, Church DB, McGreevy PD, et al. **Longevity and mortality of cats attending primary care veterinary practices in England.** *J Feline Med Surg* 2015; 17: 125–133.
- McLeland SM, Cianciolo RE, Duncan CG, et al. **A comparison of biochemical and histopathologic staging in cats with chronic kidney disease.** *Vet Pathol* 2015; 52: 524–534.
- Chakrabarti S, Syme HM, Brown CA, et al. **Histomorphometry of feline chronic kidney disease and correlation with markers of renal dysfunction.** *Vet Pathol* 2013; 50: 147–155.
- Reynolds BS and Lefebvre HP. **Feline CKD: pathophysiology and risk factors – what do we know?** *J Feline Med Surg* 2013; 15 Suppl 1: 3–14.
- White JD, Malik R and Norris JM. **Feline chronic kidney disease: can we move from treatment to prevention?** *Vet J* 2011; 190: 317–322.
- Furuya T, Sassa Y, Omatsu T, et al. **Existence of feline morbillivirus infection in Japanese cat populations.** *Arch Virol* 2014; 159: 371–373.
- Furuya T, Wachi A, Sassa Y, et al. **Quantitative PCR detection of feline morbillivirus in cat urine samples.** *J Vet Med Sci* 2016; 77: 1701–1703.
- Woo PC, Lau SK, Wong BH, et al. **Feline morbillivirus, a previously undescribed paramyxovirus associated with tubulointerstitial nephritis in domestic cats.** *Proc Natl Acad Sci USA* 2012; 109: 5435–5440.
- DiBartola SP, Rutgers HC, Zack PM, et al. **Clinicopathologic findings associated with chronic renal disease in cats: 74 cases (1973–1984).** *J Am Vet Med Assoc* 1987; 190: 1196–1202.
- Bartlett PC, Van Buren JW, Bartlett AD, et al. **Case-control study of risk factors associated with feline and canine chronic kidney disease.** *Vet Med Int* 2010; 2010: 957570.
- Greene JP, Lefebvre SL, Wang M, et al. **Risk factors associated with the development of chronic kidney disease in cats evaluated at primary care veterinary hospitals.** *J Am Vet Med Assoc* 2014; 244: 320–327.
- Hughes KL, Slater MR, Geller S, et al. **Diet and lifestyle variables as risk factors for chronic renal failure in pet cats.** *Prev Vet Med* 2002; 55: 1–15.
- Jepson RE, Brodbelt D, Vallance C, et al. **Evaluation of predictors of the development of azotemia in cats.** *J Vet Intern Med* 2009; 23: 806–813.
- National Kidney Foundation. **Clinical practice guidelines for chronic kidney disease: evaluation, classification and stratification.** http://www2.kidney.org/professionals/KDOQI/guidelines_ckd/toc.htm (2002, accessed 4 August 2015).
- AAFP and AFM. **American Association of Feline Practitioners/Academy of Feline Medicine Panel Report on Feline Senior Care.** *J Feline Med Surg* 2005; 7: 3–32.
- Hoyumpa Vogt A, Rodan I, Brown M, et al. **AAFP-AAHA: feline life stage guidelines.** *J Feline Med Surg* 2010; 12: 43–54.
- Finch N. **Measurement of glomerular filtration rate in cats: methods and advantages over routine markers of renal function.** *J Feline Med Surg* 2014; 16: 736–748.
- Baral RM, Dhand NK, Morton JM, et al. **Bias in feline plasma biochemistry results between three in-house analysers and a commercial laboratory analyser: results should not be directly compared.** *J Feline Med Surg* 2015; 17: 653–666.
- Rishniw M and Bicalho R. **Factors affecting urine specific gravity in apparently healthy cats presenting to first opinion practice for routine evaluation.** *J Feline Med Surg* 2015; 17: 329–337.
- Adams LG, Polzin DJ, Osborne CA, et al. **Effects of dietary protein and calorie restriction in clinically normal cats and in cats with surgically induced chronic renal failure.** *Am J Vet Res* 1993; 54: 1653–1662.
- Minkus G, Reusch C, Hörauf A, et al. **Evaluation of renal biopsies in cats and dogs – histopathology in comparison with clinical data.** *J Small Anim Pract* 1994; 35: 465–472.
- Baral RM, Dhand NK, Freeman KP, et al. **Biological variation and reference change values of feline plasma biochemistry analytes.** *J Feline Med Surg* 2014; 16: 317–325.
- International Renal Interest Society. **IRIS staging of CKD.**

- <http://iris-kidney.com/guidelines/staging.aspx> (2013, accessed 4 August 2015).
- 28 Paepe D, Lefebvre HP, Concordet D, et al. **Simplified methods for estimating glomerular filtration rate in cats and for detection of cats with low or borderline glomerular filtration rate.** *J Feline Med Surg* 2015; 17: 889–900.
 - 29 Braff J, Obare E, Yerramilli M, et al. **Relationship between serum symmetric dimethylarginine concentration and glomerular filtration rate in cats.** *J Vet Intern Med* 2014; 28: 1699–1701.
 - 30 Hall JA, Yerramilli M, Obare E, et al. **Comparison of serum concentrations of symmetric dimethylarginine and creatinine as kidney function biomarkers in cats with chronic kidney disease.** *J Vet Intern Med* 2014; 28: 1676–1683.
 - 31 Koch A, Weiskirchen R, Bruensing J, et al. **Regulation and prognostic relevance of symmetric dimethylarginine serum concentrations in critical illness and sepsis.** *Mediators Inflamm* 2013; 2013: 413826.
 - 32 Ghys LF, Paepe D, Duchateau L, et al. **Biological validation of feline serum cystatin C: the effect of breed, age and sex and establishment of a reference interval.** *Vet J* 2015; 204: 168–173.
 - 33 Ghys LF, Paepe D, Lefebvre HP, et al. **The effect of feeding, storage and anticoagulant on feline serum cystatin C.** *Vet J* 2015; 206: 91–96.
 - 34 Finch NC, Syme HM and Elliott J. **Parathyroid hormone concentration in geriatric cats with various degrees of renal function.** *J Am Vet Med Assoc* 2012; 241: 1326–1335.
 - 35 Finch NC, Geddes RF, Syme HM, et al. **Fibroblast growth factor 23 (FGF-23) concentrations in cats with early nonazotemic chronic kidney disease (CKD) and in healthy geriatric cats.** *J Vet Intern Med* 2013; 27: 227–233.
 - 36 Bijsmans ES, Jepson RE, Chang YM, et al. **Changes in systolic blood pressure over time in healthy cats and cats with chronic kidney disease.** *J Vet Intern Med* 2015; 29: 855–861.
 - 37 Syme HM, Markwell PJ, Pfeiffer D, et al. **Survival of cats with naturally occurring chronic renal failure is related to severity of proteinuria.** *J Vet Intern Med* 2006; 20: 528–535.
 - 38 Elliott J and Barber PJ. **Feline chronic renal failure: clinical findings in 80 cases diagnosed between 1992 and 1995.** *J Small Anim Pract* 1998; 39: 78–85.
 - 39 White JD, Stevenson M, Malik R, et al. **Urinary tract infections in cats with chronic kidney disease.** *J Feline Med Surg* 2013; 15: 459–465.
 - 40 Geddes RF, Finch NC, Elliott J, et al. **Fibroblast growth factor 23 in feline chronic kidney disease.** *J Vet Intern Med* 2013; 27: 234–241.
 - 41 Boyd LM, Langston C, Thompson K, et al. **Survival in cats with naturally occurring chronic kidney disease (2000–2002).** *J Vet Intern Med* 2008; 22: 1111–1117.
 - 42 King JN, Tasker S, Gunn-Moore DA, et al. **Prognostic factors in cats with chronic kidney disease.** *J Vet Intern Med* 2007; 21: 906–916.
 - 43 Geddes RF, Elliott J and Syme HM. **Relationship between plasma fibroblast growth factor-23 concentration and survival time in cats with chronic kidney disease.** *J Vet Intern Med* 2015; 29: 1494–1501.
 - 44 Chakrabarti S, Syme HM and Elliott J. **Clinicopathological variables predicting progression of azotemia in cats with chronic kidney disease.** *J Vet Intern Med* 2012; 26: 275–281.
 - 45 Kuwahara Y, Ohba Y, Kitoh K, et al. **Association of laboratory data and death within one month in cats with chronic renal failure.** *J Small Anim Pract* 2006; 47: 446–450.
 - 46 Langston C. **Managing fluid and electrolyte disorders in renal failure.** *Vet Clin North Am Small Anim Pract* 2008; 38: 677–697.
 - 47 Polzin DJ. **Chronic kidney disease.** In: Bartges J and Polzin DJ (eds). *Nephrology and urology of small animals*. Ames: Blackwell Publishing, 2011, pp 431–471.
 - 48 Seefeldt SL and Chapman TE. **Body water content and turnover in cats fed dry and canned rations.** *Am J Vet Res* 1979; 40: 183–185.
 - 49 Wei A, Fascetti AJ, Villaverde C, et al. **Effect of water content in a canned food on voluntary food intake and body weight in cats.** *Am J Vet Res* 2011; 72: 918–923.
 - 50 Fouque D and Laville M. **Low protein diets for chronic kidney disease in non diabetic adults.** *Cochrane Database Syst Rev* 2009; 2: CD001892.
 - 51 National Research Council. **Nutrient requirements of dogs and cats.** Washington, DC: National Academies Press, 2006. DOI: 10.17226/10668.
 - 52 Laflamme DP and Hannah SS. **Discrepancy between use of lean body mass or nitrogen balance to determine protein requirements for adult cats.** *J Feline Med Surg* 2013; 15: 691–697.
 - 53 Kidder AC and Chew D. **Treatment options for hyperphosphatemia in feline CKD: what's out there?** *J Feline Med Surg* 2009; 11: 913–924.
 - 54 Plantinga EA, Everts H, Kastelein AM, et al. **Retrospective study of the survival of cats with acquired chronic renal insufficiency offered different commercial diets.** *Vet Rec* 2005; 157: 185–187.
 - 55 Elliott J, Rawlings JM, Markwell PJ, et al. **Survival of cats with naturally occurring chronic renal failure: effect of dietary management.** *J Small Anim Pract* 2000; 41: 235–242.
 - 56 Ross SJ, Osborne CA, Kirk CA, et al. **Clinical evaluation of dietary modification for treatment of spontaneous chronic kidney disease in cats.** *J Am Vet Med Assoc* 2006; 229: 949–957.
 - 57 Harte JG, Markwell PJ, Moraillon RM, et al. **Dietary management of naturally occurring chronic renal failure in cats.** *J Nutr* 1994; 124: 2660S–2662S.
 - 58 Adams LG, Polzin DJ, Osborne CA, et al. **Influence of dietary protein/calorie intake on renal morphology and function in cats with 5/6 nephrectomy.** *Lab Invest* 1994; 70: 347–357.
 - 59 Finco DR, Brown SA, Brown CA, et al. **Protein and calorie effects on progression of induced chronic renal failure in cats.** *Am J Vet Res* 1998; 59: 575–582.
 - 60 Polzin DJ, Osborne CA, Ross S, et al. **Dietary management of feline chronic renal failure: where are we now? In what direction are we headed?** *J Feline Med Surg* 2000; 2: 75–82.
 - 61 Ross LA, Finco DR and Crowell WA. **Effect of dietary phosphorus restriction on the kidneys of cats with reduced renal mass.** *Am J Vet Res* 1982; 43: 1023–1026.
 - 62 Barber PJ, Rawlings JM, Markwell PJ, et al. **Effect of dietary phosphate restriction on renal secondary hyperparathyroidism in the cat.** *J Small Anim Pract* 1999; 40: 62–70.
 - 63 Geddes RF, Elliott J and Syme HM. **The effect of feeding a renal diet on plasma fibroblast growth factor 23 concentra-**

- tions in cats with stable azotemic chronic kidney disease. *J Vet Intern Med* 2013; 27: 1354–1361.
- 64 Larsen JA, Parks EM, Heinze CR, et al. **Evaluation of recipes for home-prepared diets for dogs and cats with chronic kidney disease.** *J Am Vet Med Assoc* 2012; 240: 532–538.
 - 65 Markovich JE, Freeman LM, Labato MA, et al. **Survey of dietary and medication practices of owners of cats with chronic kidney disease.** *J Feline Med Surg* 2015; 17: 979–983.
 - 66 Laflamme D and Gunn-Moore D. **Nutrition of aging cats.** *Vet Clin North Am Small Anim Pract* 2014; 44: 761–74.
 - 67 Schmidt BH, Dribusch U, Delport PC, et al. **Tolerability and efficacy of the intestinal phosphate binder Lantharenol® in cats.** *BMC Vet Res* 2012; 8: 14.
 - 68 Wagner E, Schwendenwein I and Zentek J. **Effects of a dietary chitosan and calcium supplement on Ca and P metabolism in cats.** *Berl Munch Tierarztl Wochenschr* 2003; 117: 310–315.
 - 69 King JN, Delport PC, Luus HG, et al. **Efficacy and acceptability of the new oral phosphate binder Lenziaren® in healthy cats fed a renal diet.** *J Vet Pharmacol Ther* 2015; 38: 278–289.
 - 70 Bernachon N, Fournel S, Gatto H, et al. **Comparative palatability of five supplements designed for cats suffering from chronic renal disease.** *Ir Vet J* 2014; 67: 10.
 - 71 International Renal Interest Society. **IRIS treatment recommendations.** <http://iris-kidney.com/guidelines/> (2013, accessed 4 August 2015).
 - 72 Barber PJ and Elliott J. **Feline chronic renal failure: calcium homeostasis in 80 cases diagnosed between 1992 and 1995.** *J Small Anim Pract* 1998; 39: 108–116.
 - 73 McLeland SM, Lunn KF, Duncan CG, et al. **Relationship among serum creatinine, serum gastrin, calcium-phosphorus product, and uremic gastropathy in cats with chronic kidney disease.** *J Vet Intern Med* 2014; 28: 827–837.
 - 74 de Brito Galvao JF, Nagode LA, Schenck PA, et al. **Calcitriol, calcidiol, parathyroid hormone, and fibroblast growth factor-23 interactions in chronic kidney disease.** *J Vet Emerg Crit Care (San Antonio)* 2013; 23: 134–162.
 - 75 Hostutler RA, DiBartola SP, Chew DJ, et al. **Comparison of the effects of daily and intermittent dose calcitriol on serum parathyroid hormone and ionized calcium concentrations in normal cats and cats with chronic renal failure.** *J Vet Intern Med* 2006; 20: 1307–1313.
 - 76 Deguchi E and Akuzawa M. **Renal clearance of endogenous creatinine, urea, sodium, and potassium in normal cats and cats with chronic renal failure.** *J Vet Med Sci* 1997; 59: 509–512.
 - 77 de Morais HA, Bach JF and DiBartola SP. **Metabolic acid-base disorders in the critical care unit.** *Vet Clin North Am Small Anim Pract* 2008; 38: 559–574.
 - 78 de Brito-Ashurst I, Varagunam M, Raftery MJ, et al. **Bicarbonate supplementation slows progression of CKD and improves nutritional status.** *J Am Soc Nephrol* 2009; 20: 2075–2084.
 - 79 Elliott J, Syme HM and Markwell PJ. **Acid-base balance of cats with chronic renal failure: effect of deterioration in renal function.** *J Small Anim Pract* 2003; 44: 261–268.
 - 80 Elliott J, Syme HM, Reubens E, et al. **Assessment of acid-base status of cats with naturally occurring chronic renal failure.** *J Small Anim Pract* 2003; 44: 65–70.
 - 81 Tonkin L and Parnell N. **Evaluation of serum fatty acids in cats with chronic kidney disease [abstract].** *J Vet Intern Med* 2015; 29: 1217.
 - 82 Aaron KJ and Sanders PW. **Role of dietary salt and potassium intake in cardiovascular health and disease: a review of the evidence.** *Mayo Clin Proc* 2013; 88: 987–995.
 - 83 Buranakarl C, Mathur S and Brown SA. **Effects of dietary sodium chloride intake on renal function and blood pressure in cats with normal and reduced renal function.** *Am J Vet Res* 2004; 65: 620–627.
 - 84 Xu H, Laflamme DP and Long GL. **Effects of dietary sodium chloride on health parameters in mature cats.** *J Feline Med Surg* 2009; 11: 435–441.
 - 85 Reynolds BS, Chetboul V, Nguyen P, et al. **Effects of dietary salt intake on renal function: a 2-year study in healthy aged cats.** *J Vet Intern Med* 2013; 27: 507–515.
 - 86 Kirk CA, Jewell DE and Lowry SR. **Effects of sodium chloride on selected parameters in cats.** *Vet Ther* 2006; 7: 333–346.
 - 87 Keegan RF and Webb CB. **Oxidative stress and neutrophil function in cats with chronic renal failure.** *J Vet Intern Med* 2010; 24: 514–519.
 - 88 Krofič Žel M, Tozon N and Nemec Svete A. **Plasma and erythrocyte glutathione peroxidase activity, serum selenium concentration, and plasma total antioxidant capacity in cats with IRIS stages I–IV chronic kidney disease.** *J Vet Intern Med* 2014; 28: 130–136.
 - 89 Yu S and Paetau-Robinson I. **Dietary supplements of vitamins E and C and beta-carotene reduce oxidative stress in cats with renal insufficiency.** *Vet Res Commun* 2006; 30: 403–413.
 - 90 Hanzlicek AS, Roof CJ, Sanderson MW, et al. **The effect of Chinese rhubarb, *Rheum officinale*, with and without benazepril on the progression of naturally occurring chronic kidney disease in cats.** *J Vet Intern Med* 2014; 28: 1221–1228.
 - 91 Rishniw M and Wynn SG. **Azodyl, a synbiotic, fails to alter azotemia in cats with chronic kidney disease when sprinkled onto food.** *J Feline Med Surg* 2011; 13: 405–409.
 - 92 Syme HM, Barber PJ, Markwell PJ, et al. **Prevalence of systolic hypertension in cats with chronic renal failure at initial evaluation.** *J Am Vet Med Assoc* 2002; 220: 1799–1804.
 - 93 Stiles J, Polzin DJ and Bistner SI. **The prevalence of retinopathy in cats with systemic hypertension and chronic renal failure or hyperthyroidism.** *J Am Anim Hosp Assoc* 1994; 30: 564–572.
 - 94 Mishina M, Watanabe T, Fujii K, et al. **Non-invasive blood pressure measurements in cats: clinical significance of hypertension associated with chronic renal failure.** *J Vet Med Sci* 1998; 60: 805–808.
 - 95 Steele JL, Henik RA and Stepien RL. **Effects of angiotensin-converting enzyme inhibition on plasma aldosterone concentration, plasma renin activity, and blood pressure in spontaneously hypertensive cats with chronic renal disease.** *Vet Ther* 2002; 3: 157–166.
 - 96 Taugner F, Baatz G and Nobiling R. **The renin-angiotensin system in cats with chronic renal failure.** *J Comp Pathol* 1996; 115: 239–252.
 - 97 Jepson RE, Syme HM and Elliott J. **Plasma renin activity and aldosterone concentrations in hypertensive cats with and without azotemia and in response to treatment with amlodipine besylate.** *J Vet Intern Med* 2014; 28: 144–153.
 - 98 Jepson RE, Hartley V, Mendl M, et al. **A comparison of CAT**

- Doppler and oscillometric Memoprint machines for non-invasive blood pressure measurement in conscious cats.** *J Feline Med Surg* 2005; 7: 147–152.
- 99 Acierno MJ, Seaton D, Mitchell MA, et al. **Agreement between directly measured blood pressure and pressures obtained with three veterinary-specific oscillometric units in cats.** *J Am Vet Med Assoc* 2010; 237: 402–406.
 - 100 da Cunha AF, Saile K, Beaufrère H, et al. **Measuring level of agreement between values obtained by directly measured blood pressure and ultrasonic Doppler flow detector in cats.** *J Vet Emerg Crit Care (San Antonio)* 2014; 24: 272–278.
 - 101 Martel E, Egner B, Brown SA, et al. **Comparison of high-definition oscillometry – a non-invasive technology for arterial blood pressure measurement – with a direct invasive method using radio-telemetry in awake healthy cats.** *J Feline Med Surg* 2013; 15: 1104–1113.
 - 102 Cannon MJ and Brett J. **Comparison of how well conscious cats tolerate blood pressure measurement from the radial and coccygeal arteries.** *J Feline Med Surg* 2012; 14: 906–909.
 - 103 Grandy JL, Dunlop CI, Hodgson DS, et al. **Evaluation of the Doppler ultrasonic method of measuring systolic arterial blood pressure in cats.** *Am J Vet Res* 1992; 53: 1166–1169.
 - 104 Gouni V, Tissier R, Misbach C, et al. **Influence of the observer's level of experience on systolic and diastolic arterial blood pressure measurements using Doppler ultrasonography in healthy conscious cats.** *J Feline Med Surg* 2015; 17: 94–100.
 - 105 Brown S, Atkins C, Bagley R, et al. **Guidelines for the identification, evaluation, and management of systemic hypertension in dogs and cats.** *J Vet Intern Med* 2007; 21: 542–558.
 - 106 Bodey AR and Sansom J. **Epidemiological study of blood pressure in domestic cats.** *J Small Anim Pract* 1998; 39: 567–573.
 - 107 Sansom J, Rogers K and Wood JL. **Blood pressure assessment in healthy cats and cats with hypertensive retinopathy.** *Am J Vet Res* 2004; 65: 245–252.
 - 108 Kobayashi DL, Peterson ME, Graves TK, et al. **Hypertension in cats with chronic renal failure or hyperthyroidism.** *J Vet Intern Med* 1990; 4: 58–62.
 - 109 Lin CH, Yan CJ, Lien YH, et al. **Systolic blood pressure of clinically normal and conscious cats determined by an indirect Doppler method in a clinical setting.** *J Vet Med Sci* 2006; 68: 827–832.
 - 110 Sparkes AH, Caney SM, King MC, et al. **Inter- and intraindividual variation in Doppler ultrasonic indirect blood pressure measurements in healthy cats.** *J Vet Intern Med* 1999; 13: 314–318.
 - 111 Belew AM, Barlett T and Brown SA. **Evaluation of the white-coat effect in cats.** *J Vet Intern Med* 1999; 13: 134–142.
 - 112 Elliott J, Barber PJ, Syme HM, et al. **Feline hypertension: clinical findings and response to antihypertensive treatment in 30 cases.** *J Small Anim Pract* 2001; 42: 122–129.
 - 113 Maggio F, DeFrancesco TC, Atkins CE, et al. **Ocular lesions associated with systemic hypertension in cats: 69 cases (1985–1998).** *J Am Vet Med Assoc* 2000; 217: 695–702.
 - 114 Nelson L, Reidesel E, Ware WA, et al. **Echocardiographic and radiographic changes associated with systemic hypertension in cats.** *J Vet Intern Med* 2002; 16: 418–425.
 - 115 Snyder PS, Sadek D and Jones GL. **Effect of amlodipine on echocardiographic variables in cats with systemic hypertension.** *J Vet Intern Med* 2001; 15: 52–56.
 - 116 Chetboul V, Lefebvre HP, Pinhas C, et al. **Spontaneous feline hypertension: clinical and echocardiographic abnormalities, and survival rate.** *J Vet Intern Med* 2003; 17: 89–95.
 - 117 Littman MP. **Spontaneous systemic hypertension in 24 cats.** *J Vet Intern Med* 1994; 8: 79–86.
 - 118 Jacob F, Polzin DJ, Osborne CA, et al. **Association between initial systolic blood pressure and risk of developing a uremic crisis or of dying in dogs with chronic renal failure.** *J Am Vet Med Assoc* 2003; 222: 322–329.
 - 119 Tozawa M, Iseki K, Iseki C, et al. **Blood pressure predicts risk of developing end-stage renal disease in men and women.** *Hypertension* 2003; 41: 1341–1345.
 - 120 Jepson RE, Elliott J, Brodbelt D, et al. **Effect of control of systolic blood pressure on survival in cats with systemic hypertension.** *J Vet Intern Med* 2007; 21: 402–409.
 - 121 Bacic A, Kogika MM, Barbaro KC, et al. **Evaluation of albuminuria and its relationship with blood pressure in dogs with chronic kidney disease.** *Vet Clin Pathol* 2010; 39: 203–209.
 - 122 Hunsicker LG, Adler S, Caggiula A, et al. **Predictors of the progression of renal disease in the modification of diet in renal disease study.** *Kidney Int* 1997; 51: 1908–1919.
 - 123 Syme HM. **Proteinuria in cats. Prognostic marker or mediator?** *J Feline Med Surg* 2009; 11: 211–218.
 - 124 Jensen J, Henik RA, Brownfield M, et al. **Plasma renin activity and angiotensin I and aldosterone concentrations in cats with hypertension associated with chronic renal disease.** *Am J Vet Res* 1997; 58: 535–540.
 - 125 Lefebvre HP and Toutain PL. **Angiotensin-converting enzyme inhibitors in the therapy of renal diseases.** *J Vet Pharmacol Ther* 2004; 27: 265–281.
 - 126 Jenkins TL, Coleman AE, Schmiedt CW, et al. **Attenuation of the pressor response to exogenous angiotensin by angiotensin receptor blockers and benazepril hydrochloride in clinically normal cats.** *Am J Vet Res* 2015; 76: 807–813.
 - 127 Huhtinen M, Derré G, Renoldi HJ, et al. **Randomized placebo-controlled clinical trial of a chewable formulation of amlodipine for the treatment of hypertension in client-owned cats.** *J Vet Intern Med* 2015; 29: 786–793.
 - 128 O'Neill J, Kent M, Glass EN, et al. **Clinicopathologic and MRI characteristics of presumptive hypertensive encephalopathy in two cats and two dogs.** *J Am Anim Hosp Assoc* 2013; 49: 412–420.
 - 129 Chalhoub S, Langston C and Eatroff A. **Anemia of renal disease: what it is, what to do and what's new.** *J Feline Med Surg* 2011; 13: 629–640.
 - 130 Cowgill LD. **Pathophysiology and management of anemia in chronic progressive renal failure.** *Semin Vet Med Surg (Small Anim)* 1992; 7: 175–182.
 - 131 Callan MB and Rentko VT. **Clinical application of a hemoglobin-based oxygen-carrying solution.** *Vet Clin North Am Small Anim Pract* 2003; 33: 1277–1293.
 - 132 Yang Q, Abudou M, Xie XS, et al. **Androgens for the anaemia of chronic kidney disease in adults.** *Cochrane Database Syst Rev* 2014; 10: CD006881.
 - 133 Harkin KR, Cowan LA, Andrews GA, et al. **Hepatotoxicity of stanozolol in cats.** *J Am Vet Med Assoc* 2000; 217: 681–684.
 - 134 Schiesser D, Binet I, Tsalis D, et al. **Weekly low-dose treat-**

- ment with intravenous iron sucrose maintains iron status and decreases epoetin requirement in iron-replete haemodialysis patients. *Nephrol Dial Transplant* 2006; 21: 2841–2845.
- 135 Chalhoub S, Langston CE and Farrelly J. The use of darbepoetin to stimulate erythropoiesis in anemia of chronic kidney disease in cats: 25 cases. *J Vet Intern Med* 2012; 26: 363–369.
 - 136 Langston CE, Reine NJ and Kittrell D. The use of erythropoietin. *Vet Clin North Am Small Anim Pract* 2003; 33: 1245–1260.
 - 137 Cowgill LD, James KM, Levy JK, et al. Use of recombinant human erythropoietin for management of anemia in dogs and cats with renal failure. *J Am Vet Med Assoc* 1998; 212: 521–528.
 - 138 Ruggerenti P, Cravedi P and Remuzzi G. Mechanisms and treatment of CKD. *J Am Soc Nephrol* 2012; 23: 1917–1928.
 - 139 Hanzlicek AS, Roof CJ, Sanderson MW, et al. Comparison of urine dipstick, sulfosalicylic acid, urine protein-to-creatinine ratio and a feline-specific immunoassay for detection of albuminuria in cats with chronic kidney disease. *J Feline Med Surg* 2012; 14: 882–888.
 - 140 Lyon SD, Sanderson MW, Vaden SL, et al. Comparison of urine dipstick, sulfosalicylic acid, urine protein-to-creatinine ratio, and species-specific ELISA methods for detection of albumin in urine samples of cats and dogs. *J Am Vet Med Assoc* 2010; 236: 874–879.
 - 141 Whittemore JC, Gill VL, Jensen WA, et al. Evaluation of the association between microalbuminuria and the urine albumin-creatinine ratio and systemic disease in dogs. *J Am Vet Med Assoc* 2006; 229: 958–963.
 - 142 Ferlizza E, Campos A, Neagu A, et al. The effect of chronic kidney disease on the urine proteome in the domestic cat (*Felis catus*). *Vet J* 2015; 204: 73–81.
 - 143 Miyazaki M, Kamiie K, Soeta S, et al. Molecular cloning and characterization of a novel carboxylesterase-like protein that is physiologically present at high concentrations in the urine of domestic cats (*Felis catus*). *Biochem J* 2003; 370: 101–110.
 - 144 Miyazaki M, Yamashita T, Hosokawa M, et al. Species-, sex, and age-dependent urinary excretion of cauxin, a mammalian carboxylesterase. *Comp Biochem Physiol B Biochem Mol Biol* 2006; 145: 270–277.
 - 145 Jepson RE, Syme HM, Markwell P, et al. Measurement of urinary cauxin in geriatric cats with variable plasma creatinine concentrations and proteinuria and evaluation of urine cauxin-to-creatinine concentration ratio as a predictor of developing azotemia. *Am J Vet Res* 2010; 71: 982–987.
 - 146 Jepson RE, Coulton GR, Cowan ML, et al. Evaluation of mass spectrometry of urinary proteins and peptides as biomarkers for cats at risk of developing azotemia. *Am J Vet Res* 2013; 74: 333–342.
 - 147 Benigni A and Remuzzi G. Glomerular protein trafficking and progression of renal disease to terminal uremia. *Semin Nephrol* 1996; 16: 151–159.
 - 148 Remuzzi A and Remuzzi G. Potential protective effects of telmisartan on renal function deterioration. *J Renin Angiotensin Aldosterone Syst* 2006; 7: 185–191.
 - 149 Porter AM. Ramipril in non-diabetic renal failure (REIN study) ramipril efficiency in nephropathy study. *Lancet* 1997; 350: 736–737.
 - 150 Tylicki L, Lizakowski S and Rutkowski B. Renin-angiotensin-aldosterone system blockade for nephroprotection: current evidence and future directions. *J Nephrol* 2012; 25: 900–910.
 - 151 Lees GE, Brown SA, Elliott J, et al. Assessment and management of proteinuria in dogs and cats: 2004 ACVIM Forum Consensus Statement (small animal). *J Vet Intern Med* 2005; 19: 377–385.
 - 152 King JN, Gunn-Moore DA, Tasker S, et al. Tolerability and efficacy of benazepril in cats with chronic kidney disease. *J Vet Intern Med* 2006; 20: 1054–1064.
 - 153 Mizutani H, Koyama H, Watanabe T, et al. Evaluation of the clinical efficacy of benazepril in the treatment of chronic renal insufficiency in cats. *J Vet Intern Med* 2006; 20: 1074–1079.
 - 154 Watanabe T and Mishina M. Effects of benazepril hydrochloride in cats with experimentally induced or spontaneously occurring chronic renal failure. *J Vet Med Sci* 2007; 69: 1015–1023.
 - 155 Sent U, Gössel R, Elliott J, et al. Comparison of efficacy of long-term oral treatment with telmisartan and benazepril in cats with chronic kidney disease. *J Vet Intern Med* 2015; 29: 1479–1487.
 - 156 Reynolds CA, Oyama MA, Rush JE, et al. Perceptions of quality of life and priorities of owners of cats with heart disease. *J Vet Intern Med* 2010; 24: 1421–1426.
 - 157 Chan DL. The inappetent hospitalised cat: clinical approach to maximising nutritional support. *J Feline Med Surg* 2009; 11: 925–933.
 - 158 Quimby JM and Lunn KF. Mirtazapine as an appetite stimulant and anti-emetic in cats with chronic kidney disease: a masked placebo-controlled crossover clinical trial. *Vet J* 2013; 197: 651–655.
 - 159 Quimby JM, Lake RC, Hansen RJ, et al. Oral, subcutaneous, and intravenous pharmacokinetics of ondansetron in healthy cats. *J Vet Pharmacol Ther* 2014; 37: 348–353.
 - 160 Quimby JM, Brock WT, Moses K, et al. Chronic use of maropitant for the management of vomiting and inappetence in cats with chronic kidney disease: a blinded, placebo-controlled clinical trial. *J Feline Med Surg* 2015; 17: 692–697.
 - 161 Goldstein RE, Marks SL, Kass PH, et al. Gastrin concentrations in plasma of cats with chronic renal failure. *J Am Vet Med Assoc* 1998; 213: 826–828.
 - 162 Liptak JM, Hunt GB, Barrs VR, et al. Gastroduodenal ulceration in cats: eight cases and a review of the literature. *J Feline Med Surg* 2002; 4: 27–42.
 - 163 Parkinson S, Tolbert K, Messenger K, et al. Evaluation of the effect of orally administered acid suppressants on intragastric pH in cats. *J Vet Intern Med* 2015; 29: 104–112.
 - 164 Barber PJ, Rawlings JM, Markwell PJ, et al. Incidence and prevalence of bacterial urinary tract infections in cats with chronic renal failure [abstract]. *J Vet Intern Med* 1999; 13: 251.
 - 165 Bailiff NL, Westropp JL, Nelson RW, et al. Evaluation of urine specific gravity and urine sediment as risk factors for urinary tract infections in cats. *Vet Clin Pathol* 2008; 37: 317–322.
 - 166 Mayer-Roenne B, Goldstein RE and Erb HN. Urinary tract infections in cats with hyperthyroidism, diabetes mellitus and chronic kidney disease. *J Feline Med Surg* 2007; 9: 124–132.

- 167 Weese JS, Blondeau JM, Boothe D, et al. **Antimicrobial use guidelines for treatment of urinary tract disease in dogs and cats: antimicrobial guidelines working group of the international society for companion animal infectious diseases.** *Vet Med Int* 2011; 2011: 263768.
- 168 Rowlands M, Blackwood L, Mas A, et al. **The effect of boric acid on bacterial culture of canine and feline urine.** *J Small Anim Pract* 2011; 52: 510–514.
- 169 Dorsch R, von Vopelius-Feldt C, Wolf G, et al. **Feline urinary tract pathogens: prevalence of bacterial species and antimicrobial resistance over a 10-year period.** *Vet Rec* 2015; 176: 201.
- 170 Jessen LR, Sørensen TM, Bjornvad CR, et al. **Effect of antibiotic treatment in canine and feline urinary tract infections: a systematic review.** *Vet J* 2015; 203: 270–277.
- 171 Quimby JM, Webb TL, Gibbons DS, et al. **Evaluation of intrarenal mesenchymal stem cell injection for treatment of chronic kidney disease in cats: a pilot study.** *J Feline Med Surg* 2011; 13: 418–426.
- 172 Quimby JM, Webb TL, Habenicht LM, et al. **Safety and efficacy of intravenous infusion of allogeneic cryopreserved mesenchymal stem cells for treatment of chronic kidney disease in cats: results of three sequential pilot studies.** *Stem Cell Res Ther* 2013; 4: 48.
- 173 Danielson KC, Hardie RJ and McAnulty JF. **Outcome of donor cats after unilateral nephrectomy as part of a clinical kidney transplant program.** *Vet Surg* 2015; 44: 914–919.
- 174 Roudebush P, Polzin DJ, Ross SJ, et al. **Therapies for feline chronic kidney disease. What is the evidence?** *J Feline Med Surg* 2009; 11: 195–210.
- 175 Schmiedt CW, Holzman G, Schwarz T, et al. **Survival, complications, and analysis of risk factors after renal transplantation in cats.** *Vet Surg* 2008; 37: 683–695.
- 176 Yeates JW. **Ethical considerations in feline renal transplantation.** *Vet J* 2014; 202: 405–407.
- 177 Langston CE, Cowgill LD and Spano JA. **Applications and outcome of hemodialysis in cats: a review of 29 cases.** *J Vet Intern Med* 1997; 11: 348–355.
- 178 Ross LA and Labato MA. **Current techniques in peritoneal dialysis.** *J Vet Emerg Crit Care (San Antonio)* 2013; 23: 230–240.
- 179 Gowan RA, Lingard AE, Johnston L, et al. **Retrospective case-control study of the effects of long-term dosing with meloxicam on renal function in aged cats with degenerative joint disease.** *J Feline Med Surg* 2011; 13: 752–761.
- 180 Gowan RA, Baral RM, Lingard AE, et al. **A retrospective analysis of the effects of meloxicam on the longevity of aged cats with and without overt chronic kidney disease.** *J Feline Med Surg* 2012; 14: 876–881.
- 181 Gunew MN, Menrath VH and Marshall RD. **Long-term safety, efficacy and palatability of oral meloxicam at 0.01–0.03 mg/kg for treatment of osteoarthritic pain in cats.** *J Feline Med Surg* 2008; 10: 235–241.
- 182 King JN, Strehlau G, Wernsing J, et al. **Effect of renal insufficiency on the pharmacokinetics and pharmacodynamics of benazepril in cats.** *J Vet Pharmacol Ther* 2002; 25: 371–378.
- 183 Ebner T, Schänzle G, Weber W, et al. **In vitro glucuronidation of the angiotensin II receptor antagonist telmisartan in the cat: a comparison with other species.** *J Vet Pharmacol Ther* 2013; 36: 154–160.
- 184 Bartges J and Martin Jimenez T. **Drug therapy with renal failure.** In: Bartges J and Polzin DJ (eds). *Nephrology and urology of small animals*. Ames: Wiley-Blackwell, 2011, pp 386–390.
- 185 van Hoek I and Daminet S. **Interactions between thyroid and kidney function in pathological conditions of these organ systems: a review.** *Gen Comp Endocrinol* 2009; 160: 205–215.
- 186 Trepanier LA. **Pharmacologic management of feline hyperthyroidism.** *Vet Clin North Am Small Anim Pract* 2007; 37: 775–788.
- 187 Barber PJ and Elliott J. **Study of calcium homeostasis in feline hyperthyroidism.** *J Small Anim Pract* 1996; 37: 575–582.
- 188 Williams TL, Elliott J and Syme HM. **Association of iatrogenic hypothyroidism with azotemia and reduced survival time in cats treated for hyperthyroidism.** *J Vet Intern Med* 2010; 24: 1086–1092.
- 189 Williams TL, Elliott J and Syme HM. **Effect on renal function of restoration of euthyroidism in hyperthyroid cats with iatrogenic hypothyroidism.** *J Vet Intern Med* 2014; 28: 1251–1255.

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