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Urinary Tract Disease Mini Series

Session Two: Investigation and Management of Chronic Renal Problems

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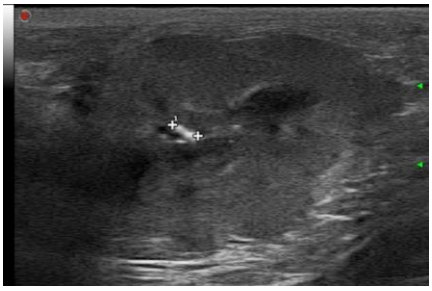

Introduction

Intrinsic chronic renal problems are traditionally divided into being either glomerular or tubular, with chronic kidney disease being used to generally refer to chronic tubulointerstitial disease. In reality, disease of either region of the nephron is intimately related to the other and current definitions of CKD consider persistent isolated glomerular disease to be an early form of CKD as it is indicative of chronic renal damage/dysfunction and will eventually lead to tubular damage. Nonetheless, it is helpful to consider the 2 regions separately in terms of pathophysiology and an appropriate clinical approach.

Glomerular Disease

Introduction

Glomerular disease is often overlooked in small animal medicine as it is apparently silent in many cases. Dogs (and cats) with glomerular disease often appear completely healthy and this can continue to be the case for months or years, making it difficult to identify and difficult to justify treatment to owners. Nonetheless, identification, investigation and treatment of this group of conditions is vitally important as left untouched it can shave years off life expectancy. Conversely, if one waits until clinical signs are apparent as a result of glomerular disease, the majority of the damage has already occurred and treatment will be limited to short term palliation in many instances.

Pathophysiology

The glomerulus is a dense, porous capillary network with a basement membrane that allows passage of water and small molecules but prevents the passage of large molecules (proteins) and cells into Bowman's capsule (the proximal nephron). It is supplied by an afferent arteriole and drained by an efferent arteriole. The potential consequences of glomerular disease include:

- Loss of significant quantities of albumin into urine, leading to hypoalbuminaemia (loss of globulins is rare)
- Passage of significant quantities of protein through nephrons, leading to nephron damage and chronic kidney disease
- Dysregulation of sodium and water balance leading to hypertension and fluid third spacing
- (Rarely - loss of RBCs through the glomerulus leading to haematuria)

Unfortunately, these effects may be self-perpetuating. Hypertension causes further glomerular damage and increases the pressure in the glomerulus leading to more protein loss. Proteinuria leads to nephron damage, fibrosis and further glomerular distortion. Hypoalbuminaemia can be associated with decreased renal perfusion, leading to AKI (see other notes).

A commonly referred to specific syndrome associated with glomerular disease is "nephrotic syndrome". This is characterized by proteinuria, hypoalbuminaemia, third spacing of fluid (oedema, pleural effusion or ascities) and hyperlipidaemia. This syndrome is a severe manifestation of glomerular disease but in itself does not represent a different problem or indicate the need for specific other therapies.

There are many potential causes of glomerular disease but it is helpful to divide them into a few different categories:

- Familial glomerulnephropathies have been described in many different breeds, with many different aetiologies, and can often be suspected if severe proteinuria is identified in a young dog. The problem is particularly common in Soft-Coated Wheaten Terriers where it may occur in association with a protein losing enteroapthy.
- Amyloidosis may be associated with severe glomerular disease. This can occur in any breed but is common in Abyssinian and Siamese cats (in association with hepatic amyloidosis) and in Shar-Peis (as part of Sharp-Pei fever complex). There is no specific treatment for this condition but the anti-fibrotic drug colchicine is often used as it may reduce further amyloid deposition.

- Glomerulosclerosis refers to non-specific changes seen in the glomerulus. The causes of this are many and range from idiopathic to hypertension and previous renal insults.
- Immune-complex glomerulonephritis (ICGN) refers to an immune mediated damage to glomeruli that may be primary or secondary. Causes of secondary ICGN include neoplasias (particularly lymphoma), any inflammatory focus, drug reactions and various infectious diseases (notably Lyme disease and Leishmania).

Investigating Proteinuria

Confirming Glomerular Disease

The hallmark of glomerular disease is proteinuria. The gold standard for identification of proteinuria is 24-hour urinary protein quantification. This is not considered practical in small animal patients and so the urine protein: creatinine ratio (UPCR) is typically used on spot urine samples as this reflects the degree of protein relative to the concentration of urine, and hence relative to the urine output. Reference ranges for proteinuria are frequently revised but UPCR in a healthy dog should certainly be <0.5 and probably <0.2 in cats. In concentrated urine (when urine creatinine concentration is high) then a dipstick can be used to rule out significant proteinuria but in dilute urine (when urine creatinine is low), the sensitivity of the dipstick is inadequate for detection of significant proteinuria and so the UPCR should be requested.

Proteinuria may be pre-renal, renal or post-renal. Pre-renal refers to proteinuria due to high plasma concentrations of proteins that get freely filtered in the glomerulus such as haemoglobin, myoglobin or Bence-Jones proteins. Post-renal proteinuria refers to protein present in the urine from lower urinary tract causes such as lower urinary tract infections or neoplasia. Pre- and post-renal proteinuria should be ruled out through investigations such as haematology/biochemistry and urinalysis (to include sediment examination and culture).

Renal proteinuria can be divided into a few potential causes. Aside from glomerular disease, as noted above, tubular proteinuria can occur with tubular dysfunction (eg Fanconi's syndrome) or renal inflammation (eg pyelonephritis). Tubular proteinuria is often mild (UPCR <2.0) and may be associated with other hallmarks of tubular disease such as azotaemia, acid-base imbalance or casts. Functional renal proteinuria can occur in the absence of any renal pathology due to fever, stress, exercise or seizures. Functional proteinuria typically resolves rapidly after removal of the inciting cause.

Once other causes of proteinuria have been excluded, then glomerular disease can be suspected. While glomerular disease can certainly be mild, it may also be strongly suspected if the UPCR is markedly elevated (some sources suggest >2.0). Within renal proteinuria, some indication of tubular vs glomerular disease can be gathered by measuring urine albumin (higher in glomerular disease) or looking for various proteins typically associated with tubular disease. In reality, these assays are not commonly required.

Investigating Glomerular Disease

Glomerular disease should be investigated with the above differential diagnoses in mind. A haematology, comprehensive biochemistry, urinalysis and urine culture should be requested to help confirm that the proteinuria is glomerular in origin and to assess the stage of disease (is azotaemia present, severity of hypoalbuminaemia etc). The labwork may also give an indication of underlying cause – eg liver enzyme elevations in feline amyloidosis, leukopenia in leishmania.

Blood pressure measurement is vital in investigation of glomerular disease as hypertension may be a cause and a consequence of the problem but in either instance it benefits form recognition and being appropriately addressed. A fundic examination may help to determine if any detected hypertension is chronic or the result of white coat syndrome.

Infectious disease testing should be considered based on individual circumstances – eg borrelia testing in dogs bitten by ticks, leishmania testing in dogs arriving from mainland Europe.

Thoracic and abdominal imaging is strongly recommended as neoplasia or inflammatory foci may be a cause of ICGN and other important lesions may be detected –eg an adrenal mass in a hypertensive patient.

Once glomerular disease has been confirmed and the presence of a systemic cause has been excluded, renal biopsy (surgical or TruCut) can be considered. The purpose of renal biopsy is primarily to look for ICGN, to justify immunosuppressive treatment. This is highly specialised histopathology and electron microscopy is required for reliable diagnosis. I tend to use the International Veterinary Renal Pathology Service, based at The Ohio State University. The laboratory should be contacted prior to performing biopsies to ensure proper sampling, handling and shipping.

Management of Glomerular Disease

Diet

Dogs with glomerular disease, of any cause, benefit from being transitioned onto a renal diet. These diets contain several features that may be beneficial:

- Restricted quantities of high quality protein. Protein entering the nephron is a cause of ongoing renal damage and reduction in dietary protein will reduce this. Protein must be sufficient to prevent catabolism, which would worsen the situation so adequate high quality protein is required.
- Sodium restriction. Glomerular disease is associated with a activation of the Renin Angiotensin Aldosterone System (RAAS), sodium retention, hypertension and third spacing. There is some evidence to suggest this can be partially mitigated through sodium restriction
- Omega-3 polyunsaturated fatty acids (n-3 PUFA). Increasing the omega-3 content of the diet to make an n-6:n-3 ratio of 5:1 is associated with a decrease in inflammation and fibrosis that may be beneficial in glomerular disease. If a diet with the appropriate ratio is not fed, omega-3 supplements containing eicosapentaenoic acid and docosahexaenoic acid can be supplemented at a dose of 0.25-0.5g/kg.

Anti-thrombotic therapy

Dogs with glomerular disease are hypercoagulable and at risk of thrombotic complications. It used to be thought that this was associated with loss of antithrombin through the glomerulus but recent evidence suggests this is not the case and dogs with adequate antithrombin may still be at risk. Dogs that have glomerular disease and that do not have invasive procedures planned or other contraindication should be started on anti-thrombotic therapy. Standard recommendations are aspirin (1-5mg/kg SID) or clopidogrel (1-2mg/kg SID). There is no data to suggest one is superior and clopidogrel is generally more costly.

RAAS inhibition

As noted above, dogs with glomerular disease have RAAS and this can have multiple deleterious effects. In addition to systemic effects of hypertension and third spacing, RAAS activation preferentially constricts the efferent arteriole leading to an increase in glomerular pressure, furthering glomerular damage and proteinuria. It also directly promotes renal fibrosis. It is therefore beneficial to block RAAS. A syndrome of “aldosterone escape” is recognised in people (and to some degree in cats and dogs) whereby RAAS blockade by any method seems to be circumvented to some degree in the chronic setting and so drug escalation and concurrent multi-modal blockade is needed in some cases.

ACE inhibitors

This is the class of drugs most commonly used for RAAS inhibition. Enalapril or benazepril are most commonly used and there is no data to suggest superiority of one over the other. For either drug a starting dose of 0.5mg/kg SID is advised but this may be gradually increased upto 1mg/kg BID (see notes on monitoring below).

Angiotensin Receptor Blockers (ARBs)

More recently RAAS blockade through blockade or angiotensin receptors has become an option and telmisartatan has a licence in cats for this purpose. At this stage there is no data comparing ACEis to ARBs in cats or dogs. Human data for similar conditions is mixed but may suggest ARBs are superior.

Similarly, data is mixed on the concurrent use but some data suggests that concurrent use of ACEis and ARBs may be synergistic in their action.

Aldosterone Antagonists

Aldosterone antagonism (using spironolactone 1-2mg/kg BID) is the final way in which RASS may be blocked. This treatment is generally reserved for cases where aggressive diuresis is also needed (eg due to ascites or pleural effusion) or in cases of refractory hypertension.

Monitoring RAAS Blockade

Blockade of RAAS by ay method will result in diuresis and potentially a decrease in GFR. Increases in creatinine of up to 50umol/L or 125% of the previous value are considered normal physiologic response to starting RAAS blockade and is generally tolerated. Nonetheless, urea and creatinine should be checked 1-2 weeks after any dose adjustment as rarely a more precipitous change will occur which necessitates dose reduction.

Hyperkalaemia will also occur in response to RAAS blockade. It is generally mild but if severe then doses should be reduced. If life threatening then treatment should be started as per AKI notes.

Reduction in blood pressure can also be expected with RAAS blockade but it is generally mild. Blood pressure should be checked after each dose adjustment at the same time as urea, creatinine and potassium. The owner should be advised to monitor for signs of hypotension.

The aim of RAAS blockade is to reduce proteinuria. Ideally this should be to a UPCR<0.5 but this is rarely achieved. A more common acceptable goal is to reduce UPCR to <50% of the starting value. UPCR shows great variation between samples and so only a change >50% is considered significant. The effects of this variation can be reduced to some degree by measuring the UPCR on urine pooled from 3 separate voidings over a 24 hour period.

Management of Hypertension

Hypertension is common in dogs with glomerular disease as a cause and a consequence. If the systolic blood pressure is above 150mmHg then therapy is indicated to reduce it to between 120-150mmHg. Initially this should occur through RAAS blockade (see above). RAAS blockade is generally not very effective in reducing blood pressure but it does dilate the efferent arteriole and thus protect the glomerulus to some degree by reducing the pressure gradient across it. If / when RAAS blockade is ineffective the calcium channel blocker amlodipine is generally used at a starting dose ~0.1mg/kg SID. This can be up titrated upto 0.3mg/kg BID with monitoring as for RAAS blockade above. If hypertension is severe then concurrent starting of amlodipine and RAAS blockade may be indicated but there is more likelihood that this will lead to significant reductions in GFR and development of azotaemia so this should be as cautious as possible.

Other drugs suggested for the treatment of hypertension include atenolol, phenoxybenzamine, prazosin or hydralazine but it is very uncommon for these to be required.

Fluid Balance

Dogs with glomerular disease can have excessive fluid retention, may be hypoalbuminaemic and may have concurrent tubular disease leading to azotaemia. These factors provide conflicting decisions with regard to adjusting fluid balance and so the general advice is to not alter a patient's fluid balance unless absolutely necessary and if it is required, to do the minimal possible to achieve the desired clinical effect rather than to adjust laboratory values.

If patients have significant oedema, ascites or pleural effusion that is directly affecting their ability to function or their quality of life then diuretics should be used. Frusemide is generally used first in patients with oedema and spironolactone is generally used first in patients with ascites or pleural effusion but in reality concurrent use of both is often needed.

In patients which have hypovolaemia/dehydration then fluid administration may be required. Fluids should not be given to treat azotaemia if there is not also significant hypovolaemia. Because patients are often hypoalbuminaemic then cautious use of colloids is often required in addition to cautious crystalloid use. Fluids should not be excessive as patients are predisposed to volume overload,

diuresis may increase protein loss and colloids may be nephrotoxic. Enteral water (by encouraging drinking or via a feeding tube) is preferred wherever possible.

Immunosuppression

In cases of ICGN immunosuppression may help to stop the disease and reduce proteinuria and progression. In severe/late stage disease then significant glomerulosclerosis may have already occurred and removal of the immune mediated component may not significantly effect the disease course. For this reason, renal biopsy is advocated in patient with stage I or stage II chronic kidney disease but not for patients with stage III or IV disease where it may be too late and biopsy risks further worsening of the situation.

Immunosuppression should be used in cases of confirmed ICGN or may be trialled in cases where it is not considered appropriate to obtain renal biopsies. The aims of immunosuppression are similar to RAAS blockade – to reduce proteinuria by a meaningful amount.

Prednisolone is generally not preferred for ICGN as it may result in fluid retention, worsening the fluid balance of many patients. There is no evidence regarding which immunosuppression protocol should be used and all of the treatments are not licensed but anecdotally, chlorambucil is preferred in cats (2mg PO q48hrs) and mycophenolate mofetil (8-10mg/kg BID) is the recommended agent in dogs. Depending on success/tolerability etc, other agents used include azathioprine or cyclopsporine. If cyclosporine is to be used, it should be noted that the immunosuppressive dose (5-10mg/kg BID) is generally much higher than the atopy treatment dose but it is highly variable between patients and is best monitored through direct measurement of plasma levels or IL-2 inhibition, making use of this drug quite complex.

Chronic Kidney Disease

Introduction

Chronic kidney Disease (CKD) is a common but poorly defined syndrome in companion animal medicine. Similar to AKI, it is important to realise that CKD does not refer to one single disease but rather a syndrome that occurs secondary to many diseases. In many (most) cases, the cause is idiopathic and histologically classified as interstitial nephritis but due consideration should be given to other diseases (previous episodes of AKI of any cause, glomerular disease, neoplasia etc) and these should be investigated as described elsewhere in this series.

There is no strict definition of CKD in veterinary patients but most would agree on the criteria that it must include the identification of persistent renal damage/dysfunction in the absence of acute kidney injury. A suggestion would be the presence of renal azotaemia, proteinuria OR polyuria secondary to renal disease in a stable, euvolaemic patient that can be documented over at least 2 weeks. An important feature of this definition is that the patient is stable and euvolaemic. If this is not the case then the patient may have CKD but it is either end stage disease or there is something else also occurring in the patient that clouds the diagnosis if CKD (eg an episode of AKI – so called “acute on chronic” kidney disease).

Staging of CKD

The International Renal Interest Society (IRIS) have produced guidelines for the staging of cats and dogs with CKD and readers are referred to those guidelines directly for specifics as they are occasionally updated and freely available online. Staging is based on serum creatinine concentration with sub-staging based on the presence or degree of proteinuria and hypertension. Investigation of CKD should therefore include these basic parameters, in addition to considering urine sediment examination and culture and imaging to look for causes of AKI.

Within the staging systems, it should be noted that Stage 1 refers to animals without any suggestion of azotaemia and the cutoffs for Stage 2 overlap with the upper end of the reference range for many laboratories. This indicates that animals do not have to be azotaemic to be diagnosed with CKD. For instance, persistent renal proteinuria is indicative of renal damage/dysfunction and the potential to develop worsening kidney disease so this would be considered a form of CKD. Similarly if an animal is PU/PD and non-azotaemic but investigations conclude that early chronic kidney disease is the

cause then this would be considered a form of CKD and appropriate monitoring/therapy should be instigated.

As noted in earlier notes, plasma creatinine concentration is related to both GFR and muscle mass. In animals with moderate to marked muscle wasting, creatinine concentration may therefore not indicate the true severity of a GFR decrease. Symmetric dimethylarginine (SDMA) is a renal biomarker that has recently become available as a commercial assay. SDMA is inversely related to GFR in a similar manner to creatinine but is not affected by muscle mass. Studies also indicate that SDMA increases may be detected before creatinine increases in animals with early CKD and modest decreases in GFR. As such, IRIS have recently updated their staging guidelines to indicate that persistent SDMA elevations with a normal serum creatinine concentration should be considered to have stage 1 CKD. Additionally animals with stage 2 or 3 CKD and muscle wasting should have their staging reassessed based on SDMA rather than creatinine.

Staging is a useful exercise because IRIS also produce guidelines of suggested therapies and targets based on staging and also because staging has been shown to be prognostic. In cats, available data are as follows:

- Stage II – Median survival time (MST) =1,151 days
- Stage III – MST=778 days
- Stage IV – MST=103 days

In dogs the data available is less clear but:

- Stage I & II – MST > 500 days
- Stage III – MST ~ 120 days
- Stage IV – MST ~ 14 days

Treatment of CKD

More than dozen different classes of drug are commonly recommended for the treatment of CKD and yet very few of them have a supportive evidence bases and these treatments are being recommended for terminal patients that may already have a decreased appetite or other gastrointestinal signs. As such, their introduction should be cautious, logical and stepwise, being tailored to the individual case. Once again, IRIS produces guidelines for treatment of CKD based on the stage of disease and readers are directed to those for specifics but the basis of those recommendations is briefly discussed below.

Management of dehydration

Patients with CKD are prone to dehydration as they may have reduced urine concentrating ability and they may have decreased water intake due to depression/nausea. Dehydration may further decrease water intake and demeanour. Hypovolaemia will cause AKI due to decreased renal blood flow. If this is thought to occur then it should be corrected and/or prevented through encouraging drinking, intravenous fluids or subcutaneous fluids as appropriate. Subcutaneous fluids can be given by the owner at home and while overhydration using fluids will lead to dilution of urea/creatinine and a reduction in lab values, there is no benefit to the patient from overhydrating them (and a risk of fluid overload). Subcutaneous fluids should therefore be reserved for cases where dehydration and hypovolaemia repeatedly occur.

Management of hypertension

As noted in the proteinuria notes above, hypertension and kidney disease are intimately related and once can cause and perpetuate the other. If present, hypertension should be addressed using RAAS blockade and or the calcium channel blocker amlodipine. In dogs introduction of RAAS blockade is recommended in the first instance but in cats amlodipine may be used as a first agent.

Management of Proteinuria

Proteinuria may be present as a primary or secondary component in CKD. Regardless, its presence is likely to progress the disease and has been shown to be associated with a worse survival. Proteinuria should be reduced using strategies outlined elsewhere in these notes. It should be noted that RAAS

inhibition has only been shown to be beneficial in proteinuric CKD and there is no basis for its use in non-protienuric CKD, with the exception of its use in canine hypertension as noted above.

RAAS inhibition causes a decrease in GFR and worsening of azotaemia. In early CKD this is tolerable and should be expected. In stage III or IV CKD, introduction of RAAS inhibition may be deleterious as it may lead to uraemic crisis so this risk of this must be weighed against the limited potential benefit given the poor prognosis associated with late stage disease and the fact that RAAS inhibition has no immediate beneficial effects on quality of life.

Reduction of serum phosphorus

Renal hyperparathyroidism is a major problem in CKD. The disease is driven by the retention of phosphorus by kidneys that are unable to excrete it and by the inability of the kidneys to hydroxylate calcidiol to calcitriol. Calcitriol is a major inhibitor of PTH secretion and so the combination of increased serum phosphorus and decreased calcitriol leads to excessive PTH secretion. PTH leads to calcium retention and mineralization, worsening kidney function. Additionally, PTH is likely to be directly nephrotoxic and associated with signs of uraemia. If secondary hyperparathyroidism is present for long periods of time then tertiary hyperparathyroidism occurs, whereby PTH secretion continues independent of Vitamin D or phosphorus concentrations.

IRIS guidelines provide target serum phosphorus concentrations that are in the lower half of the reference range. A value that falls within the reference range is not sufficient.

Initially, phosphorus concentrations should be reduced through dietary restriction and this is a property that is common to renal diets. In fact, introduction of an exclusive renal diet to patients with upwards of stage II CKD has been more conclusively shown to affect longevity and quality of life than any other intervention and this must be stressed to owners at the time of diagnosis. It is worth persisting with a transition to a renal diet at a stage when patients are relatively bright and have good appetite and some authors suggest going as far as placement of a feeding tube to enforce this transition if animals are stubborn on the issue.

Beyond transition to a low phosphorus diet, use of phosphate binders can reduce serum concentrations further (but this should preferably be on top of a suitable diet, not as a replacement). Licensed products for this purpose in the UK include lanthanum carbonate, a combined calcium carbonate & magnesium carbonate product and a combined chitosan and calcium carbonate product. Aluminium hydroxide may also be used for this purpose but is not licensed. Care must be used with calcium containing salts as they may lead to hypercalcaemia, actually worsening mineralization. Aluminium toxicity may be seen if formulary doses of aluminium hydroxide are exceeded. Aluminium hydroxide has the added advantage of being an antacid so it may help with some of the gastrointestinal problems seen in CKD (see below).

Calcitriol administration

As noted above, hyperparathyroidism occurs due to a lack of calcitriol and so it can be treated using supplemented calcitriol or 1-alpha Vitamin D. These products do not have a veterinary license and they must be used with extreme caution as they will lead to increases in serum calcium and phosphorus which may precipitate mineralization. They should only be introduced once phosphorus has been reduced to the desired target and have only been shown to be beneficial in one small group of dogs with stage III CKD and so this is the only situation under which IRIS recommend the use of Vitamin D analogues. Careful monitoring of Ca and P is advised and measurement of PTH is also recommended so that dosing can be to the lowest dose that effectively reduces PTH.

Management of Acidosis

Metabolic acidosis is quite common, particularly in stage III or IV disease. Again this can contribute towards malaise and inappetance and also progress CKD. Monitoring of HCO_3^- is recommended and if low, supplementation with sodium bicarbonate is advised. It should be noted that this treatment provides a lot of sodium and so care should be particularly used if giving this to patients with hypertension or nephrotic syndrome.

Management of Hypokalaemia

Hypokalaemia may be present in patients with CKD due to their decreased food intake and excessive polyuria. If present it may lead to weakness, fatigue and worse malaise and so treatment with potassium chloride or potassium gluconate oral salts is advised. Excessive oral potassium salts may cause gastritis.

Treatment of Anaemia

Anaemia is common in stage III or IV CKD and is multifactorial. The major contributing factors are a lack of EPO production and iron deficiency due to chronic GI ulceration and blood loss but other factors have their role. If present and severe, ferrous sulphate supplementation should be considered, although again, this may cause further GI upset. If the anaemia is severe and impacting on a patient's daily quality of life then recombinant human EPO or darbopoetin, a synthetic analogue, may be given to alleviate the anaemia. Recombinant human EPO should certainly be reserved as a treatment of last resort as its use will eventually stimulate the production of anti-EPO antibodies and lead to a refractory, fatal, pure red cell aplasia. It is less clear if this occurs with darbopoetin. In either instance, if EPO analogues are used the iron supplementation is also required to provide substrate for erythropoiesis.

Treatment of Gastrointestinal Signs

Gastrointestinal signs are common in CKD. Gastric hyperacidity and ulceration may occur, in part due to decreased gastrin excretion from the kidneys. Additionally, the build-up of nitrogenous waste and other uraemic toxins will lead to nausea, altered GI motility and appetite suppression. For these reasons, food intake and weight should be carefully monitored and if any concern exists in these regards antacids or central anti-emetics should be instituted.

Decreased food intake is a self-perpetuating problem as lack of intake leads to muscle catabolism, causing further release of nitrogenous waste that cannot be excreted and making animals feel worse. This cycle should be broken at all costs and so it is more important that patients with late stage CKD eat, rather than focussing on what they eat. Of course, the deal is that they get adequate and optimised nutrition and so a feeding tube may be warranted in such circumstances if the owner will accommodate it and if the patient otherwise has a good quality of life. In late stage CKD, a feeding tube also allows administration of medications and top-ups of enteral water, potentially avoiding the need or risks of subcutaneous fluids.

Other Treatments

Numerous additional treatments have been advocated or marketed for patients with varying degrees of evidence and rationale. This list is by no means comprehensive:

- B-vitamins – These water soluble vitamins may be depleted in patients with polyuria and decreased appetite, leading to a range of clinical signs from severe obtundation to anorexia and vomiting. Consideration should be given to supplementing B-vitamins in hospitalised patients with CKD or if there is reason to suspect low levels but if patients are receiving adequate quantities of a renal diet this is generally not necessary.
- Chinese rhubarb is the main ingredient on one veterinary neutraceutical marketed for CKD as it has anti-fibrotic properties in experimental models. A study in cats with CKD failed to demonstrate any effect but this may have been underpowered.
- A probiotic is marketed in the US for CKD as it contains bacteria that breakdown nitrogenous compounds leading to a reduction in azotaemia and alleviation in uraemia. It has no direct effect on renal function per se and while it may do what it is supposed to, one experimental model suggests it is associated with weight loss and so it should be used with caution.
- Haemodialysis is occasionally offered for treatment of CKD in other countries. Although useful in AKI and potentially in the stabilisation of CKD patients prior to transplantation, it my opinion it should not be used as a chronic treatment in CKD due to its aggressive and invasive nature and the fact that it may be associated with improved longevity without corresponding improvements in quality of life.
- Renal transplantation is used as the ultimate treatment of CKD in some other countries but this practice is not currently available in the UK for ethical and legislative reasons.

Acute-on-Chronic Kidney Disease

CKD pre-disposes animals to various causes of AKI. Animals may not drink adequately for their degree of polyuria, leading to renal hypoperfusion. Dilute urine and abnormal renal architecture predisposes animals to pyelonephritis. Increased calciuresis in CKD may lead to stone formation and post-renal obstruction. Hypertension and proteinuria are both associated with increased risk of thromboembolism and renal ischaemia. Alternatively, animals with CKD may be unfortunate enough to have an unrelated cause of AKI. In any instance, the AKI in these patients is particularly problematic as even if it is successfully treated, it will inevitably lead to progression of their CKD. Additionally, in patients with AKI that had previously healthy kidneys, there is capacity for the remaining normal renal tissue to hypertrophy to compensate for damaged areas. In patients with CKD, this limited ability to hypertrophy has already been maximally utilised and so there is no ability to respond to further injury.

If patients with CKD acutely deteriorate then AKI should be suspected with aggressive investigation for the above considerations and rapid treatment should be instituted in order to minimise any further problems.

Further Reading

As noted above, this is an area of much active investigation and recommendations are complex and continually changing. The flowing reading list is all freely available for download:

- ACVIM Consensus Statement: Assessment and Management of Proteinuria in Dogs and Cats – JVIM 19(2005):377-385
- International Renal Interest Society Consensus Clinical Practice Guidelines for Glomerular Disease in Dogs. JVIM Volume 27 (2013) Supplement s1
- IRIS Guidelines for staging and management of Chronic Kidney Disease (www.iris-kidney.com)