Urinary System Failure

OBJECTIVES

This section deals with the clinical problems of azotemia, uremia, polyuria and oliguria.

At the end of this section, the student should be able to:

1. define polyuria, oliguria and anuria
2. define azotemia and uremia;understand what “GFR” means, how it is calculated, and how it relates to azotemia
3. list the 3 general categories of azotemia
4. explain the pathophysiology of pre-renal azotemia and give representative examples; be able to distinguish hypoadrenalcorticism from renal failure in a clinical case of azotemia in a dog
5. explain the pathophysiology of post-renal azotemia and give representative examples
6. explain the pathophysiology of renal failure as a rule out for a dog with polyuria/polydipsia and for a dog or cat with azotemia.
7. identify the diagnostic tests necessary to differentiate pre-renal, renal, and post-renal azotemia
8. determine whether azotemia in a dog or cat is more likely to be pre-renal, renal or post-renal in origin given the history, physical examination and laboratory data
9. list the clinical signs and recognize clinical laboratory changes associated with uremia
10. describe the diagnostic tests which can be used to evaluate a polyuric/polydipsic dog which is not azotemic and what outcome would be expected on these tests when renal failure is the cause of the polyuria/polydipsia
11. explain the difference in clinical course and prognosis between acute and chronic renal failure
12. given the serum creatinine, place a dog or cat into the correct stage of renal failure; know the relationship between stage and treatment needed
13. list some common causes of acute and chronic renal failure
14. list what tests usually need to be performed to determine whether a given case has acute or chronic renal failure
15. determine whether a case of renal failure is more likely to be acute or chronic given the animal's history, physical examination, and laboratory data
16. describe the complex of clinical and laboratory findings usually associated with ethylene glycol toxicity and with leptospirosis.
17. describe how a diagnosis of ethylene glycol toxicity or leptospirosis can be

confirmed

18. know the factors that affect prognosis in CRF in dogs and cats

19. explain the difference in prognosis between oliguric and polyuric renal failure

20. design a regimen of therapy for a uremic patient of given weight with oliguric renal failure

21. design a regimen of therapy for a uremic patient of given weight with polyuric renal failure

22. design a regimen of therapy for an azotemic (but not uremic) patient of given weight

23. design a regimen of therapy for a non-azotemic dog with polyuria of renal origin

Additional Resources

Urologic Surgery Pages: 5-10; 24-29; 37-47; 53-60;
Textbook of Veterinary Internal Medicine, 6th edition, Chapters 257, 258, 260
Small Animal Medical Diagnosis, 2nd edition, Chapters 5,61,62,63
Current Veterinary Therapy XIII, 831-834, 856-858, 861-863
Canine and Feline Nephrology and Urology, Chapters 10, 11, 12, 16, 18, 22, 24, 27, 28, 29

Urinary System Failure

I Definition:urinary system dysfunction of sufficient severity to result in:

A. Abnormalities in urine output and/or
B. Accumulation of nitrogenous wastes and/or
C. Alterations in H_20, electrolyte, acid-base status which, if sufficiently severe, lead to dysfunction of other organ systems;

II. Signs of Urinary System Failure

A. Abnormality in urine output: polyuria, oliguria, anuria

1. Basal Urine Output – 10-20 ml/kg/day

2. “Normal” Urine Output – 20-45 ml/kg/day

3. In dogs, a reduction in GFR of approximately 67% (33% of normal) results in an obligatory polyuria. Oliguria and anuria indicate that GFR is extremely low (no number determined).

B. Azotemia/Uremia

1. Azotemia indicates that GFR is reduced by 75% (25% of normal).

2. Uremia indicates that clinical signs (usually GI and neurologic) are present due to accumulation of nitrogenous wastes and alteration in water, electrolyte, and acid base balance; associated with marked azotemia (generally BUN > 100 mg/dl and creatinine > 5 mg/dl, although severity of azotemia does not correlate well with clinical signs as the body can adjust if azotemia develops slowly.

III. Glomerular Filtration Rate:

A. The kidneys have three roles: filtration, reabsorption, and secretion. GFR is the measure of filtration.

B. The primary driving force for filtration is the hydrostatic pressure in the glomerular capillaries (review autoregulation of renal blood flow).

C. The primary opposing force is plasma oncotic pressure, but in obstructive diseases, pressure within the urinary space becomes an important opposing force.

D. Thus, GFR is affected by pre-renal factors (hydrostatic pressure, oncotic pressure) and post-renal factors (obstruction) as well as renal factors (renal pathology).

E. GFR is measured by determining the clearance of a compound that is neither reabsorbed nor secreted. In clinical practice, this is usually exogenous creatinine or iohexol, with iohexol currently most popular.

F. BUN and creatinine are easily performed laboratory tests to estimate GFR. Unfortunately, they are not very sensitive and are affected by extrarenal factors (review clinical pathology).

III. Causes of Urinary System Failure

A. pre-renal - insufficient hydrostatic pressure or increased oncotic pressure leading to decreased GFR; urine well concentrated as tubular function is initially unaffected, unless the causative disease also affects water reabsorption .

1. Causes:

   a. Cardiovascular Failure

   b. Decreased effective arterial blood volume/pressure

      1). hypotension

      2). dehydration

      3). Hypovolemia

2. Dogs with normal kidneys concentrate urine to 1.048 (average) when subjected to 5% dehydration. Cats concentrate to 1.052 (average). Note that normal cats typically have urine specific gravities > 1.050.

3. Some diseases affect renal ability to concentrate urine. These include complicated diabetes mellitus, diabetes insipidus, systemic E. coli infections, hypoadrenalcorticism, hyperadrenalcorticism. Hypoadrenalcorticism mimics renal failure most closely, yet the prognosis is considerably different. Be sure to be able to distinguish these two conditions.

4. Urine specific gravity should always be assessed prior to administration of fluids or diuretics in order to make a correct assessment of renal function.

5. Treatment involves correcting the predisposing factor (usually administering fluid therapy) and correcting the underlying disease. Azotemia resolves as soon as euhydration is re-established.

B. renal - abnormal signs are due to generalized renal dysfunction; includes and may be exclusively polyuria, polydipsia

1. Dogs with experimentally induced renal failure to the point of azotemia (75% reduction in functional renal mass) can still concentrate to 1.027 so a specific gravity of 1.008-1.029 is considered indicative of a renal concentrating defect in the face of dehydration.

2. The situation is more complicated in cats which retain renal concentrating ability even with loss of 75% functional renal

mass. However, cats have usually lost concentrating ability, similar to dogs, by the time a uremic crisis occurs.

3. Although ability to dilute urine is clinically less important in dogs and cats, it is important to know that ability to dilute urine is also lost with generalized renal disease (review physiology of renal handling of water).

C. post-renal - obstruction to urine outflow; rupture leading to urine retention in body; usually diagnosed by history, physical exam findings and radiography; chronic, partial obstruction to urine outflow can lead to renal injury/disease; treatment is removal of obstruction or repair of rupture;

Primary Renal Failure

I. Definition

Renal disease indicates a pathologic lesion of any size, distribution or cause in one or both kidneys; may be subclinical since kidneys have marked functional reserve plus ability to compensate and since clinical tests are limited in their ability to detect disease; renal <u>failure</u> when clinical signs are present due to renal disease.

II. Pathophysiology of Renal Failure

A. Nephron - functional unit of the kidney; all parts - glomeruli, tubules, peritubular capillaries, interstitial tissue are inter-related; if one part destroyed, rest eventually become non-functional; e.g. glomerular disease leads to decreased peritubular capillary perfusion which leads to tubular cell degeneration.

new nephrons cannot be formed (number fixed after three weeks of age);

B. repair of glomerular injury - occurs but usually without return of normal function;

C. repair of tubular injury - occurs only if basement membrane remains intact;

D. if nephron severely injured - repair by fibrosis, leads to decreased kidney size

E. fortunately - remaining nephrons can compensate within limits for those lost; body homeostasis maintained until the number of functioning nephrons greatly reduced.

F. if more than 67% of nephrons non-functional in dogs (GFR reduced to 33% of normal) - PU/PD due to decreased ability to concentrate urine; each remaining nephron must excrete more water to excrete the solute load; although a decrease in concentrating ability also occurs in cats, it is not able to be detected clinically as PU/PD because of cat's great concentrating ability (e.g. maximal urine specific gravity may only decline from 1.065 to 1.045)

G. In addition to specific gravity, the urinalysis is also important in detecting abnormal degrees of proteinuria and the presence of casts. Both of these are useful in assessing renal injury.

H. if more than 75% of nephrons non-functional (GFR reduced to 25% of normal) – azotemia develops; as azotemia worsens, acid/base, electrolyte and mineral abnormalities become evident in biochemical profiles

I. increased BUN and creatinine are the result of decreased GFR: how does PU occur in face of decreased GFR? due to the normally great reabsorption of H_20 and electrolytes being also reduced.

J. What is responsible for clinical signs in uremia?

not BUN or creatinine, but the accumulation of many metabolites; no single "toxin" of uremia has been identified; such substances as PTH, gastrin, serum phosphorus, certain amino acids have been implicated.

III. Data Base for Renal Failure

A. History
B. Physical Examination
C. CBC/Biochemical Profile
D. Urinalysis/Assessment of Proteinuria
E. Urine Culture
F. Renal Imaging (Abdominal Radiographs/Renal Ultrasound)
G. Measurement of Systolic Blood Pressure

IV. Classification of Renal Failure

A. By Severity of Clinical Signs: Polyuric, Nonazotemic; Azotemic, Non-uremic; Uremic, Polyuric; Uremic, Oliguric

1. Polyuric, Non-Azotemic Renal Failure (Usually a dog because of cat's great urine concentrating ability)

a. Diagnostic Plan

1) History (Documentation of PU/PD)
2) Physical Examination
3) Urinalysis
4) CBC, Biochemical Profile
5) Water Deprivation/ ADH Response Testing
6) Measurement of GFR (Creatinine or Iohexol Clearance)

b. Always interpret urine concentrating ability in light of animal's hydration status; inadequately concentrated urine in the face of dehydration always indicates renal dysfunction but not necessarily renal disease; can also occur with osmotic diuresis as in diabetic ketoacidosis, or if absence of ADH such as diabetes insipidus or if change in responsiveness to ADH as when there is insufficient cortisol as is hypoadrenalcorticism or too much cortisol as in Cushing's disease or bacterial toxins (pyometra, pyelonephritis, prostatic abscessation).

c. Water deprivation must always be done in a carefully controlled environment with frequent monitoring.

2. Azotemic, Non-Uremic Renal Failure

a. Only clinical sign is PU/PD in dogs; may be no clinical signs in cats; abnormality in renal size or shape may be palpated in cats.

b. Increased BUN and creatinine (GFR reduced to 25% of normal; 75% of nephrons are dysfunctional) with urine specific gravity of 1.008-1.029 in dogs; cats may retain concentrating ability greater than 1.030.

c. Increased phosphorus (reflects decreased GFR). Varies with diet .

d. Radiography is often used to evaluate kidney size - survey radiographs or excretory urography; (normal kidney size: 2.5-3.5 x length of L2 in dogs; 2.4-3.0 x length of L2 in cats); radiography may also be used to try to identify a cause of renal failure (such as uroliths in the renal pelvis).

e. Renal ultrasonography may be used to further evaluate size and compare echogenicity to normal echogenicity (most renal diseases are associated with hyperechogenicity).

3. Polyuric Uremic Renal Failure

a. Clinical Signs: those associated with uremia

1) Neurologic: depression, lethargy, seizures, coma, trembling, weakness

2) GI signs: nausea, anorexia, stomatitis, vomiting, diarrhea

3) Dehydration

b. Laboratory abnormalities

1) As for azotemic renal failure; except cats also have urine specific gravities of 1.008-1.029

2) May be a stress leukogram

3) May be hyperglycemia - lack of responsiveness to insulin

4) Metabolic acidosis may be present

a) Decreased clearance of nonvolatile acids of protein catabolism

b) Decreased tubular exertion of H+

due to decreased renal tubular production of NH_3: NH_3 within tubular lumens binds with H+ to form NH 4+ which cannot diffuse out of tubular lumen and is excreted; if no NH_3, H+ concentration in tubular fluid increases, lowering pH and preventing further secretion of H+ against the pH gradient.

5) May be abnormalities in serum calcium concentration (either hypocalcemia or hypercalcemia possible depending on underlying cause of renal failure).

6) Tendency toward hypokalemia (anorexia, increased urine output) which may be masked by acidemia; especially in cats.

7) Hyperamylasemia and hyperlipasemia in dogs (not usually measured in cats) due to decreased renal excretion (not to pancreatitis).

c. Radiography/Ultrasonography: as for azotemic, non-uremic

4. Oliguric, Uremic Renal Failure

a. History: owner may note decreased urine output

b. Physical Examination

1) As for polyuric, uremic except little urine.

2) Signs of overhydration may develop when fluids are given parenterally (pulmonary edema, peripheral edema, clear ocular or nasal discharge).

c. Clinicopathologic Evaluation

1) Hematology - As for polyuric, uremic

2) Blood chemistry - as for polyuric uremic except

Tendency toward hyperkalemia (decreased excretion plus acidemia)

a) Potassium is mainly intracellular and released into extracellular compartment by normal cell death.

b) Without urinary excretion, extracellular component steadily increases;

c) Increased serum concentration of K is often cause of death in anuric states

3) Reduced urine output (<10ml/kg/day).

d. Radiography/Ultrasonography - As for polyuric, uremic.

B. By Severity of Abnormality in Serum Creatinine: IRIS (International Renal Interest Society) Staging System for Kidney Disease

Stage	Plasma Creatinine (mg/dl)	Comments
I	<1.4 in dogs; <1.6 in cats (non-azotemic)	Dogs may have subnormal urine concentrating and diluting ability; may have abnormal renal palpation
II	1.4-2 in dogs; 1.6-2.8 in cats; (very mild azotemia)	Dogs usually have subnormal urine concentrating and diluting ability; other clinical signs usually absent; may have abnormal renal palpation
III	2.1-5 in dogs; 2.9-5 in cats (mild to moderate azotemia)	In addition to above, extra-renal signs (such as nausea, decreased activity) may be present
IV	> 5 in dogs and cats (marked azotemia)	Usually require fluid or dialysis therapy

C. Glomerular, Tubular, or Generalized Renal Disease

D. Acute vs Chronic Renal Disease: important prognostically since acute diseases have greater potential for reversibility.

Acute Renal Failure

I. Pathophysiololgy

A. In dogs and cats, acute renal failure is primarily due to acute tubular damage.

1. This results in necrosis and sloughing of tubular cells into the tubular lumen, causing tubular obstruction, and in loss of tight

junctions between tubular cells leading to tubular fluid leaking out of tubule and into renal interstitial space, leading to inflammation.

2. Renal arteriolar vasoconstriction is another component of acute renal failure. This leads to decreased GFR and renal ischemia with secondary tubular damage.

3. As a result of acute renal injury, GFR is decreased and tubular function is abnormal.

B. Since nephrons rapidly become dysfunctional, there is no time for compensation.

1. Although fewer nephrons may be dysfunctional than in chronic disease, the signs are severe. Animals with acute renal failure usually appear more ill at a given level of azotemia than animals with chronic renal failure.

2. Because of the potential for repair and compensation, animals with acute disease have the potential to recover (depending on the severity of injury).

3. Two to three months are required for maximal compensation and repair to occur.

II. Common Causes

A. Toxins (Acute Nephrosis)

1. Ethylene glycol -

a. most common cause of acute renal failure in dogs and a common cause in cats; requires only small amounts

b. generally oliguric in type due to tubular obstruction with crystals and renal tubular cell injury

c. first signs - CNS (ataxia) plus severe metabolic acidosis; renal failure in 24-48 hours

d. Presumptive diagnosis based on history of CNS signs (ataxia) plus severe acidemia plus markedly increased anion gap plus renal failure; serum calcium may be decreased; on ultrasonography kidneys are mildly, symmetrically enlarged and markedly hyperechoic

e. confirm diagnosis by finding large numbers of oxalate crystals in urine or in renal biopsy specimen or by a blood test for ethylene glycol in first 24-48 hours

2. Aminoglycoside antibiotics (all except streptomycin)

a. <u>too</u> common a cause of nephrotoxicity; remember the motto "above all else, try to do no harm"

b. Proximal tubular toxins - cause mild proteinuria, isosthenuria, occasionally glucosuria, cylindruria

c. progressive course if administration continues: starts as polyuric, non-azotemic, then to polyuric azotemic, then polyuric, uremic, and terminally oliguric, uremic

d. risk factors

1) fever

2) dehydration

3) old age

4) pre-existing renal disease

5) hypokalemia

6) overdosage

7) sepsis

8) some cephalosporins

9) other or prior aminoglycosides

10) furosemide

11) frequency of administration

12) route of administration (IV more toxic than SQ or IM)

e. median onset of toxicity - 9 days (range 5-17)

f. maximal toxicity does not occur until at least 4 days <u>after</u> the drug is stopped

g. recommended monitoring - daily urinalysis; if wait until BUN increases, it is <u>too</u> late - gentamycin blood levels can be monitored in some hospitals

3. Other Drugs - For example, amphotericin B, banamine, other non-steroidal anti-inflammatory drugs

4. Hemoglobin or myoglobin: hemoglobinuria, myoglobinuria only impair renal function in the presence of hypotension, dehydration or acidosis; when these are present, tubules can become obstructed by hemoglobin or myoglobin casts; in small animals, myoglobinuria is primarily a problem in racing greyhounds

5. Plant toxicities – Lilly toxicity in cats is the best described in small

animals

6. Food toxicities – Raisins, grapes, and chocolate in dogs

B. Infectious - acute nephritis: for example, leptospirosis, bacterial sepsis, Rocky Mt. Spotted Fever

1. Leptospirosis is currently the second most common cause of acute renal failure in dogs. Cats are resistant to leptospirosis. Humans are susceptible to infection and so infected, untreated dog's urine is a public health risk.

2. The serovars of leptospirosis most associated with acute renal failure in dogs in Georgia are grippotyphosa and pomona, which are not included in the bivalent vaccine. Unfortunately, vaccination against one serovar does not protect against other serovars. Fort Dodge currently makes a vaccine with four serovars: icterohemorrhagiae, canicola, grippotyphosa, pomona.

3. Clinical signs are those of uremia (vomiting, anorexia). There may be abdominal or muscle pain and occasionally muscle fasciculations. Only 50% of cases are febrile or have leukocytosis, despite this being an infectious disease. Approximately 30% of cases are thrombocytopenic. Since thrombocytopenia also occurs with Rocky Mt Spotted Fever and bacterial sepsis, the concurrent presence of thrombocytopenia and renal failure suggests an acute infectious etiology.

4. If diagnosed early, this is the most reversible cause of acute renal failure, responding to antibiotic therapy (penicillins, ampicillin) and fluid support. This is why many clinicians treat all canine cases of acute renal failure of unknown cause with intravenous ampicillin.

5. Diagnosis is based on a 4 fold rise in titer over a 2 week period, or identification of the organism in the urine or on a renal biopsy specimen; a single titer of $\geq$1:800 establishes a presumptive diagnosis.

C. Acute ureteral obstruction due to uroliths in a cat in which the other kidney (or both kidneys) have chronic renal disease is currently the most common cause of ARF in cats.

D. Acute Bacterial Pyelonephritis: rare cause of renal failure

E. Metabolic: Severe hypercalcemia caused by Vitamin D containing rodenticides

F. Hemodynamic/Infarction - associated with embolic shower from bacterial endocarditis or disseminated intravascular coagulation (DIC) of any cause, such as in heat stroke; associated with profound hypotension;

G. The one acute glomerulopathy is a vasculitis seen in racing greyhounds (renal vascular glomerulopathy) associated with the feeding of raw or undercooked meat (due to toxin associated with E. coli).

III. Extended data base when suspect acute renal failure
   A. Ethylene Glycol Test
   B. Leptospirosis titers in dogs
   C. Ultrasonograpy/abdominal radiographs for evidence of ureteral obstruction/ureteral stones in cats
   D. Renal Biopsy if cause remains undetermined

IV. Stages of acute Renal Failure: most begin as uremic because of severity of the injury, but some causes (such as aminoglycoside toxicity) begin as polyuric and progress over days to uremic.

V. Signs which suggest that the renal injury is acute

   A. History: acute onset with no previous problems related to the urinary system; exposure to a toxin?; exposure to lakes/streams/marshes/puddles? (leptospirosis in dogs)

   B. Physical Findings

      1. Kidney size (palpation): symmetrical, normal or mildly enlarged in size.

      2. Renal pain - due to swelling and stretching of renal capsule (uncommonly recognized)

   C. Clinicopathologic Evaluation

      1. Hematology

         a. Leukocytosis - Uncommon even in inflammatory renal disease with the following exceptions:

            1. Acute pyelonephritis (acute bacterial injection of the renal pelvis and adjacent renal tissue)

            2. In association with a systemic inflammatory disease, such as bacterial endocarditis

         b. Thrombocytopenia: seen with Rocky Mountain Spotted Fever; 50% of cases of leptospirosis; DIC.

      2. Blood Chemistry: changes characteristic of primary renal failure but none specific to acuteness

      3. Urinalysis

         a. <u>May</u> see increased number of granular casts;

b. Specific gravity is 1.008-1.029 (neither concentrated nor hyposthenuric); similar to chronic diseases.

c. Acute infarction can result in hematuria.

d. Acute bacterial pyelonephritis causes pyuria, bacteriuria.

e. Proximal tubular injury may result in glucosuria (with normal blood glucose) and mild proteinuria.

f. May see large numbers of calcium oxalate monohydrate crystals with ethylene glycol toxicity.

D. Radiography - in acute renal failure the kidneys are symmetrical, either normal in size or mildly enlarged.

E. Ultrasonography - echogenicity may be normal to increased; kidneys with ethylene glycol toxicity are very hyperechoic; kidneys in dogs with acute leptospirosis often have mild US changes, even though severely azotemic

F. Histopathologic Evaluation - Varies with etiology; may be used to differentiate acute from chronic renal failure and to identify the cause of acute renal failure.

V. Prognosis - From complete recovery to death, dependent on degree of injury; in general, better than in chronic disease since potential for repair and compensation; time required for recovery: days to months. Chronic renal failure may develop if renal injury not resolvable.

Chronic Renal Failure

I. Pathogenesis

A. Gradual decrease in nephron population with compensation by remaining nephrons-maximal compensation has occurred when only 33% of nephrons remain; even at this point, the remaining nephrons can maintain homeostasis as long as no sudden changes occur and as long as water intake is not restricted. As nephrons drop out, fibrosis occurs leading to decreased renal size unless the cause is an infiltrative disease such as neoplasia in which case asymmetric renomegaly occurs.

B. First sign in dogs: obligatory PU/PD - at point when only 33% of nephrons remain functional (GFR is 33% of normal).

C. Azotemia, Uremia: occurs when only 25% of functional nephron mass remains (GFR is 25% of normal) or when a pre-renal factor is superimposed on maximally compensating nephrons - e.g. restricted access to water or any disease which results in dehydration or decreased water consumption.

D In cats, first sign may be azotemia with retained concentrating ability; as disease progresses in cats, polyuria/polydipsia will become evident.

E. The kidney is important in red cell production through erythropoietin and in maintenance of bone mass through 1,25 Vitamin D. With advanced chronic disease, these functions are diminished, leading to non-regenerative anemia and renal hyperparathyroidism leading to osteoporosis.

F. The kidney is important in regulation of blood pressure; hypertension is common in dogs and cats with renal failure

II. Common Causes in Dogs

A. Degenerative

1. Chronic renal failure may follow an acute renal injury; for example about 50% of cases of leptospirosis in dogs remain azotemic after recovery due to 75% of the injured nephrons having been beyond repair; injured tissue is replaced with fibrous tissue.

2. Aging - nephrons are lost with advancing age; however, because renal reserve is so great the majority of animals will die of another disease process prior to the onset of renal failure; chronic renal failure is a major problem and 2-5% of aged dogs (>10yr).

B. Congenital

1. Chronic renal disease in young dogs, unknown whether inherited or acquired during gestation

2. Many Different Purebreeds -some examples: Lhasa Apso/Shih Tzu, Cockers, Norwegian Elkhounds, Pekingese, Alaskan Malamutes, GSD, Miniature Schnauzers, Dachshunds, Chows, Shelties, Dobermans.

3. Amyloidosis in Shar Pei dogs may be due to a genetic predisposition; in contrast to amyloid deposition in other breeds which is in the glomerulus; amyloid deposition in the Shar Pei is mainly interstitial so affected dogs are minimally proteinuric

C. Metabolic: Hypercalcemia

1. Due to hyperparathyroidism or pseudohyperparathyroidism or vitamin D toxicity (due to cholecalciferol containing rodenticides)

2. Results

a. initially in polyuria with isosthenuria or hyposthenuria and inability to concentrate. This is due to:

1) Calcium interfering with ADH action.

2) Interference with Na reabsorption leading to saline diuresis.

b. there is also increased afferent arteriolar resistance in glomerulus causing decreased GFR.

c. eventually deposition of $CaPO_4$ in tubular cells and interstitium causes injury and fibrosis which may progress even after serum calcium is returned to normal.

D. Neoplastic: Most neoplasms in dogs affect only 1 kidney so that renal failure does not result;

E. Inflammatory/Infectious

1. Chronic pyelonephritis: chronic bacterial infection of the kidneys, which begins in the renal pelvis; rare cause of CRF but may complicate it

2. Bilateral Renal/Ureteral Calculi: injure renal tissue through pressure necrosis and renal pelvic or ureteral obstruction;

G. Inflammatory/Immune Mediated: glomerulonephritis is generally chronic and usually immune mediated in origin

H. Amyloidosis :a markedly proteinuric disease in most dogs due to primary deposition in the glomerulus

I. Idiopathic: Often find “End Stage Renal Disease” (small fibrotic, mineralized kidneys) with no prior history of renal problems and with no obvious underlying cause.

III. Common Causes in Cats

A. Degenerative: about 15% of geriatric cats (>15 yr); this is 3x higher than

dogs or humans; the incidence of CRF in cats has been increasing dramatically from 16/1000 cats in 1990 to 112/1000 cats in 2000; about 20% of old cats with CRF also have nephrolithiasis

B. Anomaly

1. Polycystic Renal Disease: Persians: autosomal dominant genetic basis; can be diagnosed by ultrasound in kittens; seen in random other cats as well
2. Amyloidosis in Abyssinians; signs do not develop until cats are several years old; as in Shar Peis, amyloid deposition is primarily interstitial so affected cats are minimally proteinuric

C. Inflammatory

1. Nephrolithiasis: usually calcium oxalate uroliths; may move into

the ureter and cause partial ureteral obstruction leading to hydronephrosis; dramatic increase in incidence over the past 10 years from 10/1000 cats in 1990 to 139/1000 cats in 2000; most cats with nephrolithiasis also have bilateral CRF and their prognosis is worse than cats with CRF without nephroliths;

2. Bacterial Pyelonephritis: rare as cause of CRF but may complicate it
3. Glomerulonephritis: associated with FeLV
4. FIP: causes increased renal size through granulomatous inflammation

D. Neoplasia: the most common type of neoplasia is renal lymphosarcoma which affects both kidneys and thus causes chronic renal failure

E. Nutritional - Renal lesions severe enough to result in azotemia have been produced in cats by feeding diets high in protein and low in potassium and magnesium, which are acidifying. In some cats on such diets, hypokalemia becomes severe, resulting in prominent signs of muscle weakness (ventral flexion of the neck) as the primary presenting signs.

III. Stages of Chronic Renal Failure

A. Polyuric, non-azotemic (usually only noted in dogs, not cats because of the cat's great urine concentrating ability)

B. Polyuric, azotemic, non-uremic

C. Polyuric, uremic

D. Oliguric, uremic

IV. Signs which suggest renal failure is chronic

A. History

1. Prior history of PU/PD in dogs (less than 1/3 of cats present with this) or other urinary tract problems, such as infection or calculi

2. Most cats present because of weight loss associated with decreased appetite and occasional vomiting and diarrhea. Dogs may have similar signs.

3. The onset of uremia is <u>often</u> <u>acute even though the disease process is chronic</u> - the owner misses the insidious onset of PU/PD and a pre-renal factor often leads to decompensation of marginal renal function.

B. Physical examination

1. Normal to reduced renal size; may also be irregular and firmer than

normal; exceptions are neoplasia, granulomatous diseases (such as FIP), hydronephrosis, and polycystic disease with which kidneys may be enlarged and asymmetric;

2. Pale mucous membranes (in some but not the majority of cases, because anemia is a problem that occurs relatively late in the course of chronic renal failure).

3. Evidence of renal osteodystrophy: swollen face in young dogs, rubber jaw in older dogs (in some but not all cases) - again a late change in chronic renal failure; rarely detected in cats

4. May be hypertensive: about 15% of dogs with CRF of tubular origin and up to 80% of dogs with CRF of glomerular origin have increased blood pressure (systolic pressure > 180 mm Hg); hypertension also occurs in cats (approximately 20% have a systolic blood pressure > 175 mm Hg; most cats have tubular disease); severe hypertension (systolic pressure > 180) leads to retinal detachment and acute blindness; severe hypertension can also cause neurologic signs such as head pressing and seizures. Important in dogs as prognosis is worse in dogs with CRF and hypertension; in contrast, prognosis in cats is not worsened by hypertension; hypertension is currently defined in dogs and cats as a systolic blood pressure >150 mm Hg with 150-159 being mild hypertension; 160-179 being moderate hypertension, and 180 and higher being marked hypertension;

5. Cats may display ventral flexion of the neck and muscular weakness if they are hypokalemic.

6. Chronic loss of weight (usually associated with a decline in appetite)

C. Clinicopathologic Evaluation

1. Hematology

    a. Anemia-normochromic, normocytic, nonregenerative

        1) Due primarily to hypoplastic erythroid series - lack of renal production of erythropoietin.

        2) Worsened by internal or external parasitism (inability to respond to chronic blood loss because of lack of erythropoietin)

        3) More common in cats than dogs; only develops in about 10% of dogs with CRF, but presence of anemia in dogs is a poor prognostic sign;

2. Urinalysis

    a. Occasionally a mild proteinuria in tubular diseases -urine protein/urine creatinine ratios of >0.4-1 in cats and >0.5 to 1 in dogs; early or mild glomerular diseases may also have UP/UC ratios in this range

b. a severe proteinuria with a normal urine sediment indicates a glomerulopathy; urine protein/urine creatinine ratio >2

c. 1.008 - 1.029 urine specific gravity in dogs and in cats with advanced disease

d. In dogs and cats with a normal urine sediment, urine protein/urine creatinine ratios are increasingly used to guide prognosis. A normal UP/UC in dogs and cats is <0.2 (note that this value is lower than you will find in older references); a urine protein to creatinine ratio of 0.2 to 0.4 in cats and 0.2 to 0.5 in dogs is considered borderline proteinuria;

e. Urinary tract infections (UTI) are common in dogs and cats with CRF; an increased predisposition to UTI is due to less concentrated urine (highly concentrated urine is inhibitory to bacteria) and to generalized impairment of the cellular immune system; UTI affecting the kidney (pyelonephritis) may worsen renal function; UTI may also be associated with nephroliths;

3. Blood Chemistry

a. Cats with polyuric CRF may be hypokalemic

b. Calcium - tendency to decrease, although serum Ca usually remains normal until very advanced stages of chronic disease.

1) why calcium decreases

a) Increased urinary excretion of Ca from decreased tubular reabsorption.

b) Increased serum phosphorus due to decreased GFR: Directly decreases serum ionized Ca.

c) Increased phosphorus in gut and formation of nonreabsorbable salts with dietary Ca.

d) Increased phosphorus in tissue leading to precipitation of Ca/P salts.

e) Decreased renal metabolism of Vit D to 1,25 dihydroxycholecalciferol leads to decreased intestinal absorption of Ca and increased skeletal resistance to PTH.

2) Tendency to decreased Ca leads to increased PTH

a) Mobilizes Ca & P from bone and leads to osteoporosis so that bones fracture easily (renal osteodystrophy); indicates prognosis is poor since reflects prolonged chronic course.

b) Enhances GI Ca absorption.

c) Enhances Ca reabsorption by kidneys and Phosphorus excretion.

d) Maintains serum phosphorus normal until GRF less than 25% of normal.

e) Maintains serum calcium normal until GFR is extremely low

3) In some cases, total serum Ca is increased in chronic renal failure - either because hypercalcemia is the cause of the renal failure or because of increases in bound calcium; certain compounds retained in azotemic states have the ability (like albumin) to bind calcium; remember that total serum calcium is the sum of ionized calcium (the biologically important component), albumin bound calcium, and other bound calcium.

D. Radiography

1. Survey Films

a. kidney size: normal to bilaterally decreased in size (<2.5 x length of L2 vertebra on DV or VD view); exceptions are that kidneys may be enlarged and asymmetric with neoplastic, granulomatous, polycystic disease, and hydronephrosis;

b. also taken to rule out renal or ureteral calculi either as a cause of renal failure or associated with renal failure in cats;

c. Osteoporosis may be evident, especially prevalent in mandible.

2. Excretory urography: to further delineate renal size; to rule out radiolucent calculi and pyelonephritis; to rule out ureteral obstruction from calculi, structures or masses

E. Ultrasonography: to delineate renal size and echogenicity; to rule out polycystic disease in which the kidneys have large hypoechoic areas; fibrosis results in increased echogenicity; to rule out ureteral or renal pelvic obstruction (evidence of hydronephrosis and hydroureter); to detect enlarged parathyroid glands.

F. Renal Biopsy

1. May give a specific diagnosis, e.g. amyloidosis, or indicate severity of chronic changes.

2. Technique – usually done percutaneously under general anesthesia in cats since kidneys are usually easy to palpate; usually done percutaneously with ultrasound guidance in dogs; can also be done via laparoscopy or by a keyhole technique in dogs; illustrated in textbooks

3. Often done in glomerular disease in dogs to differentiate amyloidosis from glomerulonephritis; often done in cats with large, lumpy kidneys to diagnose lymphosarcoma and FIP; rarely done in animals in which other findings suggest chronic, end-stage disease, since therapy rarely changed by biopsy findings.

V. Prognosis

A. Chronic renal disease tends to be progressive and the patient will not be cured, but the rate may be very slow (over months to years); thus if the disease is discovered at the polyuric only or azotemic/polyuric stages, the outlook is good

B. If the patient is polyuric and uremic, the chances are fair that it can be returned to a non-uremic condition if it remains polyuric especially if a pre-renal factor has caused the decompensation; will eventually become uremic again; may have a good short term prognosis if a pre-renal problem caused the decompensation and that problem can be avoided in the future.

C. If the patient is oliguric, the prognosis is very poor as this is the terminal stage of chronic renal disease

D. Non-regenerative anemia due to CRF is a poor prognostic indicator in dogs as most with this finding on presentation die or are euthanized due to poor quality of life within 6 months. Dogs that are not anemic and well managed for renal failure have a median survival of two years. Anemia is not a poor prognostic indicator in cats as most live >300 days despite presenting with anemia

E. Hypertension (SBP > 160) in association with CRF is a poor prognostic indicator in dogs. Hypertension is not a poor prognostic indicator in acute renal failure or in CRF in cats.

F. A urine protein/urine creatinine ratio > 1 was associated with a poorer prognosis in dogs and a ratio > 0.4 was associated with a shorter survival time in cats with CRF (but the median survival was still almost 9 months as opposed to two years with a UP/UC < 0.4).

Therapy of Renal Failure

I. Prevention

A. Evaluate renal function by measuring BUN/serum creatinine/urinalysis before anesthesia in all animals with a history of PU/PD (this should be a standard question before any anesthetic episode) and in all older dogs and cats (> 5 years)

B. Rapidly correct pre and post renal azotemia.

C. If poor renal function present, use adequate fluid therapy before, during, and after any anesthetic episode; if renal failure is known to exist and appropriate fluid therapy is given, mild to moderate renal failure is not a contraindication for anesthesia.

II. General Principles

A. Do diagnostic lab work, particularly the UA, before treatment instituted; time usually available for hx, p.e., lab work before treatment necessary in renal failure. If cystocentesis by palpation is unsuccessful, ultrasound can be used. If ultrasound is unavailable, catheterization of the bladder via the urethra to obtain urine is indicated in all sick dogs prior to fluid therapy. Catheterization is more difficult in cats, usually requiring sedation and sedation is generally avoided in sick animals until they are stabilized.

B. Clinical signs of uremia not due to renal disease itself but due to fluid, acid-base, and electrolyte abnormalities, retention of metabolic wastes; basis of tx - keep patient alive until kidney can re-establish homeostasis compatible with life - can be expensive and prolonged - why establishing reversibility, acute or chronic nature, so important to client.

III. Specific therapy for renal failure

A. Limited to eliminating precipitating cause if identifiable to prevent further renal damage; especially important in acute renal failure; for example, Leptospirosis, drug toxicity, and heat stroke

B. Renal lesions already present must heal or be compensated; currently no therapy for renal tubules or glomeruli specifically (although research continues in this area)

IV. General Principles of Supportive Therapy

A. Avoid giving anything unnecessarily - drugs eliminated by kidney can accumulate, become toxic, and add to problems;

1. Drugs metabolized by the liver require little change in dosage - chloramphenicol, macrolides, short-acting barbiturates.

2. With some drugs, higher than normal blood levels are relatively nontoxic - penicillin and its derivatives, cephalothin.

3. Avoid nephrotoxic drugs - aminoglycoside antibiotics, NSAIDs

4. Avoid corticosteroids and tetracycline - increase protein catabolism.

5. With other drugs - Adjust dosage or increase interval between doses - check before using any drug whose excretion you do not

know.

6. If using a drug for urinary tract infection, be sure the drug will still be effective - reduced renal function may prevent excretion of effective urine concentrations, e.g. sulfonamides, nitrofurantoin.

B. Basic premise - maintenance of fluid, electrolyte, acid-base and caloric balance as much as possible; specific requirements for therapy will depend on severity of renal failure (oliguric uremic, polyuric uremic, azotemic but non-uremic, or only polyuric).

C. Be careful with catheterization of vascular and urinary systems - the patients have depressed cell mediated immunity.

D. Monitor animal's physical examination often to determine whether it is improving or worsening; monitor body weight to help determine hydration status; monitor BUN, creatinine, calcium, phosphorus, acid/base, and electrolytes to evaluate response to and efficacy of therapy

V. Estimation of the degree of dehydration as a percentage of body weight from physical examination findings

Percentage of Dehydration	Physical Examination Findings
< 5 %	No abnormalities
5%	Slightly doughy inelasticity of the skin
7%	Definite inelasticity of the skin; capillary refilling time 2-3 seconds (normal < 2 seconds); slight depression of eye into orbit
10%	Severe skin inelasticity; capillary refilling time > 3 seconds; markedly sunken eyeballs; shock in debilitated animals; involuntary muscle twitching
12%	Shock; imminent death

VI. Treatment of Oliguric Uremic Renal Failure

A. Remember the R/O for Oliguria

1. Severe Pre-renal insult

2. Urinary Tract Obstruction or Rupture

3. Severe Renal Failure: acute or chronic

4. BE SURE to r/o #1 and #2 before concluding that the animal has #3 since most animals with #3 are euthanized because of the poor prognosis, while conditions #1 and #2 are usually reversible.

B. Treatment problems with oliguric renal failure: need fluid therapy to correct dehydration and improve renal perfusion/stimulate GFR, but tendency to overhydration with fluid therapy; need to reduce serum K when increased;

C. Insert an intravenous catheter (jugular vein) and an indwelling urinary catheter; record body weight and respiratory rate and character

*D. Correct fluid deficit over 2=4 hours - body weight (kg) x % dehydration; maximal rate of fluid administration in dogs/cats is 90 ml/kg/hr . (*required formula)

1. Fluid of choice is usually lactated Ringer's solution (LRS) or Normosol R because these fluids are more similar to plasma (less Na and Cl load) and combat acidosis;

Fluid	Na	Cl	K	pH	Buffer	Cost
0.9% NaCl	154	154	0	5	None	a
LRS	130	109	4	6.5	Lactate	a + 5%
Normosol R	140	98	5	6.4	Acetate	a + 100%

2. Monitor for signs of overhydration - increasing body weight, pulmonary edema, increasing central venous pressure, clear nasal discharge, peripheral edema.

3. Check for urine production.

E. Try osmotic diuresis with hypertonic dextrose (10%)

1. Mechanism

   a. Expands cardiac output and extracellular fluid volume and thus increases renal blood flow and glomerular filtration rate.

   b. Increases urine flow through the nephron due to increased intratubular osmolarity.

2. Technique

   a. Administer 10% dextrose at 5 ml/kg for 20 minutes depending on patient size.

   b. After 20 minutes, check urine for presence of glucose.

      1. If +: Decrease rate of flow to administer a total calculated dose of 22 ml/kg over 2 hrs; should produce an almost equal volume of urine. If this occurs, manage as a polyuric, uremic patient (described in next section).

      2. If - and less than 1 ml urine produced/min -

discontinue therapy and observe for 30 minutes; if no increase in urine production, try natriuretic diuretics.

F. Natriuretic diuresis - Furosemide IV in increasing doses beginning at 2.2 mg/kg; can increase to 10 mg/kg if no response; diuresis should begin within 15 minutes of an IV dose; will be maximal at 30-45 minutes and persist for 2 hours;

1. Mechanism - Inhibits tubular reabsorption of Cl; therefore induces urine flow in spite of low GRF and may work in patients unresponsive to osmotic diuretics.
2. Complications if effective - hypokalemia, dehydration, hypotension
3. Often ineffective

G. If unable to induce urine production, must reduce fluid intake to amount needed for maintenance and meet losses (urine, GI tract) or dialysis or euthanasia if prognosis for underlying disease is poor (remember that prognosis to return from an oliguric state to normal renal function is poor because of the severity of the renal injury, but does occur with ARF not due to ethylene glycol on occasion).

1. Supply insensible fluid losses – 15 ml/kg/day
2. Replace measured urinary losses (adjusted every 4 hours)
3. Replace estimated losses from vomiting/diarrhea and correct any evident dehydration.

H. Peritoneal or hemodialysis: rarely used in general veterinary practice but available in a limited number of referral centers

I. To monitor oliguric patient for improvement:

1. Urine output
2. Clinical signs
3. Degree of azotemia
4. Serum K (if originally increased)

VII. Treatment of Polyuric Uremic Renal Failure

A. Insert intravenous catheter (jugular vein)

B. Correct dehydration with fluid therapy - do this over 2-4 hours rather than the usual 24-48 hours for other causes of dehydration; generally use Lactated Ringers or Normosol R because of acidemia;

C. Anti-emetics - Anti-emetics may be necessary to control vomiting from uremia; H2 blockers often used because of hypergastrinemia associated with renal failure, even though H2 blockers are not direct anti-emetics.

D. Lactated Ringers or Normosol R for Maintenance

1. Calculate maintenance at 60 ml/kg/day; give throughout the day intravenously if uremic *(required formula)

2. Tendency to hypokalemia with polyuria usually necessitates additional K in maintenance fluids; (see F)

E. Intensive diuresis using osmotic agents

1. Purpose - To increase turnover of body water and to establish and maintain adequate renal perfusion.

2. Mechanism

a. Increases renal blood flow by expanding ECV and Cardiac Output.

b. Increases tubular urine flow due to increased osmolarity in tubule (increased fluid in tubule, decreased Na reabsorption via decreased Na concentration).

3. Drug used: Dextrose (10%)

4. Technique

a. Weigh patient so can determine if overhydration developing.

b. Monitor urine production by palpation of the bladder and observation.

c. Administer 20 ml/kg 10% Dextrose IV over 90 minutes; do this 2 to 3 times per day

F. Management of hypokalemia

1. If patient is polyuric (producing > 2.2 ml/kg/hr) and is on osmotic diuresis, will become hypokalemic if not supplemented; can supplement by

a. Oral elixirs 1-3mEq/Kg/day if <u>not</u> vomiting.

b. SQ KCl, 36 mEq/L in Lactated Ringers (total 40 mEq/L).

c. IV KCl, 16 mEq/L Lactated Ringers (total 20 mEq/L).

d. Adjust the above doses by monitoring serum K.

2. <u>Never</u> exceed 0.5mEq K/Kg/hour intravenously *(required formula)

3. Hypokalemia is a serious problem in some cases of renal failure in

cats; in fact, muscle weakness may be the principle presenting sign; in these cases, much higher doses of potassium may be needed:

Serum Potassium (mEq/250 ml)	IV/SQ Supplementation
3.0-3.5	5/10
2.5-3.0	7/14
2.0-2.5	10/20
<2.0	12/24

G. If patient requires osmotic diuresis for more than 24 hours and cannot (continued vomiting) or will not eat, institute nutritional support. If patient will not eat, but is not vomiting, insert a feeding tube and utilize this to provide sufficient calories. If patient cannot tolerate feeding because of vomiting, parenteral nutrition is required.

H. While patient is on diuresis, must monitor each day and correct dehydration each day - we usually estimate a minimum of 5%.

I. Example of Patient Management - e.g 10 kg dog, 5% dehydrated, uremic, polyuric

1. To correct fluid deficit

   5% x 10 kg = .5L = 500 ml over 2-4 hours = 125-250 ml/hour for 2-4 hours; Lactated Ringers. (maximum fluid rate is 90 ml/kg/hr = 900 ml/hr)

2. Maintenance fluid requirement

   60 ml/kg/day = 600 ml/day Lactated Ringers supplemented with KCl at 20 mEq/L iv or 40 mEg/L SQ.

3. Osmotic diuresis with 10% dextrose

   22 ml/kg = 220 ml tid 10% dextrose
   220 ml x 3 times/day = 660 ml/day

5. Therefore one schedule of fluid therapy for the dog would be as follows assuming starting treatment at 4:00 PM on the first day:

   a. 4pm-6pm: 250 ml/hr Lactated Ringers IV (to correct dehydration)

   b. 6pm-8pm: 110 ml/hr 10% dextrose IV(for diuresis)

   c. 8pm-8am: 40 ml/hr Lactated Ringers IV plus 16 mEq KCL/L (for maintenance of hydration); if monitoring an IV infusion overnight is not possible you could give 500 ml Lactated Ringers + 16 mEq KCl SQ

d. 8am-10am: 110 ml/hour 10% dextrose IV(for diuresis)

e. 10am-2:00pm: 30 ml/hr LRS plus 16 mEq KCL/L IV(for maintenance)

f. 2pm-4pm: 110 ml/hr 10% dextrose IV (for diuresis)

J. Monitoring therapy - Serial evaluations of BUN, creatinine, electrolytes, albumin, PCV/TS, patient's clinical status, body weight; adjust therapy as necessary; it is not necessary to reduce BUN or creatinine to normal - just return patient to point of being able to maintain itself;

K. When patient stable, discontinue fluid therapy gradually by about 33% per day, continuing to monitor BUN, creatinine, electrolytes, clinical status and body weight.

VIII. Treatment of the Polyuric, Azotemic, Non-Uremic Patient

A. Maintain euhydration: free access to water, subcutaneous fluid support if needed, avoid pre-renal insults which result in dehydration

B. Maintain appetite and normal body weight

1. Correct electrolyte disorders and acidemia; anemia if PCV < 20%

2. If nauseous, oral H2 blocker

3. Avoid unnecessary drugs

4. Avoid abrupt dietary changes

5. Improve food palatability: warming, flavoring agents, more frequent small meals

6. Treat gum and tooth disease

C. Manage Azotemia

1. The purpose of restricting protein intake to maintenance levels is to reduce the concentrations of metabolic products of protein metabolism. BUN will decrease as an indication of efficacy of therapy. Fats and carbohydrates are metabolized to $C0_2$ and H_20 and eliminated; protein is incompletely metabolized. Byproducts include urea, aromatic acids, amines, indoles, phenols, peptides which must be excreted by kidneys. These are the "middle molecules of uremia" and are thought to be responsible for the signs of uremia. Urea itself is not a uremic toxin but is an indicator of other molecules; BUN levels correlate better with uremic signs in man than other renal function tests: BUN levels in renal failure dogs and cats are <u>markedly</u> influenced by protein intake. Protein quality is as important as quantity. Essential amino acids must be

supplied in appropriate quantities if dietary protein is to be used for structural protein synthesis rather than metabolized for energy.

2. Although reducing protein intake helps ameliorate the signs of uremia, restricting protein intake has not been proven to slow the progression of chronic renal injury.

3. One must feed at least maintenance amounts of protein or the animal will lose weight and become malnourished - dog 1.29 g protein/Kg, 66 Kcal/kg/day; cat 3.73 g protein/Kg, 80 Kcal/kg/day. Some studies show that maintenance for normal dogs and cats may be insufficient for some renal failure animals so you must re-evaluate your patients frequently when making dietary changes to be sure the animal is doing well nutritionally. Providing adequate caloric intake is as essential as protein quality and intake; animal should maintain ideal weight; if caloric intake insufficient - will digest own body proteins and lose weight/muscle mass.

4. Diets

   a. Homemade (see textbooks for recipes)

   b. commercial; for examples, Hill's canine K/D or Purina canine NF Diet = 1.8 g protein/Kg when fed at appropriate caloric needs (regular dog foods - >3.0 g/Kg);

   c. Feline k/d contains about 21% protein which should supply about 3.7 gm/kg/day when fed to meet caloric needs.

   d. The clinician needs to adjust protein intake as needed to reduce BUN and yet maintain normal food intake; protein restricted diets tend to be less palatable than regular diets.

5. When to institute protein restriction - when moderate azotemia (BUN > 75 mg/dl) exists; only known benefit at lower levels of azotemia is to assist in phosphorus restriction

D. Manage Hyperphosphatemia

1. Basis - Phosphorus restriction shown to reduce mortality and renal lesions in experimentally induced renal failure in rats and dogs; also assists in prevention of renal osteodystrophy

2. Goal: normal serum P and serum Ca X P < 70

3. When to institute - whenever hyperphosphatemia due to renal failure identified

4. Means

   a. Phosphorus restricted diets - Often correspond with protein restricted diets (want phosphorous to be < 0.35 % dry matter),

b. If diet alone does not maintain normophosphatemia, phosphate binders - Al (OH_3) (for example, Amphogel) is added. Calcium carbonate and calcium acetate can also be used as P binders but must monitor for development of hypercalcemia with calcium containing products; must give with meals to be effective (bind phosphate in the diet in the intestinal tract so it is not absorbed).

E. Renal Secondary Hyperparathyroidism

1. Consequence of chronic renal failure; osteodystrophy is a poor prognostic sign because indicates advanced, chronic disease

2. Therapy

a. establish and maintain normal serum phosphorus concentrations

b. establish and maintain normal acid-base status

c. calcitriol: used only if serum P is normal and Ca x P product can be maintained <60; risk of soft tissue mineralization if hypercalcemia develops or if Ca x P > 60; renal mineralization will potentiate existing renal disease; thus, use carries risk to patient; use of calcitriol under carefully controlled conditions (monitoring of serum ionized calcium and PTH every 2 weeks for 1 month and then every 2 months) did increase duration of survival in dogs with CRF from 250 to 365 days (mean serum creatinine at start was 4 mg/dl);

F. Alter Dietary Lipids

1. Dogs in renal failure fed a diet with a high concentration of omega-3 fatty acids (menhaden fish oil) had less proteinuria, lower serum creatinine, higher GFR, and less severe renal interstitial fibrosis than dogs fed a high concentration of omega-6 fatty acids (safflower oil). The beneficial effect is thought due to decreased inflammation, vasoconstriction and platelet aggregation.

2. The current recommendation is an omega 6: omega 3 ratio of 5:1 (generally been incorporated into commercial renal failure diets).

G. Hypertension

1. Diet

a. Too much Na leads to extracellular fluid volume expansion which has the potential to worsen hypertension; generally restrict Na if animal is hypertensive, although there is little evidence in naturally occurring canine and feline renal failure that blood pressure is “sodium sensitive”; in fact, Dr. Scott Brown has shown that salt has no effect on blood pressure in experimentally induced CRF in cats;

b. Too little Na leads to extracellular fluid volume depletion which leads to reduced renal blood flow and GFR;

c. Therefore change Na intake gradually (remember diseased kidney cannot adjust to rapid changes in dietary intake of sodium).

d. Most renal failure, commercial diets (e.g. Hill's k/d, Purina NF) are currently low in Na as compared to regular dog foods; therefore, if starting these diets, change from animal's regular diet gradually over at least 2 weeks (this also may help with palatability of renal failure diets).

2. Anti-hypertensive drug therapy: amlodipine effective in cats; hypertension associated with CRF in dogs is usually refractory to treatments tried to date. Enalapril may be used in dogs if serum creatinine is less than 3 mg/dl. Enalapril can cause GFR to decrease so renal function must be carefully monitored when it is used.

H. ACE Inhibitors and Chronic Renal Failure

1. Benefits

a. Reduce proteinuria (lower glomerular pressure by vasodilation of the afferent arteriole)

b. Slow progression in some diseases/models

c. Less severe renal lesions in experimental models

d. Blood pressure control – better in humans than dogs/cats

2. Adverse Effects

a. Occasionally worsen azotemia

b. Can cause anorexia

H. Acidemia

1. Acidemia of mild renal failure is usually compensated by lungs;

2. Renal failure patient is more susceptible to acidemia from pre-renal causes - diarrhea, sepsis, fever, catabolism, oral administration of acids (e.g. NH_4Cl, ascorbic acid as urinary acidifiers or diets designed to acidify the urine). Such products should be avoided.

3. Supplement $HC0_3$ when $TC0_2 < 15$; dose of $HC0_3$ is that which will raise $TC0_2$ to >15;

4. Renal failure dogs on protein restricted diets have greater tendency

to acidemia - perhaps due to lesser ability to excrete ammonia; therefore $TC0_2$ should be measured 1-2 weeks after starting these diets and $NaHC0_3$ supplemented as necessary; remember this is given to effect so you must recheck the laboratory work and adust as needed

5. Therapy: either sodium bicarbonate (baking soda) or potassium citrate can be used

I. Hypokalemia in Cats

1. Avoid acidifying diets (Hill's c/d, s/d, Purina UR, etc.)

2. Therapy: oral potassium gluconate or potassium citrate

J. Water soluble vitamins (B-vitamins)

K. Non-regenerative anemia

1. Anabolic steroids: to increase RBC production (not very potent and some potential adverse effects such as hepatopathy).

2. Human Erythropoietin (Epogen) - very effective for anemia due to CRF, but expensive; vehicle is human albumin so anaphylaxis possible; about 25% of cats and 60% of dogs treated develop anti-erythropoietin antibodies leading to severe anemia which is slowly reversible when the drug is stopped. Approximately 40% of cats also developed neurologic signs (seizures, bizarre behavior). Because of these side effects, human erythropoietin is not usually used unless the anemia is of sufficient severity to have a negative effect on the quality of life. Canine and feline erythropoietin have been synthesized and tested to a limited degree. They are not commercially available at present.

3. Be sure that all blood sucking parasites (internal and external) are eliminated.

L. Urinary Tract Infection

1. Animals with renal failure are immunosuppressed and don't concentrate their urine, both of which increase susceptibility to UTI (urinary tract infection)

2. Renal failure animals are not routinely placed on antibiotics to avoid this because of side effects of antibiotic therapy and because of potential development of antibiotic resistant infections; however, urinalyses should be re-evaluated frequently and any infections detected are treated.

M. Monitoring Therapy

1. Patients should be rechecked two weeks after any changes are made in therapy and every 3 months otherwise. These rechecks include history, physical examination, measurement of body weight,

CBC, biochemical profile, and urinalysis. Blood pressure measurement is also recommended.

2. The purpose is to detect and correct any developing abnormalities to keep the patient as healthy and stable as possible for as long as possible.

3. In humans, frequent re-evaluation significantly slows progression of renal failure.

IX. Treatment of the Polyuric, Non-Azotemic Renal Failure Patient

A. Abundant fresh water and avoid pre-renal insults

B. Dietary sodium restriction - optional, may minimize polyuria to make pet easier to manage; institute gradually.