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Popular Article

Renal Dysfunction: Acute Kidney Injury and Chronic Kidney Disease

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Abstract

Kidney diseases in dogs present significant veterinary concerns due to their impact on morbidity and mortality. Canine kidneys are essential for filtering waste, balancing electrolytes, and regulating blood pressure, with each kidney containing approximately a million nephrons responsible for these critical functions. Kidney diseases in dogs are broadly classified into acute kidney injury (AKI) and chronic kidney disease (CKD), each with distinct etiologies and clinical manifestations. AKI results abruptly from factors like reduced blood flow or toxin exposure, while CKD develops progressively, often associated with aging. The pathophysiology of AKI involves prerenal, intrinsic renal, and postrenal causes, each contributing differently to the onset and progression of renal failure. CKD is characterized by irreversible and progressive loss of renal function, often due to congenital or acquired conditions. Diagnosis involves a combination of clinical history, physical examination, laboratory findings, and diagnostic imaging. Management strategies are complex, integrating fluid therapy, medications, and in some cases, advanced interventions like dialysis.

Introduction

Canine kidney disease, a significant health concern, manifests in two primary forms: acute and chronic. Acute kidney disease emerges abruptly, often resulting from sudden decreases in blood flow, trauma, or exposure to harmful substances. In contrast, chronic kidney disease develops gradually over time, frequently associated with the aging process in dogs. Symptoms of kidney disease in canines can be subtle, including increased urination, excessive thirst, decreased appetite, lethargy, and weight loss. Early detection and intervention are vital for effective management, which may involve intravenous fluid therapy, nutritional monitoring, and medications to alleviate symptoms and support kidney function. Furthermore, addressing electrolyte imbalances and ensuring proper hydration are critical components of treatment, emphasizing the importance of proactive care and regular veterinary check-ups for our beloved canine companions.

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Anatomical and Functional Overview of Canine Kidneys

The kidneys in dogs are essential organs that lie against the back abdominal wall, lateral to the spine, in the lumbar region. The right kidney is slightly cranial to the left kidney, and they are encapsulated, bean-shaped organs that vary in size depending on the dog's size. The functional unit of the kidney is the nephron, which is responsible for filtering waste and regulating fluid balance. Each kidney contains approximately a million nephrons, each comprised of a glomerulus and a long tubule that eventually empties into the ureter. kidneys perform various functions, including removing toxins, balancing water and electrolytes, maintaining blood pressure, and releasing hormones to produce red blood cells.

Kidney disease

Kidney disease in dogs encompasses a spectrum of conditions characterized by functional or structural abnormalities in one or both kidneys. Acute renal failure is marked by a sudden decline in renal function, leading to the retention of nitrogenous wastes, while acute kidney injury represents a range of renal injuries from mild, clinically silent nephron loss to severe acute renal failure. On the other hand, chronic kidney disease is defined by kidney damage persisting for at least three months, with or without a decreased glomerular filtration rate. This chronic condition poses a significant challenge as kidney tissue cannot regenerate once damaged, emphasizing the importance of early detection and intervention.

Various factors contribute to kidney diseases in dogs, including old age, trauma, parasites, cancer, autoimmune diseases, inflammation, kidney stones, genetics, and inherited disorders. Additionally, fungal, viral, and bacterial infections, as well as toxicity from poisons or medications, can also lead to kidney issues in dogs. Understanding the multifaceted nature of these causes is crucial for effective diagnosis, treatment, and management of kidney diseases in canine companions. Further research into the intricate mechanisms underlying these conditions is essential for advancing veterinary care and improving outcomes for dogs affected by kidney disease.

Acute Kidney Injury in Dogs: Etiology, Clinical Features, and Prognosis

Acute kidney injury (AKI) is a sudden and potentially life-threatening condition in dogs, characterized by a rapid decline in renal function. The etiology of AKI in dogs can be divided into three categories: prerenal, intrinsic renal, and postrenal causes.

- **Prerenal causes**, such as severe dehydration, hypotension, and sepsis, result in reduced blood flow to the kidneys, leading to AKI.

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- **Intrinsic renal causes**, such as ischemia, inflammation, and infection, involve direct damage to the renal parenchyma, leading to AKI.
- **Postrenal causes**, such as urinary tract obstruction and urolithiasis, result in increased pressure on the kidneys, leading to AKI.

Clinical signs of AKI in dogs include lethargy, anorexia, vomiting, diarrhea, abdominal pain, polyuria, polydipsia, and oliguria. The severity of AKI is classified into five grades based on the serum creatinine concentration. The prognosis of AKI in dogs depends on the underlying cause and the severity of the injury. The mortality rate of AKI in dogs is high, with approximately 30-50% of dogs with AKI dying or being euthanized due to the severity of the condition. Understanding the etiology, clinical features, and prognosis of AKI in dogs is essential for effective management and improving outcomes.

Table-1: Types and Features of Acute Kidney Injury in Dogs

Type	Causes	Prognosis
Pre-Renal	Severe dehydration, hypotension, sepsis	Fair to good with appropriate treatment
Intrinsic Renal	Ischemia, inflammation, infection	Poor to fair, depending on the severity and duration of the injury
Post Renal	Urinary tract obstruction, urolithiasis	Fair to good with appropriate treatment

Table-2: Normal Values of BUN and Serum Creatinine in Dogs

Parameter	Normal Range
Blood Urea Nitrogen (BUN)	10-30 mg/dL
Serum Creatinine	0.5-1.5 mg/dL

Pathophysiology of Acute Renal Failure

Acute kidney injury (AKD) is characterized by a rapid deterioration or loss of renal function, substantial morbidity, and fatality rates. Treatment and prognostic evaluation might be guided by the underlying pathology. Prerenal, intrinsic, or obstructive (postrenal) factors may be the etiology of the AKI. Patients with acute or chronic renal failure develop renal failure as a result of prerenal AKI, which is caused by nonvolume responsive hepatorenal syndrome. Damage to the tubules, glomeruli,

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interstitium, or intrarenal blood arteries can cause intrinsic AKI. The hallmark of postrenal AKI is an abrupt blockage of urine flow, which raises intratubular pressure and lowers glomerular filtration rate (GFR). The proximal tubules and thick ascending limb, two extremely metabolically active nephron segments located in the renal outer medulla, have decreased energetics, which contributes to the pathogenesis of AKI.

Injury to kidney cells can be lethal or sublethal, with sublethal injury profoundly influencing GFR and renal blood flow. The nature of the recovery response is mediated by the degree to which sublethal cells can restore normal function, which may be compromised in some cases. The pathogenesis of ischemic and nephrotoxic AKI involves vascular, tubular, and inflammatory perturbations. The underlying basis of renal injury appears to be impaired energetics of the highly metabolically active nephron segments, which can trigger conversion from transient hypoxia to intrinsic renal failure. Inflammation represents an important additional component of AKI, leading to the extension phase of injury, which may be associated with insensitivity to vasodilator therapy.

Risk factors causing Renal damage:

Nephrotoxins:

- ✓ Ethylene glycol
- ✓ Plants (e.g., Easter lily, raisins, grapes)
- ✓ Phosphate enemas
- ✓ Heavy metals
- ✓ Hypervitaminosis D (e.g., cholecal-ciferol-containing rodenticides, pharmaceuticals)
- ✓ Drugs (e.g., aminoglycosides, amphotericin B, cisplatin, sulfonamides, tetracyclines, nonsteroidal antiinflammatory drugs, radiocontrast agents, ACE inhibitors)
- ✓ Diet-associated nephrotoxicity (melamine/cyanuric aci)
- ✓ Pigmenturia (hemoglobinuria, myoglobinuria)

Ischemia: hypotension, trauma, shock, sepsis, systemic inflammatory response syndrome, hypoadrenocorticism, congestive heart failure, temperature extremes, prolonged anesthesia, anaphylaxis

Infection:

Dogs: leptospirosis, pyelonephritis, borreliosis

Cats: pyelonephritis, feline infectious peritonitis

Others: Thromboembolic disease, hypercalcemia, transfusion reaction, myoglobin/hemoglobinuria,

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vasculitis, envenomation, trauma, urinary tract obstruction, renal lymphoma (cats >dogs)

Associated conditions & disorders: Uremia, pulmonary edema, acute lung injury, hypertension, hyperkalemia with bradyarrhythmia.

Four phases of AKI pathophysiology:

1. Initiation phase: starts with the insult/injury to the kidney. At this time the GFR decreases but obvious clinical signs are unlikely to be observed. If the cause can be identified and removed during this stage it may prevent further disease progression.
2. Extension phase: during this phase, the kidney insult continues as a result of hypoxia, ischaemia and an ongoing inflammatory response. The GFR continues to decrease as cells undergo apoptosis and necrosis.
3. Maintenance phase: the GFR stabilises during this phase as kidney blood flow improves and cellular repair begins. Uraemic complications (vomiting, diarrhoea, changes to drinking and urinating) may become more noticeable; therefore, this is the phase when AKI is generally diagnosed.
4. Recovery phase: This is the final stage which can last for months to years. GFR continues to increase due to cellular repair. However, progression to fibrosis might also occur and patients might develop chronic kidney disease (CKD). It is important to avoid further injury/insult during this stage to prevent relapse.

Clinical presentation of disease forms/Subtypes

- Oliguric/anuric ARF
- Polyuric ARF

History, Chief Complaint: Some or all may be present:

- ✓ Lethargy, depression
- ✓ Vomiting, anorexia
- ✓ Abdominal/general discomfort
- ✓ Recent onset polydipsia, polyuria
- ✓ No urination (no urine production and no attempts to urinate)
- ✓ Multiple animals in same household developing ARF is consistent with toxin-associated renal failure, especially dietassociated.

Physical Exam Findings

Common findings:

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- Dehydration, halitosis, oral cavity debris/secretions, vomitus, ptyalism, normal-sized/enlarged kidneys

May also include:

- ✓ Small bladder
- ✓ Abdominal/renal pain
- ✓ Oral (uremic) mucosal ulcerations
- ✓ Tachycardia, tachypnea

Etiology And Pathophysiology

- ➢ Renal injury initiated by various causes (e.g., ischemia, toxicant, infection)
- ➢ Renal response causes extension of insult through four mechanisms:

i. Impaired glomerular filtration via reduced ultrafiltration coefficient
ii. Tubular obstruction (cellular casts, protein, hemoglobin, crystals)
iii. Tubular backleak of ultrafiltrate
iv. Intrarenal vasoconstriction

Diagnosis:

- ✓ Clinical history
- ✓ Physical examination
- ✓ Laboratory findings
- ✓ Diagnostic imaging

Haematology:

Red blood cell (RBC) count is typically within the reference interval but erythrocytosis might be as a result of dehydration/haemoconcentration. Anaemia is often associated with CKD and a lack of eryrthropoetin production, but might occur in patients with AKI due to blood loss (which might have been the primary cause for the AKI) or secondary to gastrointestinal (GI) bleeding associated with uraemic complications.

Biomarkers in Kidney Injury:

1. Blood Creatinine Concentration:

Increases with the severity of AKI.

Most commonly used biomarker for glomerular filtration rate (GFR).

1. Blood Urea Nitrogen (BUN):

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- ✓ Rises as kidney function decreases.
- ✓ Influenced by factors like gastrointestinal bleeding, hence less specific than creatinine for kidney injury.

2. Blood Symmetric Dimethylarginine (SDMA):
   - ✓ Another biomarker for GFR.
   - ✓ Neither creatinine nor SDMA alone can differentiate between AKI and CKD.
3. Liver Enzymes and Bilirubin:
   - ✓ Levels of alanine transferase (ALT), alkaline phosphatase (ALP), and bilirubin may be elevated in diseases like leptospirosis.
4. Electrolyte and Acid-Base Disorders in AKI:
   - ✓ Accumulation of creatinine and urea.
   - ✓ Hyperkalemia and fluid overload are serious concerns, potentially causing pulmonary edema.
   - ✓ Hyperphosphatemia due to phosphate retention.
   - ✓ Hypocalcemia due to decreased calcitriol production and calcium phosphate precipitation.
   - ✓ Acidosis from impaired hydrogen ion excretion.
   - ✓ Possible coagulation impairment and pericarditis from significant uremia.
   - ✓ Varied urine output depending on AKI type and cause.
5. Cystatin C as a Biomarker:
   - ✓ Small protein (13 kD), used as a GFR or kidney function marker, especially in CKD in dogs.
   - ✓ Produced constantly by all body cells and functions as a cysteine protease inhibitor.
   - ✓ Normally filtered by the glomerulus and reabsorbed in the proximal convoluted tubules; thus, urinary concentrations are low unless there is proximal renal tubular damage.
   - ✓ Increased serum concentrations indicate reduced GFR, making it a potential marker of kidney damage.
   - ✓ Increased urinary concentrations suggest proximal renal tubular injury.
   - ✓ Measurement alongside protein and creatinine values is recommended for accurate assessment due to potential interference from proteinuria.
   - ✓ Its normal concentration is 0.5 – 1.5 mg/dl, so value greater than this is considered as kidney damage.

Increased cystatin C concentration in urine: This could be a potential marker of proximal renal tubular injury. Proteinuria can affect results (by inhibiting renal tubular absorption), so measurement of protein concurrently along with creatinine values (and determination of a cystatin C/creatinine ratio)

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is recommended.

Urine analysis:

- ✓ Measures the concentration of urine.
- ✓ Typical USGs(urine specific gravity) in healthy hydrated dogs and cats are 1.015–1.045 and 1.035–1.060 respectively .
- ✓ Highly concentrated urine (>1.045 in dogs and >1.060 in cats) might indicate a pre-renal cause of azotaemia (such as dehydration), whereas isosthenuria (USG 1.008–1.015) in the face of azotaemia suggests there is intrinsic renal disease .
- ✓ Glucosuria with normoglycaemia and proteinuria are indicators of tubular damage/dysfunction. A fresh urine sample should be prepared and examined under the microscope to look for evidence of white blood cells, red blood cells (RBCs), and bacteria which may indicate an infection.

Measurement of urine output

Assess following complete rehydration. Although polyuric ARF can occur, the classic presentation is oliguria (urine production 2 mL/kg/h) volumes of urine.

Abdominal radiographs Renomegaly is often present (contrasts with small kidneys often identified with chronic kidney disease).

Abdominal ultrasound: Renomegaly; renal pelvic dilation in association with pyelonephritis; alterations in renal parenchymal echogenicity often identified; loss of corticomedullary distinction often identified; hyperechoic cortices (associated with ethylene glycol toxicity but also seen in some healthy cats)

Electrocardiogram (ECG): Altered by pronounced hyperkalemia (bradycardia [more common in dogs than cats], absent P waves, wide QRS complexes).

Factors to be find in AKI patient :

- ✓ Hydration status
- ✓ Blood pressure
- ✓ PCV
- ✓ Cardiac monitoring
- ✓ Electrolytes monitoring
- ✓ Urine output

Treatment Strategies for Acute Kidney Injury and Related Conditions:

1. Fluid Therapy:

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- ✓ Failure to induce diuresis suggests severe parenchymal damage or underestimation of fluid needs.
- ✓ Use diuretics or dopamine if rehydration does not initiate diuresis.

2. Medications and Infusions:
   - ✓ Hypertonic Mannitol: 0.5-1.0 g/kg IV over 15-30 minutes, continue as needed every 4-6 hours.
   - ✓ Furosemide: 2-6 mg/kg IV as an alternative to or following mannitol.
   - ✓ Dopamine: 2-5 mcg/kg/min IV in 5% dextrose; consider dialysis if no diuresis after 4-6 hours.
3. Supportive Medications:
   - ✓ Anti-nausea: Ondansetron.
   - ✓ Antacids: Famotidine.
   - ✓ Blood Pressure Control: Amlodipine (0.18 to 0.3 mg/kg PO SID for cats, 0.2 to 0.4 mg/kg PO SID for dogs).
   - ✓ Gastroprotectants: Sucralfate.
4. Phosphorus Binders:
   - ✓ Administer Aluminum hydroxide or aluminum carbonate at 30 to 90 mg/kg/day with meals.
5. Supplements:
   - ✓ Omega 3 & 6 fatty acids to support overall health.
6. Treatment for Anemia and Infections:
   - ✓ Address anemia and manage infections with appropriate antibiotic therapy.
7. Glomerulonephritis Treatment:
   - ✓ Occurs when immune complexes become trapped in the glomeruli, causing inflammation and damage.
   - ✓ Treatment involves managing the immune response to prevent further kidney damage.

Causes of glomerulonephritis:

Any condition that causes chronic stimulation of the immune system, resulting in the formation of immune complexes, can cause glomerulonephritis. Some possible inciting causes include:

- chronic periodontal (dental) disease o cancer o heartworm infection
- Ehrlichia infection (a tick-borne disease)
- lyme disease (a tick-borne disease)
- pyometra (a bacterial infection in the uterus)
- endocarditis (a bacterial infection in the heart, often secondary to periodontal disease)
- chronically inflamed skin
- immune-mediated diseases (such as lupus erythematosus or discoid lupus)

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- chronic pancreatitis

Clinical signs:

- ✓ Elevated amount of protein in the urine and a reduced amount of protein in the blood.
- ✓ Due to this loss of protein, mild to moderate clinical signs may include weight and muscle loss.
- ✓ More severe clinical signs are referred to as _nephrotic syndrome‘ and include fluid in the abdominal cavity (ascites), increased respiratory effort (due to fluid within the lungs), and swelling of the limbs (peripheral edema).

"The most common clinical sign of glomerulonephritis is blood in the urine”

Diagnosis:

- ✓ "To definitively diagnose glomerulonephritis, a biopsy of the kidney is needed.
- ✓ Other tests include: Complete blood count (CBC) to identify anemia, inflammation, infection or low platelet count
- ✓ Serum chemistry tests to identify low blood protein concentration and high blood cholesterol concentration
- ✓ blood pressure measurement to identify systemic hypertension
- ✓ kidney biopsy to identify glomerulonephritis conclusively and differentiate it from amyloidosis, which is another kidney disease that affects the glomeruli.

Treatment:

- ✓ Immunosuppressive drugs to suppress immune complex formation.
- ✓ A very low dose of aspirin to prevent clotting within the glomeruli.
- ✓ omega-3 fatty acid supplementation to help reduce the inflammatory response and prevent clotting.
- ✓ Specialized prescription diets may be used in some instances. These include: -low protein, low phosphorus diets fed to pets in kidney failure -low sodium diets fed to pets with hypertension
- ✓ Angiotensin-converting enzyme (ACE) inhibitors such as enalapril to minimize protein loss in the urine and to help control blood pressure Medications to control high blood pressure.

Chronic kidney disease —”Chronic” in the context of CKD means an irreversible and usually progressive loss of kidney function and/ or structure. In contrast , acute kidney injury is potentially reversible either by : Resolution of at least part of the kidney injury Development of adaptive compensatory enhancements in kidney function , or a combination of these events.

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Causes of CKD:

1. Congenital
    - Amyloidosis
    - Dysplasia
    - Glomrulopathy
    - Polycystic disease
1. Acquired Infections
    - Metabolic causes (hypokalemia and hypercalcemia)
    - Infections
    - Obstructive nephropathy
    - Neoplasms
    - Proteinuric kidney disease (amyloidosis,gomerulopathies)
    - Chronic nephrotoxin exposurrenal ischemia
    - Immune mediated diseases

Pathophysiology of chronic renal failure

- Reduction of functional nephrons → loss of ability to concentrate urine and retention of waste products.
- Hyperfiltration of remaining nephrons → self-perpetuating destruction of remaining nephrons.
- Metabolic acidosis → renal ammoniagenesis → toxic and inflammatory effect on renal interstitium.
- Uremia → erythropoietin deficiency and shortened RBC lifespan → normochromic, normocytic, non-regenerative anemia.
- Hyperphosphatemia , due to inability to excrete phosphate → hyperparathyroidism → renal osteodystrophy and soft tissue mineralisation (including nephrocalcinosis which may potentiate renal damage).
- Lack of active vitamin D3 (calcitriol) → initiates and exacerbates hyperparathyroidism.
- Proteinuria → increased tubular reabsorption potential to promote tubulointerstitial inflammation → progression of tubulointerstitial nephritis.
- Systemic hypertension → transfer of high systemic pressure to glomerular capillaries → development of glomerular hypertension, glomerular hyperfiltration and glomerulosclerosis perpetuating renal damage.

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Symptoms:

- Excess urinating and drinking
- Weight loss
- Poor appetite (anorexia)
- Weakness
- Vomiting (emesis)
- Seizures
- Ulcers
- Blindness can occur due to the high blood pressure (hypertension)

Peritoneal dialysis (PD) and hemodialysis (HD) are dialysis options for end-stage renal disease patients in whom preemptive kidney transplantation is not possible. Peritoneal dialysis, although associated with a high complication rate, was a successful technique for reducing azotemia in dogs with acute and chronic renal failure.

Fluid therapy:

- ✓ A balanced polyionic solution: lactated Ringer ‘s solution is appropriate in most situations.
- ✓ Physiologic saline (0.9% Nacl) contains no potassium and is suitable when treating hyperkalemia.
- ✓ Fluids low in sodium are more appropriate after rehydration.
- ✓ Determination of the volume to be administered involves consideration of a variety of factors.
- ✓ In patients with signs consistent with chronic or recurrent dehydration, long term subcutaneous fluid therapy may be considered.
- ✓ Peritoneal dialysis (PD) and hemodialysis (HD) are dialysis options for end-stage renal disease patients in whom preemptive kidney transplantation is not possible

Conclusion

In conclusion, kidney diseases in dogs and cats encompass a wide range of conditions with diverse etiologies and clinical presentations. Timely diagnosis, appropriate treatment, and vigilant monitoring are essential for improving outcomes and enhancing the quality of life for affected animals.

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