CHAPTER 12

RENAL DISORDERS

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Abstract

Pharmacological management of renal conditions requires precise medication selection and dosing based on kidney function parameters. Acute kidney injury protocols incorporate preventive strategies, supportive measures, and specific interventions based on underlying etiology and severity markers. Chronic kidney disease management utilizes multiple drug classes targeting complications including anemia, mineral disorders, and cardiovascular risk with systematic monitoring of disease progression. Electrolyte disorder treatment requires careful assessment of underlying mechanisms with targeted replacement or elimination strategies based on severity and chronicity. Drug dosing protocols in renal dysfunction incorporate pharmacokinetic principles with systematic adjustment based on estimated glomerular filtration rate and specific drug properties. Dialysis considerations include medication removal characteristics, timing of administration, and supplemental dosing requirements. Treatment strategies emphasize prevention of further kidney damage while managing multiple comorbid conditions.

Keywords: *Renal pharmacotherapy, Kidney injury, Electrolyte disorders, Drug dosing, Dialysis*

Learning Objectives

After completion of the chapter, the learners should be able to:

- Identify and manage causes of acute kidney injury
- Develop treatment plans for different stages of chronic kidney disease
- Correct electrolyte imbalances using evidence-based approaches
- Calculate appropriate drug doses for patients with renal dysfunction
- Design medication regimens for patients on different types of dialysis
- Monitor renal function and adjust therapy based on patient response.

ACUTE KIDNEY INJURY (AKI)

Acute Kidney Injury represents a sudden deterioration in kidney function, occurring over hours to days. The current standard definition follows the KDIGO criteria, which has unified previous varying definitions to establish a clear diagnostic framework. According to KDIGO, AKI is diagnosed when there is an increase in serum creatinine by 0.3 mg/dL or more within 48 hours, or an increase to 1.5 times baseline within 7 days. Alternatively, a reduction in urine output to less than 0.5 mL/kg/h for 6 hours can also establish the diagnosis.

The staging system for AKI provides a framework for severity assessment and guides management decisions. Stage 1 represents mild disease, characterized by a creatinine elevation of 1.5-1.9 times baseline or an absolute increase of 0.3 mg/dL. Urine output may decrease to less than 0.5 mL/kg/h for 6-12 hours. Stage 2 indicates moderate disease severity, with creatinine increasing to 2.0-2.9 times baseline and urine output dropping below 0.5 mL/kg/h for 12 hours or more. Stage 3, the most severe form, is diagnosed when creatinine rises to three times baseline, reaches or exceeds 4.0 mg/dL, or when renal replacement therapy becomes necessary. At this stage, urine output falls below 0.3 mL/kg/h for 24 hours or longer, or complete anuria develops for at least 12 hours.

Table 12-1: Stages and Characteristics of Acute Kidney Injury (AKIN Criteria)

Stage	Serum Creatinine Criteria	Urine Output Criteria	Typical Clinical Features
1	Increase 1.5-1.9× baseline or ≥0.3 mg/dL	<0.5 mL/kg/h for 6-12h	Minimal symptoms, early volume changes
2	Increase 2.0-2.9× baseline	<0.5 mL/kg/h for ≥12h	Moderate symptoms, early uremic signs
3	Increase >3.0× baseline or ≥4.0 mg/dL or RRT initiation	<0.3 mL/kg/h for ≥24h or anuria ≥12h	Severe symptoms, overt uremia

Pathophysiology

The understanding of AKI's pathophysiology is fundamental to appropriate management, and the condition is traditionally divided into three main categories based on the anatomical location of the injury. This classification helps guide both diagnostic evaluation and therapeutic interventions.

Pre-renal AKI represents the most common form, accounting for approximately 55-60% of cases. This category results from renal hypoperfusion without intrinsic damage to the kidney tissue itself. The kidney's structural integrity remains intact, but its function is compromised due to inadequate blood flow. Common scenarios leading to pre-renal AKI include volume depletion from hemorrhage or dehydration, decreased cardiac output in heart failure, systemic vasodilation in sepsis, and renal vasoconstriction from various medications or disease states.

Intrinsic renal AKI constitutes approximately 35-40% of cases and involves direct damage to the kidney parenchyma. This form represents actual structural injury to the kidney tissue, particularly affecting the tubules, glomeruli, interstitium, or vasculature. Acute tubular necrosis (ATN) stands as the most prevalent form of intrinsic renal injury, occurring through either ischemic or nephrotoxic mechanisms. Ischemic ATN often develops when pre-renal conditions persist or worsen, leading to cellular damage. Nephrotoxic ATN results from direct injury by medications, contrast media, or other chemical agents.

Other forms of intrinsic renal injury include acute interstitial nephritis, typically triggered by medication reactions or autoimmune conditions. This variant features inflammation within the kidney's interstitial space, often accompanied by systemic manifestations. Glomerulonephritis represents another significant cause, characterized by inflammation of the glomeruli, which may occur in isolation or as part of a systemic disease process. Vascular diseases affecting the kidneys, such as vasculitis or thrombotic microangiopathy, can also precipitate intrinsic AKI.

Post-renal AKI, while least common at 5-10% of cases, remains clinically significant due to its potential reversibility when promptly recognized and treated. This form results from obstruction to urinary flow at any level from the renal pelvis to the urethra. The obstruction must typically be bilateral to cause AKI, except in cases involving a solitary functioning kidney. The presentation varies based on the level and chronicity of obstruction.

The most frequent causes of post-renal AKI vary by age and gender. In older males, benign prostatic hyperplasia represents a common culprit, while urinary tract malignancies can affect both genders. Retroperitoneal processes, whether malignant or fibrotic, may cause external compression of the ureters. Nephrolithiasis, though usually unilateral, can cause AKI in cases of bilateral obstruction or when affecting a solitary functioning kidney.

Each category of AKI demonstrates distinct pathophysiological mechanisms and characteristic laboratory findings. Pre-renal AKI typically shows preserved tubular function with appropriate concentrated urine and sodium conservation. Intrinsic renal AKI often manifests with evidence of tubular dysfunction, including granular casts and renal epithelial cells in the urinary sediment. Post-renal AKI may present with alternating oliguria and polyuria, and diagnostic imaging often reveals hydronephrosis.

Management

The management of AKI follows a systematic approach based on severity, underlying cause, and associated complications. Initial management focuses on identifying and treating life-threatening complications, followed by addressing the underlying cause while providing supportive care. Volume status assessment represents a critical first step, as both volume depletion and overload can worsen outcomes.

Immediate interventions include discontinuation of nephrotoxic agents, dose adjustment of medications, and optimization of hemodynamics. In pre-renal AKI, fluid resuscitation with crystalloids often proves beneficial, while careful volume removal may be necessary in overload states. Electrolyte and acid-base disturbances require close monitoring and correction. Hyperkalemia, metabolic acidosis, and volume overload often necessitate urgent intervention.

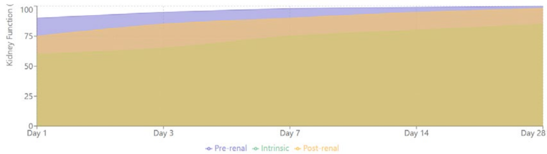

Figure 12.1 Acute Kidney Injury Recovery Pattern

The timing of renal replacement therapy remains individualized, though absolute indications include severe metabolic acidosis, refractory hyperkalemia, volume overload unresponsive to diuretics, and uremic manifestations. The choice between continuous and intermittent modalities depends on hemodynamic stability, facility resources, and specific patient factors.

CHRONIC KIDNEY DISEASE (CKD)

Chronic Kidney Disease represents a progressive decline in kidney function occurring over months to years. The current classification system incorporates both glomerular filtration rate (GFR) and albuminuria categories, providing a comprehensive assessment of disease severity and risk stratification.

GFR Categories

Stage 1 encompasses normal or high GFR (≥90 mL/min/1.73m^2) with evidence of kidney damage. Stage 2 represents mild reduction (60-89 mL/min/1.73m^2), often asymptomatic but indicating early disease. Stage 3 subdivides into 3a (45-59 mL/min/1.73m²) and 3b (30-44 mL/min/1.73m²), marking moderate reduction where complications begin to emerge. Stage 4 (15-29 mL/min/1.73m²) indicates severe reduction, requiring intensive management and preparation for renal replacement therapy. Stage 5 (<15 mL/min/1.73m²) represents kidney failure, often necessitating dialysis or transplantation.

Table 12-2: CKD Classification and Management Focus

Stage	GFR (mL/min/1.73m²)	Management Priorities
1	≥90	Risk factor modification, BP control
2	60-89	Cardiovascular risk assessment
3a	45-59	Bone-mineral disorder screening
3b	30-44	Anemia evaluation
4	15-29	RRT planning, access preparation
5	<15	RRT initiation or conservative care

Albuminuria Categories shape risk assessment and treatment decisions. Category A1 represents normal to mildly increased albuminuria (<30 mg/g creatinine), indicating minimal kidney damage. Category A2 encompasses moderately increased albuminuria (30-300 mg/g creatinine), suggesting significant kidney damage and increased cardiovascular risk. Category A3, severely increased albuminuria (>300 mg/g creatinine), correlates with substantial kidney damage and markedly increased complications risk.

The combination of GFR and albuminuria categories creates a matrix that better predicts outcomes than either measure alone. This system guides monitoring frequency, specialist referral timing, and therapeutic interventions. Higher albuminuria categories at any GFR stage indicate increased risk and may necessitate more aggressive management approaches

Common Complications

Cardiovascular Complications

Cardiovascular disease represents the leading cause of death in CKD patients, with risk increasing as kidney function declines. Traditional risk factors combine with CKD-specific factors to accelerate atherosclerosis and vascular calcification. Left ventricular hypertrophy commonly develops due to volume overload, hypertension, and anemia. Uremia-induced endothelial dysfunction contributes to widespread vascular disease. Heart failure frequently coexists, creating complex management challenges as volume status becomes increasingly difficult to optimize.

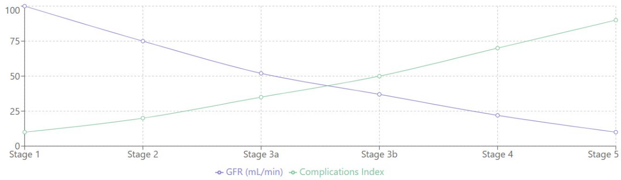

Figure 12.2 CKD Progression and complications

Bone-Mineral Disorders

CKD-Mineral and Bone Disorder (CKD-MBD) encompasses a spectrum of abnormalities in bone and mineral metabolism. As GFR declines, phosphate retention occurs, leading to secondary hyperparathyroidism through complex mechanisms involving reduced calcitriol production and increased FGF-23 levels. These changes result in bone disease manifestations ranging from high-turnover osteitis fibrosa to low-turnover adynamic bone disease. Vascular calcification accelerates, contributing to cardiovascular morbidity. Patients may experience bone pain, increased fracture risk, and extraskeletal calcifications.

Anemia

Anemia in CKD primarily results from decreased erythropoietin production by the failing kidneys. Additional contributing factors include iron deficiency, chronic inflammation, and shortened red blood cell survival. The severity typically correlates with CKD stage, becoming more pronounced as kidney function declines. Anemia contributes to reduced quality of life, decreased exercise tolerance, and increased cardiovascular complications.

Management

The management of CKD requires a comprehensive approach addressing both disease progression and complications. Core strategies include:

Blood Pressure Control

Strict blood pressure control, particularly using ACE inhibitors or ARBs, forms a cornerstone of CKD management. Target blood pressure goals may vary based on proteinuria and comorbidities, but generally aim for <130/80 mmHg. Medication choice considers both antiproteinuric effects and cardiovascular protection.

Risk Factor Modification

Lifestyle modifications play crucial roles, including smoking cessation, weight management, and dietary modifications. Dietary interventions focus on sodium restriction, protein modification based on CKD stage, and phosphate control. Regular exercise is encouraged within individual capabilities.

Complication-Specific Management

For cardiovascular complications, management includes aggressive risk factor modification, appropriate antiplatelet therapy, and careful attention to volume status. Regular cardiovascular monitoring helps detect