CHAPTER 10

TREATMENT ALGORITHMS FOR RENAL DISORDERS

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Abstract

Treatment algorithms for renal disorders are stratified by acuity, etiology, and the pattern of glomerular injury. The management of Chronic Kidney Disease (CKD) is a staged algorithm based on GFR and albuminuria (KDIGO criteria). This pathway focuses on slowing progression via foundational therapies, including aggressive blood pressure control (primarily with RAS blockade), glycemic control (notably with SGLT2 inhibitors), and lifestyle modifications. The algorithm extends to the systematic management of secondary complications, including anemia with iron and erythropoiesis-stimulating agents, and mineral-bone disorder with phosphate binders and vitamin D sterols. In contrast, the Acute Kidney Injury (AKI) algorithm is a diagnostic pathway to rapidly determine and reverse the etiology. It bifurcates into pre-renal (requiring volume resuscitation), intrinsic (supportive care, nephrotoxin removal), and post-renal (urinary decompression). The algorithm for glomerulonephritis (GN) is driven by serology and renal biopsy. Crescentic, rapidly progressive GN (RPGN) necessitates an emergent algorithm of high-dose corticosteroids combined with either cyclophosphamide or rituximab, and plasmapheresis for anti-GBM disease. Nephrotic syndrome management is also etiology-specific based on biopsy, with the algorithm for adult minimal change disease centered on high-dose corticosteroids, while algorithms for focal segmental glomerulosclerosis or membranous nephropathy involve more complex immunosuppressive regimens.

Keywords: *Chronic Kidney Disease, Acute Kidney Injury, Glomerulonephritis, Nephrotic Syndrome, KDIGO, RAS Blockade*

Learning Objectives

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

- Define the stages of Chronic Kidney Disease (CKD) based on GFR and albuminuria.
- Explain the management algorithm for life-threatening hyperkalemia in a patient with Acute Kidney Injury (AKI).
- Apply the KDIGO guideline algorithm for managing blood pressure and proteinuria in a patient with diabetic nephropathy.
- Differentiate the diagnostic and therapeutic algorithms for pre-renal, intra-renal, and post-renal AKI.
- Justify the use of immunosuppressive therapy in the algorithm for a patient with biopsy-proven, new-onset nephrotic syndrome

CHRONIC KIDNEY DISEASE

Chronic Kidney Disease (CKD) is defined as abnormalities of kidney structure or function, present for more than 3 months, with implications for health. The management algorithm is a long-term strategy focused on staging, slowing progression, and managing systemic complications.

Pathophysiology

The pathophysiology is a final common pathway resulting from numerous primary insults, such as diabetes mellitus and hypertension. The initial insult (e.g., hyperglycemic damage to the glomerulus) leads to the loss of functional nephrons. In response, the remaining, viable nephrons undergo **adaptive hyperfiltration** to maintain the overall glomerular filtration rate (GFR). This compensatory hyperfiltration, while beneficial in the short term, is the central mechanism of progressive disease. The increased intra-glomerular pressure and flow (hyperfiltration) leads to mechanical stress, podocyte injury, and glomerulosclerosis. This, in turn, causes the loss of more nephrons, creating a vicious, self-perpetuating cycle of nephron loss, adaptive hyperfiltration, and further nephron loss, leading to end-stage renal disease (ESRD).

Diagnosis and Staging

The diagnostic and staging algorithm for CKD is based on the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines. This framework classifies CKD using two main parameters: the cause, the Glomerular Filtration Rate (GFR) category (G1-G5, based on eGFR), and the albuminuria category (A1-A3, based on urine albumin-to-creatinine ratio, ACR). GFR categories range from G1 (GFR ≥ 90 ml/min/1.73m^2) to G5 (GFR < 15, or End-Stage Renal Disease, ESRD). Albuminuria categories range from A1 (< 30 mg/g) to A3 (> 300 mg/g). This GFR/ACR grid forms a "heat map" that stratifies the risk for progression and mortality, thereby guiding the algorithm for monitoring frequency and therapeutic intensity.

Differential Diagnosis (Etiology)

The differential diagnosis for CKD is an investigation into its underlying cause, which is a critical part of the initial algorithm. The most common causes in Western populations are diabetic nephropathy and hypertensive nephrosclerosis. Other important etiologies include glomerulonephritis (e.g., IgA nephropathy), genetic disorders (e.g., autosomal dominant polycystic kidney disease), chronic tubulointerstitial nephritis (e.g., from drugs or autoimmune disease), and chronic obstructive uropathy.

Treatment Algorithm

The treatment algorithm for CKD is multifactorial, with the primary goal of slowing GFR decline and managing complications. The foundational algorithm for slowing progression involves:

1. **Blood Pressure Control:** Aggressive BP targets are important. Angiotensin-Converting Enzyme (ACE) inhibitors or Angiotensin II Receptor Blockers (ARBs) are first-line agents, especially in the presence of albuminuria (A2 or A3), due to their specific renal-protective, anti-proteinuric effects.
2. **Glycemic Control:** In patients with diabetes, strict glycemic control is essential. SGLT2 inhibitors (e.g.,

dapagliflozin, empagliflozin) are now a pillar of therapy for both diabetic and non-diabetic proteinuric CKD, as they have been shown to significantly slow GFR decline.

3. **Lifestyle Modification:** This includes sodium restriction (to enhance diuretic and RAS blockade efficacy), dietary protein moderation, and smoking cessation.

Table 10.1: CKD Staging and Core Management Algorithm (KDIGO)

GFR Stage	GFR (mL/min/1.73 m^2)	Albuminuria (AER)	Management Goals
G1 / G2	≥ 60 (with damage)	A1 (<30) / A2 (30-300) / A3 (>300)	Diagnose/Treat underlying cause. **BP Control.** Risk reduction.
G3a / G3b	45-59 / 30-44	(as above)	All above + **SGLT2i** (if T2DM/HF/proteinuria). Monitor anemia, bone health.
G4	15-29	(as above)	All above + Prepare for Renal Replacement Therapy (RRT). Manage hyper-K, acidosis.
G5	< 15	(as above)	**Initiate RRT** (Dialysis or Transplant). Manage uremia, fluid overload.

AER = Albumin Excretion Rate (mg/day or mg/g creatinine)

A parallel algorithm involves the systematic management of CKD complications:

- **Anemia:** The algorithm is triggered when hemoglobin

levels fall. It involves first repleting iron stores (oral or IV iron) and then, if Hb remains low, initiating an erythropoiesis-stimulating agent (ESA).

- **Mineral and Bone Disorder (CKD-MBD):** This algorithm involves monitoring phosphorus, calcium, and parathyroid hormone (PTH). Treatment is stepwise, beginning with dietary phosphate restriction, followed by oral phosphate binders, and finally, the use of active vitamin D sterols (e.g., calcitriol) or calcimimetics to control secondary hyperparathyroidism.
- **Metabolic Acidosis:** If serum bicarbonate falls, the algorithm dictates initiation of oral sodium bicarbonate or sodium citrate to maintain levels within the normal range, which may slow CKD progression.
- **Renal Replacement Therapy (RRT):** For G5 CKD, the algorithm involves timely patient education on RRT modalities (hemodialysis, peritoneal dialysis, transplantation) and surgical referral for dialysis access (e.g., AV fistula) creation.

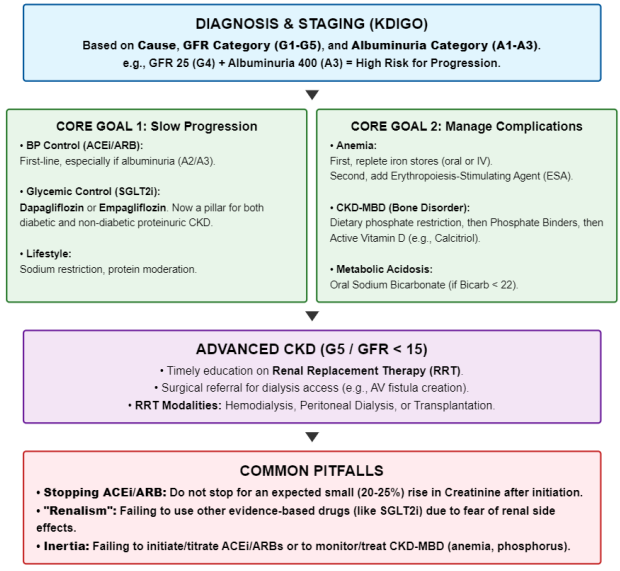

Figure 10.1: Chronic Kidney Disease

Monitoring and Follow-Up

CKD management requires lifelong, vigilant monitoring of two main parameters: GFR (estimated by serum creatinine and eGFR) and albuminuria (measured by a urine albumin-to-creatinine ratio, UACR). Patients are monitored at 3- to 6-month intervals. The goal is to slow the *rate of eGFR decline* and *reduce albuminuria*. Monitoring also includes:

1. **Blood Pressure:** This is the most critical parameter to monitor. Strict BP control is paramount.
2. **Electrolytes:** Monitoring for hyperkalemia, hyperphosphatemia, and hypocalcemia.
3. **Anemia:** A CBC is monitored to screen for anemia of CKD (due to decreased erythropoietin production by the failing kidney).
4. **Bone Health:** Monitoring PTH and phosphate levels to manage secondary hyperparathyroidism.

Long-Term Management / Secondary Prevention

The goal is to slow the progression to ESRD. The entire management algorithm is built on **RAAS blockade** (Angiotensin-Converting Enzyme inhibitors or Angiotensin II Receptor Blockers). These agents are first-line, even in non-hypertensive patients with albuminuria, because they preferentially dilate the efferent arteriole, which *reduces the intra-glomerular pressure* and directly targets the pathophysiology of hyperfiltration.

A new pillar of therapy is **SGLT2 inhibitors** (e.g., dapagliflozin, empagliflozin). These agents, originally for diabetes, are now a standard of care for non-diabetic CKD as well, as they have been shown to significantly slow GFR decline.

Secondary prevention involves:

1. **Strict Blood Pressure Control:** Target < 130/80 mmHg.
2. **Glycemic Control:** In diabetics, an HbA1c target of ~7.0%.
3. **Dietary Management:** Sodium restriction, and in advanced CKD, potassium and phosphate restriction.
4. **Nephrotoxin Avoidance:** This is a critical preventive measure.

Patient Counseling Points

1. **"This is a 'Silent' Disease":** "This is the most important thing to know. Kidney disease is silent; you will not *feel* sick until your kidney function is less than 10-15%. Our goal is to treat this disease now, while you feel well, to *prevent* you from ever feeling sick or needing dialysis."
2. **"Your Kidneys are 'Leaking' Protein":** "The main sign of kidney damage is a 'leaky filter,' which lets protein spill into your urine. Our primary goal is to stop this leak. The most important medicine for this is an 'ACE inhibitor' or 'ARB' (e.g., Lisinopril). This pill is *more* than a blood pressure pill; it is a 'kidney-protection' pill, and you must take it even if your blood pressure is normal."
3. **The "No-Fly List" for Your Kidneys:** "There are medicines that are now dangerous for you. You must *never* take NSAIDs, which are pills like Ibuprofen (Advil, Motrin) or Naproxen (Aleve). These can permanently damage your kidneys. You must use Tylenol (acetaminophen) for pain. You must also be very careful with CT scan contrast dye."
4. **Blood Pressure is Everything:** "Controlling your blood pressure is the single most important thing you can do, besides your kidney-protection pill, to slow this disease down."

Common Pitfalls in Management

A common pitfall is therapeutic inertia, particularly the failure to initiate or titrate ACE inhibitors/ARBs in patients with albuminuria. A critical error is stopping an ACE inhibitor due to a small, expected "bump" (e.g., 20-25%) in serum creatinine upon initiation; this rise reflects a beneficial change in glomerular hemodynamics and the drug should be continued. Another pitfall is "renalism," where other evidence-based therapies (e.g., for heart failure) are withheld due to fear of renal side effects. Finally, failing to monitor and treat CKD-MBD can lead to severe bone disease and cardiovascular calcification.

Case Study

A 62-year-old male (Mr. Singh) with a 10-year history of Type 2 Diabetes and Hypertension presents for a routine check-up. His BP is 145/88 mmHg. His labs show: Serum Creatinine 1.8 mg/dL (eGFR **40 mL/min/1.73m²**) and a Urine Albumin-to-Creatinine Ratio (UACR) of **350 mg/g**.

Discussion

This patient meets the criteria for **Chronic Kidney Disease (CKD)**. The algorithm requires staging based on GFR and Albuminuria (KDIGO criteria).

- **G-Stage:** GFR is 40, placing him in **Stage G3b** (30-44).
- **A-Stage:** UACR is 350, placing him in **Stage A3** (>300).
- This is **CKD Stage G3bA3**, placing him at very high risk for progression. The algorithm mandates aggressive treatment to slow this progression, especially BP control and SGLT2 inhibition.

Treatment Algorithm

1. **Diagnosis:** CKD Stage G3bA3, secondary to Diabetic Nephropathy.
2. **Algorithm (BP Control):** His BP is 145/88, which is above the goal of <130/80. He is already on Lisinopril (an ACEi).
    - **Action:** Increase **Lisinopril** dose and add a diuretic.
3. **Algorithm (Progression Slowing):** He has T2DM, a GFR > 20, and a UACR > 200. The algorithm **mandates** a new pillar of therapy:
    - **Action:** Start an **SGLT2 inhibitor**, such as **Dapagliflozin 10 mg daily**, for its proven renal and cardiovascular benefits.
4. **Follow-up:** Re-check labs (K+, Creatinine) in 2 weeks. A small, expected bump in creatinine after starting an SGLT2i is acceptable.

Outcome

Mr. Singh is started on Dapagliflozin 10 mg daily and his BP

regimen is intensified. The goal is to reduce his UACR and slow his GFR decline.

ACUTE KIDNEY INJURY

Acute Kidney Injury (AKI) is an abrupt decline in kidney function. Unlike the chronic management algorithm of CKD, the AKI algorithm is a rapid diagnostic pathway to identify and reverse the underlying cause.

Pathophysiology

The pathophysiology is classified by location.

- **Pre-renal AKI:** This is the most common cause and is a purely hemodynamic problem. The kidney structure is *normal*, but it is being under-perfused. This is due to true volume depletion (e.g., dehydration, hemorrhage) or a decrease in effective arterial blood volume (e.g., in heart failure or sepsis). The kidney responds appropriately by avidly conserving sodium and water (producing concentrated, low-sodium urine).
- **Post-renal AKI:** This is an obstructive problem. Kidney function is normal, but urine is blocked from being excreted, causing back-pressure that stops filtration. This is commonly due to benign prostatic hyperplasia (BPH) or a kidney stone.
- **Intrinsic AKI:** This is true kidney *damage*. The most common cause is **Acute Tubular Necrosis (ATN)**. ATN pathophysiology is ischemic or toxic damage to the renal tubular cells. In a "pre-renal" state (hypoperfusion), if the low blood flow is severe and prolonged, it converts to an "intrinsic" injury (ATN), and the tubular cells die. This "muddy brown cast" in the urine is the sloughed, dead tubular cells.

Diagnosis and Staging

AKI is diagnosed based on a rise in serum creatinine (sCr) or a fall in urine output (UOP), as defined by KDIGO. Staging (Stage 1-3) is based on the magnitude of sCr rise (e.g., Stage 1: 1.5-1.9x baseline; Stage 3: > 3.0x baseline or initiation of RRT).

Differential Diagnosis (Etiology)

The AKI treatment algorithm is fundamentally an algorithm to differentiate its three main etiological categories:

1. **Pre-renal:** Caused by renal hypoperfusion. This is the most common cause and includes hypovolemia (e.g., dehydration, hemorrhage), low cardiac output (e.g., cardiorenal syndrome), and systemic vasodilation (e.g., sepsis).
2. **Intrinsic:** Caused by direct damage to the kidney parenchyma. This is most commonly Acute Tubular Necrosis (ATN) from ischemia (e.g., prolonged pre-renal state) or nephrotoxins (e.g., contrast dye, NSAIDs, antibiotics). Other intrinsic causes include Acute Interstitial Nephritis (AIN), glomerulonephritis, and vascular causes.
3. **Post-renal:** Caused by downstream urinary tract obstruction (e.g., benign prostatic hyperplasia, kidney stones, pelvic malignancy).

Treatment Algorithm

The algorithm is a stepwise process of exclusion and intervention:

- **Step 1: Rule out Post-renal Obstruction.** The first step is a renal/bladder ultrasound. If obstruction is found (e.g., hydronephrosis), the algorithm is urinary decompression (e.g., Foley catheter, urology consultation for stents or nephrostomy tubes).
- **Step 2: Assess Volume Status.** If non-obstructive, the algorithm differentiates pre-renal from intrinsic. This involves a thorough physical exam (orthostatics, JVP, edema) and diagnostic aids (e.g., passive leg raise, ultrasound of IVC).
- **Step 3: Treat Pre-renal AKI.** If the patient is hypovolemic (pre-renal), the algorithm is immediate volume resuscitation with intravenous fluids.
- **Step 4: Treat Intrinsic AKI (ATN).** If the patient is euvolemic or hypervolemic, or does not respond to fluids, a diagnosis of intrinsic AKI (most commonly