Acute Kidney Injury (AKI)

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BRACE YOURSELVES

DETAILED NEPHROLOGY IS COMING

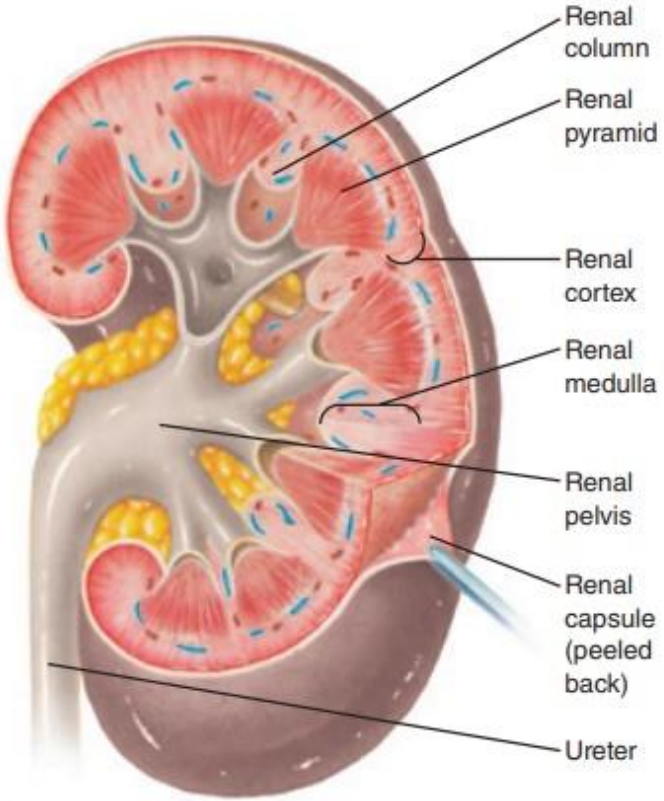


FIGURE 22-2 Gross anatomy of the kidney.

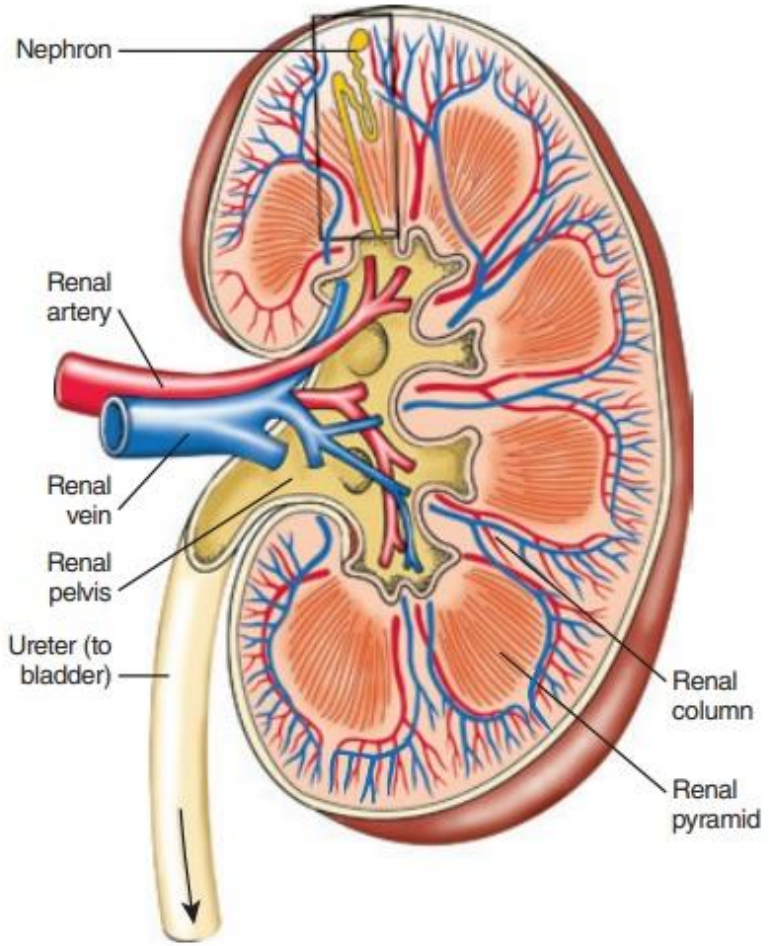
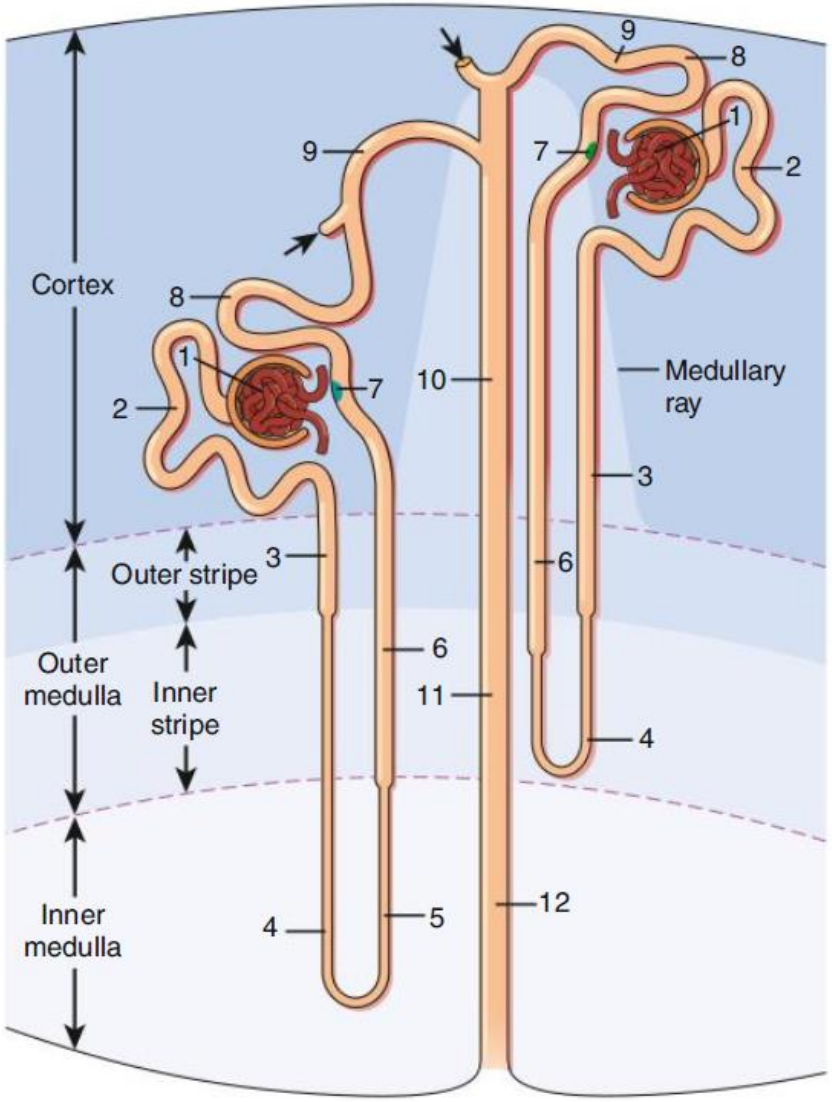


FIGURE 22-3 Kidney structures, showing renal artery and its branches.

Nephrons and the Collecting Duct System



1. Renal corpuscle
2. Proximal convoluted tubule
3. Proximal straight tubule
4. Descending thin limb
5. Ascending thin limb
6. Distal straight tubule (thick ascending limb)
7. Macula densa
8. Distal convoluted tubule
9. Connecting tubule
10. Cortical collecting duct
11. Outer medullary collecting duct
12. Inner medullary collecting duct


Perfectly balanced...
...As all things should be

Definition:

- AKI is **deterioration in renal function** manifested by an **acute rise in serum creatinine (Cr)** and **blood urea nitrogen (BUN)** caused by the inability to clear water, electrolytes, and nitrogenous wastes, occurring over hours to days.
- **Doubling of serum Cr indicates approximately 50% reduction in renal function.**
- AKI results in altered urine output, classified as either **oliguric** (<400 mL/day) or **non-oliguric** (>400 mL/day).

RIFLE (risk, injury, failure, loss, and ESRD) criteria

	Serum Creatinine	Glomerular filtration Rate	Urine output
Risk	1.5× increase in the serum Cr.	GFR decrease by 25%.	urine output less than 0.5 mL/kg/hr. for 6 hours.
Injury	2× increase in the serum Cr.	GFR decrease by 50%.	urine output less than 0.5 mL/kg/hr. for 12 hours.
Failure	3× increase in the serum Cr. or serum Cr more than 4 mg/dL .	GFR decrease by 75%.	or urine output less than 0.3 mL/kg/hr. for 24 hours or anuria for 12 hours.
Loss	complete loss of renal function for more than 4 weeks.		
ESRD	Persistent AKI more than 3 months.		

AKIN (Acute Kidney Injury Network)-modified RIFLE criteria

	Serum Creatinine	Urine output
Stage 1	Increase in serum Cr of 0.3 mg/dL from baseline. *or* Cr increase of 1.5 to 2 times baseline.	Urine output less than 0.5 mL/kg/hr. for more than 6 hours.
Stage 2	Serum Cr concentration increase of 2 to 3 times baseline.	urine output less than 0.5 mL/kg/hr. for more than 12 hours.
Stage 3	Serum Cr concentration increase over 3 times baseline. *or* Cr value greater than 4 mg/dL with acute increase of Cr greater than 0.5 mg/dL.	Urine output less than 0.3 mL/kg/hr. for 24 hours. or anuria for 12 hours.

Kidney Disease: Improving Global Outcomes Composite Staging of Acute Kidney Injury

Stage	Serum Creatinine	Urine Output
Stage 1	1.5–1.9 × baseline or ≥0.3 mg/dL (≥29 μmol/L) increase	<0.5 mL/kg/h for 6–12 h
Stage 2	2.0–2.9 × baseline	<0.5 mL/kg/h for ≥12 h
Stage 3	3.0 × baseline or Increase in serum creatinine to ≥4.0 mg/dL (≥352 μmol/L) or Initiation of kidney replacement therapy or In patients younger than 18 yr, decrease in estimated glomerular filtration rate <35 mL/min/1.73 m2	<0.3 mL/kg/h for ≥24 h or Anuria for ≥12 h

Causes of AKI

Prerenal:

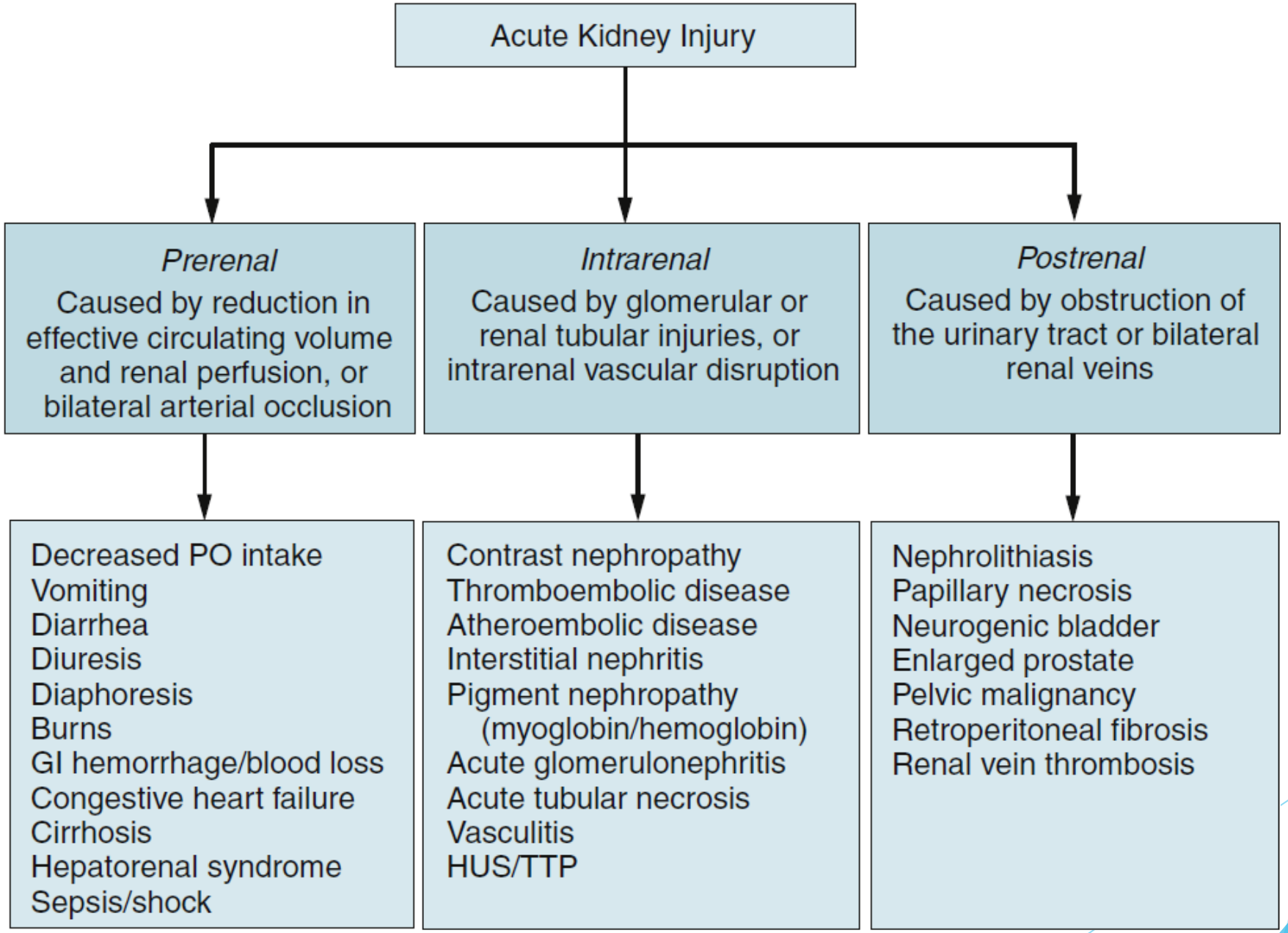
- Reduction in effective circulating volume and renal perfusion or bilateral renal artery occlusion.

Intrarenal:

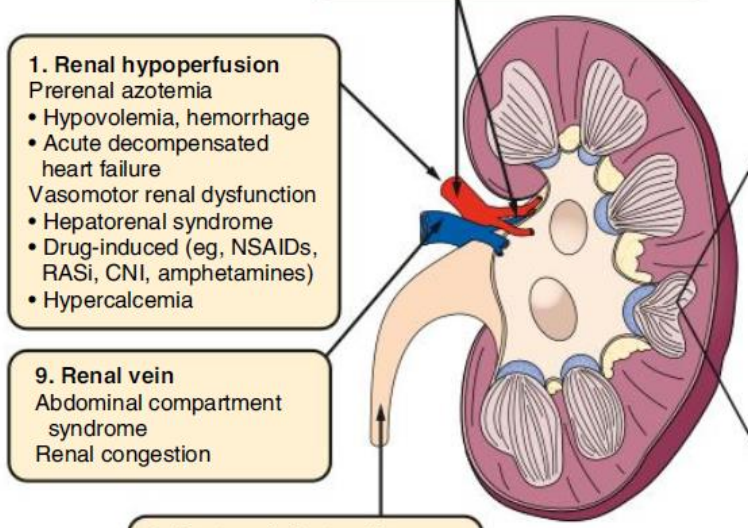
- Vascular, glomerular, or tubular injuries.

Postrenal:

- Obstruction of urinary tract or bilateral renal veins.


Acute Kidney Injury
Prerenal
Caused by reduction in effective circulating volume and renal perfusion, or bilateral arterial occlusion
Intrarenal
Caused by glomerular or renal tubular injuries, or intrarenal vascular disruption
Postrenal
Caused by obstruction of the urinary tract or bilateral renal veins
Decreased PO intake
Vomiting
Diarrhea
Diuresis
Diaphoresis
Burns
GI hemorrhage/blood loss
Congestive heart failure
Cirrhosis
Hepatorenal syndrome
Sepsis/shock
Contrast nephropathy
Thromboembolic disease
Atheroembolic disease
Interstitial nephritis
Pigment nephropathy (myoglobin/hemoglobin)
Acute glomerulonephritis
Acute tubular necrosis
Vasculitis
HUS/TTP
Nephrolithiasis
Papillary necrosis
Neurogenic bladder
Enlarged prostate
Pelvic malignancy
Retroperitoneal fibrosis
Renal vein thrombosis

Causes of AKI



1. Renal hypoperfusion
Prerenal azotemia
- Hypovolemia, hemorrhage
- Acute decompensated heart failure

Vasomotor renal dysfunction
- Hepatorenal syndrome
- Drug-induced (eg, NSAIDs, RASi, CNI, amphetamines)
- Hypercalcemia

2. Renal artery
Renal artery occlusion or dissection
Large- or medium-vessel vasculitis

3. Small-vessel disease
Thrombotic microangiopathy
Renal atheroembolism

4. Glomerular disease (ANCA+ or –)
Small-vessel vasculitis
Anti-GBM disease
Lupus nephritis
Postinfectious glomerulonephritis
Infective endocarditis
Membranoproliferative glomerulonephritis
Cryoglobulinemia
IgA nephropathy/collapsing glomerulopathy

5. Acute tubular injury
Ischemic
Toxic
- Endogenous toxins
  - Light chains (eg, myeloma)
  - Uric acid (eg, tumor lysis)
  - Myoglobin (eg, rhabdomyolysis)
  - Hemoglobin (eg, massive hemolysis)
  - Bile salts (eg, obstructive cholestasis)
- Exogenous toxins
  - Antimicrobials (eg, aminoglycosides)
  - Chemoagents (eg, cisplatin)
  - Radiocontrast media
  - Phosphate (eg, Na-Phos bowel prep)
  - Oxalate (eg, ethylene glycol)
  - Acetaminophen (intoxication level)
  - Synthetic cannabinoids

6. Acute interstitial nephritis
Non-granulomatous
- Allergic due to drugs
- Infection (eg, viral)

Granulomatous
- Drugs
- Infection
- Systemic disease

Pyelonephritis

8. Postrenal obstruction
Bladder outlet obstruction
Tumors
Renal calculi
Papillary necrosis
Retroperitoneal fibrosis
Neurogenic bladder (eg, drugs)

9. Renal vein
Abdominal compartment syndrome
Renal congestion

General principles for treatment of AKI

- **Correct any reversible causes.**
- Assess **potassium**, **acid-base status**, **fluid status**, **toxin accumulation**, and need for dialysis.
- **Adjust dosage** of renally cleared medications.
- Fluid challenge if appropriate.
- Discontinue all **nephrotoxic** drugs.

General principles for treatment of AKI

Indications for Dialysis	
Indication	**Findings**
Volume overload	Congestive heart failure. Uncontrolled hypertension. Massive edema.
Severe metabolic acidosis	Hyperventilation. Hyperkalemia.
Hyperkalemia	Cardiac arrhythmias.
Uremia	Pericarditis; stupor; seizures; asterixis; platelet dysfunction.
Drug toxicity (e.g., lithium, digoxin)	Specific to drug.

Prerenal Causes of Acute Kidney Injury

Prerenal Causes of Acute Kidney Injury

- AKI that is **caused by reduction of effective circulating volume** or decreased renal blood flow.
- Prerenal causes are the **second most common general cause of AKI in the hospital setting** (most common is acute tubular necrosis).
- Patients can present with severe oliguric renal failure.
- Once the **effective circulating volume has been restored**, **renal recovery is the general rule**.

Prerenal Causes of Acute Kidney Injury

True volume depletion:

- **GI loss:** Bleeding or diarrhea, Lack of oral intake or vomiting.
- **Renal loss:** Diuretics, hyperglycemia, salt-wasting nephropathy, diabetes insipidus.
- **Skin loss:** Sweats or burns.

Prerenal Causes of Acute Kidney Injury

Reduction in effective circulating volume

- Congestive heart failure (cardiorenal syndrome).
- Cirrhosis.
- Nephrotic syndrome.
- Sepsis and shock.
- Hepatorenal syndrome:
  - A poorly understood, relentless worsening of renal function in the patient with advanced liver disease, with no other apparent cause (a diagnosis of exclusion).
  - Pathophysiology includes dilation of the splanchnic bed vasculature, which pools blood and results in a fall in the systemic vascular resistance and blood pressure, with reduced renal perfusion.
  - The renin-angiotensin and sympathetic nervous systems are activated, and vasopressin is released, resulting in renal artery vasoconstriction.

Prerenal Causes of Acute Kidney Injury

Medications

- **Diuretics:** volume depletion.
- **ACE inhibitor/ARB/renin inhibitor:** Decreases the formation of angiotensin II or blocks the effects of angiotensin II, thus resulting in efferent arteriolar vasodilation and reduced intraglomerular pressure and reduced GFR
- **NSAID:** Inhibits the production of vasodilatory prostaglandins, resulting in afferent arteriolar vasoconstriction and reduced GFR.
- **Calcineurin inhibitors (tacrolimus, cyclosporine):** Cause renal artery vasoconstriction, resulting in reduced GFR.

Prerenal Causes of Acute Kidney Injury

Diagnosis:

- **BUN/Cr ratio greater than 20:1** because of increased water and urea reabsorption.
- Low **urine sodium** concentration (usually **<20 mEq/L**).
- Low **urine fractional excretion of sodium** (**FENa <1%**).
- **Urine osmolality greater** than **500 mOsm/kg**.

Prerenal Causes of Acute Kidney Injury

Treatment

- **Volume depletion:**
  - Vigorous IV fluid resuscitation typically improves renal function and urine output within 24 to 48 hours.
- **Reduced effective volume:**
  - Treatment of the underlying disease process; maximize cardiac output.
- **Hepatorenal syndrome is best treated by liver transplantation:**
  - Dialysis may be needed in the interim.
  - Peritoneal-venous shunt or trans-jugular intrahepatic portosystemic shunt (TIPS) may prolong renal function but can cause worsening of encephalopathy of liver disease.
  - Terlipressin (an antidiuretic hormone analogue that constricts the splanchnic bed) may be administered with IV albumin, which may improve renal function but can cause ischemia.
  - Midodrine (systemic vasoconstrictor) and octreotide (blocks vasodilator release) may be of some benefit.

Intrarenal Causes of Acute Kidney Injury

Intrarenal Causes of Acute Kidney Injury

- Acute tubular Injury.
- Interstitial nephritis.
- Contrast nephropathy.
- Thromboembolic disease.
- Athero-embolic disease.
- Pigment nephropathy (myoglobin/hemoglobin).
- Acute glomerulonephritis.
- Vasculitis.
- HUS/TTP.

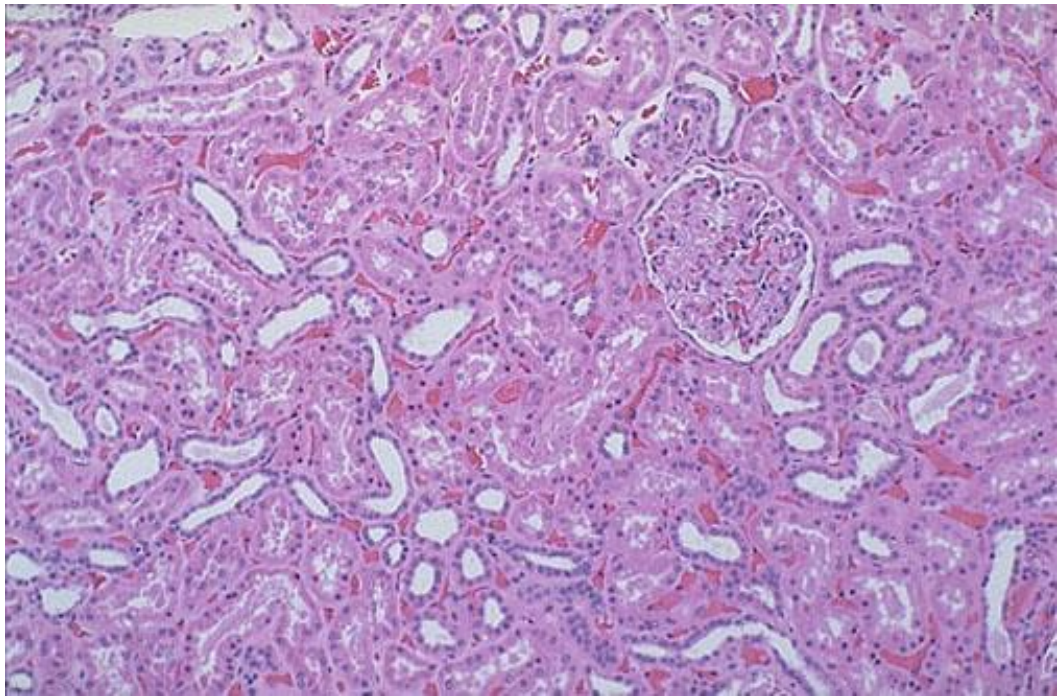
Intrarenal: Acute Tubular Injury (ATI)

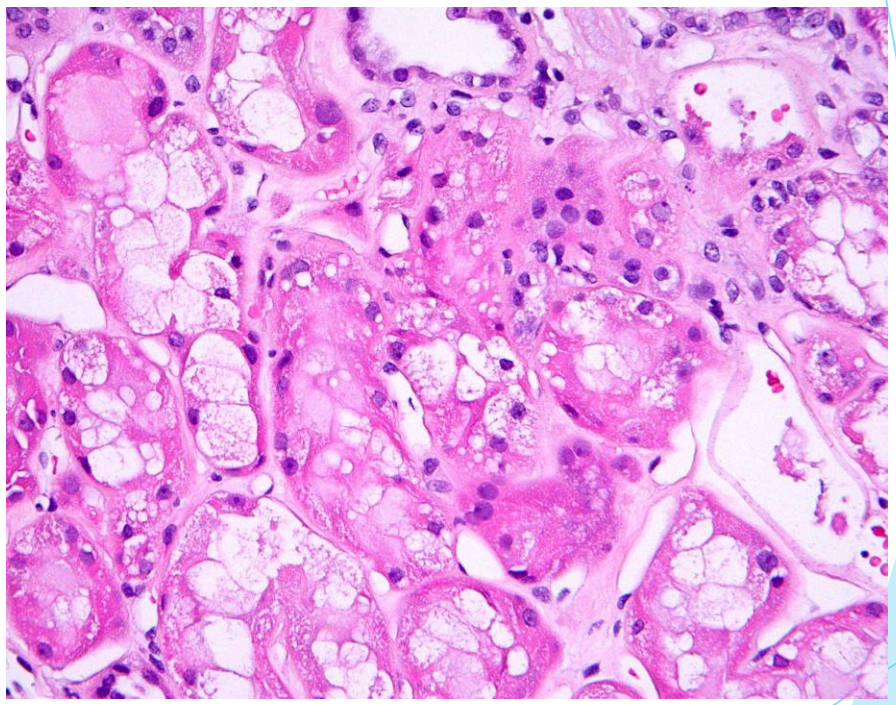
- The **most common cause of AKI** in the hospital setting.
- Results from **ischemic** (i.e., prerenal) or **nephrotoxic** (i.e., intrarenal) injury to renal tubules.
- Damaged tubular cells accumulate in tubular lumen, resulting in occlusion.
- Injury commonly **most severe in early proximal tubule** and medullary segment.
- Appropriate clinical setting, such as ischemic event or exposure to nephrotoxin, precedes deterioration in renal function.
- Clinical course typically progresses, then **resolves over 1 to 3 weeks**.

Intrarenal: Acute Tubular Injury (ATI)

- **Diagnosis:**
- **BUN/Cr ratio** is normal, usually **less than 20:1**.
- Urinalysis shows **muddy brown granular casts** and epithelial cell casts.
- **High urine sodium concentration** (usually **>40 mEq/L**) is caused by tubular injury and decreased sodium reabsorption.
- **High urine fractional excretion of sodium** (**FENa >2%**).
- **Urine osmolality less than 350 to 450 mOsm/kg**.
- Urine Cr/Plasma Cr ratio less than 20:1 (measure of tubular water reabsorption).
- **Treatment:**
  - Supportive care until renal function returns
  - Avoid nephrotoxins

Intrarenal: Acute Tubular Injury (ATI)





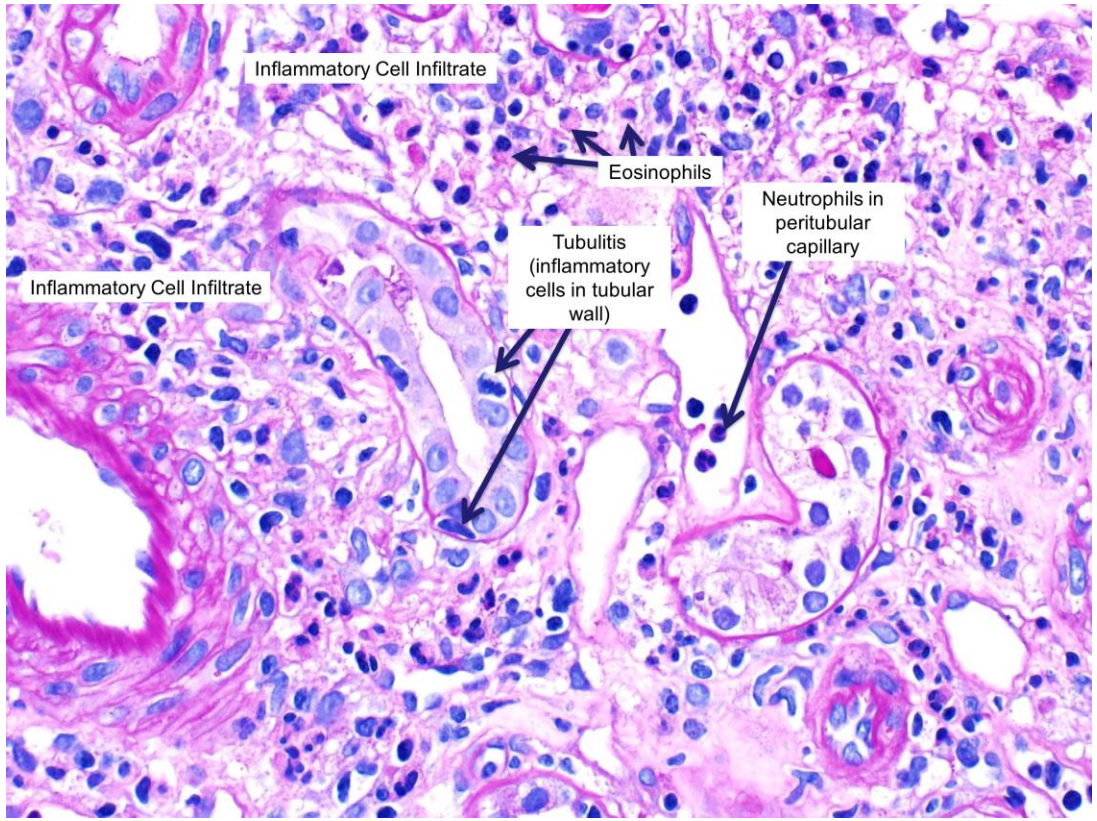
Intrarenal: Acute Interstitial Nephritis (AIN)

- Results from the **infiltration of the interstitial space by inflammatory cells** (mostly T cells and monocytes).
- Process initiated by **reaction to medications**.
- **ß-Lactam antibiotics** and **cephalosporins** are the most common.
- **NSAIDs** are associated with Either pure interstitial disease or additional glomerular disease (minimal change disease or membranous glomerulonephritis).
- NSAIDs can also cause acute ischemic renal injury (hemodynamic change), analgesic nephropathy, or papillary necrosis Urine sediment may not contain significant eosinophils.
- **Rifampin** is associated with acute tubulointerstitial disease even with intermittent dosing or after discontinuation of the drug.
- **Sulfonamides** can cause vasculitis.

Intrarenal: Acute Interstitial Nephritis (AIN)

- Acute worsening of renal function after starting a new medication.
- **Fever** and **skin rash** are also common.
- **Diagnosis:**
- Made based on clinical presentation or renal biopsy and is supported by Hematuria, pyuria, and white blood cell casts in urine.
- **Eosinophilia** and **eosinophiluria** are seen.
- **Mild proteinuria** also seen.
- **Treatment:**
  - Discontinuation of offending agent(s).
  - Corticosteroids: Prednisone 1 mg/kg/day.

Intrarenal: Acute Interstitial Nephritis (AIN)



Intrarenal: Contrast-Induced Nephropathy (CIN)

- Caused by **renal vasoconstriction** from the release of endothelin and adenosine as well as from the **high osmolality of the contrast material**.
- Also caused by direct tubular injury by the contrast agent.
- **Those at greatest risk include those with:**
  - Underlying renal insufficiency with plasma Cr greater than 1.5 mg/dL Diabetic nephropathy with renal insufficiency.
  - Poor renal perfusion: Heart failure, dehydration, or liver failure.
  - Multiple myeloma.
  - High doses of contrast agent.
- Magnetic resonance gadolinium contrast media may also be associated with nephrotoxicity in high concentrations.
- Use of gadolinium in the setting of advanced renal failure has been associated with **nephrogenic systemic fibrosis**.

Intrarenal: Contrast-Induced Nephropathy (CIN)

- Acute **rise of serum BUN/Cr occurs within 24 to 48 hours of IV contrast exposure**.
- **Cr peaks within 7 days** and usually returns to baseline within 10 days.
- Renal failure is **usually reversible**.
- Clinical diagnosis based on history of exposure in appropriate time period.
- Imaging of the kidneys, ureter, and bladder reveals enhanced outline of kidneys secondary to retained IV contrast.

Intrarenal: Contrast-Induced Nephropathy (CIN)

- **Treatment:**
  - **No specific therapy**; supportive measures only Maintain renal perfusion with IV hydration, but with risk of volume overload.
  - Avoid repeated contrast exposure.
  - **Best treatment is prevention**.
  - IV hydration with normal saline 1 mL/kg/hr, 12 hours before and after administration of IV contrast agent.
  - **Sodium bicarbonate hydration** may also be of benefit before IV contrast
  - **N-Acetylcysteine** 600 to 1200 mg PO twice a day for 2 days, starting 1 day before IV contrast exposure. (not used now)
  - **Minimize IV contrast volume**
  - Use **nonionic contrast** or dilute contrast media
  - Prophylactic dialysis to remove contrast has no proven benefit

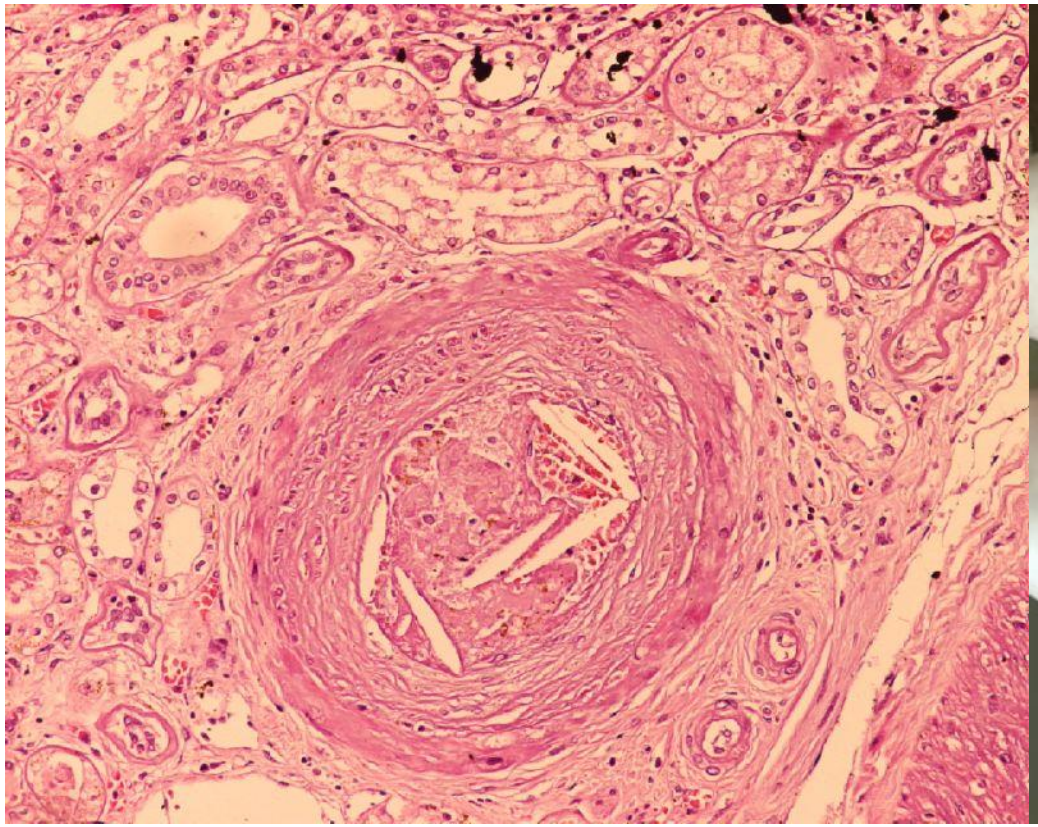
Intrarenal: Renal Artery Embolic Disease

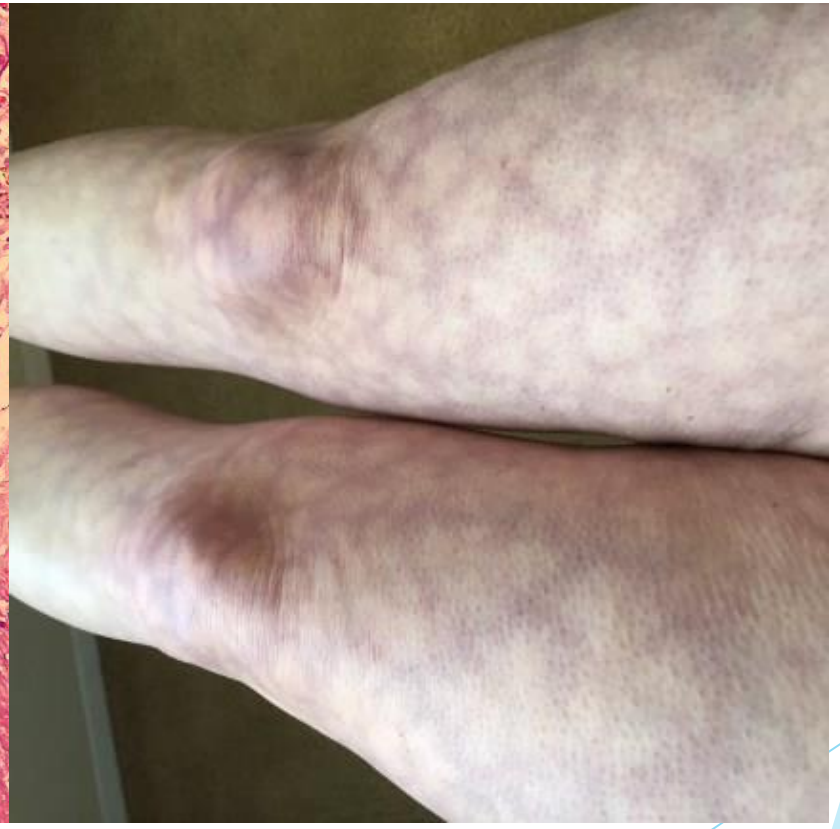
- AKI results from cholesterol emboli, which lodge in medium or small renal arteries.
- Inflammatory reaction causes intimal proliferation, fibrosis, and **irreversible blockages**.
- Two common presentations, caused by either thromboembolic or atheroembolic event.
- **Thromboembolic:**
  - Occurs after myocardial infarction or with atrial arrhythmias, resulting in complete arterial obstruction and renal infarction.
  - Individual notes **flank pain**, **hematuria**, **Lactate dehydrogenase is elevated**.
- **Atheroembolic:**
  - Occurs spontaneously or following a catheter manipulation in aorta or surgery; produces incomplete obstruction and renal atrophy; renal function worsens acutely and continues to progress over several weeks
  - Other physical findings include **cyanosis**, **gangrene of toes or feet**, **livedo reticularis**.
  - If pancreatic or mesenteric emboli also occur, abdominal pain may result.

Intrarenal: Renal Artery Embolic Disease

- **Diagnosis:**
- Clinical suggestion in appropriate setting Laboratory findings include **eosinophilia**, **eosinophiluria**, and **hypocomplementemia**
- Cholesterol crystals may be present on renal or skin biopsy, or elsewhere in body
- **Treatment:**
  - Supportive care only; prognosis is poor.
  - Consider anticoagulation with thromboembolic disease.

Intrarenal: Renal Artery Embolic Disease





Intrarenal: Pigment Nephropathy

- Acute renal tubular injury from **myoglobin** or **Hemoglobin**.
- Pathogenesis is tubular cell injury from free chelatable iron (ferrihemate), which results in intrarenal vasoconstriction.
- Obstruction of tubules with pigment casts, which results in renal failure.
- Patient often notes dark urine ("Coca-Cola urine") because of presence of myoglobin/hemoglobin pigments in urine.
- Usually associated with **traumatic muscle injuries** (extreme exercises, trauma, seizures, ischemia), **muscle toxins** (drugs, including cocaine and statins), or other causes (**infections**, **electrolyte abnormalities**, endocrine, inflammatory myopathies).
- Release of intracellular electrolytes results in **hyperkalemia**, **hyperphosphatemia**, and **hyperuricemia**.
- Sequestration of fluid and calcium into injured muscles leading to volume depletion and **hypocalcemia**.

Intrarenal: Pigment Nephropathy

- **Diagnosis:**
- AKI in appropriate clinical setting Associated with high serum creatine phosphokinase (CPK); renal injury often associated with **CPK greater than 10,000** IU/L.
- **Hyperkalemia**, **hyperphosphatemia**, and **hypocalcemia** also common and support the diagnosis.
- Urinalysis reveals **pigmented casts** (but no red blood cells) with myoglobin or hemoglobin in the urine.
- **Treatment:**
  - Aggressive IV hydration.
  - Alkalinize urine to pH above 6.5 (2–3 ampules of bicarbonate mixed in 1 L of 5% dextrose in water) to prevent formation of ferrihemate from myoglobin or hemoglobin.
  - Recovery is the general rule, but dialysis may be needed until renal function returns.

Clinical and Laboratory Variables in the Differential Diagnosis Between Prerenal and Acute tubular Injury

Parameter	Prerenal	Intrarenal
History	Volume loss from GI, urinary, skin, or blood or reduced EABV (e.g., heart failure, pancreatitis)	Drugs or toxin exposure, hemodynamic change
Clinical presentation	Hypotension or volume depletion	No specific symptoms or signs
Laboratory studies		
BUN/SCr	>20	<20
Sediment	Normal to few hyaline casts	Muddy brown casts
Uosm (mmol/kg)	>500	>350
Proteinuria	None to trace	Mild to moderate
UNa (mmol/L)	<20	>40
FENa (%)	<1	>1
FEUrea (%)	<35	>35

Postrenal Causes of Acute Kidney Injury

Postrenal Causes of Acute Kidney Injury

- Group of disorders resulting from the **physical obstruction** of:
  - the ureters (e.g., obstructing nephrolithiasis, malignancy, retroperitoneal fibrosis).
  - the bladder (e.g., prostatic hypertrophy, clots, tumors).
  - renal veins (e.g., renal vein thrombosis) .
- If onset sudden, patient will note flank pain.
- If **obstruction complete, anuria results**.
- **Partial obstruction may result in polyuria or oliguria**.
- Physical examination may note abdominal mass from hydronephrosis, or pelvic mass from distended bladder.

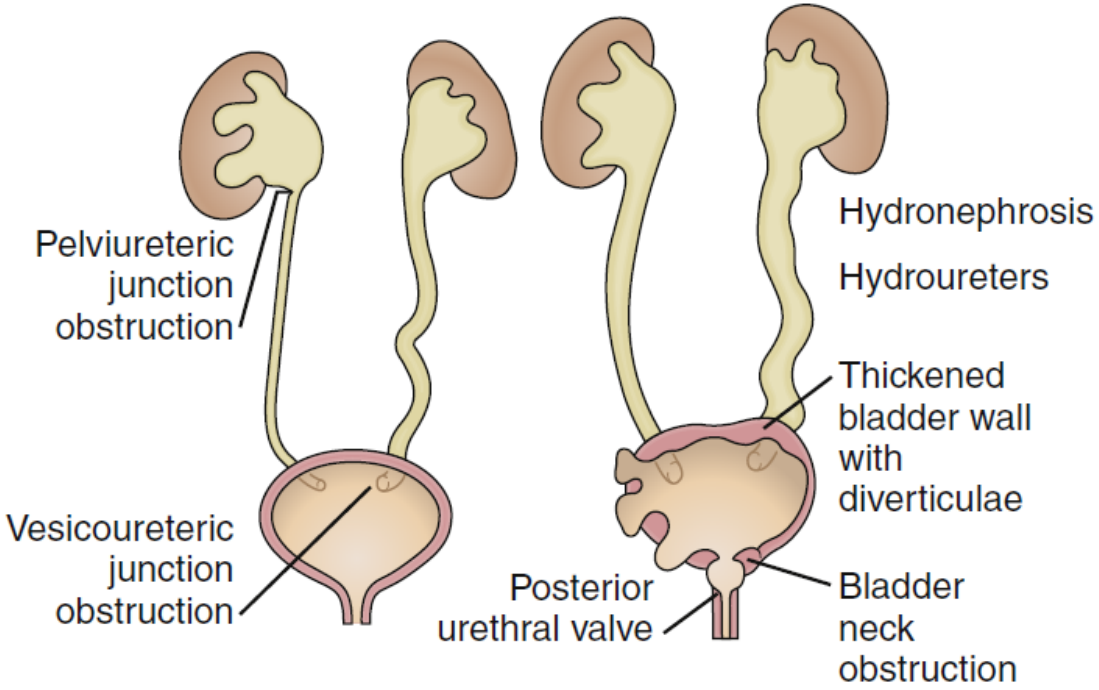
Postrenal Causes of Acute Kidney Injury

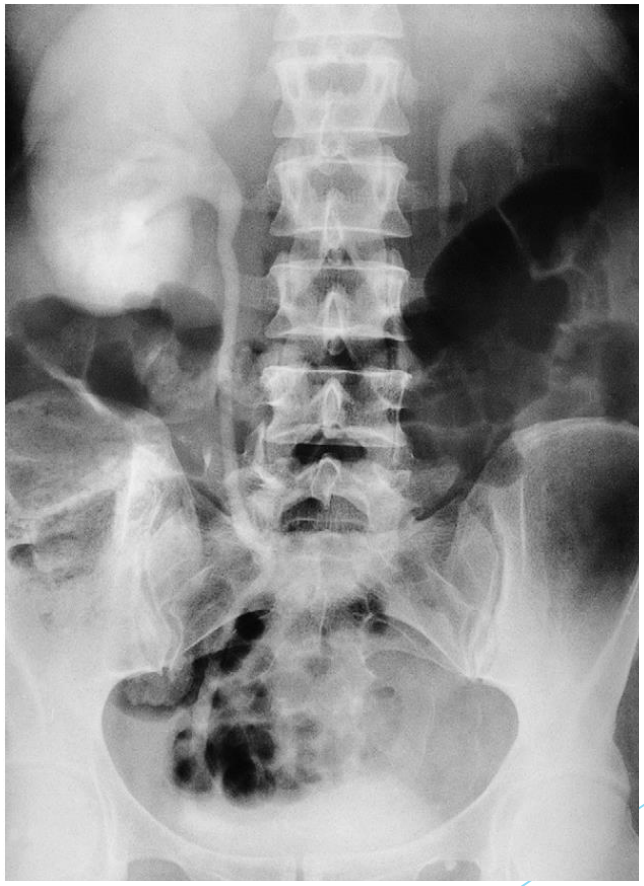
- **Diagnosis:**
- **Ultrasound is the test of choice** to determine the presence of obstruction because of high sensitivity (90%) and specificity (90%), low cost, and safety.
- **IV pyelography** is the test of choice to define the location of obstruction and anatomy of the ureters; however, one must consider the potential toxicity of IV contrast medium and poor visualization of the kidneys with low GFR.
- **Computed tomography** is able to diagnose hydronephrosis without IV contrast and is useful in determining extrinsic mass, hematoma, or stones.
- **Nuclear medicine furosemide renogram** can provide functional status of the kidneys and avoid risk of IV contrast; however, anatomic visualization is poor.

Postrenal Causes of Acute Kidney Injury

- **Treatment**
- The most effective treatment is **determined by the location of the obstruction**.
- Emergency relief of the obstruction is indicated if AKI or urosepsis has resulted.
- Obstruction distal to the bladder can be relieved by a **Foley catheter** or a **suprapubic catheter**.
- Upper urinary tract obstruction can be relieved by either a **percutaneous nephrostomy tube** or **ureteral stent placement**.
- Recovery of renal function depends on the duration of the obstruction.
- **Post obstructive diuresis:** Marked polyuria with loss of water, sodium, potassium, and other electrolytes.
- Replacement fluid should be half-normal saline initially and readjusted according to serum electrolyte changes.
- Etiology of massive diuresis is volume expansion, urea accumulation, tubular damage, and accumulation of natriuretic factors.
- Prolonged fluid replacement should be avoided, as it will perpetuate post obstructive diuresis by continued replacement of sodium and water.

Postrenal Causes of Acute Kidney Injury

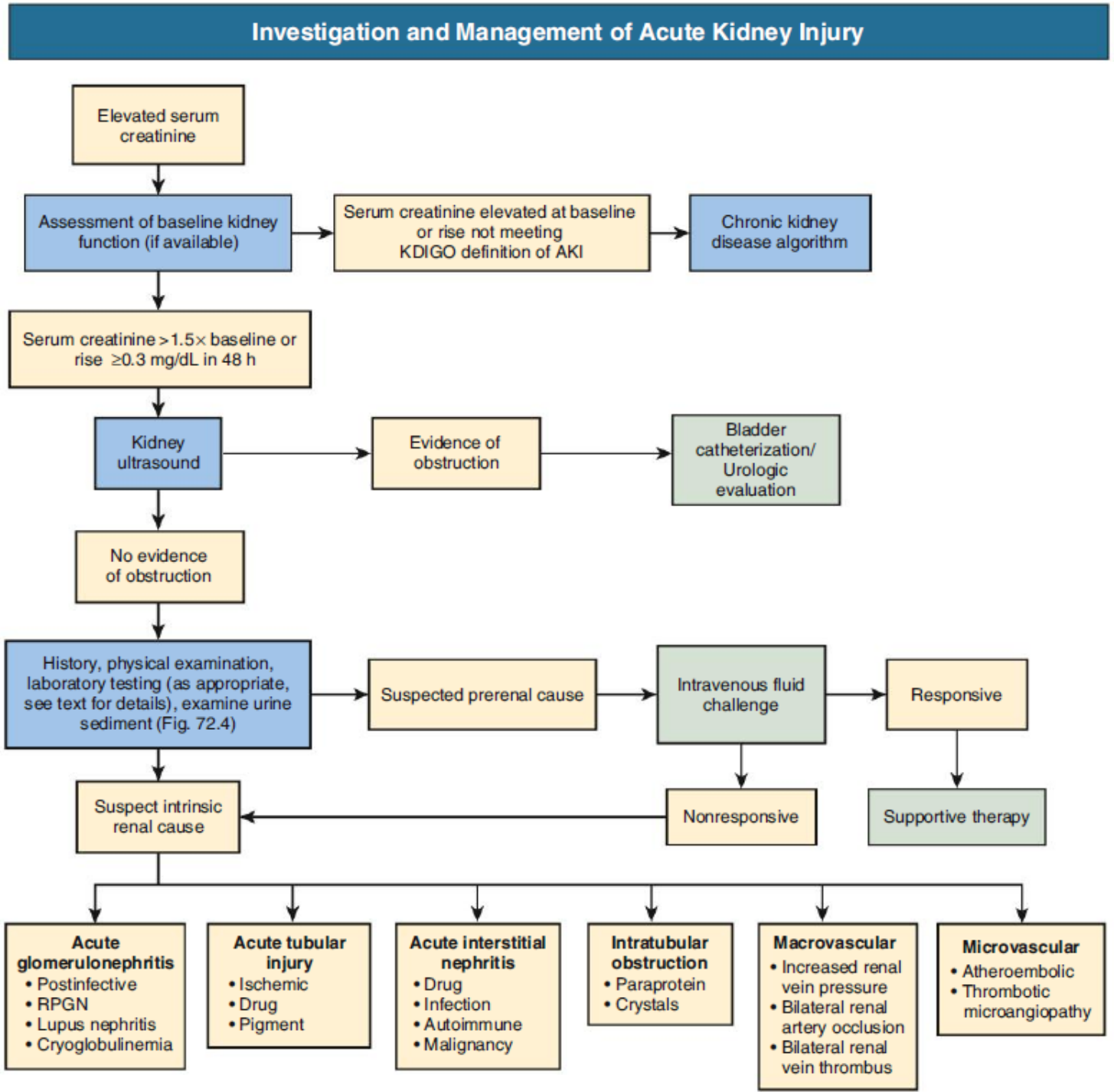


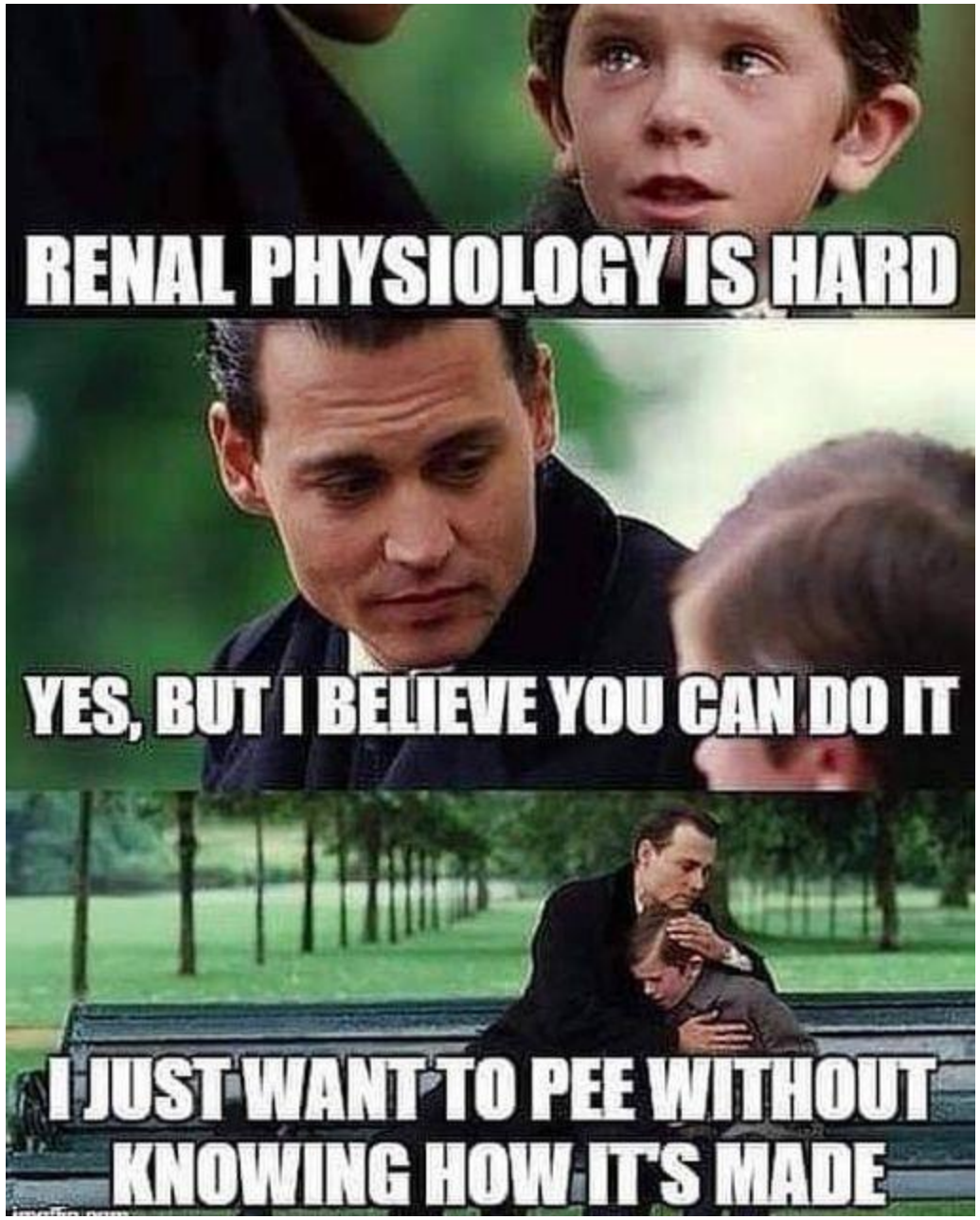


Approach to AKI

History	Ask about existing and new medications, toxin exposure, volume depletion, invasive tests, and hypotensive episodes
Physical exam	Check BP/pulse (with orthostatics), look for skin tenting or edema, palpate for full bladder, check skin for palpable purpura or rash, check fundi and skin for evidence of thromboemboli
Urinalysis	Presence of protein and RBC casts suggests glomerulonephritis; WBCs or WBC casts suggest infection or interstitial nephritis; hyaline casts suggest acute tubular necrosis; granular casts suggest ATN, ischemia, or nephrotoxin
Other labs	Serum: electrolytes, uric acid, LFTs, CPK, CBC, toxicology screen Urine: sodium, FE_{Na}* (eosinophils)
Imaging studies	Renal ultrasound, CT scan, IVP, MRI/MRA,† furosemide renogram
When to biopsy	H&P, labs, and imaging have ruled out prerenal and postrenal causes. Intrarenal cause due to primary renal disease felt to be likely. Biopsy also if glomerulonephritis is suspected.

Approach to AKI




RENAL PHYSIOLOGY IS HARD
YES, BUT I BELIEVE YOU CAN DO IT
I JUST WANT TO PEE WITHOUT KNOWING HOW IT'S MADE

Thank You