ARF

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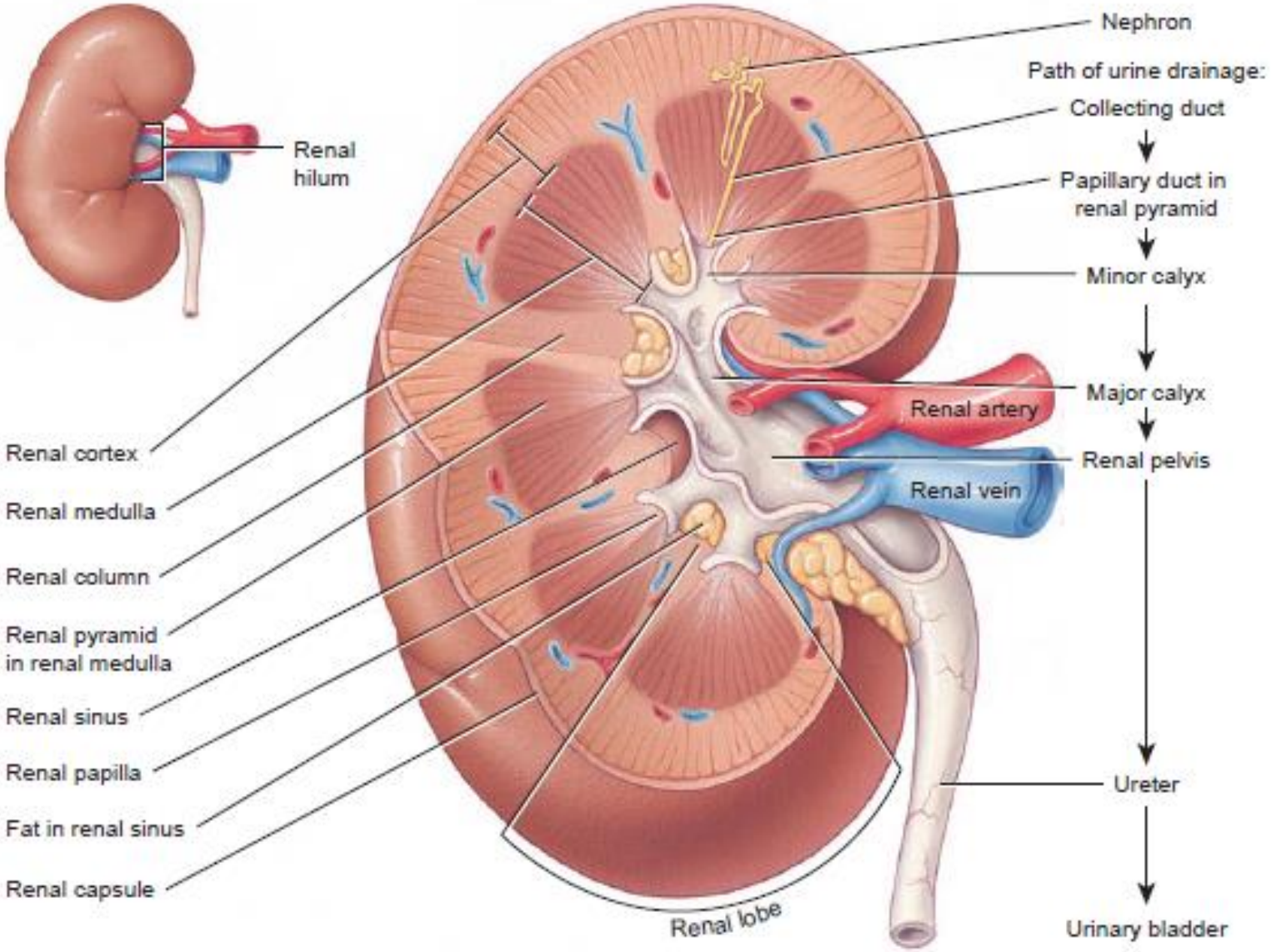
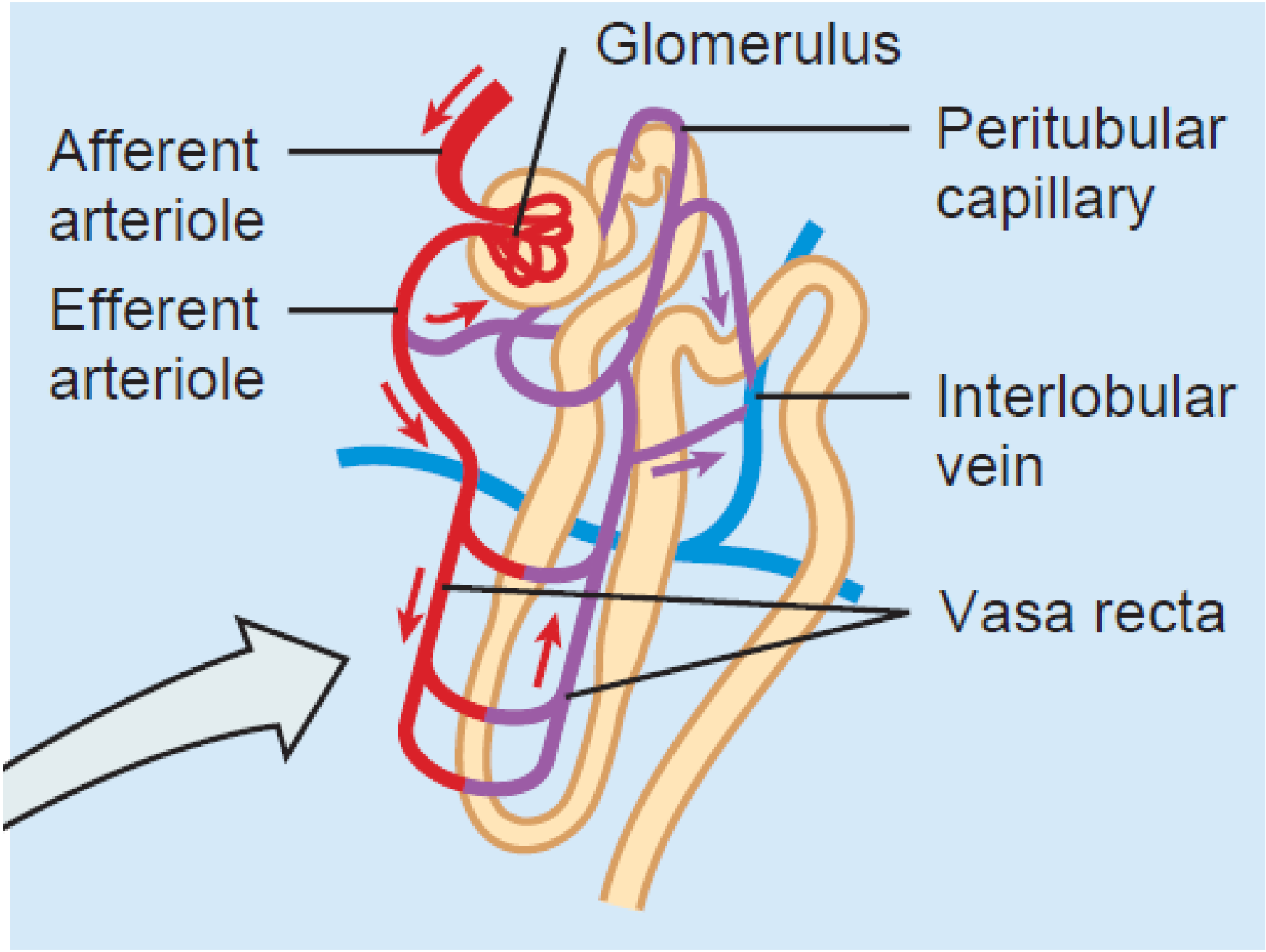
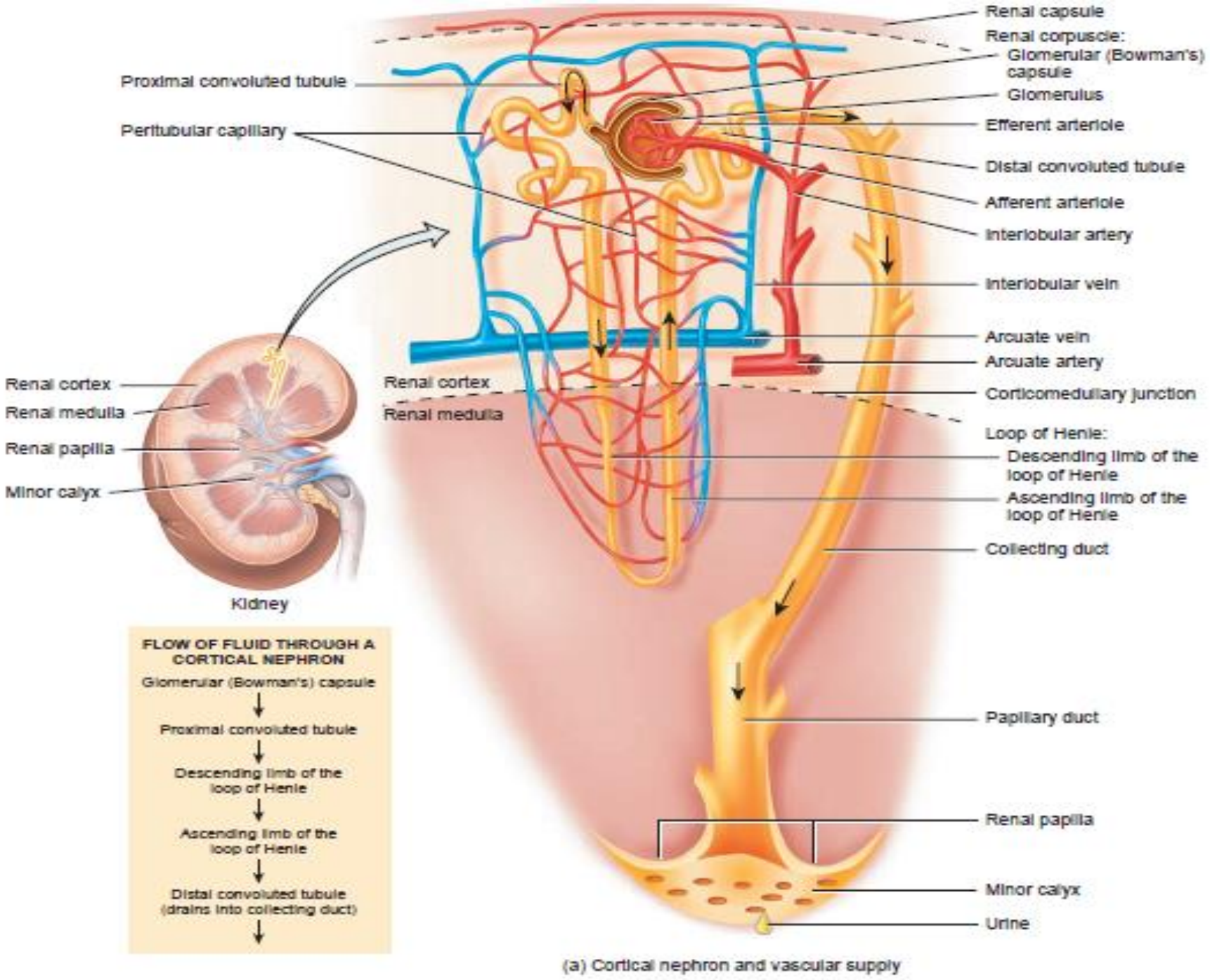


(a) Frontal section of right kidney


Glomerulus
Afferent arteriole
Efferent arteriole
Peritubular capillary
Interlobular vein
Vasa recta



(a) Cortical nephron and vascular supply

Production and elimination of urine requires 3 basic physiologic events

- **Blood flow to glomeruli**
- **Formation and processing of ultrafiltrate by glomeruli and tubular cells**
- **Urine excretion through ureters, bladder and urethra**

- **Alteration in these physiological events leads to ARF or CRF**

- **Renal failure is a condition in which the kidneys fail to remove metabolic end products from the blood and regulate the fluid, electrolyte, and pH balance of the extracellular fluids.**

- **Renal failure can occur as an acute or a chronic disorder**

- **ARF is broadly defined as a decrease in glomerular filtration rate (GFR), generally occurring over hours to days, sometimes over weeks, that is associated with an accumulation of waste products, including urea and creatinine.**

- **Acute renal failure often is reversible if recognized early and treated appropriately**

- **Chronic kidney disease, also called chronic renal insufficiency or progressive kidney disease by some, is defined as a progressive loss of function occurring over several months to years, and is characterized by the gradual replacement of normal kidney architecture with interstitial fibrosis.**

- **Chronic renal failure is the end result of irreparable damage**

ARF is predominantly categorized based on the anatomic area of injury or malfunction:

- **prerenal—decreased renal blood flow,**
- **Functional –impaired glomerular ultrafiltrate production or intraglomerular pressure**
- **intrinsic—a structure within the kidney is damaged, and**
- **postrenal—an obstruction is present within the urine collection system.**

- **Normal urine output of ≥1,200 mL/day**

Patients with ARF are often categorized as being

- **anuric (urine output <50 mL/day),**
- **oliguric (urine output <500 mL/day), or**
- **nonoliguric (urine output >500 mL/day).**

- **The most common indicator of acute renal failure is azotemia, an accumulation of nitrogenous wastes (urea nitrogen,uric acid, and creatinine) in the blood.**

Causes of Acute Renal Failure

Prerenal

Hypovolemia
- Hemorrhage
- Dehydration
- Excessive loss of gastrointestinal tract fluids
- Excessive loss of fluid due to burn injury

Decreased vascular filling
- Anaphylactic shock
- Septic shock

Heart failure and cardiogenic shock

Decreased renal perfusion due to vasoactive mediators, drugs, diagnostic agents

Intrinsic or intrarenal

Acute tubular necrosis
- Prolonged renal ischemia
- Exposure to nephrotoxic drugs, heavy metals, and organic solvents
- Intratubular obstruction resulting from hemoglobinuria, myoglobinuria, myeloma light chains, or uric acid casts
- Acute renal disease (acute glomerulonephritis, pyelonephritis)

Postrenal

Bilateral ureteral obstruction

Bladder outlet obstruction

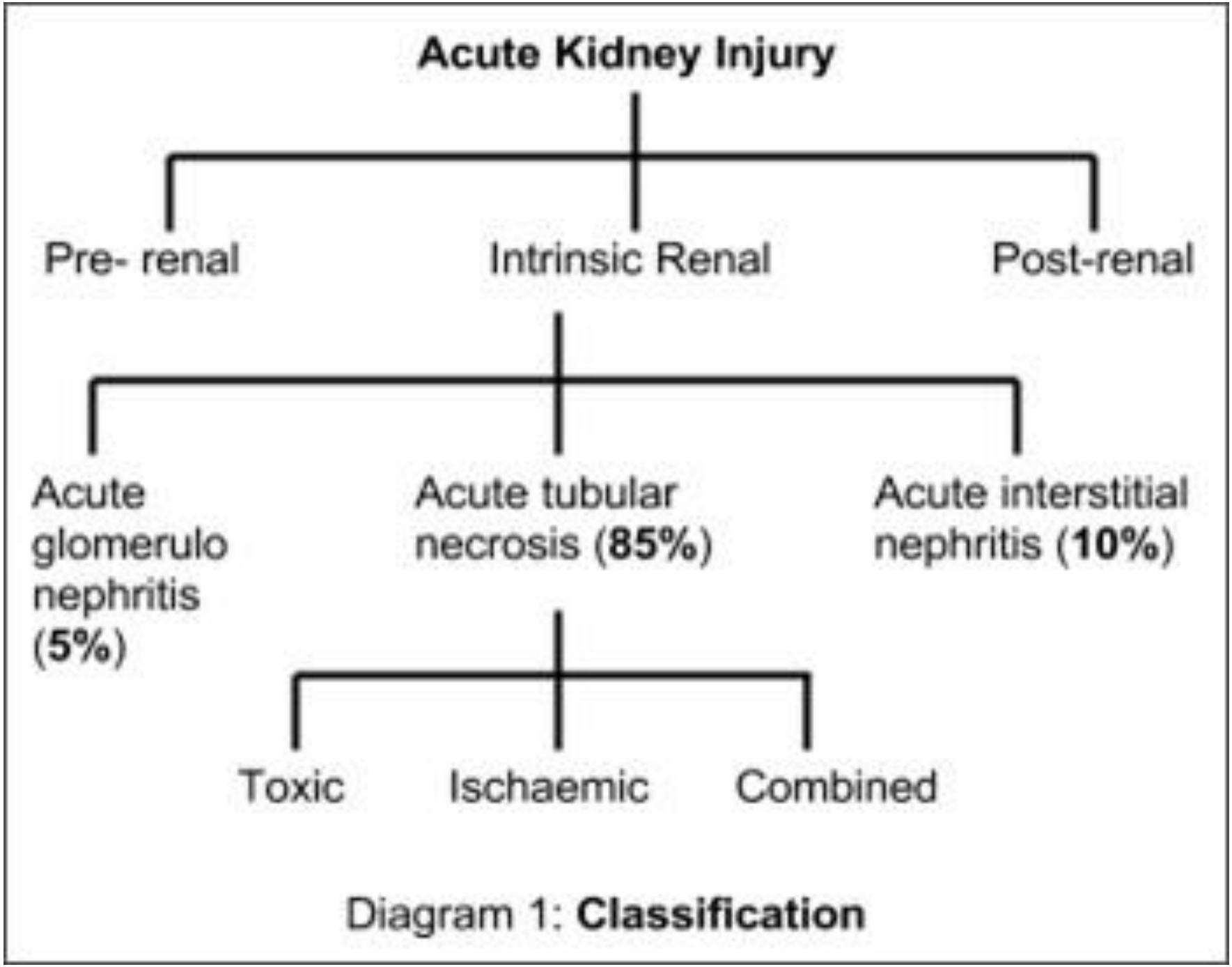


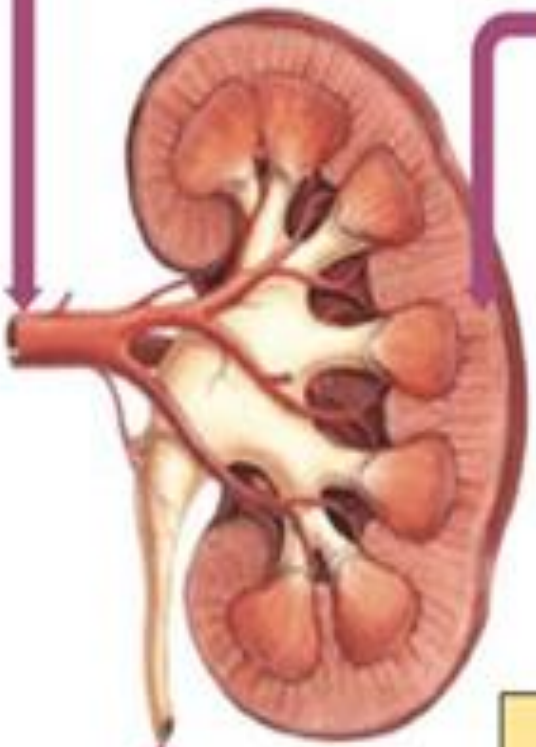
Diagram 1: **Classification**

Pre Renal Disease

- Blood or fluid loss
- Blood pressure medications
- Haemorrhage
- Heart attack
- Heart disease
- Liver failure
- Severe burns
- Severe dehydration
- Use of aspirin, ibuprofen or other related drugs
- Severe allergic reaction

Intrinsic Renal Disease

- Blood clots in the veins and arteries in the kidney
- Cholesterol deposits that block blood flow in the kidneys
- Glomerulonephritis(glo-mer-u-loe-neh-fry-tis):inflammation of tiny filters(glomeruli) of kidney
- Infection
- Medications such as certain chemotherapy drugs, antibiotics
- Toxins such as alcohol, heavy metals and cocaine



Post Renal Disease

Urinary tract obstruction at any site
e.g. Stones
Tumor
Prostatic enlargement

Diagram 2: **Causes of AKI**

Prerenal ARF

- Results from hypoperfusion of the renal parenchyma, with or without systemic arterial hypotension.

- Renal hypoperfusion with systemic arterial hypotension may be caused by a decline in intravascular or effective blood volume that can occur in those with acute blood loss (hemorrhage), dehydration, hypoalbuminemia, or diuretic therapy.

- **Renal hypoperfusion without systemic hypotension is most commonly associated with Renal artery stenosis bilateral renal artery occlusion, or unilateral occlusion in a patient with a single functioning kidney.**

- **The most common cause is atherosclerosis, with severe abrupt occlusion sometimes occurring as the result of an embolism.**

- **Homeostatic mechanisms are often able to maintain arterial pressure and renal perfusion, potentially averting the progression to ARF**

- **If, however, the decreased renal perfusion is severe or prolonged, these compensatory mechanisms may be overwhelmed and ARF will then be clinically evident.**

Functional

- **Impaired glomerular ultrafiltrate production or impaired intraglomerular pressure**

- **The afferent and efferent arterioles work in concert to maitain adequate glomerular capillary hydrostatic pressure to form ultrafiltrate**

- **Many drugs reduce this intraglomerular hydrostatic pressure.**

- **NSAID and cyclosporine—afferent vasoconstriction**
- **ACE inh ARB ---efferent vasodilation.**

Intrinsic ARF

- **Renal vasculature damage**
- **Glomeruli damage**
- **Tubular damage (ATN)**
- **Interstitial damage**

Intravascular Volume Depletion

- Hemorrhage (surgery, trauma)
- Dehydration (gastrointestinal losses, aggressive diuretic administration)
- Severe burns
- Hypovolemic shock
- Sequestration (peritonitis, pancreatitis)
- Decreased Effective Circulating Volume
- Cirrhosis with ascites
- Congestive heart failure

Hypotension, Shock Syndromes

- Antihypertensive vasodilating medications
- Septic shock
- Cardiomyopathy

Increased Renal Vascular Occlusion or Constriction

- Bilateral renal artery stenosis
- Unilateral renal stenosis in solitary kidney
- Renal artery or vein thrombosis (embolism, atherosclerosis)
- Vasopressor medications (phenylephrine, norepinephrine)

Renovascular damage

- Occlusion large atheroemboli or thromboemboli in the bilateral renal arteries, or one vessel of the patient with a single kidney.

- Susceptible to inflammatory processes that lead to microvascular damage and vessel dysfunction when the renal capillaries are affected.

- Neutrophils invade the vessel wall, causing damage that can include thrombus formation, tissue infarction, and collagen deposition within the vessel structure

- **Diffuse renal vasculitis can be mild or severe, with severe forms promoting concomitant ischemic acute tubular necrosis (ATN).**

- **Accelerated hypertension that is not treated may also compromise renal microvascular blood flow, and thus cause diffuse renal capillary damage.**

Glomerular Damage

- Only 5% of the cases of intrinsic ARF are of glomerular origin.

- The glomerulus serves to filter fluid and solute into the tubules while retaining proteins and other large blood components in the intravascular space.

- glomerular damage can occur by the same mechanisms described for the renal vasculature, and severe inflammatory processes specific to the glomerulus.

- **Immune mediated injury**
- **Antigen-antibody complexes localize in glomerulus lead to ⟹ triggering of biological events cell injury and proteinuria.**

Tubular damage

- 85% of all cases of intrinsic ARF are caused by ATN
- 50% are a result of renal ischemia
- 35% are the result of exposure to direct tubule toxins,
  - endogenous (myoglobin, hemoglobin, or uric acid)
  - exogenous (contrast agents, heavy metals, or aminoglycoside antibiotics).

- **The tubules located within the medulla of the kidney are particularly at risk from ischemic injury, as this portion of the kidney is metabolically active and thus has high oxygen requirements.**

- **Thus, ischemic conditions affect the tubules more than any other portion of the kidney.**

- **Initial injury causing tubule epithelial cell necrosis or apoptosis, followed by an extension phase with continued hypoxia and an inflammatory response involving the nearby interstitium.**

- **The onset of ATN can occur over days to weeks, and rarely longer than that depending on the factors responsible for the damage to the tubular epithelial cells.**

- Once tubular cells die
- They slough off into the tubular lumen.
- The debris causes increased tubular pressure and reduces glomerular filtration
- The loss of epithelial cells leaves only the basement membrane between the filtrate and the interstitium
- Which results in dysregulation of fluid and electrolyte transfer across the tubular epithelium

- Tubular injury leads to a loss in the ability to concentrate urine
- Defective distal sodium reabsorption, and, ultimately, to a reduction in the GFR
- Continued kidney hypoxia or toxin exposure after the original insult, kills more cells and propagates the inflammatory response
- Extend the injury and delay the recovery Process
- With prolonged ischemia, the tubular epithelial cells in the cortico-medullary junction are damaged and die

- When the toxin or ischemia is removed, a maintenance phase ensues (typically 2 to 3 weeks), followed by a recovery phase (2 to 3 weeks) during which new tubule cells are regenerated.

- The recovery phase is associated with a notable diuresis, which requires attention to fluid balance to ensure that a secondary prerenal injury does not occur.

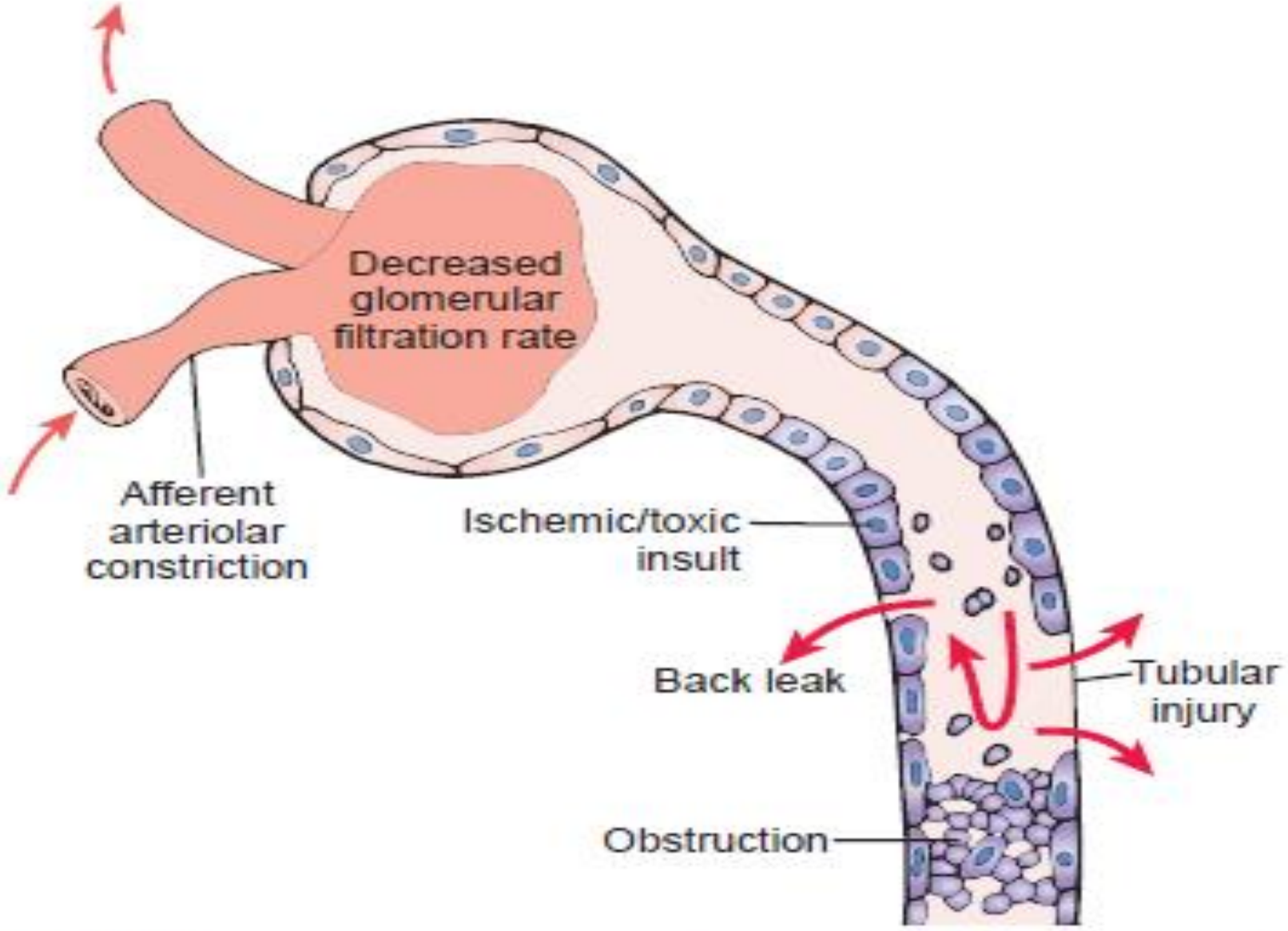
- if the ischemia or injury is extremely severe or prolonged, cortical necrosis may occur, preventing any tubule cell regrowth in the affected areas.

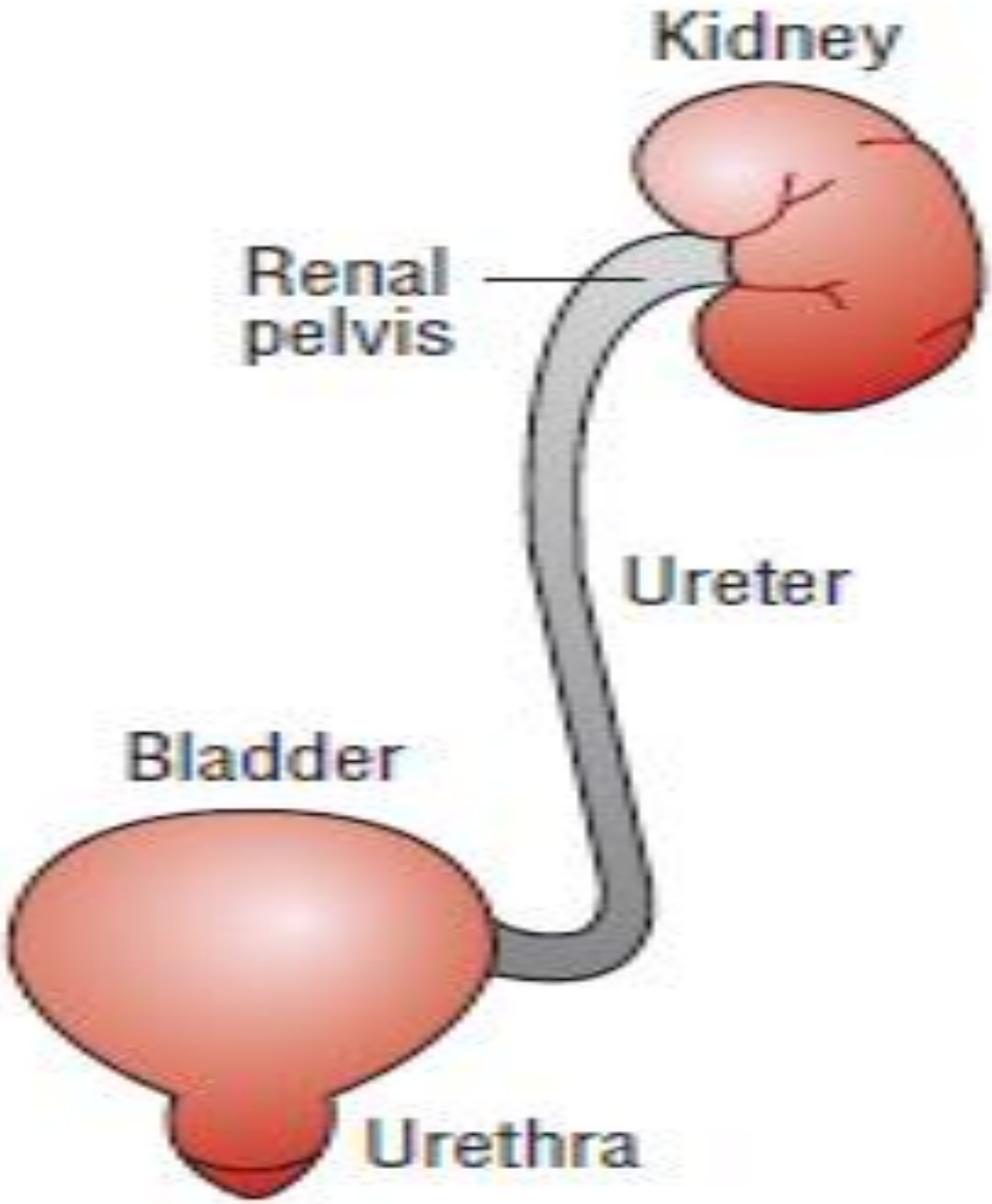
Interstitial Damage

- The interstitium of the kidney is rarely the primary cause of end-stage renal disease (ESRD)
- Acute interstitial nephritis is most commonly caused by medications or bacterial or viral infections
- Up to 30% of cases have no identifiable cause

- **Interstitial nephritis is characterized by lesions comprised of monocytes, macrophages, B cells, or T cells, clearly identifying an immunologic response as the injurious process affecting the interstitium**

- **Widespread inflammation and edema affect the function of the tubules, and may cause fibrosis if the administration of the nephrotoxin is not discontinued and inflammation quickly**


Decreased glomerular filtration rate
Afferent arteriolar constriction
Ischemic/toxic insult
Back leak
Tubular injury
Obstruction


Kidney
Renal pelvis
Ureter
Bladder
Urethra

POSTRENAL ACUTE RENAL FAILURE

- Postrenal ARF may develop as the result of obstruction at any level within the urinary collection system from the renal tubule to urethra

- Wherever the location of the obstruction, urine will accumulate in the renal structures above the obstruction and cause increased pressure upstream.

- The ureters, renal pelvis, and calyces all expand, and the net result is a decline in GFR.
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- **The blockage may occur at the ureter level, secondary to nephrolithiasis, blood clots, a sloughed renal papillae, or physical compression by an abdominal process such as retroperitoneal fibrosis, cancer, or an abscess**

- **Bladder outlet obstruction, the most common cause of obstructive uropathy, is often caused by a prostatic process (hypertrophy, cancer or infection)**

- **Improperly placed urinary catheter.**

- **Neurogenic bladder or anticholinergic medications may also prevent bladder emptying and cause ARF.**
- **Crystal deposition within the tubules from oxalate**
- **Insufficient urine volume to prevent crystal precipitation in the urine**
- **Extremely elevated uric acid concentrations from chemotherapy- induced tumor lysis syndrome**

Clinical presentation

- Acute change in urinary habits,
- Weight gain, and flank pain.
- Signs include edema, colored or foamy urine, and, in volume depleted patients, orthostatic hypotension.

Complications of ARF?

- Anemia
- Bone disease and high phosphorus (hyperphosphatemia)
- Heart disease
- High potassium (hyperkalemia)
- Fluid buildup