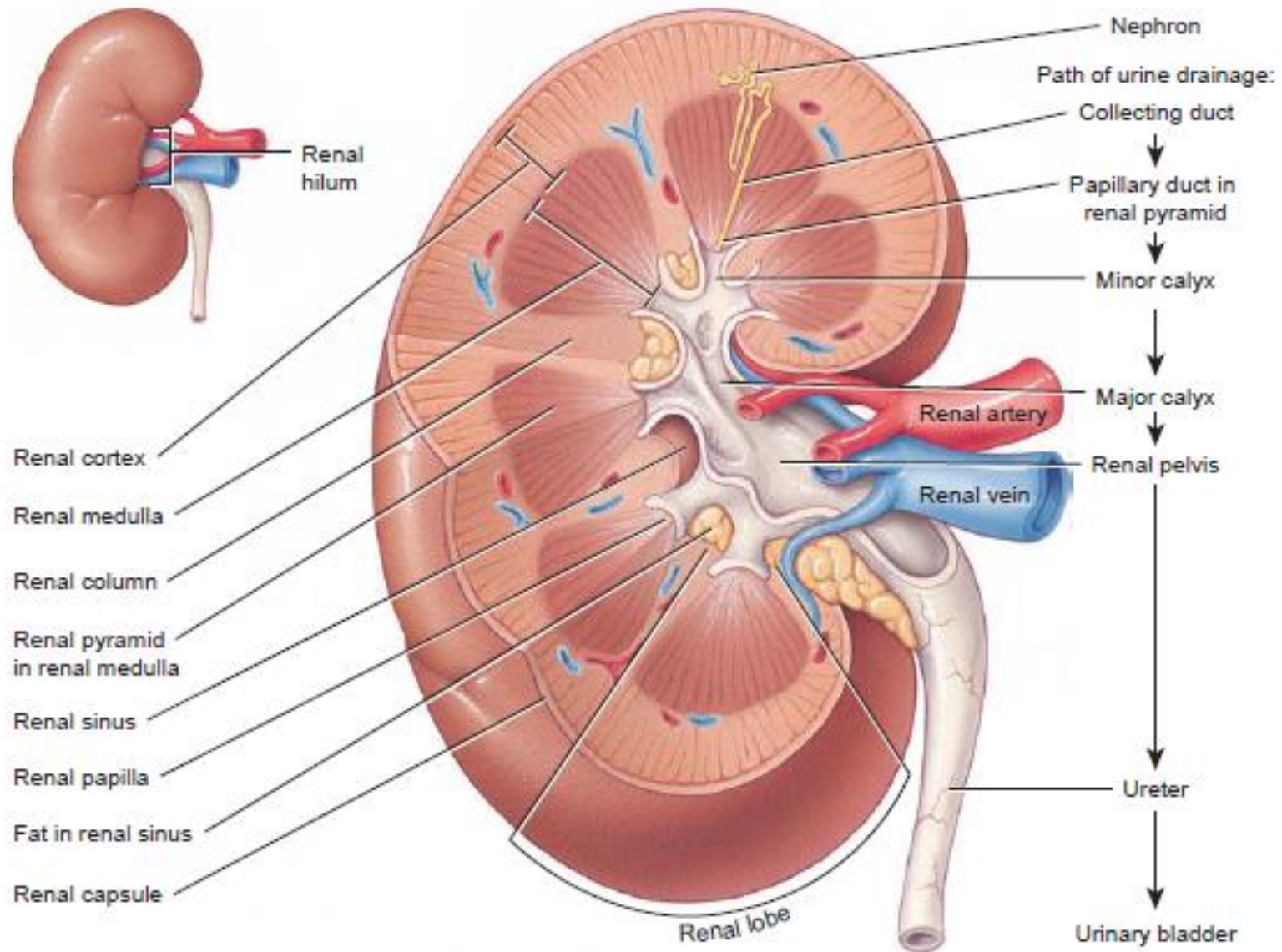
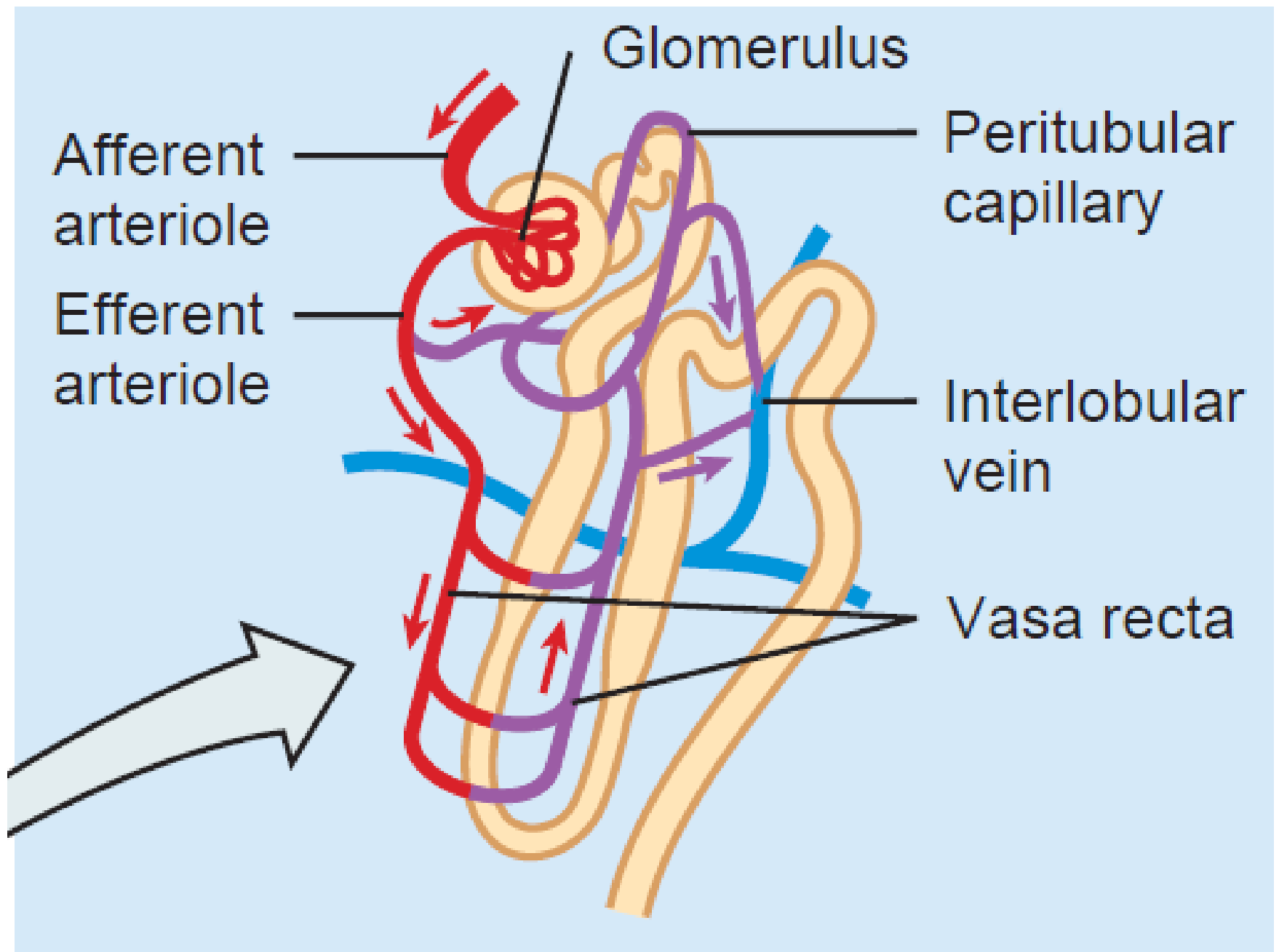


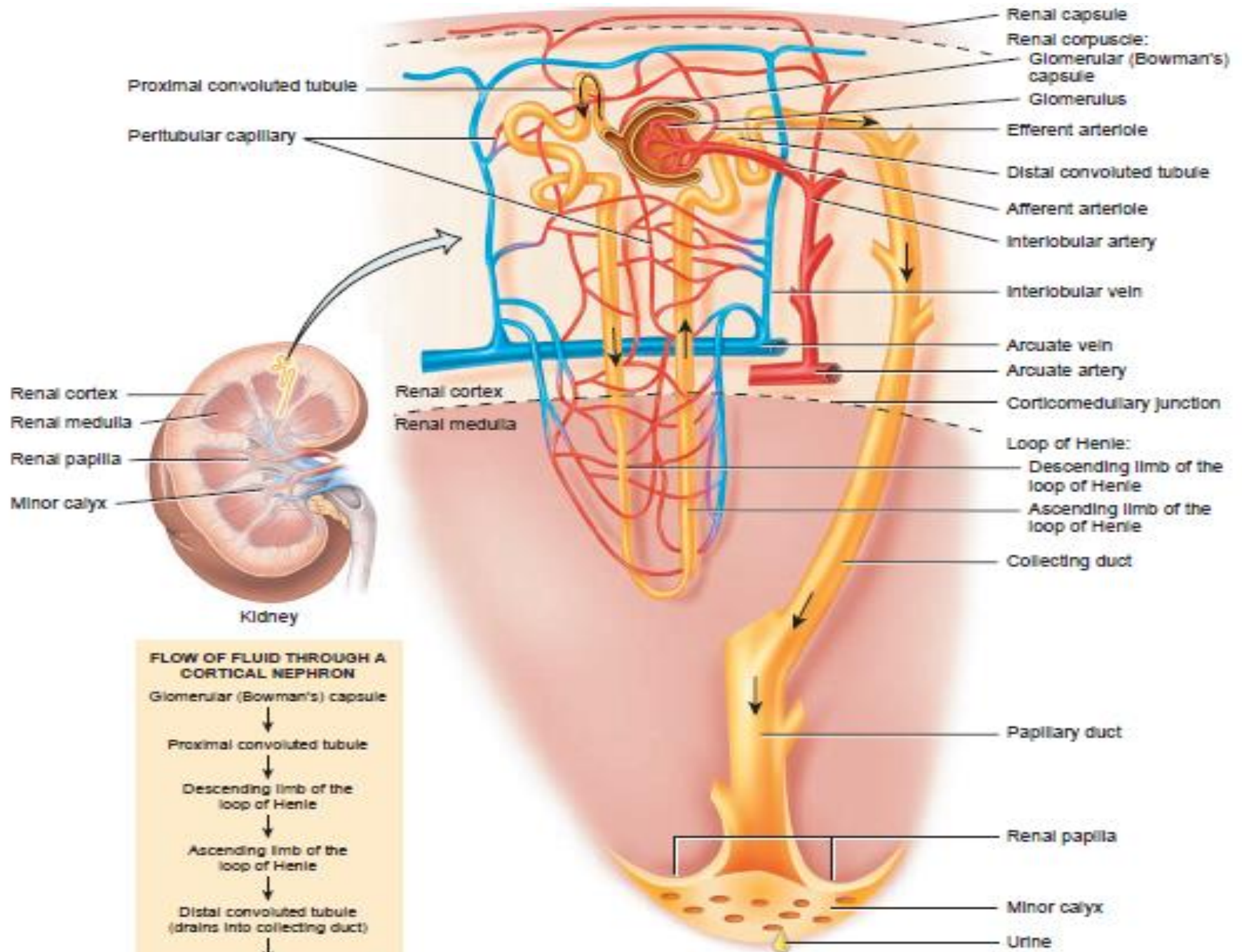
ARF

BY DR SWATHI SWAROOPA.B



(a) Frontal section of right kidney





(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**
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- **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.
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- Normal urine output of $\geq 1,200$ 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).**
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- **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 hemoglobin-
uria, myoglobinuria, myeloma light chains, or
uric acid casts

- Acute renal disease (acute glomerulonephritis,
pyelonephritis)

Postrenal

Bilateral ureteral obstruction

Bladder outlet obstruction

Acute Kidney Injury

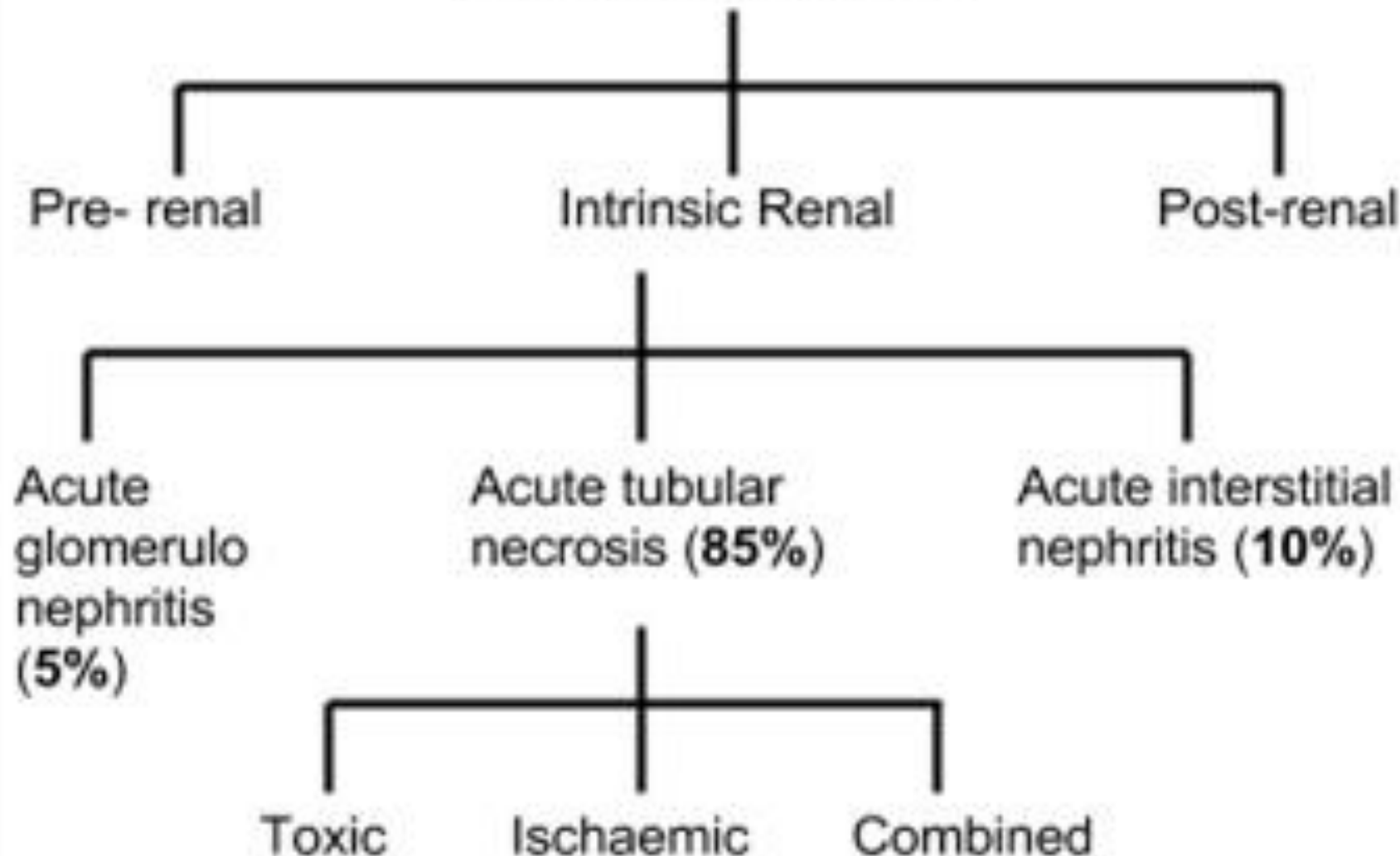


Diagram 1: **Classification**

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 maintain 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

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

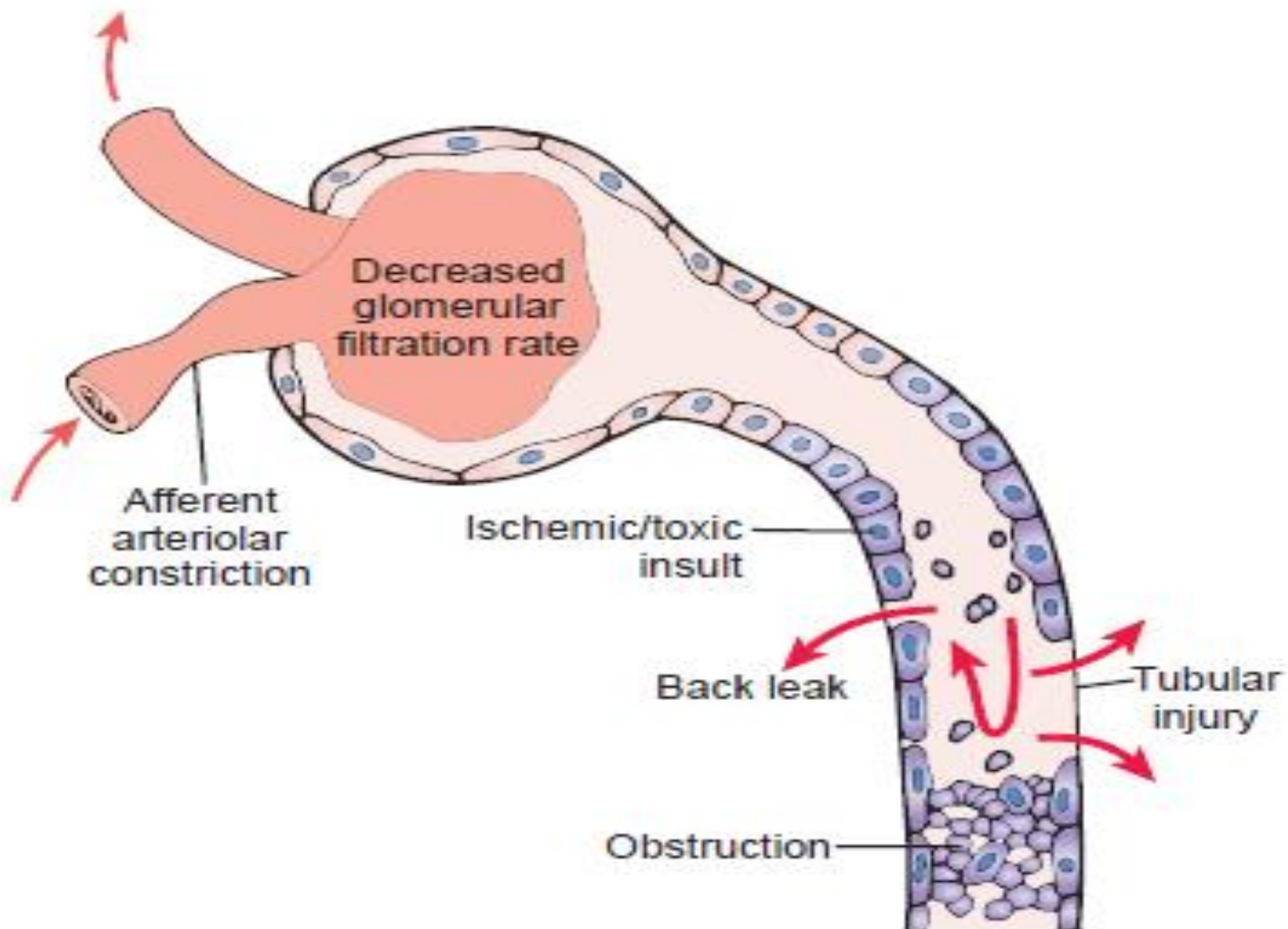
- Tubular injury leads to a **loss in the ability to concentrate urine**
- **Defective distal sodium reabsorption, and, ultimately, to a reduction in the GFR**
- Continued kidney hypoxia or toxin exposure after the original insult, kills more cells and **propagates the inflammatory response**
- **Extend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

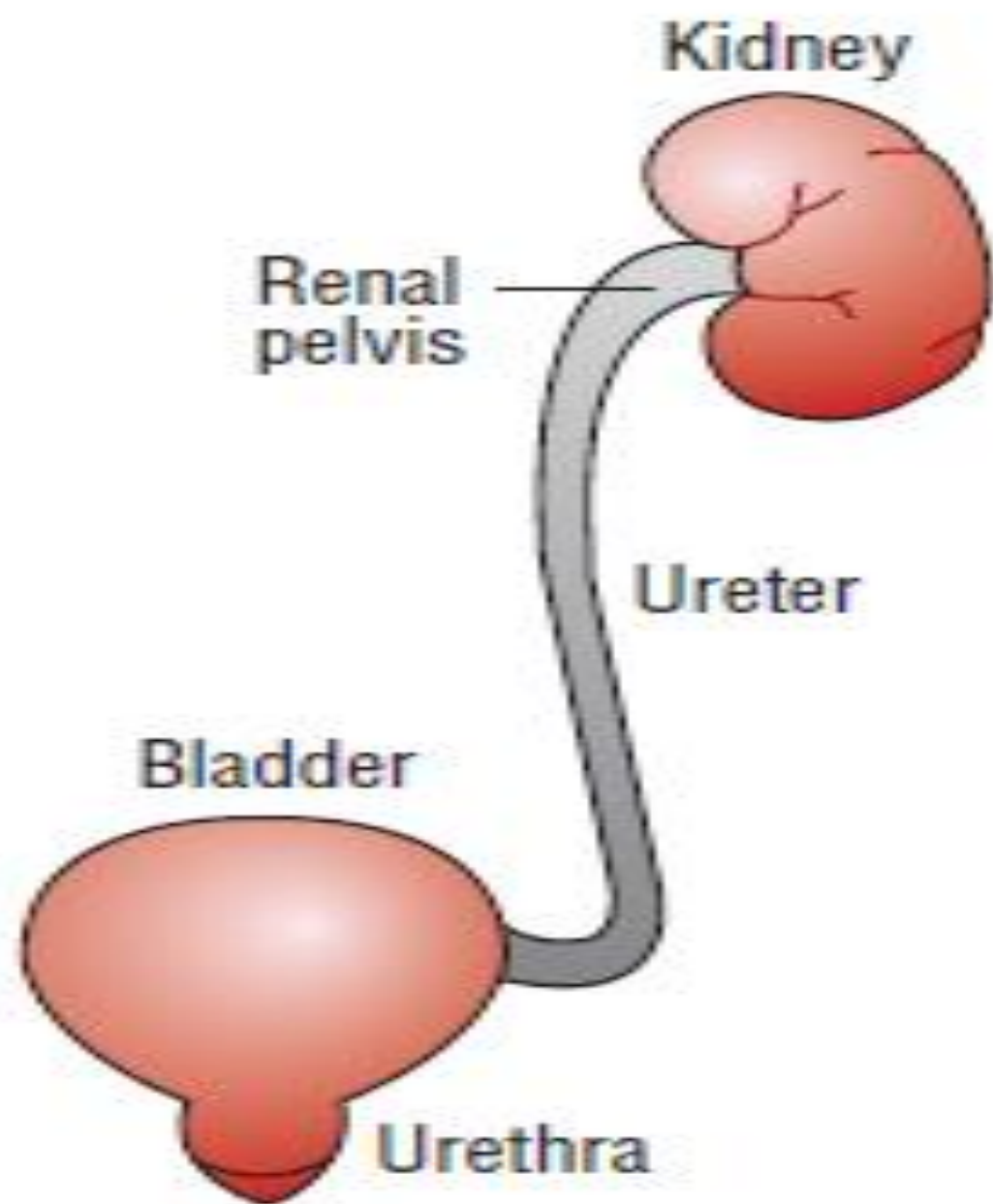
- When the toxin or ischemia is removed, a **maintenance phase ensues** (typically 2 to 3 weeks), followed by **a recovery phase** (2 to 3 weeks) during which new tubule cells are **regenerated**.
- The **recovery phase** is associated with a notable **diuresis**, which requires attention to fluid balance 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





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?