Drug Induced Acute Renal Failure

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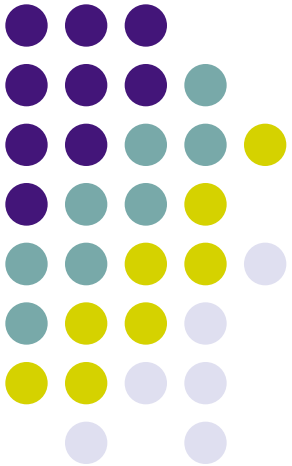


Acute renal failure (ARF)

- An abrupt or rapid decline in renal function
- Marked by a rise in BUN (azotemia) or serum creatinine concentration
  - Immediately after a kidney injury, BUN or creatinine levels may be normal
    - The only sign of a kidney injury may be decreased urine production
    - Use RIFLE Criteria to evaluate Risk.

RIFLE Criteria for ARF

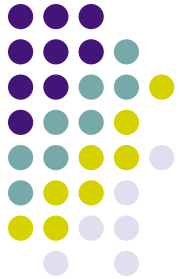
- Risk
- Injury
- Failure
- Loss of Function
- End Stage Renal Disease

- Oliguria 6 hours
- Oliguria 12 hours
- Creatinine
- Dialysis < 90 days
- Dialysis > 90 days

Acute renal failure (ARF)

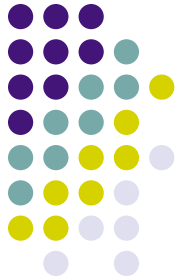
- Causes:
  - A rise in the BUN level can occur without renal injury, such as in GI or mucosal bleeding, steroid use, or protein loading
  - A rise in the creatinine level can result from medications (eg, cimetidine, trimethoprim) that inhibit the kidney's tubular secretion, or an increase of muscle breakdown such as seen in Rhabdomyolysis.

Acute renal failure (ARF)



- History and Physical examination:
  - Nephrotoxic drug ingestion
  - History of trauma or unaccustomed exertion
  - Blood loss or transfusions
  - Congestive heart failure
  - Exposure to toxic substances, such as ethyl alcohol or ethylene glycol

Acute renal failure (ARF)



- History and Physical examination:
  - Exposure to mercury vapors, lead, cadmium, or other heavy metals, which can be encountered in welders and miners
  - Hypotension
  - Volume contraction
    - Vomiting/Diarrhea/Sweating/Nursing Home
  - Evidence of connective tissue disorders or autoimmune diseases

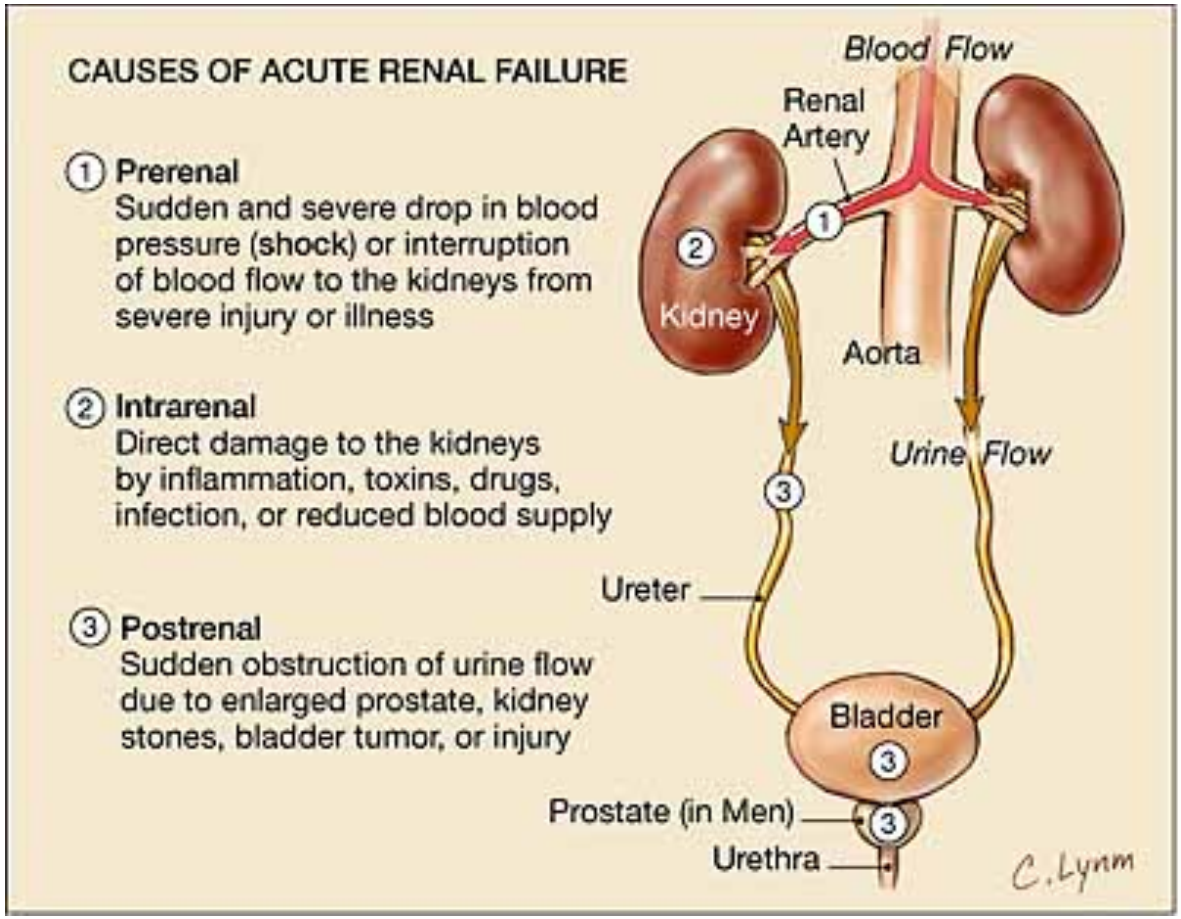
Pathophysiology

- ARF may occur in 3 clinical patterns

BUN:Cr > 20:1

BUN:Cr 10-20:1

BUN:Cr > 20:1

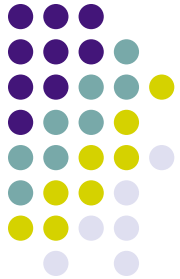


Pathophysiology

- ARF may occur in 3 clinical patterns
- Suggested by labwork:

BUN:Cr > 20:1	Pre-Renal
BUN:Cr 10-20:1	Intra-Renal
BUN:Cr < 10:1	Extrinsic Production of Creatinine

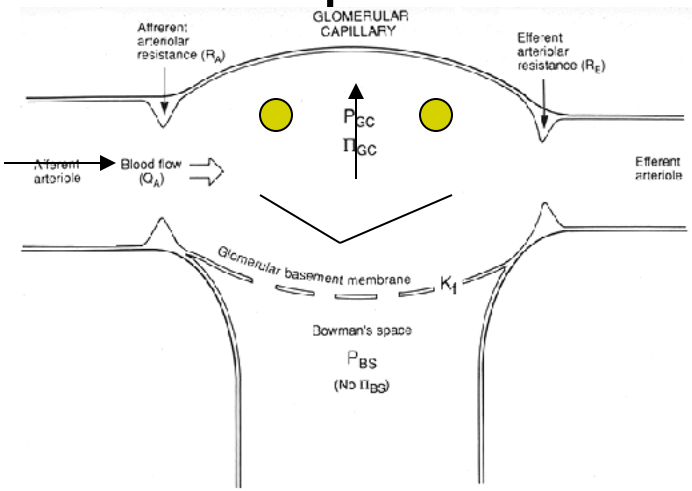
Acute renal failure (ARF)



- Patients can have:
  - Oliguria
    - Daily urine volume of less than 400 mL/d and has a worse prognosis, except in prerenal failure
    - Anuria is urine output of less than 100 mL/d and, if abrupt in onset, is suggestive of bilateral obstruction or catastrophic injury to both kidneys
  - Rapid or slow rise in creatinine levels
  - Differences in urine solute concentrations and cellular content

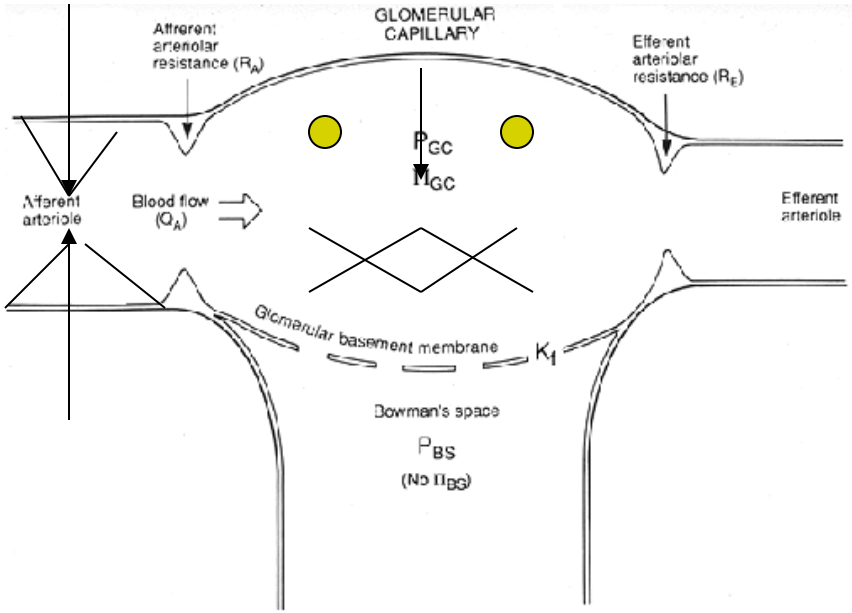
Prerenal ARF

- Prerenal ARF represents the most common form of kidney injury and often leads to **intrinsic** ARF if it is not promptly corrected
- From any form of extreme volume loss
  - GI, renal (diuretics, polyuria), cutaneous (eg, burns), and internal or external hemorrhage can result in this syndrome
- Systemic vasodilation or decreased renal perfusion
  - Anesthetics
  - Drug overdose
  - Heart failure
  - Shock (eg, sepsis, anaphylaxis)



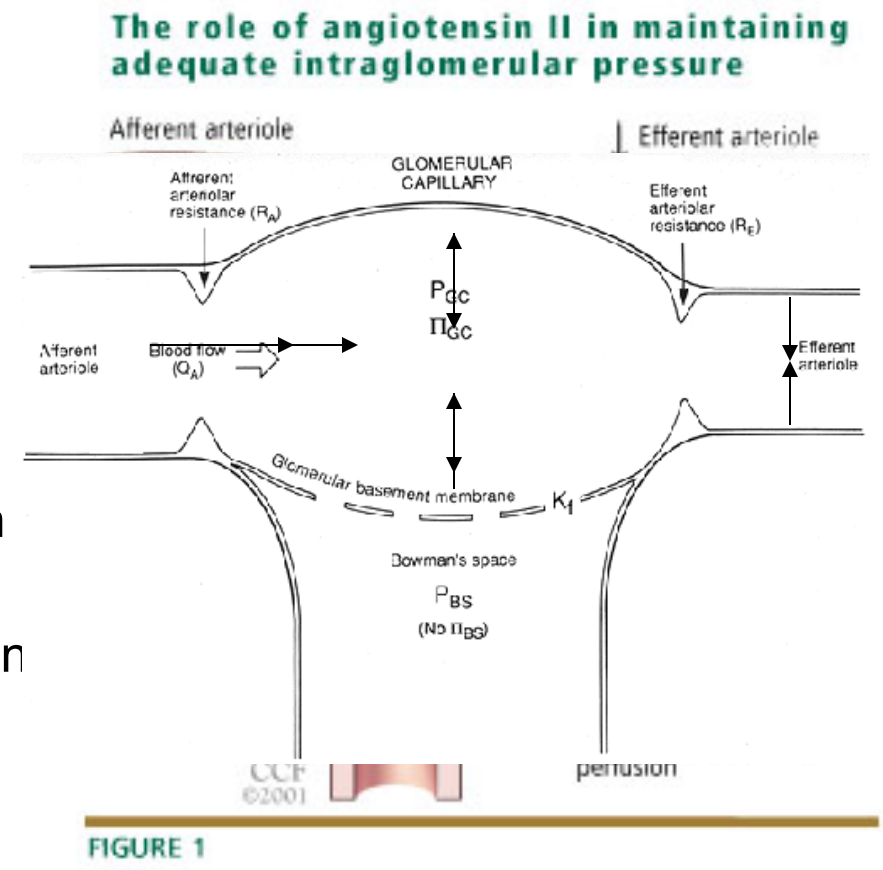
Prerenal ARF

- **<u>Afferent</u>** Arteriolar vaso**<u>constriction</u>** leading to prerenal ARF
  - Hypercalcemic states
  - Radiocontrast agents
  - NSAIDs
  - Amphotericin
  - Calcineurin inhibitors
  - Norepinephrine
  - Other pressor agents
  - Hepatorenal syndrome
    - Functional renal failure develops from diffuse vasoconstriction in vessels supplying the kidney.



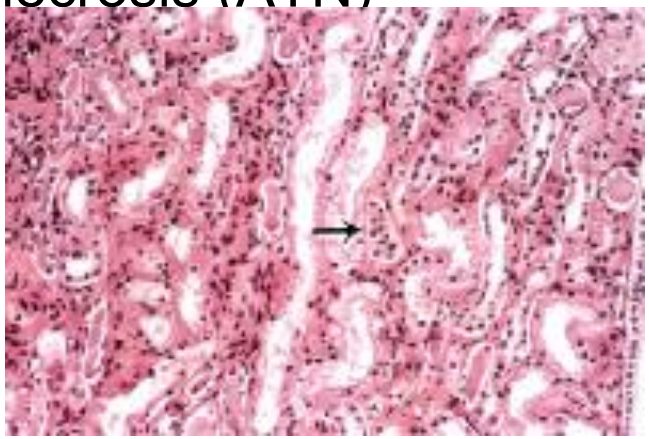
Prerenal ARF

- **Efferent** arteriolar vaso**dilation** can induce prerenal ARF in volume-depleted states in the face of :
  - ACE Inhibitors
  - ARBs
    - Otherwise safely tolerated and beneficial in most patients with chronic kidney disease
    - Both cause afferent and efferen dilation, but efferent more



Intrinsic ARF

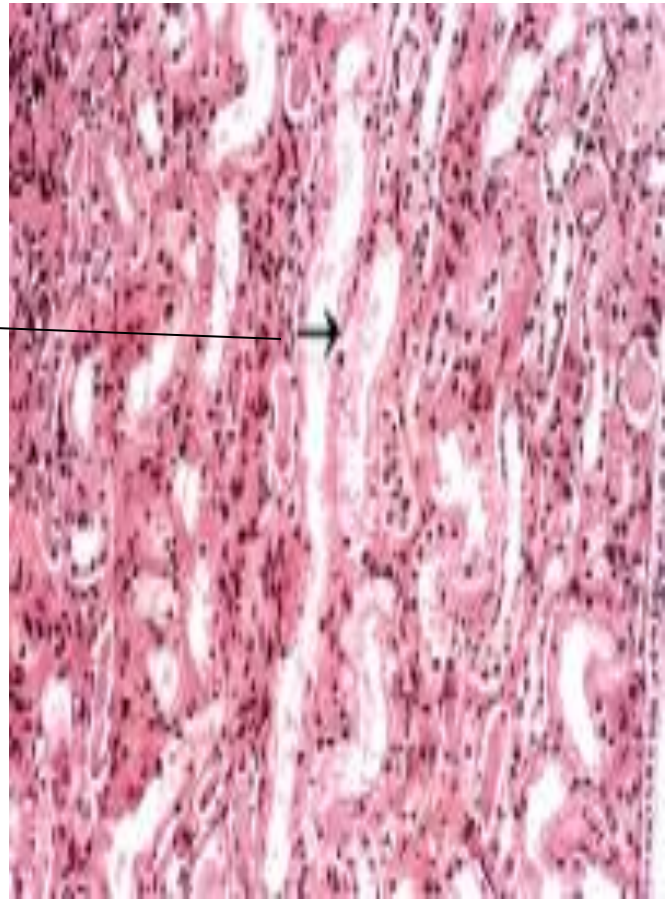
- Structural injury in the kidney
  - Most common form is acute tubular necrosis (ATN)
    - Either ischemic or cytotoxic
    - Loss of brush borders
    - Flattening of the epithelium
    - Detachment of cells
    - Formation of intratubular casts
    - Dilatation of the lumen



  - Although these changes are observed predominantly in **proximal tubules**, injury to the distal nephron can also be demonstrated. The distal nephron may also be subjected to obstruction by desquamated cells and cellular debris.

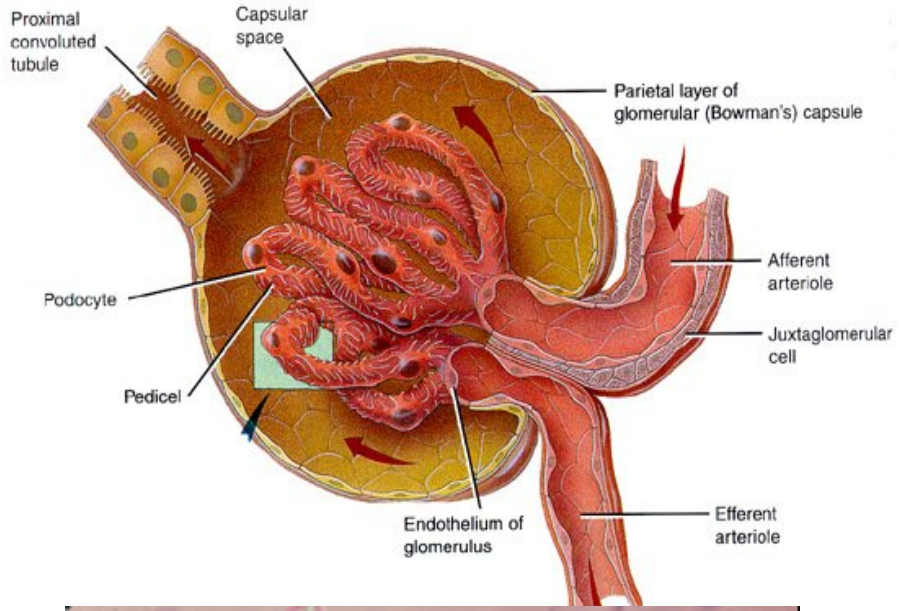
Intrinsic ARF

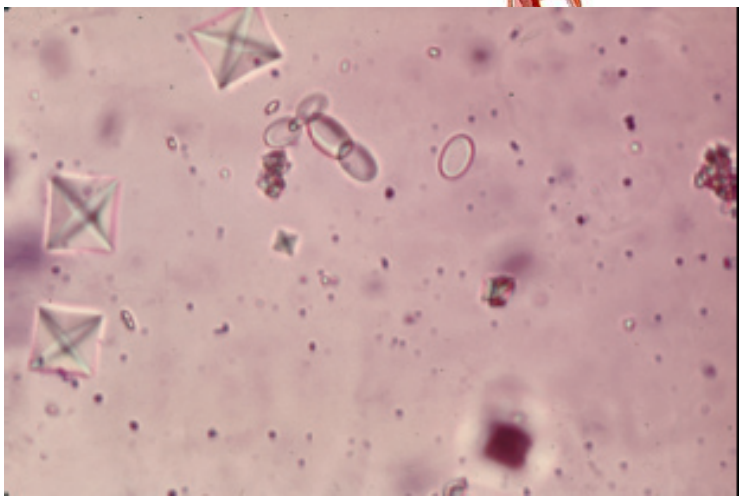
- Intrarenal vasoconstriction is the dominant mechanism for the reduced glomerular filtration rate (GFR) in patients with ATN.
- Tubular injury seems to be an important concomitant finding
  - Urine backflow and intratubular obstruction (from sloughed cells and debris) = reduced net ultrafiltration.
- Stressed renal microvasculature is more sensitive to potentially vasoconstrictive drugs and otherwise tolerated changes in systemic blood pressure.
  - Injured kidney vasculature has an impaired vasodilatory response and loses its autoregulatory behavior
  - Dialysis may re-injure the kidneys as a result



Intrinsic ARF

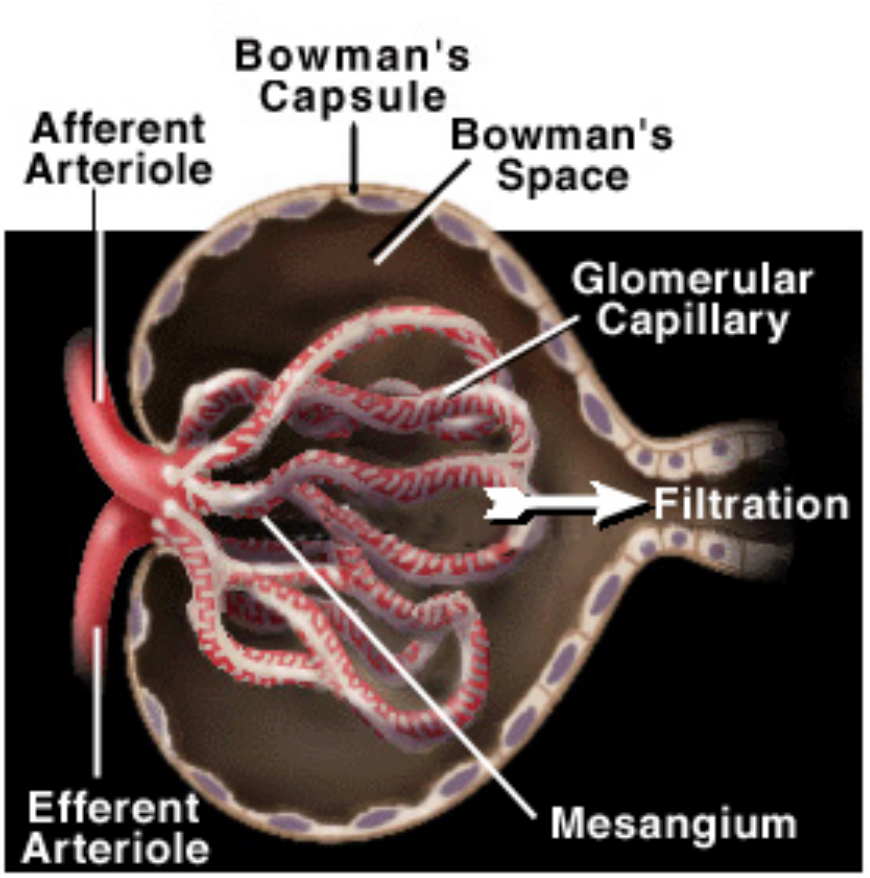
- Tubular
  - Cytotoxic
    - Crystals
      - Tumor lysis syndrome
      - Ethylene glycol poisoning
      - Megadose vitamin C
      - Acyclovir
      - Indinavir
      - Methotrexate
    - Drugs
      - Aminoglycosides
      - Lithium
      - Amphotericin B
      - Pentamidine
      - Cisplatin
      - Ifosfamide
      - Radiocontrast agents





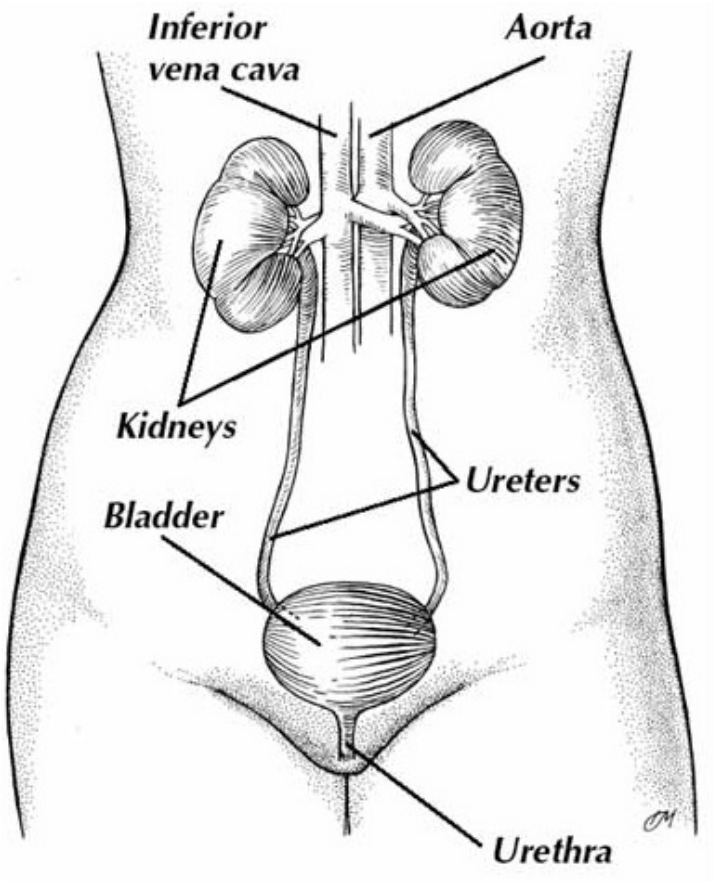
Intrinsic ARF

- Interstitial
  - Drugs
    - Penicillins
    - Cephalosporins
    - NSAIDs
    - Proton-pump inhibitors
    - Allopurinol
    - Rifampin
    - Indinavir
    - Mesalamine
    - Sulfonamides



Postrenal ARF

- Mechanical obstruction of the urinary collecting system
  - Renal pelvis, ureters, bladder, or urethra
- Causes of obstruction
  - Stone disease
  - Stricture
  - Intraluminal, extraluminal, or intramural tumors



Postrenal ARF

- Bladder neck obstruction
  - Tricyclic antidepressants
  - Facilitates urine storage by decreasing bladder contractility and increasing outlet resistance.
    - Imipramine
    - Desipramine
    - Trimipramine
    - Clomipramine
    - Lofepramine
    - Amitriptyline
    - Nortriptyline
    - Protriptyline
    - Dothiepin hydrochloride
    - Doxepin
  - Ganglion blockers
    - Trimethaphan
    - Mecamylamine
  - ACEIs
  - Gentamicin