

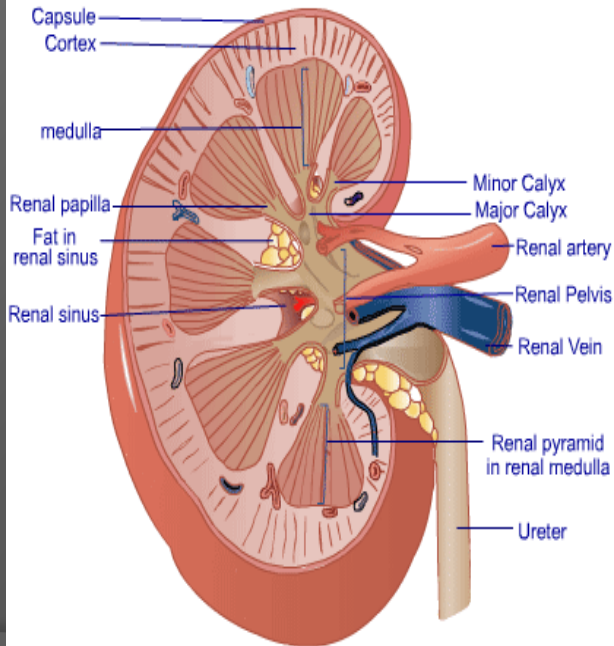
V. N. Karazin Kharkiv National University

Internal medicine department



# ACUTE RENAL FAILURE

Cut Section of Kidney



Performed: student of V  
course, gr. 527  
SHRADDHA .D.TARAL

Scientific adviser: ass.prof Makharynska O.S  
Head of department: prof. Yabluchansky M.I.

# Structure:

- ⦿ Acute Renal failure (ARF) – definition
- ⦿ Anatomy and physiology of kidneys
- ⦿ ARF diagnostic criterias
- ⦿ ARF - classification
- ⦿ Etiology and pathophysiology
- ⦿ Diagnostic evaluation
- ⦿ Prerenal ARF
- ⦿ Intrinsic ARF
- ⦿ Postrenal ARF
- ⦿ Differential diagnosis
- ⦿ Complications
- ⦿ Management: prevention and treatment

**Acute kidney injury**, previously known as acute renal failure, encompasses a wide spectrum of injury to the kidneys, not just kidney failure, and characterized by the sudden impairment of kidney function resulting in retention of nitrogenous and other waste products normally cleared by the kidneys.

- AKI complicates 5-7% of acute care hospital admissions and up to 30% of admissions to the intensive care unit
- AKI is associated with a marked-increased risk of death in hospitalized individuals
- Risk factors for developing ARF: age, IDDM, CKD, LV dysfunction
- AKI may be **community-acquired** (volume depletion, adverse effects of medications, obstruction of the urinary tract) or **hospital-acquired** (sepsis, major surgical procedures, liver failure, intravenous iodinated contrast administration, and nephrotoxic medication).

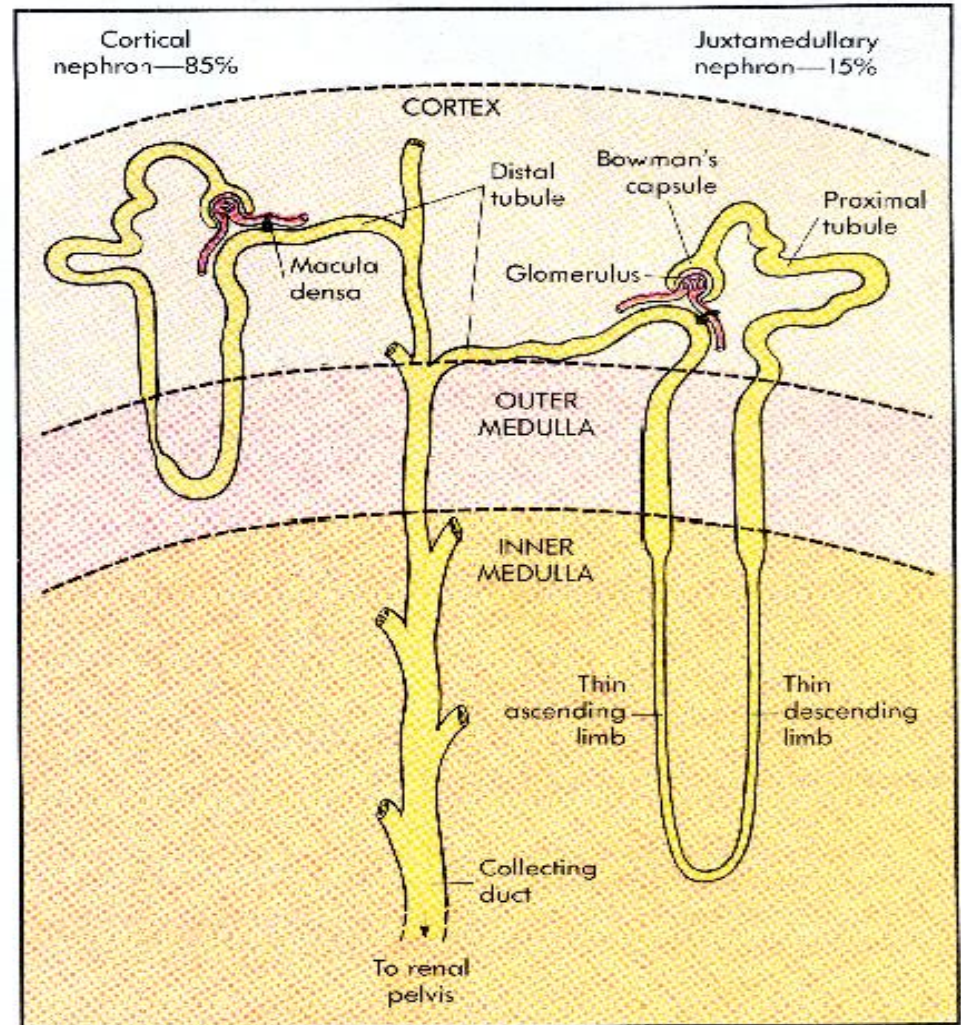
# Structural organization

- ◎ renal parenchyma:

- cortex
- medulla

- ◎ nephrons:

- cortical
- juxtamedullary

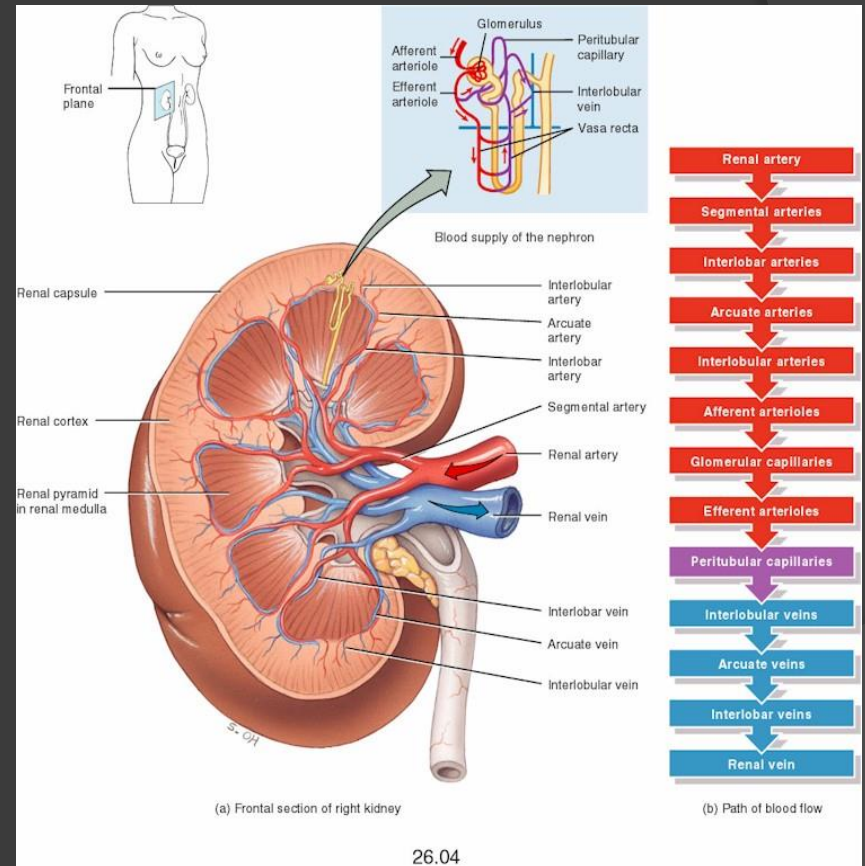


# Renal blood supply:

the kidneys receive 20% of the cardiac output

## ○ vascular supply:

- renal arteries
- interlobar arteries
- arcuate arteries
- interlobular arteries
- afferent arterioles
- glomerular capillaries
- efferent arterioles
- peritubular capillaries

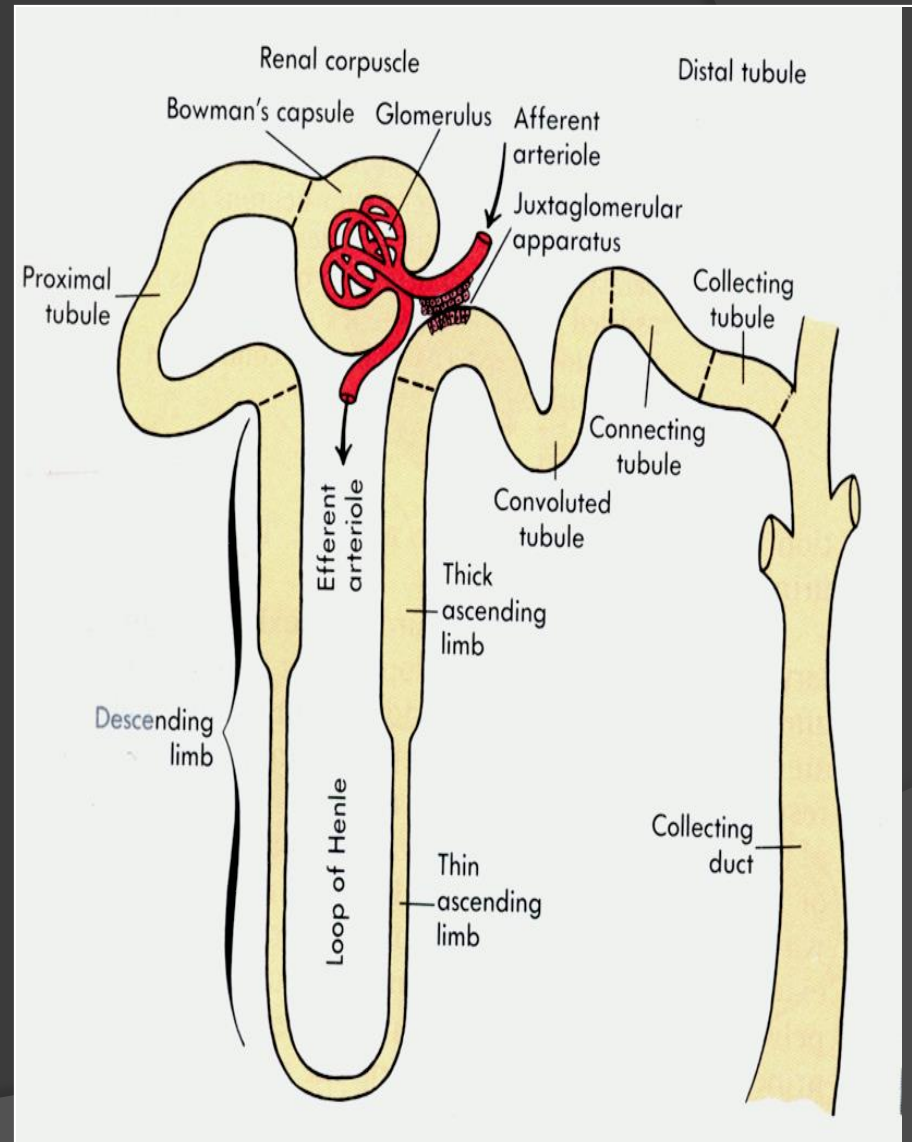


# Basic Renal Physiology

## Nephron is

the functional unit of the kidney, capable of forming urine has two major components:

- glomerulus
- tubule:
  - proximal
  - loop of Henle
  - distal
  - collecting



# Determinants of renal blood flow (RBF)

$$\text{RBF} = \frac{\text{renal artery pressure} - \text{renal vein pressure}}{\text{total renal vasculature resistance}}$$

Adjusting the resistances of the afferent and efferent arterioles, the kidneys can regulate both the hydrostatic pressures in the glomerular and peritubular capillaries, changing the rate of glomerular filtration and/or tubular reabsorption in response to homeostatic demands.

# Glomerular filtration rate (GFR)

- is widely accepted as the best overall index of kidney function in health and disease. Depends on the interplay between hydrostatic and oncotic pressures within the nephron
- ⊙ *hydrostatic pressure* is usually higher in the glomerulus than within the tubule, forcing filtrate out of the capillary bed into the tubule
- ⊙ *oncotic pressure* is generated by non-filtered proteins: it helps to retain fluid in the intravascular space
- ⊙ GFR:  $K_f^*$  (hydrostatic pressure - oncotic pressure)
- ⊙ Normal GFR: 100 ml/min/1.72m<sup>2</sup>

\*K<sub>f</sub> - filtration coefficient in the glomerulus

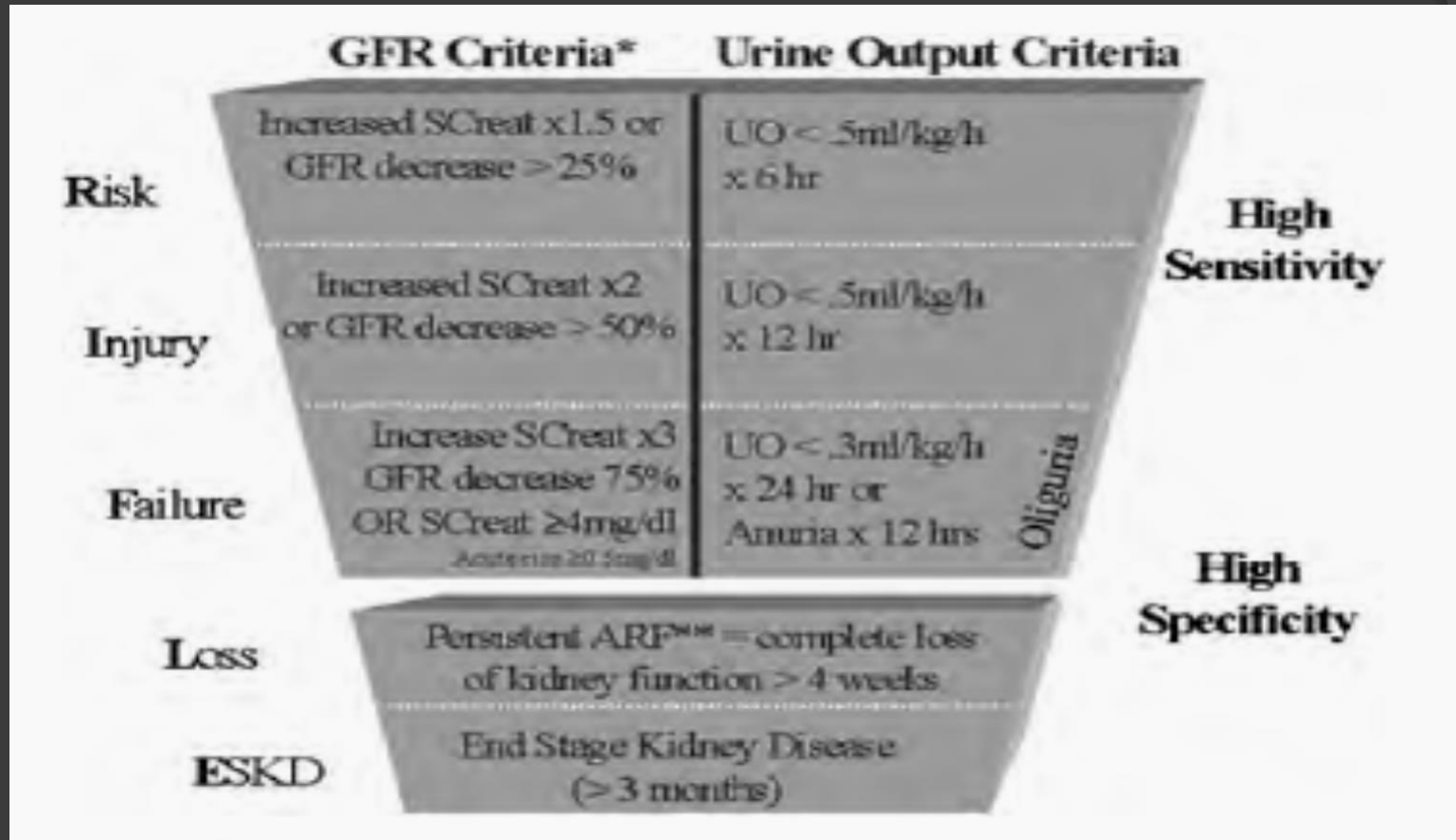
# Evidence of decreasing renal function (reduced GFR):

- Rising BUN (blood urea nitrogen) – nl about 10 mg/dL (nr = 7-25 mg/dL)
- Rising creatinine – nl about 1 mg/dL (nr = 0.6 – 1.2 mg/dL)
- **Note!** *normal BUN: creatinine ratio = 10-20:1*

AM

# The RIFLE criteria for AKI

The acronym RIFLE stands for the increasing severity classes Risk, Injury, and Failure; and the two outcome classes, Loss and End-Stage Renal Disease (ESRD).



ARF, acute renal failure; GFR, glomerular filtration rate; Screat, serum creatinine concentration; UO, urine output.

# AKIN criteria for AKI

- ⦿ Abrupt (within 48 h) reduction in kidney function currently defined as an absolute increase in serum creatinine of 0.3 mg/dL or more ( $\geq 26.4 \mu\text{mol/L}$ ) or
- ⦿ A percentage increase in serum creatinine of 50% or more (1.5-fold from baseline) or
- ⦿ A reduction in urine output (documented oliguria of  $< 0.5 \text{ mL/kg/h}$  for  $> 6 \text{ h}$ )

The RIFLE criteria are defined as changes within 7 days, while the AKIN criteria suggest using 48 hours.

**Table 3 | Comparison of RIFLE and AKIN criteria for diagnosis and classification of AKI**

AKI staging	Urine output	RIFLE	
Serum creatinine	(common to both)	Class	Serum creatinine or GFR
Stage 1 Increase of more than or equal to 0.3 mg/dl ( $\geq 26.5 \mu\text{mol/l}$ ) or increase to more than or equal to 150% to 200% (1.5- to 2-fold) from baseline	Less than 0.5 ml/kg/h for more than 6 hours	Risk	Increase in serum creatinine $\times 1.5$ or GFR decrease $> 25\%$
Stage 2 Increased to more than 200% to 300% ( $> 2$ - to 3-fold) from baseline	Less than 0.5 ml/kg per hour for more than 12 hours	Injury	Serum creatinine $\times 2$ or GFR decreased $> 50\%$
Stage 3 Increased to more than 300% ( $> 3$ -fold) from baseline, or more than or equal to 4.0 mg/dl ( $\geq 354 \mu\text{mol/l}$ ) with an acute increase of at least 0.5 mg/dl ( $44 \mu\text{mol/l}$ ) or on RRT	Less than 0.3 ml/kg/h for 24 hours or anuria for 12 hours	Failure	Serum creatinine $\times 3$ , or serum creatinine $> 4 \text{ mg/dl}$ ( $> 354 \mu\text{mol/l}$ ) with an acute rise $> 0.5 \text{ mg/dl}$ ( $> 44 \mu\text{mol/l}$ ) or GFR decreased $> 75\%$
		Loss	Persistent acute renal failure=complete loss of kidney function $> 4$ weeks
		End-stage kidney disease	ESRD $> 3$ months

# KDIGO criteria for AKI

AKI is defined as any of the following (Not Graded):

- ⦿ K Increase in SCr by  $\geq 0.3$  mg/dl ( $\geq 26.5$   $\mu\text{mol/l}$ ) within 48 hours; or
- ⦿ K Increase in SCr to  $\geq 1.5$  times baseline, which is known or presumed to have occurred within the prior 7 days; or
- ⦿ K Urine volume  $< 0.5$  ml/kg/h for 6 hours.

**Table 2 | Staging of AKI**

Stage	Serum creatinine	Urine output
1	1.5–1.9 times baseline OR $\geq 0.3$ mg/dl ( $\geq 26.5$ $\mu\text{mol/l}$ ) increase	$< 0.5$ ml/kg/h for 6–12 hours
2	2.0–2.9 times baseline	$< 0.5$ ml/kg/h for $\geq 12$ hours
3	3.0 times baseline OR Increase in serum creatinine to $\geq 4.0$ mg/dl ( $\geq 353.6$ $\mu\text{mol/l}$ ) OR Initiation of renal replacement therapy OR, In patients $< 18$ years, decrease in eGFR to $< 35$ ml/min per $1.73$ m <sup>2</sup>	$< 0.3$ ml/kg/h for $\geq 24$ hours OR Anuria for $\geq 12$ hours

# Types of Acute Kidney Injury

## 1. **PRERENAL**

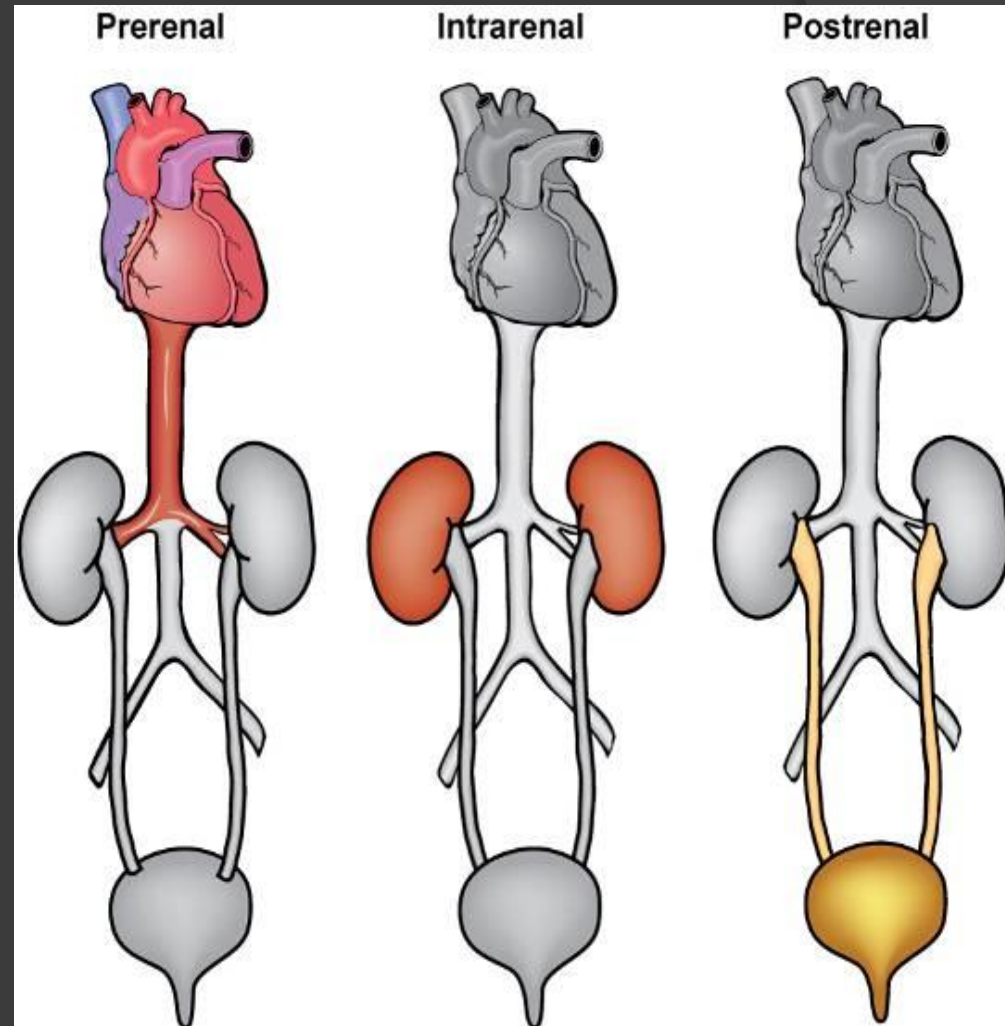
**Impaired renal perfusion** (*shock, hypovolemia, volume shifts,  $\uparrow$ CO,  $\uparrow$ PVR(pulmonary vascular resistance), renal artery obstruction*)

## 2. **INTRARENAL**

**Involves parenchymal changes** (*renal trauma, acute tubular necrosis, infectious diseases, glomerulonephritis*)

## 3. **POSTRENAL**

**Obstruction to urinary tract** (*prostate disease, obstruction, spinal cord injury, pelvic trauma*)



# Classification of the major causes of acute kidney injury

## Types of Acute Renal Failure

**Prerenal**, caused by transient renal hypoperfusion due to:  
Hypotension  
Decreased cardiac output  
Decreased effective arterial blood volume

**Postrenal**, due to obstruction of the urinary tract.

### **Intrinsic**

**Acute glomerulonephritis** involves inflammation and damage to the glomerular membrane.

**Acute interstitial nephritis**, an allergic reaction, may be caused by a variety of drugs.

**Acute tubular necrosis** accounts for more than 50% of cases of acute renal failure.

*Causes:* nephrotoxic agents, prolonged renal hypoperfusion.

# Acute kidney injury: pathophysiology

- **Increase in NaCl delivered to macula densa.**

Damage to proximal tubule cells increases NaCl delivery to distal nephron. This causes disruption of feedback mechanism.

- **Obstruction of tubular lumen.**

Casts (necrosis of tubular cells and sloughed basement membrane) clog the lumen. This will increase the tubular pressure and then GFR will fall.

- **Backleak of fluid through the tubular basement membrane.**

# Acute Kidney Injury Stages (1)

## 1. INITIATING PHASE

- ⦿ Begins at time of insult until S&S seen (hours to days)

## 2. OLIGURIC or ANURIC PHASE

- ⦿ Oliguria caused by GFR decrease
- ⦿ Begins 1-7 days after insult depending on cause
- ⦿ Usually lasts usually 10-14 days (may last up to 8 weeks)
- ⦿ Longer the phase, poorer prognosis of renal recovery

Manifestations are changes in UOP, fluid & electrolyte balances, & uremia in serum levels of urea, creatinine, uric acid, K<sup>+</sup> & Mg

# Acute Kidney Injury Stages (2)

## 3. DIURETIC PHASE

- Gradual increase of UOP can reach 1-2 (or more) L per day. Nephrons are still not fully functional
- Caused by osmotic diuresis and inability of tubules to concentrate.
- Recovered ability to excrete wastes, but not concentrate.
- Monitor for hypokalemia, hyponatremia & dehydration
- Hypovolemia and hypotension can occur Lasts 1-3 weeks
- Acid-base, electrolyte and waste product levels begin to normalize.

## 4. RECOVERY PHASE

Begins when GFR increases allowing BUN and creatinine to reach a plateau and decrease

May still have glycosuria and decreased ability to concentrate urine

Major improvements first 1-2 weeks but may take 12 months to stabilize.

Investigate for acute kidney injury, by measuring serum creatinine and comparing with baseline, in adults with acute illness if any of the following are likely or present:

- heart failure
- liver disease
- diabetes
- history of acute kidney injury
- oliguria (urine output less than 0.5 ml/kg/hour)
- neurological or cognitive impairment or disability, which may mean limited access to fluids because of reliance on a carer
- hypovolaemia
- use of drugs with nephrotoxic potential (such as non-steroidal anti-inflammatory drugs [NSAIDs], aminoglycosides, angiotensin-converting enzyme [ACE] inhibitors, angiotensin II receptor antagonists [ARBs] and diuretics) within the past week, especially if hypovolaemic
- use of iodinated contrast agents within the past week
- symptoms or history of urological obstruction, or conditions that may lead to
- obstruction
- sepsis
- deteriorating early warning scores
- age 65 years or over.

# Monitoring and preventing deterioration in patients with or at high risk of acute kidney injury

- **Detecting acute kidney injury** with the RIFLE, AKIN or KDIGO definitions
- **Identifying the cause(s) of acute kidney injury:**
  - Urinalysis
  - Ultrasound (useful for obstructive forms)
  - Doppler (to assess renal blood flow)
  - Nuclear Medicine Scans
- **Managing acute kidney injury:**
  - Relieving urological obstruction
  - Pharmacological management
  - Referring for renal replacement therapy
  - Referring to nephrology

# Acute kidney injury: common clinical features

- azotemia
- hypervolemia
- electrolytes abnormalities:
  - $\uparrow\uparrow$   $K^+$      $\uparrow\uparrow$  phosphate
  - $\downarrow\downarrow$   $Na^+$      $\downarrow\downarrow$  calcium
- metabolic acidosis
- hypertension
- oliguria – anuria (a biomarker of tubular injury)
- atheroembolies in small vessels



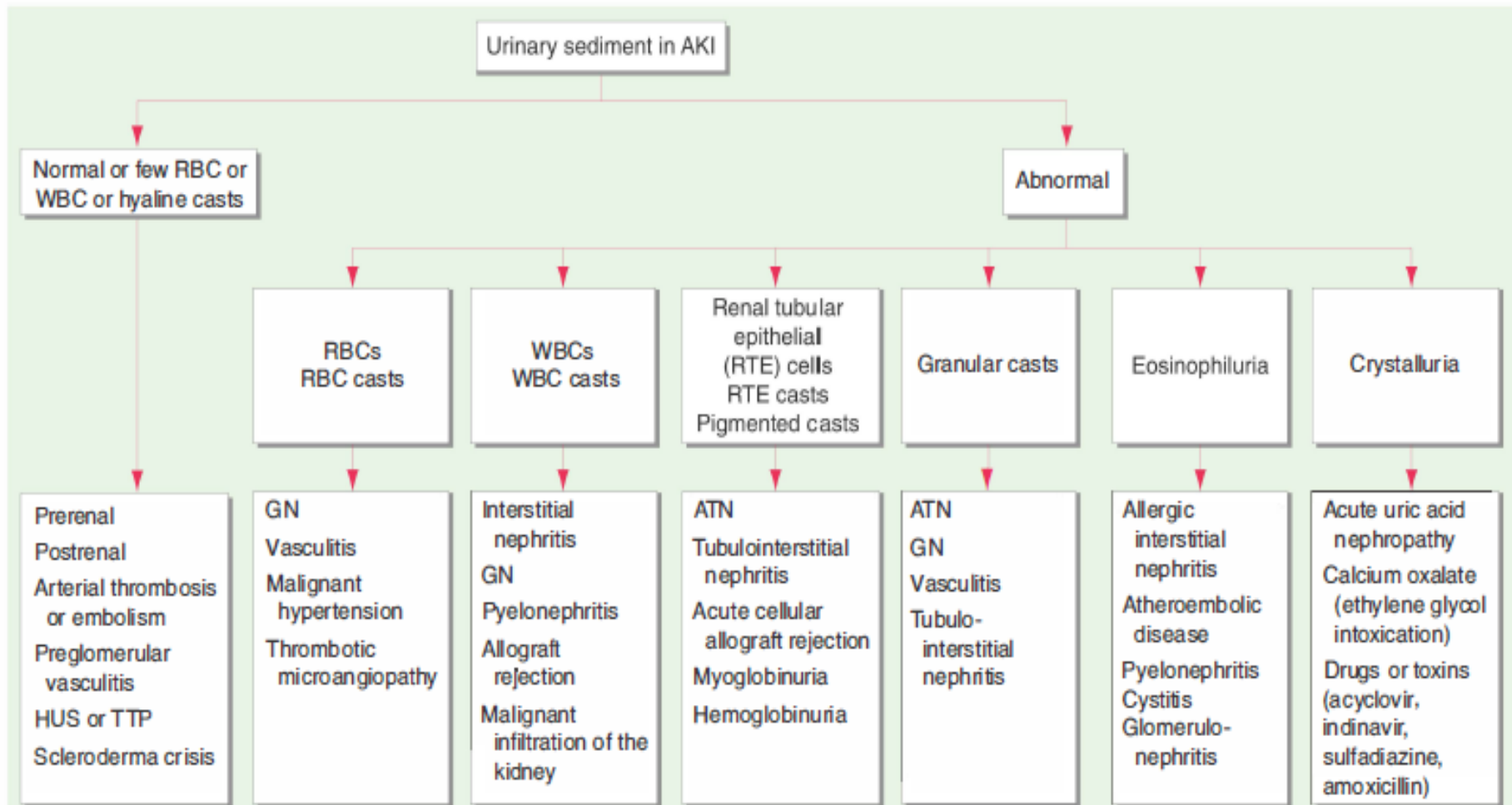
# Urine Findings

- ⦿ Complete **anuria** early in the course of AKI is uncommon except in the following situations: complete urinary tract obstruction, renal artery occlusion, overwhelming septic shock, severe ischemia (often with cortical necrosis), or severe proliferative glomerulonephritis or vasculitis.
- ⦿ **Oliguria**, defined as  $<500$  mL/24 h) usually denotes more severe AKI (i.e., lower GFR) than when urine output is preserved.
- ⦿ Proteinuria  $> 1$  g/d in AKI suggests damage to the glomerular ultrafiltration barrier or excretion of myeloma light chains
- ⦿ Extremely heavy proteinuria ("nephrotic range"  $>3.5$  g/d) can occasionally be seen in glomerulonephritis, vasculitis, or interstitial nephritis

# Acute Kidney Injury: Urine Volume

- ⊙ Anuria (< 100 ml/24h)
  - Acute bilateral arterial or venous occlusion
  - Bilateral cortical necrosis
  - Acute necrotizing glomerulonephritis
  - Obstruction (complete)
  - ATN (very rare)
- ⊙ Oliguria (100-500 ml/24h)
  - Pre-renal azotemia
  - ATN
- ⊙ Non-Oliguria (> 500 ml/24h)
  - ATN
  - Obstruction (partial)

# Interpretation of urinary sediment findings in acute kidney injury



# Red Blood Cells

- ⦿ Monomorphic (non-dysmorphic) RBC suggest non-glomerular source of bleeding – i.e., bleeding from the calyces, pelvis, ureter(s), bladder, prostate or urethra. Dysmorphic red blood cells suggest glomerular injury.
- ⦿ Red or brown urine may be seen with or without gross hematuria

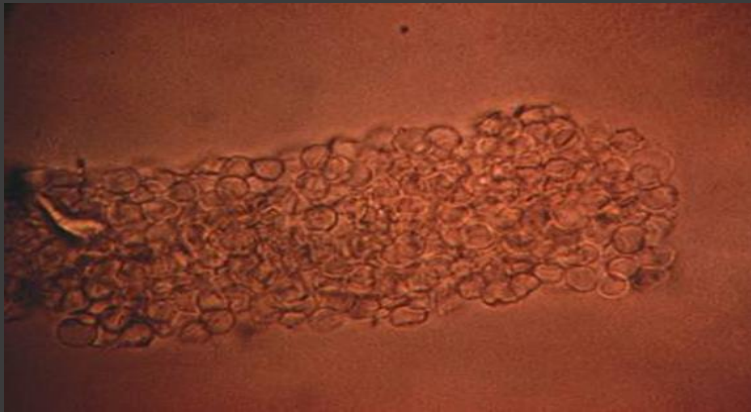
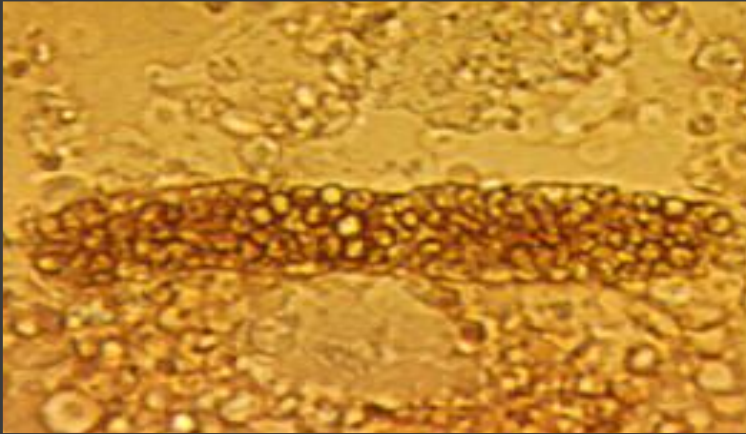


dysmorphic



monomorphic

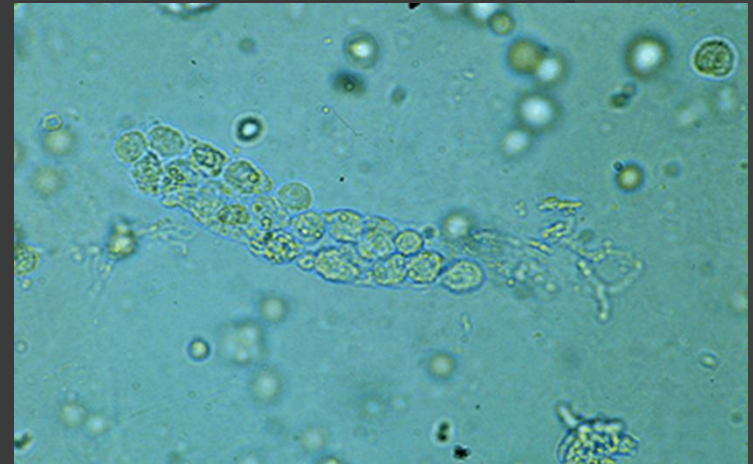
## Red Blood Cell Cast



Two examples of red blood cell casts, typical of glomerular bleeding.

Glomerulonephritis may lead to dysmorphic red blood cells or red blood cell casts.

## White Blood Cell Cast

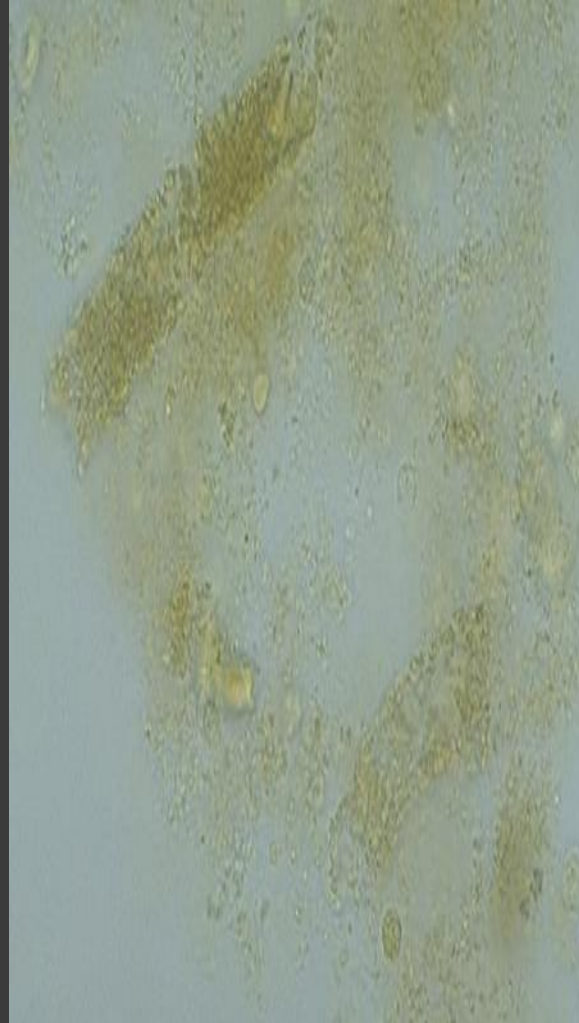


Interstitial nephritis may lead to white blood cell casts. Urine eosinophils have a limited role in differential diagnosis; they can be seen in interstitial nephritis, pyelonephritis, cystitis, atheroembolic disease, or glomerulonephritis.

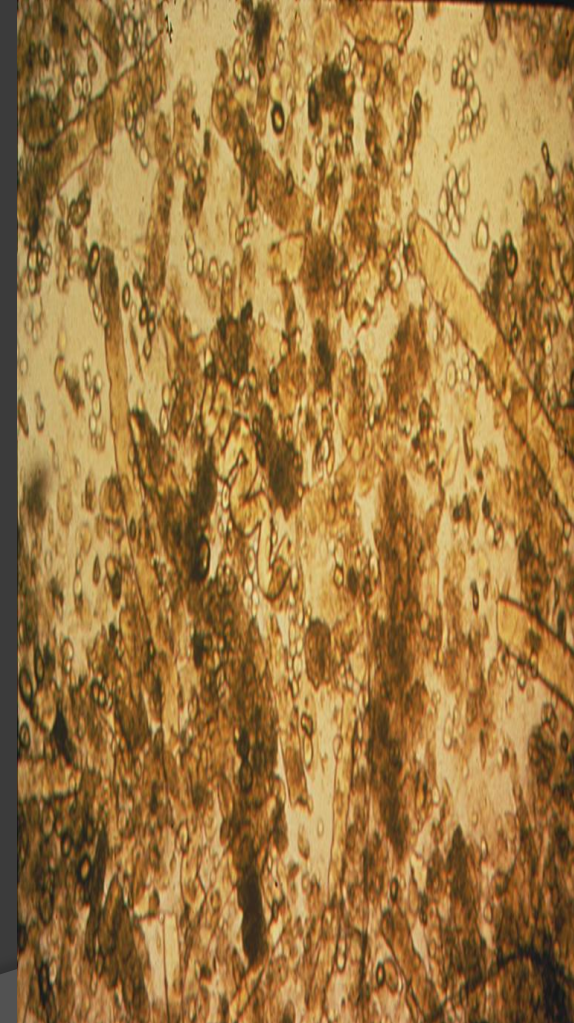
## Renal Tubular Epithelial Cell Cast



## Granular casts



## Pigmented Granular Casts



Pigmented granular (“muddy brown”) casts are characteristic of acute tubular necrosis

# Renal Failure Indices

Several indices have been used to help differentiate prerenal azotemia from intrinsic AKI when the tubules are malfunctioning.

- **The fractional excretion of sodium (FeNa)** is the fraction of the filtered sodium load that is reabsorbed by the tubules, and is a measure of both the kidney's ability to reabsorb sodium as well as endogenously and exogenously administered factors that affect tubular reabsorption.
- **Urine osmolality** - in the patient not taking diuretics and with good baseline kidney function, urine osmolality may be above 500 mOsm/kg in prerenal azotemia. Loss of concentrating ability is common in septic or ischemic AKI, resulting in urine osmolality below 350 mOsm/kg

$$\text{Renal Failure Index (RFI)} = \frac{\text{urine [Na]}}{\text{urine creatinine / serum creatinine}}$$

# Urine Chemistries

## Fractional Excretion of Na and Urea

- *Since urinary indices depend on urine sodium concentration, they should be interpreted cautiously if the patient has received diuretic*
- Spot urine Na may be affected (raised) by diuretic use and baseline impaired kidney function (chronic renal disease where maximum urine Na reabsorption is impaired)
- Fractional excretion of Na accounts for this by including creatinine:

$$FE_{Na} = \frac{\text{urine [Na]} \div \text{plasma [Na]}}{\text{urine creatinine} \div \text{plasma creatinine}} \times 100$$

FxEx<sub>urea</sub> – substitute urine urea nitrogen for Na useful if patient receiving diuretics

# AKI: Ultrasound Findings

Normal kidney on ultrasound



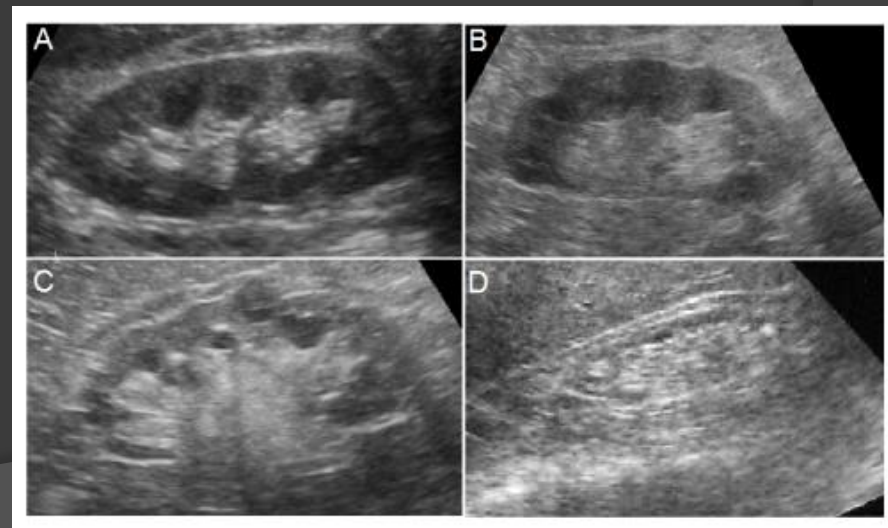
Hydronephrosis on ultrasound



Kidney Cancer Ultrasound



Diabetic Kidney Ultrasound



# AKI: Novel Biomarkers

- ⦿ BUN and creatinine are functional biomarkers of glomerular filtration rather than tissue injury biomarkers
- ⦿ **Kidney injury molecule-1 (KIM-1)** is a type 1 transmembrane protein that is abundantly expressed in proximal tubular cells injured by ischemia or nephrotoxins such as cisplatin, can be detected shortly after ischemic or nephrotoxic injury in the urine
- ⦿ **Neutrophil gelatinase associated lipocalin (NGAL, also known as lipocalin-2 or siderocalin)** - a protein in granules of human neutrophils, can be detected in the plasma and urine within 2 h of cardiopulmonary bypass-associated AKI.
- ⦿ **Interleukin (IL) 18** - a pro-inflammatory cytokine of the IL- 1 superfamily that may mediate ischemic proximal tubular injury
- ⦿ **L-type fatty acid binding protein** - from ischemic proximal tubule cells

# Acute Kidney Injury: Pre-renal Causes

Prerenal azotemia (from "azo" meaning nitrogen, and "-emia") is the most common form of AKI.

- ⊙ Decreased effective perfusion without cellular injury
  - Hemorrhage
  - Sodium depletion
  - Pump failure
  - Increased vascular capacity e.g., sepsis
  - Increased renal vascular resistance (hepatorenal, NSAIDs)
  - Vasoconstriction drugs (radio contrast, cyclosporine, amphotericin B)
  - Decreased intraglomerular pressure (ACEI, ARB)
- ⊙ Redistribution of ECF
  - “Third space” accumulation
  - Edematous disorders
- ⊙ Drugs
- ⊙ Renal tubular and glomerular functions are intact
- ⊙ Reversible if underlying cause is corrected

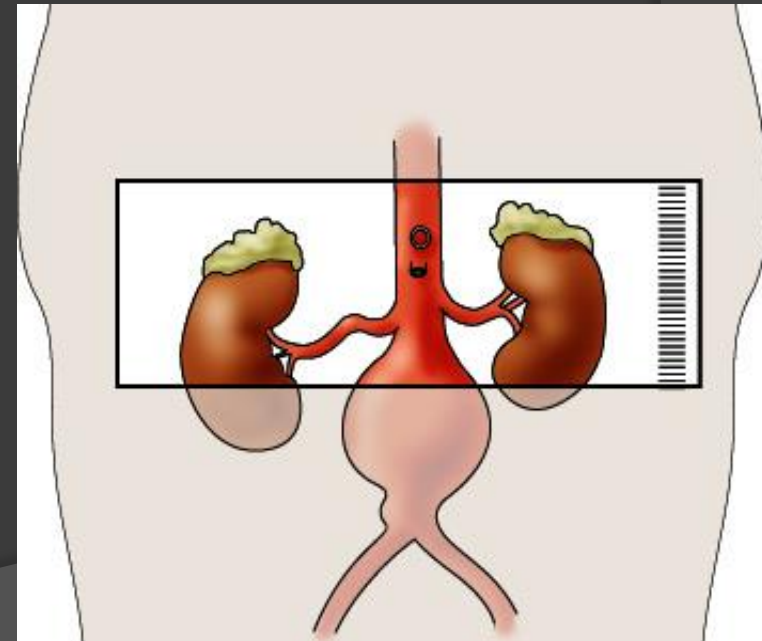
# Pre-Renal Azotemia Pathophysiology

- ⦿ Renal hypoperfusion
  - Decreased RBF (renal blood flow) and GFR
  - Increased filtration fraction (GFR/RBF)
- ⦿ Increased Na and H<sub>2</sub>O reabsorption
  - Oliguria, high  $U_{osm}$ , low  $U_{Na}$
  - Elevated BUN/Cr ratio

In the absence of renal artery stenosis, renal arterial pressure (RAP) is the same as systemic mean arterial pressure (commonly referred to by nephrologists as “renal perfusion pressure”).

Renal venous pressure (RVP) is usually, but not always, low and relatively constant.

The glomerular afferent and efferent arterioles are the major sites of renal vascular resistance (Raff and Reff, respectively); changes in either will affect renal blood flow (RBF).



# Pre-renal AKI

- ◎ **Physical examination** – focus on volume status
  - Vital signs – current and preceding the development of AKI
  - Neck veins, lungs, heart, mucous membranes
  - Edema – presacral and extremity
- ◎ **Laboratory studies**
  - BUN : creatinine ratio – *elevated in pre-renal; >10-20:1*
  - Unremarkable urinary sediment, high specific gravity
  - May see hyaline casts
  - Urine dipstick negative (no blood or protein)

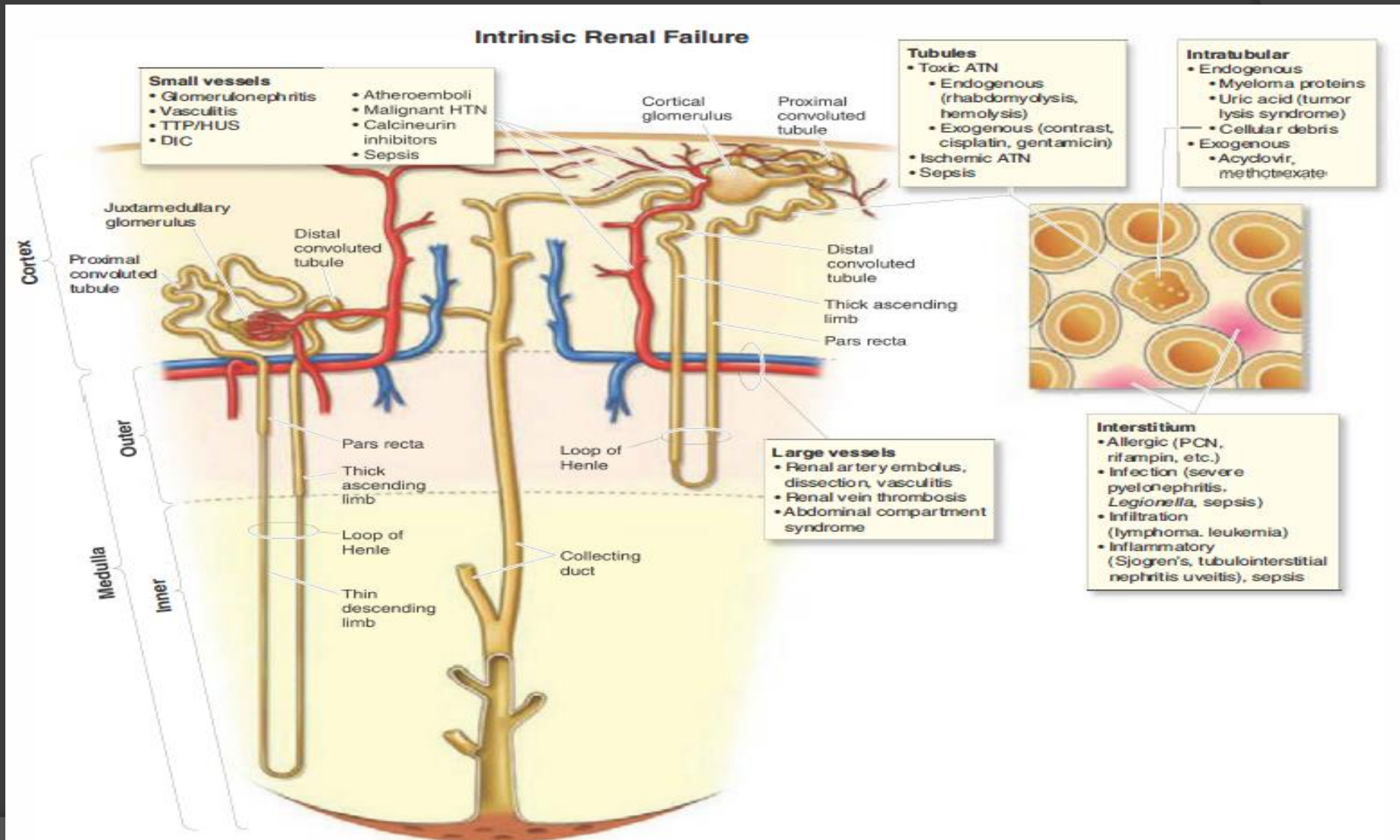
There is no intrinsic kidney damage in pre-renal ARF; rising BUN and creatinine occur because the kidneys are inadequately perfused.

# Pre-renal AKI Urine Electrolytes

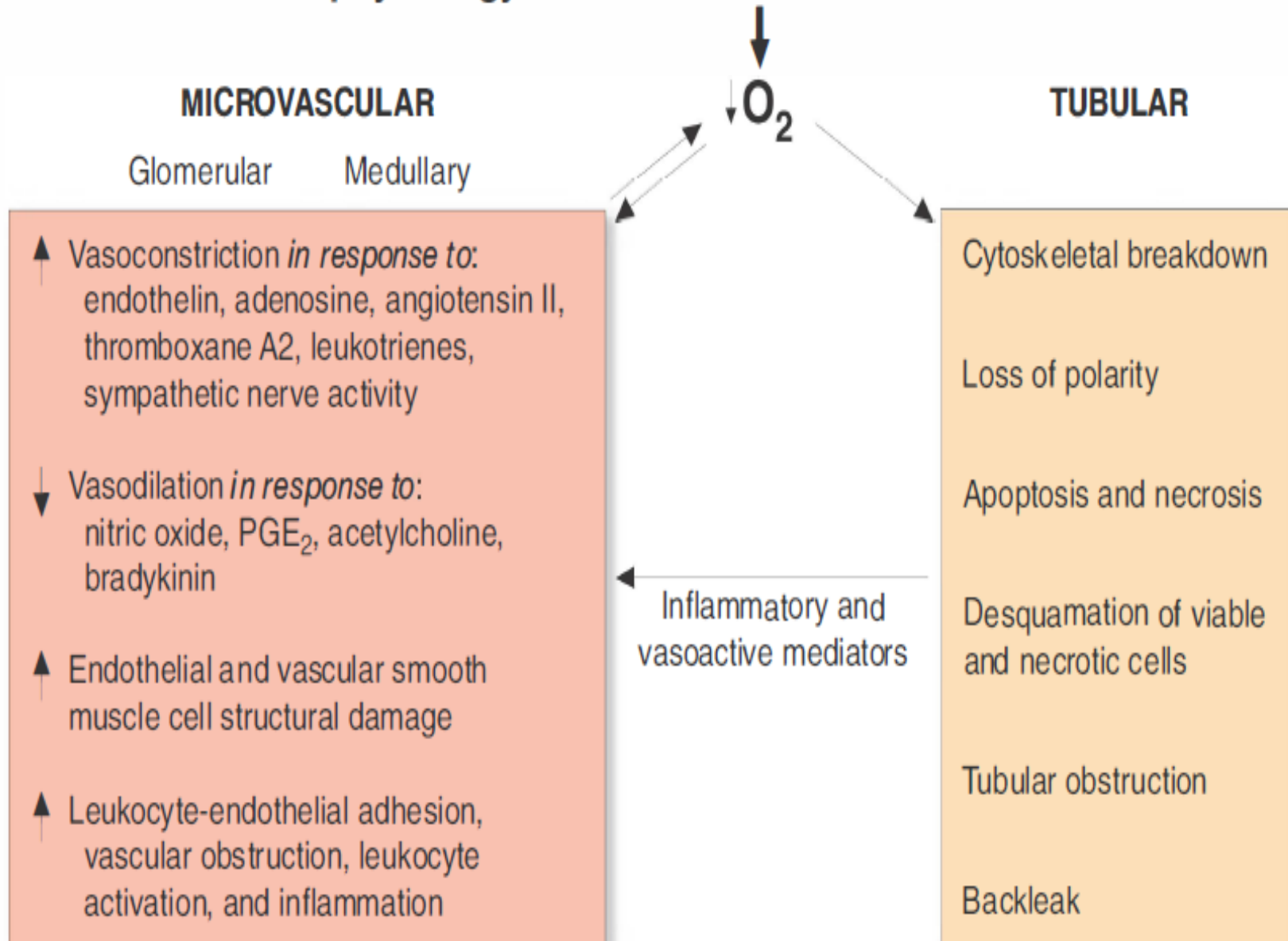
- ⦿ Intact renal tubular function in the setting of impaired renal perfusion (due either to volume loss, pump failure, renal vasoconstriction , etc) results in *avid tubular reabsorption of sodium*.
- ⦿ *Therefore, low urine Na (<20 mEq/L) and low fractional excretion of Na (<1%) and of urea (<35%) in pre-renal ARF.*
- ⦿ Therefore, normal renal physiologic responses occur, manifested in urine electrolytes that reflect intact kidney tubular function.
- ⦿ Prerenal azotemia and ischemic tubular necrosis represent a continuum. Azotemia progresses to necrosis when blood flow is sufficiently compromised to result in the death of tubular cells.

# AKI: Renal or Intrinsic

The most common causes of intrinsic AKI are sepsis, ischemia and nephrotoxins, both endogenous and exogenous



# Pathophysiology of Ischemic Acute Renal Failure



# Renal or Intrinsic AKI

- ⦿ In all types of intrinsic ARF, BUN : creatinine ratio preserved (10-20:1)
- ⦿ The history, PE, and especially, urine analysis will help to differentiate

Classified according to primary site of injury:

- ⦿ Vascular
- ⦿ Glomerular (acute glomerulonephritis)
- ⦿ Tubular (acute tubular necrosis or ATN)
- ⦿ Interstitial (acute interstitial nephritis)

# Renal or Intrinsic AKI – Vascular Type

## ⊙ Large vessels – *must be bilateral*

- Renal vein thrombosis
- Renal artery stenosis
- Urine eosinophils
- Low C3

### Large vessels

- Renal artery embolus, dissection, vasculitis
- Renal vein thrombosis
- Abdominal compartment syndrome

## ⊙ Small vessels

- Vasculitis
- Atheroembolic
- Malignant hypertension
- Thrombotic microangiopathies.

### Small vessels

- Glomerulonephritis
- Vasculitis
- TTP/HUS
- DIC
- Atheroemboli
- Malignant HTN
- Calcineurin inhibitors
- Sepsis

# Renal or Intrinsic AKI – Vascular Type

- ◎ Small vessels – atheroembolic
  - Relatively common
  - Risk factors = catheter manipulation and anticoagulation in the setting of atherosclerosis
  - PE may reveal livedo reticularis
  - Progressive rise then stabilization of BUN, creatinine usually without significant recovery of kidney function
  - Cholesterol clefts occ seen on kidney biopsy but transient so bx not suggested; Dx clinically



# Renal or Intrinsic AKI – Glomerular Type

- ⊙ History – systemic or primary kidney  
– edema
- ⊙ PE – BP (usually hypertensive)  
– edema
- ⊙ BUN : creatinine ratio preserved
- ⊙ *Urine analysis: + protein, blood (RBCs, RBC casts)*
- ⊙ Often will require kidney biopsy

**RBC Casts**

# Renal or Intrinsic AKI – Interstitial Type

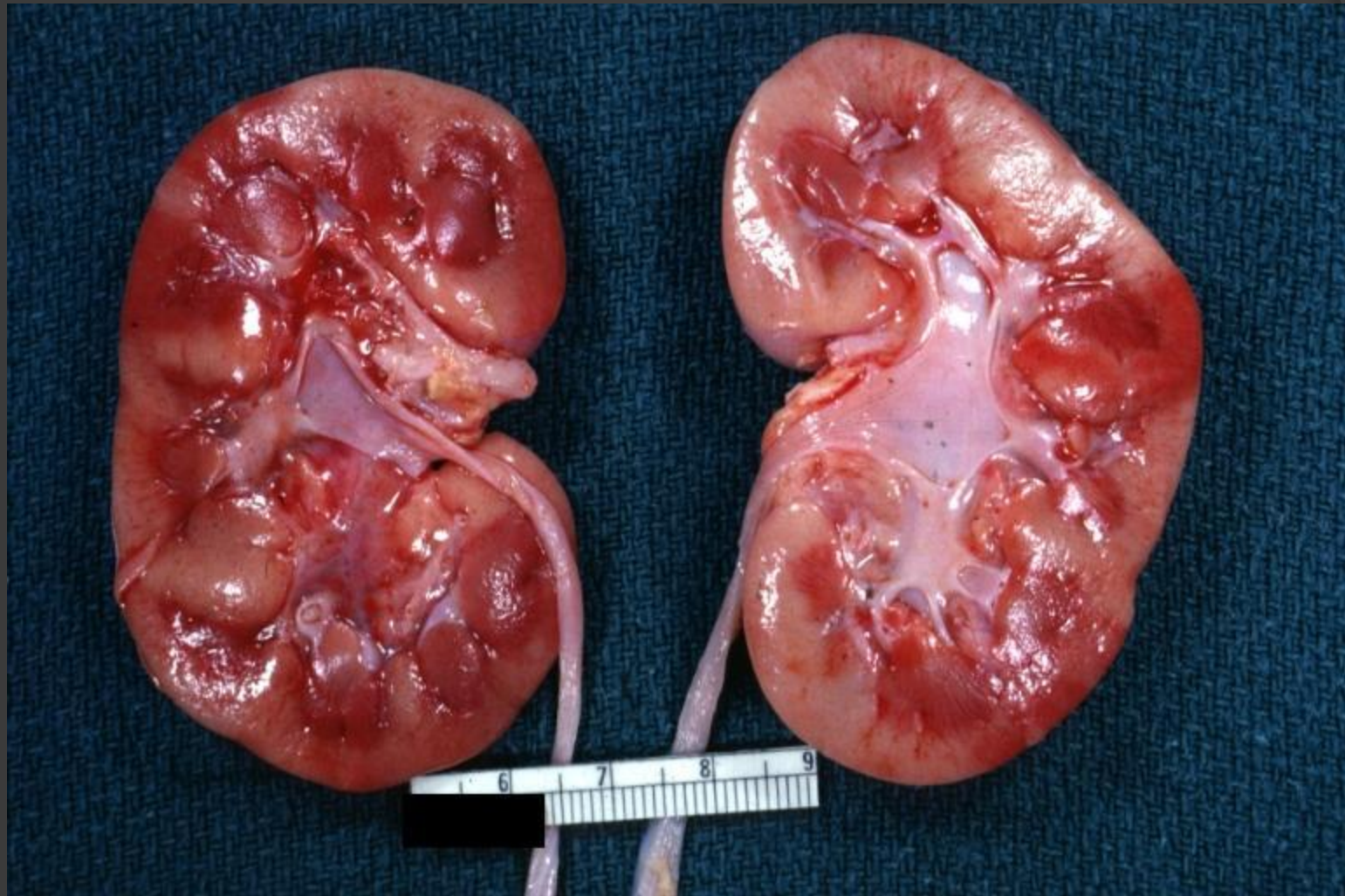
- History – *exposure to medications* usually 7- 14 days earlier – penicillin, cephalosporin, dilantin
- PE – maculopapular erythematous skin rash – 1/3 have fever, arthralgias
- BUN : creatinine ratio 10-20:1
- Urine analysis -- + protein, blood (*WBCs, WBC casts, eosinophils*)
- The most common type of Hospital - acquired ARF
- May Be:
  - 1) **Ischemic** (ATN) or 2) **Nephrotoxic** (in etiology)
- Most common Acute Tubular Necrosis is Ischemic, most often due to a prolonged pre-renal state (prolonged reduced renal perfusion)

# Renal or Intrinsic AKI – Acute Tubular Necrosis

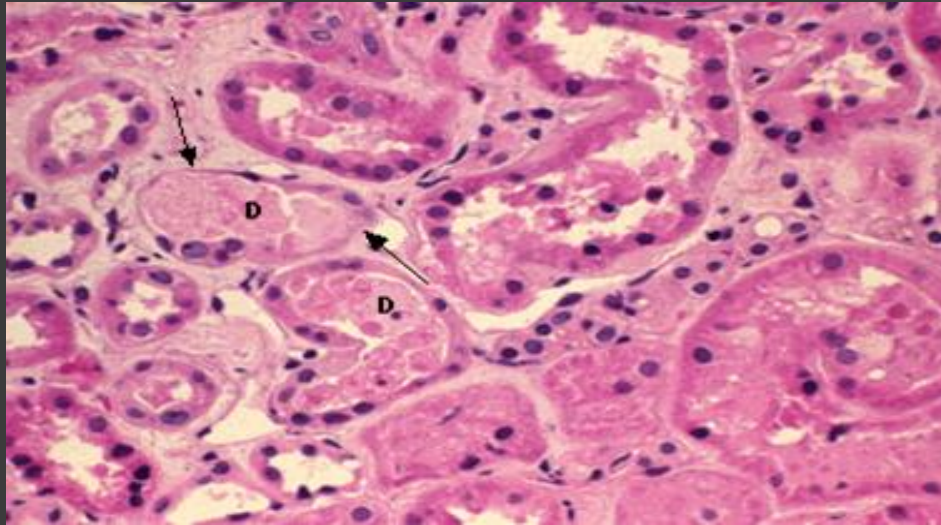
- History – prolonged pre-renal state
  - exposure to nephrotoxin
    - aminoglycoside antibiotics
    - ethylene glycol
    - pigments (myoglobin, hemoglobin)
- PE – volume status (to exclude pre-renal ARF)
- BUN:creat ratio preserved (10-20:1)
- Urine analysis – usually negative protein, blood
  - *granular casts (dirty brown casts)*
  - renal tubular epithelial cells
- Urine chemistries – urine Na > 40 meq/L

- ◎ The increased incidence of non-oliguric ATN during the past 25 years is most likely due to the increased usage of nephrotoxins, more frequent chemical testing, and more aggressive use of fluids, potent diuretics, and vasodilators in the management of ATN. The reduced mortality of non-oliguric compared to oliguric ATN is probably not because of the increased urine volume but rather due to a lower associated mortality of the conditions causing non-oliguric compared to oliguric ATN. (Data from Anderson et al: Non-oliguric Acute Renal Failure. New Engl J Med 296:134, 1977.)
- ◎ Prior to the article by Anderson , it was believed that most cases of ATN were oliguric. Today, we know that ATN can present with oliguria or non-oliguria and that both presentations are common. Any cause of ATN can present with nonoliguria ; non-oliguria is more likely with nephrotoxic causes of ATN such as aminoglycosides, contrast media, cis-platinum, and amphotericin.

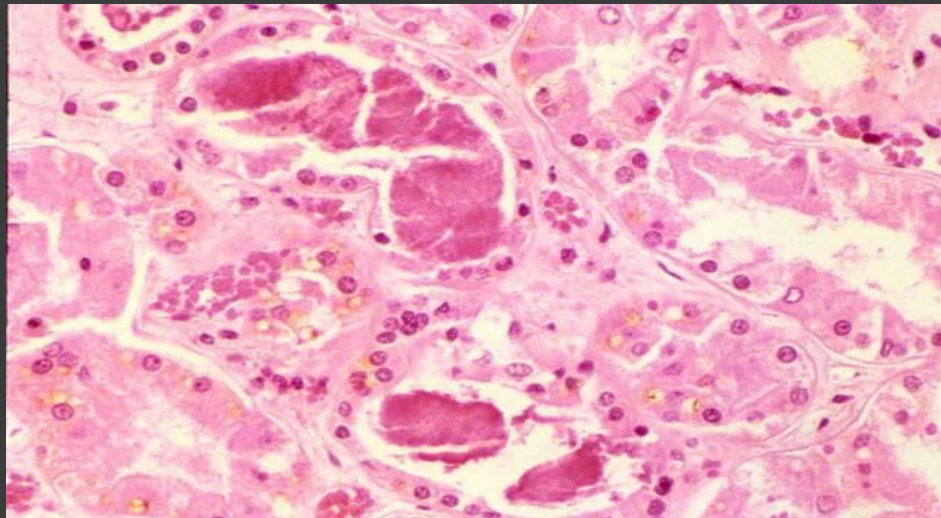
# Acute Tubular Necrosis



# Acute Tubular Necrosis



- Acute tubular necrosis showing focal loss of tubular epithelial cells (arrows) and partial occlusion of tubular lumens by cellular debris (D) (H&E stain).



- Tubular epithelial degeneration and hyaline amphophilic casts (positive with immunologic stains for myoglobin) in a patient with rhabdomyolysis and myoglobinuric acute tubular necrosis.

The kidney biopsy can provide definitive diagnostic and prognostic information about acute kidney diseases and CKD.

# Acute Interstitial Nephritis

## Causes:

- ⊙ Allergic interstitial nephritis
  - Drugs (aminoglycosides, cisplatin and carboplatin)
- ⊙ Infections
  - Bacterial (sepsis)
  - Viral
- ⊙ Sarcoidosis
- ⊙ Radiation nephritis
- ⊙ Iodinated contrast agents
- ⊙ Risk factors for nephrotoxicity include older age, chronic kidney disease, and prerenal azotemia

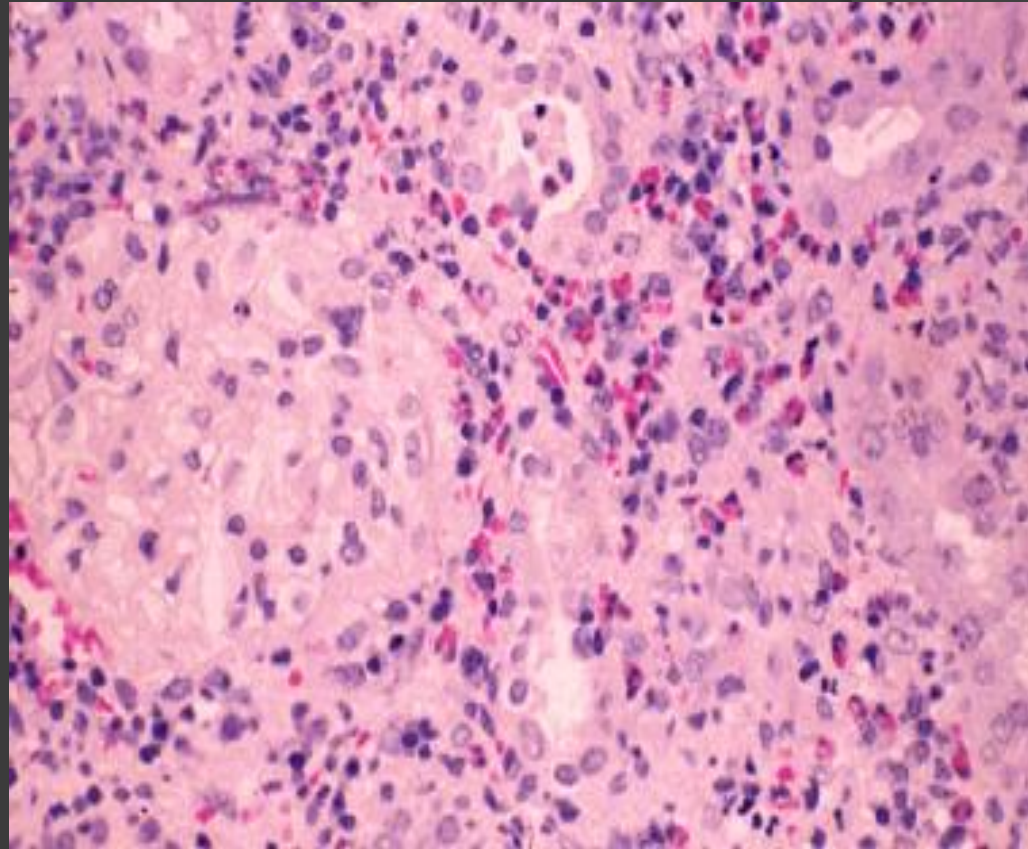
# Acute Interstitial Nephritis

## Clinical Characteristics

- ⊙ Fever
- ⊙ Rash
- ⊙ Arthralgias
- ⊙ Eosinophilia
- ⊙ Urinalysis
  - Microscopic hematuria
  - Sterile pyuria
  - Eosinophiluria

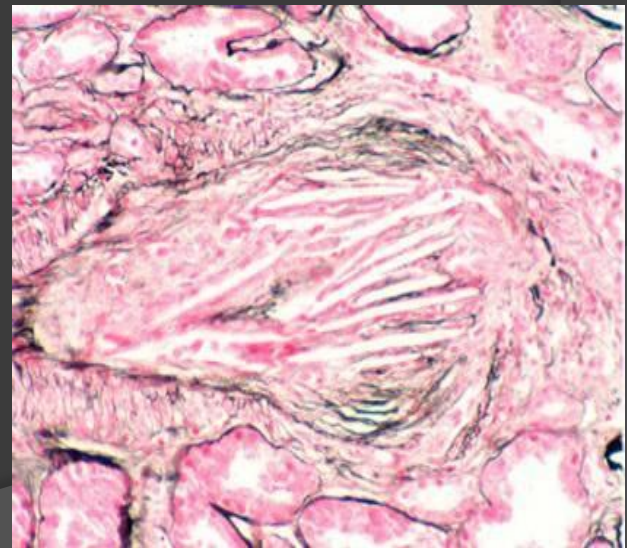
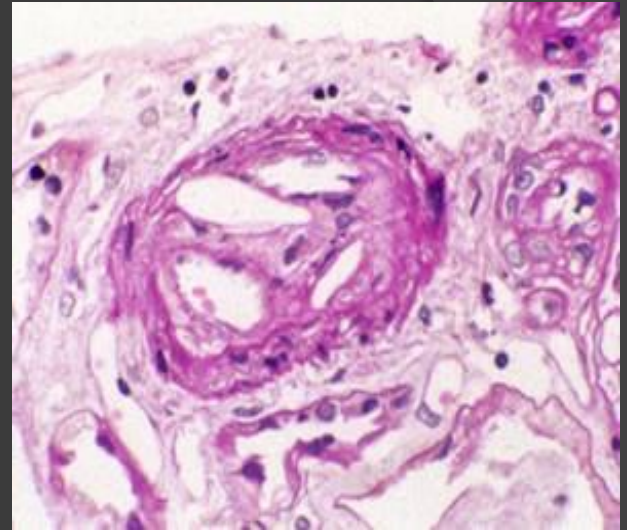
# Acute Interstitial Nephritis

- ⦿ Drug-induced allergic interstitial nephritis (H&E stain). Note the diffuse interstitial infiltrate, many red-staining eosinophils, and sparing of the glomerulus (on the left).



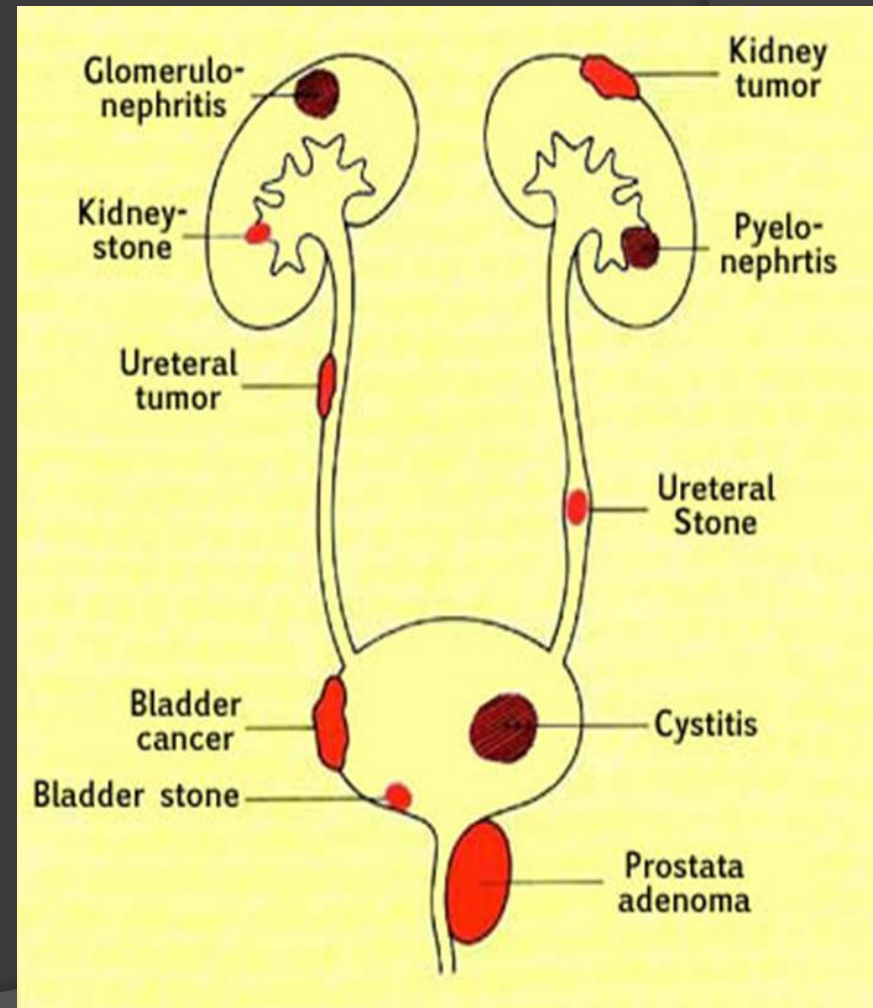
# AKI - Cholesterol Embolization

Cholesterol embolization may occur after a “sentinel” procedure (e.g., cardiac catheterization) or be associated with slowly progressive renal failure over a period of months or years. Whatever the time course, it is generally irreversible. Cholesterol emboli usually lodge in vessels 100 to 200 microns in diameter, and are visualized as clear spaces where the cholesterol crystals have been dissolved by routine processing. The early response of platelets and occasional mononuclear cells is seen in the medium size artery occluded by acute cholesterol emboli in the left panel (Jones Silver stain). In later stages of organization the lumen may have more fibrous reorganization surrounding the cholesterol clefts, as shown in the right lower diagram (PAS stain).



# Acute Kidney Injury: Post-renal Causes

- ⊙ Intra-renal Obstruction
  - Acute uric acid nephropathy
  - Drugs (e.g., acyclovir)
- ⊙ Extra-renal Obstruction
  - Renal pelvis or ureter ;must be **bilateral** unless solitary kidney (e.g., stones, clots, tumors, papillary necrosis, retroperitoneal fibrosis)
  - Bladder (e.g., BPH, neuropathic bladder)
  - Urethra (e.g., stricture)



# Acute Kidney Injury: Post-renal

- ⦿ Postrenal AKI occurs when the normally directional flow of urine is acutely blocked either partially or totally, leading to increased retrograde hydrostatic pressure and interference with glomerular filtration.
- ⦿ Obstruction to urinary flow - from the renal pelvis to the tip of the urethra. For AKI to occur in healthy individuals, obstruction must affect both kidneys unless only one kidney is functional, in which case unilateral obstruction can cause AKI.
- ⦿ Elevated pressure in urinary conduits results in renal parenchymal destruction if unrelieved - an initial period of hyperemia from afferent arteriolar dilation is followed by intrarenal vasoconstriction from the generation of angiotensin II, thromboxane A<sub>2</sub>, and vasopressin, and a reduction in NO production
- ⦿ Important to rule out quickly:
  - potential for recovery of renal function is often inversely related to the duration of the obstruction

# Acute Kidney Injury: Post-renal

- History – symptoms (frequency, hesitancy, etc)
  - carcinoma, DM, stones, medications in anamnesis
- PE – distended bladder, prostatic enlargement, pelvic masses, lymph nodes
- Laboratory studies
  - *elevated BUN:creat ratio*
  - *unremarkable urine sediment*
  - variable urine chemistries
- Bladder catheterization
- Renal ultrasound – hydronephrosis
- Treatment is to relieve the obstruction:
  - Bladder catheterization
  - Nephrostomy tubes

# AKI: Differential Diagnosis

	Functional criteria	Structural criteria
AKI	Increase in SCr by 50% within 7 days, <i>OR</i> Increase in SCr by 0.3 mg/dl (26.5 $\mu$ mol/l) within 2 days, <i>OR</i> Oliguria	No criteria
CKD	GFR <60 ml/min per 1.73 m <sup>2</sup> for >3 months	Kidney damage for >3 months
AKD	AKI, <i>OR</i> GFR <60 ml/min per 1.73 m <sup>2</sup> for <3 months, <i>OR</i> Decrease in GFR by $\geq$ 35% or increase in SCr by >50% for <3 months	Kidney damage for <3 months
NKD	GFR $\geq$ 60 ml/min per 1.73 m <sup>2</sup> Stable SCr	No damage

AKD, acute kidney diseases and disorders; AKI, acute kidney injury; CKD, chronic kidney disease; GFR, glomerular filtration rate; NKD, no known kidney disease; SCr, serum creatinine.

# Prerenal azotemia vs Renal azotemia

- Urine sediment: hyaline and fine granular casts
- Urinary to plasma creatinine ratio: high
- Urinary Na: low
- FENa: low

*Increased urine output in response to hydration*

- Urine sediment: brown granular casts and tubular epithelial cells
- Urinary to plasma creatinine ratio: low
- Urinary Na: high
- FENa: high

# Prerenal azotemia vs Renal azotemia

	Prenal	Renal
BUN/Cr	>20	<20
FeNa	<1%	>1%
RFI	<1%	>1%
UNa (mEq/L)	<20	> 40
Specific gravity	high	low

# AKI vs progression of Chronic Kidney Disease

- ⦿ Distinction important (etiology, prognosis, therapy differ)
- ⦿ Past BUN, creatinine values; course of BUN, creatinine rise
- ⦿ Half and half nails
- ⦿ Kidney size and echogenicity by ultrasound (10 cm lower limit of normal; normal size usually 11-12 cm depending on height)

# AKI: Complications

- ⦿ Uremia
- ⦿ Hypo- or hypervolemia
- ⦿ Hyponatremia
- ⦿ Hyperkalemia
- ⦿ Acidosis
- ⦿ Hyperphosphatemia and hypocalcemia
- ⦿ Bleeding
- ⦿ Infections
- ⦿ Cardiac complications
- ⦿ Malnutrition

# Acute Kidney Injury: Prevention

- ⦿ Recognize Patients At Risk (Postoperative States, Cardiac Surgery, Septic Shock)
- ⦿ The management of individuals with and at risk for AKI varies according to the underlying cause
- ⦿ Prevent Progression From Prerenal To Renal
- ⦿ Preserve Renal Perfusion:
  - Isovolemia, Cardiac Output, Normal Blood Pressure
  - Avoid Nephrotoxins (Aminoglycosides, NSAIDS, Amphotericin)

# Treatment of AKI

## General Issues

1. Optimization of systemic and renal hemodynamics through volume resuscitation and judicious use of vasopressors
2. Elimination of nephrotoxic agents (e.g., ACE inhibitors, ARBs, NSAIDs, aminoglycosides) if possible
3. Initiation of renal replacement therapy when indicated

- Based on type/etiology of AKI (acute kidney injury) i.e., pre-renal, post-renal, or intrinsic renal initially
  - Pre-renal – volume, improve renal perfusion
  - Post-renal – relieve obstruction
  - Intrinsic – glomerular, tubular, interstitial, vascular depends on type

# Treatment of AKI

## Specific Issues

1. Nephrotoxin-specific
  - a. Rhabdomyolysis: aggressive intravenous fluids; consider forced alkaline diuresis
  - b. Tumor lysis syndrome: aggressive intravenous fluids and allopurinol or rasburicase
2. Volume overload
  - a. Salt and water restriction
  - b. Diuretics
  - c. Ultrafiltration
3. Hyponatremia ( $\text{Na} < 125 \text{ mEq/L}$ )
  - a. Restriction of enteral free water intake, minimization of hypotonic intravenous solutions including those containing dextrose
  - b. Hypertonic saline is rarely necessary in AKI. Vasopressin antagonists are generally not needed.

# Treatment of AKI

4. Hyperkalemia
  - a. Restriction of dietary potassium intake
  - b. Discontinuation of potassium-sparing diuretics, ACE inhibitors, ARBs, NSAIDs
  - c. Loop diuretics to promote urinary potassium loss
  - d. Potassium binding ion-exchange resin (sodium polystyrene sulfonate)
  - e. Insulin (10 units regular) and glucose (50 mL of 50% dextrose) to promote entry of potassium intracellularly
  - f. Inhaled beta-agonist therapy to promote entry of potassium intracellularly
  - g. Calcium gluconate or calcium chloride (1 g) to stabilize the myocardium
5. Metabolic acidosis
  - a. Sodium bicarbonate (if pH <7.2 to keep serum bicarbonate >15 mmol/L)
  - b. Administration of other bases, e.g., THAM
  - c. Renal replacement therapy

# Treatment of AKI

6. Hyperphosphatemia
  - a. Restriction of dietary phosphate intake
  - b. Phosphate binding agents (calcium acetate, sevelamer hydrochloride, aluminum hydroxide—taken with meals)
7. Hypocalcemia
  - a. Calcium carbonate or calcium gluconate if symptomatic
8. Hypermagnesemia
  - a. Discontinue  $Mg^{2+}$  containing antacids
9. Hyperuricemia
  - a. Acute treatment is usually not required except in the setting of tumor lysis syndrome (see above)
10. Nutrition
  - a. Sufficient protein and calorie intake (20–30 kcal/kg per day) to avoid negative nitrogen balance. Nutrition should be provided via the enteral route if possible.
11. Drug dosing
  - a. Careful attention to dosages and frequency of administration of drugs, adjustment for degree of renal failure
  - b. Note that serum creatinine concentration may overestimate renal function in the non–steady state characteristic of patients with AKI

# AKI: Hemoglobinuria + Myoglobinuria

## Hemoglobinuria:

Transfusion Reactions, HUS (Hemolytic Uremic Syndrome),  
ECMO (Extra-corporeal Membrane Oxygenation)

## Myoglobinuria:

Crush Injuries, Rhabdomyolysis

Urine (+) Blood, But (-) Red Blood Cells

↑↑ CFK, ↑↑ K<sup>+</sup>

## Treatment

Aggressive Hydration + Urine Alkalinization,  
Mannitol / Furosemide

# Acute Kidney Injury: fluid therapy

## **If patient is fluid overloaded**

- fluid restriction (insensible losses)
- attempt furosemide 1-2 mg/kg
- Renal replacement therapy (see later)

## **If patient is dehydrated:**

- restore intravascular volume first
- then treat as euvolemic (below)

## **If patient is euvolemic:**

- restrict to insensible losses (30-35 ml/100kcal/24 hours)  
+ other losses (urine, chest tubes, etc)

# AKI – Indications for Dialysis

Dialysis is indicated when medical management fails to control volume overload, hyperkalemia, or acidosis. The timing of dialysis is still a matter of debate. Late initiation of dialysis carries the risk of avoidable volume, electrolyte and metabolic complications of AKI. On the other hand, initiating dialysis too early may unnecessarily expose individuals to intravenous lines and invasive procedures, with the attendant risks of infection, bleeding, procedural complications, and hypotension. The initiation of dialysis should not await the development of a life-threatening complication of renal failure.

**A** – acidosis

**E** – electrolyte disturb., usually *hyperkalemia*

**I** – intoxications (lithium, ethylene glycol, etc)

**O** – overload (volume overload)

**U** – uremia (symptoms, signs)

Thank you!

