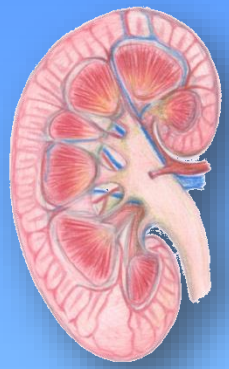
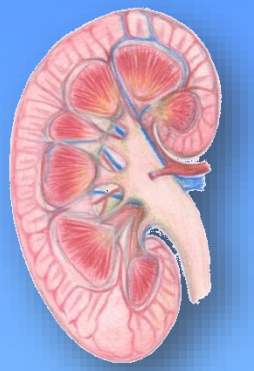


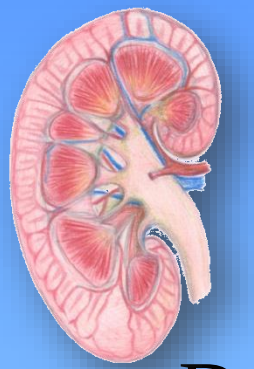
Approach to Acute Kidney Injury

Dr. Mohammed Al-Ghonaim
MBBS,FRCP(C)



Objective

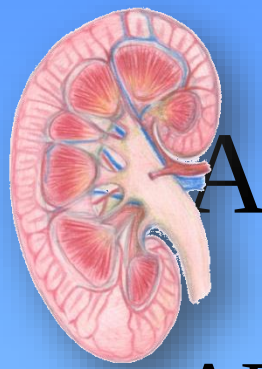
- At the end of this tutorial you will be able to:
  - Define AKI
  - Know the epidemiology of AKI
  - Know the etiology of AKI
  - Manage AKI
    - Diagnose AKI
    - Treat AKI



Acute Kidney Injury (AKI)

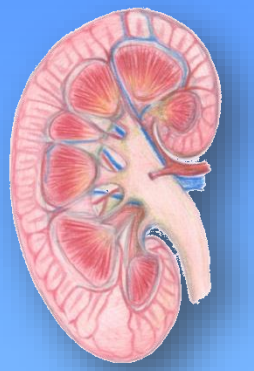
- Deterioration of renal function over a period of hours to days, resulting in
  - the failure of the kidney to excrete nitrogenous waste products and
  - to maintain fluid and electrolyte homeostasis

- Oliguria: <400 ml urine output in 24 hours
- Anuria: <100 ml urine output in 24 hours



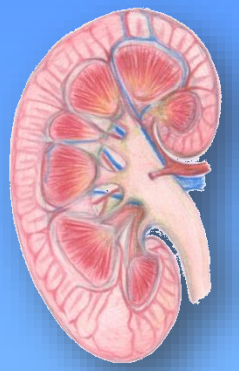
Acute Kidney Injury (definition)

- ARF in one study was defined as:
  - a 0.5 mg/dL increase in serum creatinine if the baseline serum creatinine was ≤1.9 mg/dL,
  - an 1.0 mg/dL increase in serum creatinine if the baseline serum creatinine was 2.0 to 4.9 mg/dL, and
  - a 1.5 mg/dL increase in serum creatinine if the baseline serum creatinine was ≥5.0 mg/dl



Acute Kidney Injury (AKI)

- An abrupt (within 48 hours) absolute increase in increase in creatinine by 0.3 mg/dl (26.4 µmol/l)or percentage increase of >50% from base line or urine output <0.5 ml/hour for 6 hours



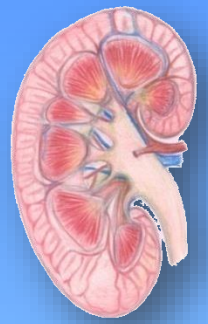
Why a creatinine of (26.4)?

"Acute kidney injury, mortality, length of stay, and costs in hospitalized patients"

19,982 pts admitted to academic medical centre in SF 9,205 pts with >1 creatinine results

Rise in creatinine	Multivariable OR (hospital mortality)
≥ 0.3 mg/dl (26.4 µmol/L)	4.1
≥ 0.5 mg/dl (45 µmol/L)	6.5
≥ 1.0 mg/dl (90 µmol/L)	9.7
≥ 2.0 mg/dl (180 µmol/L)	16.4

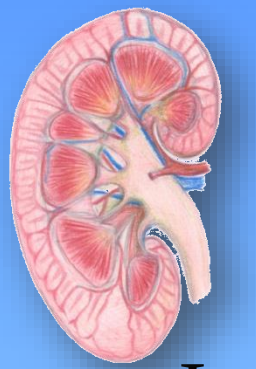
Chertow et al. JASN 2005; 16:3365-3370



Definition of Acute Kidney Injury (AKI) based on "Acute Kidney Injury Network"

Stage	Creatinine criteria	Urine Output criteria
AKI stage I	1.5-2 times baseline **OR** 0.3 mg/dl increase from baseline (≥ 26.4 µmol/L)	<0.5 ml/kg/h for >6 h
AKI stage II	2-3 times baseline	<0.5 ml/kg/h for >12 h
AKI stage III	3 times baseline **OR** 0.5 mg/dl (44 µmol/L) increase if baseline>4mg/dl(≥ 354 µmol/L) **OR** Any renal replacement therapy given	<0.3 ml/kg/h for >24 h **OR** Anuria for >12 h

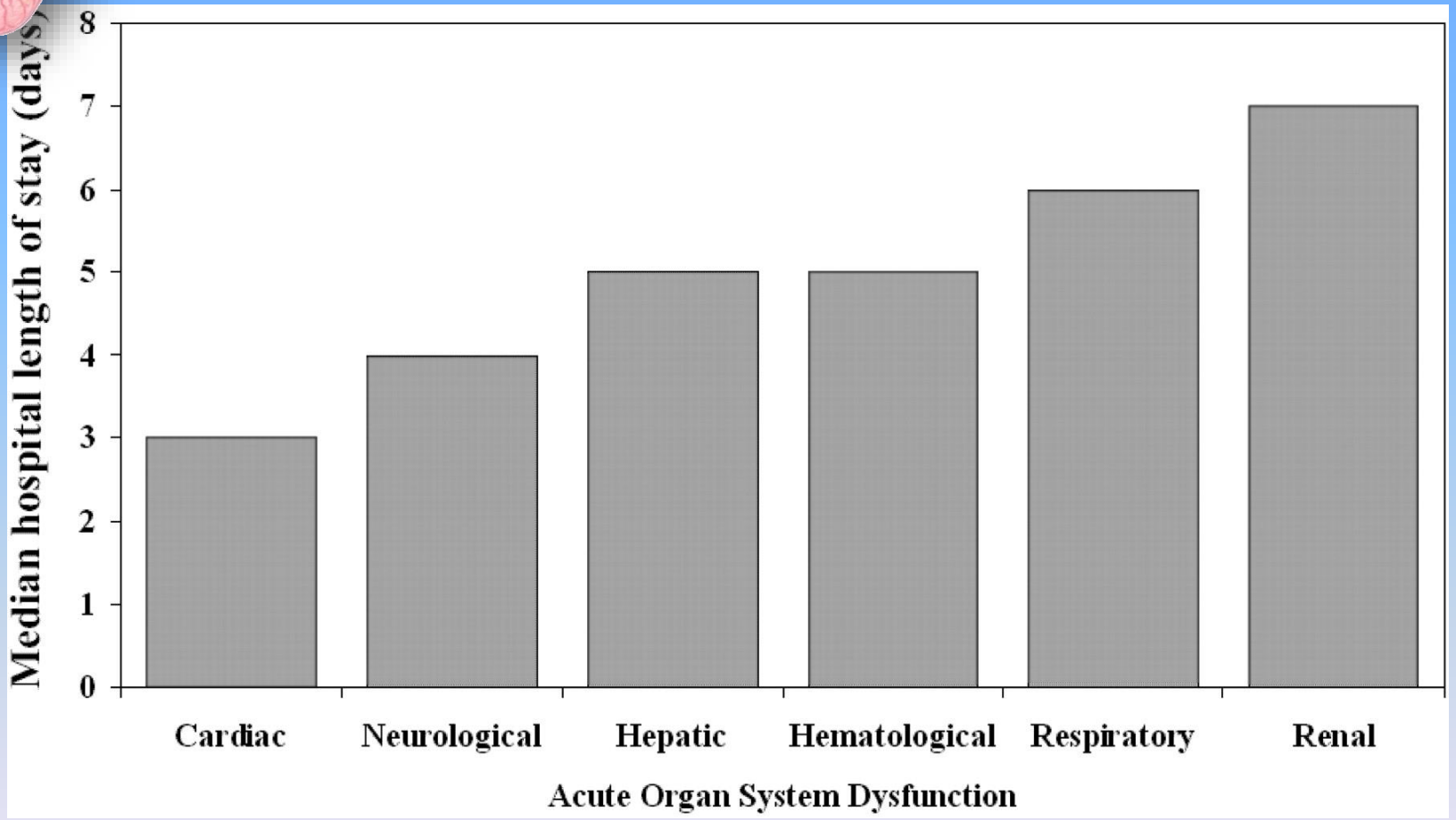
Mehta R et al. Crit Care 2007;11(2):R31
Ostermann *et al. Critical Care* 2008 **12**:R144

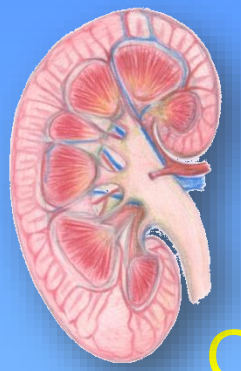


Epidemiology

- It occurs in
  - 5%of all hospitalized patients and
  - 35% of those in intensive care units
- Mortality is high:
  - up to 75–90% in patients with sepsis
  - 35–45% in those without

dian hospital length of stay (LOS) stratified by single acute organ system dysfunction (AOSD), including acute renal failure (ARF).





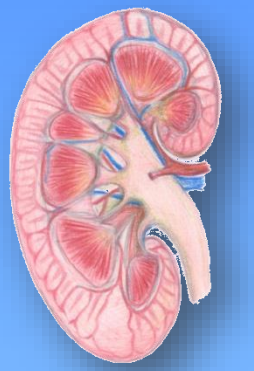
Impact of AKI

Correlation between AKI classification and outcome

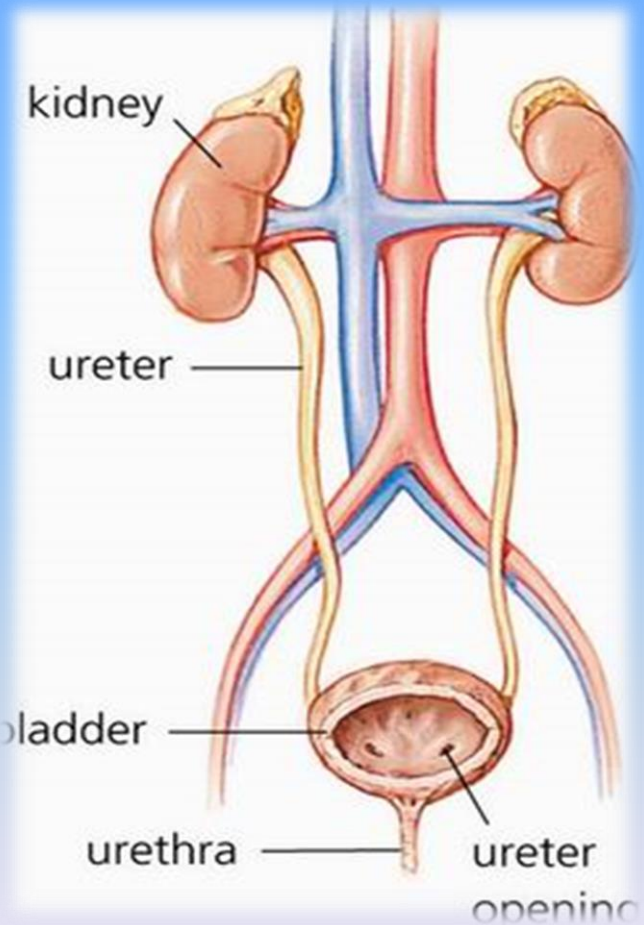
22,303 adult patients admitted to 22 ICUs in UK and Germany between 1989–1999 with ICU stay ≥24 hours

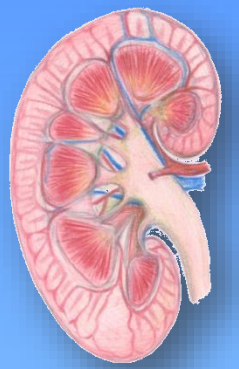
	No AKI	**AKI I**	**AKI II**	**AKI III**
	65.6%	19.1%	3.8%	12.5%
Mean age	60.5	62.1	60.4	61.1
ICU mortality	10.7%	20.1%	25.9%	49.6%
Hospital mortality	16.9%	29.9%	35.8%	57.9%

Ostermann et al, Critical Care 2008;12:R144

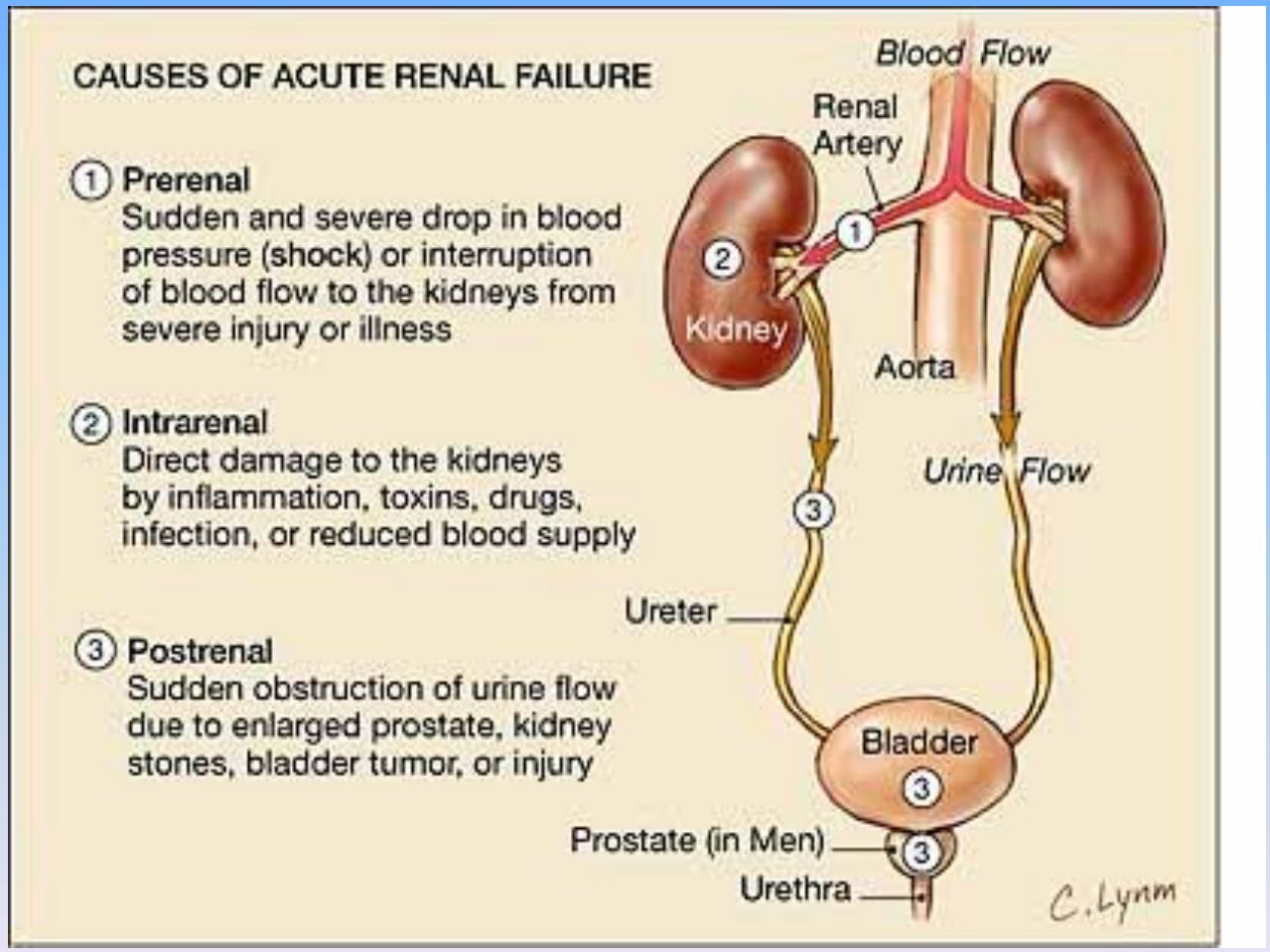


Etiology of ARF

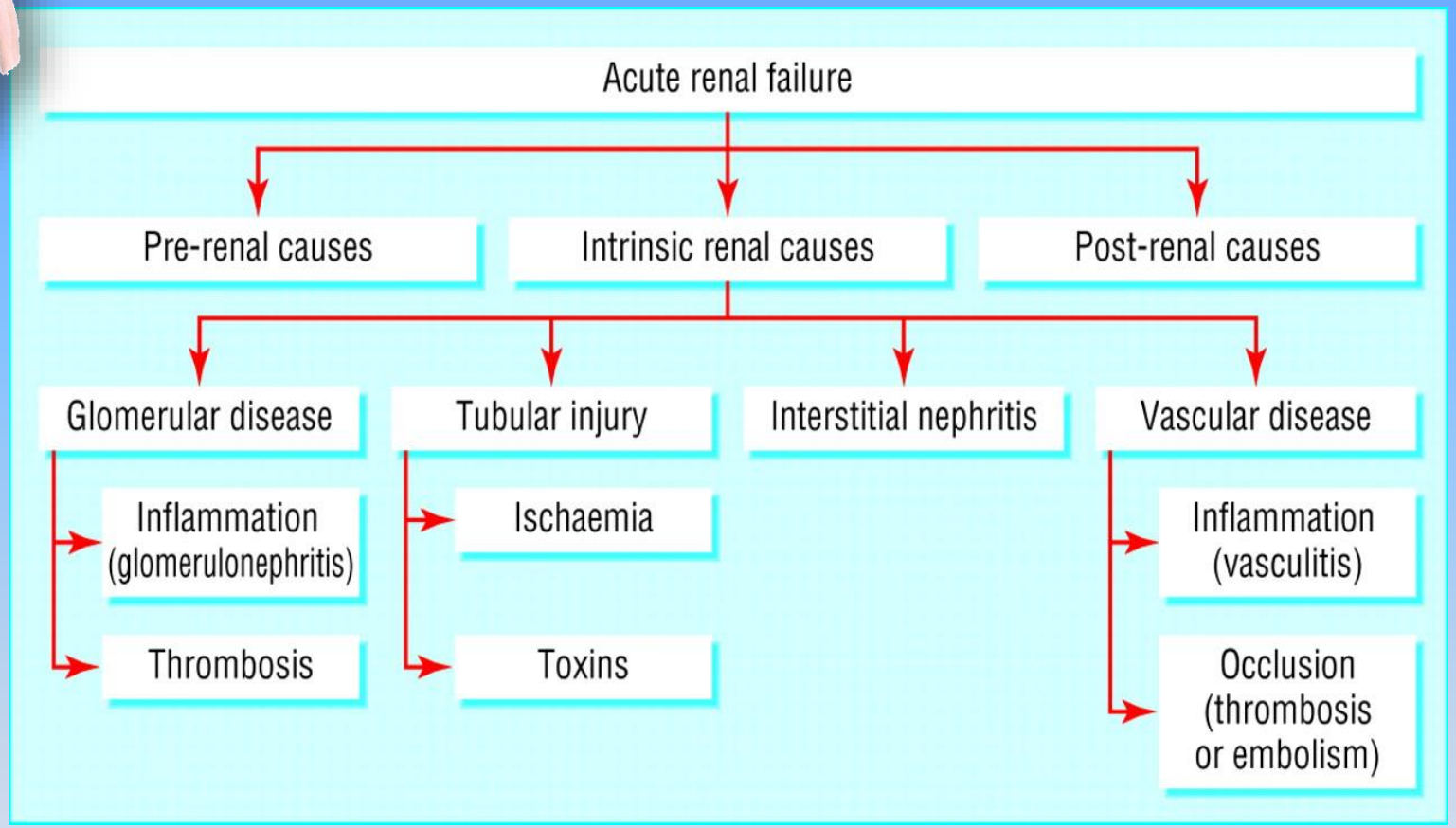




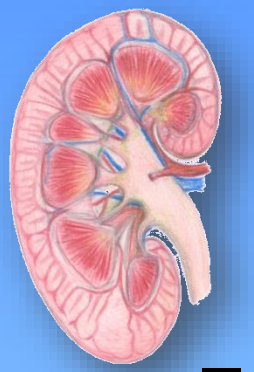
Etiology of ARF



Causes of AKI

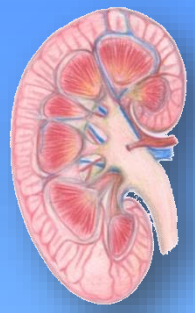


Hilton, R. BMJ 2006;333:786-790



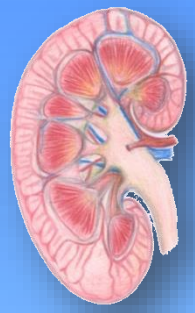
Pre-renal AKI

- **Volume depletion**
  - Renal losses (diuretics, polyuria)
  - GI losses (vomiting, diarrhea)
  - Cutaneous losses (burns, Stevens-Johnson syndrome)
  - Hemorrhage
  - Pancreatitis
- **Decreased cardiac output**
  - Heart failure
  - Pulmonary embolus
  - Acute myocardial infarction
  - Severe valvular heart disease
  - Abdominal compartment syndrome (tense ascites)



Case -1

- 75 years old female, known to have:
  - DM II
  - HTN
- Presented with nausea, vomiting and diarrhea for 3 days
- Medication: Insulin, lisinopril,
- Serum Creatinine 205

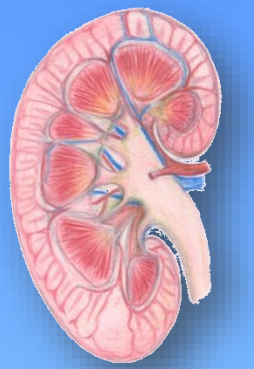


Case-1

- What other information do you want to know?
  - History:
  - Physical examination:
  - Investigations
- What is your diagnosis?
  - Acute Kidney Injury.
- What is the etiology of AKI?
  - Pre renal (dehydration)

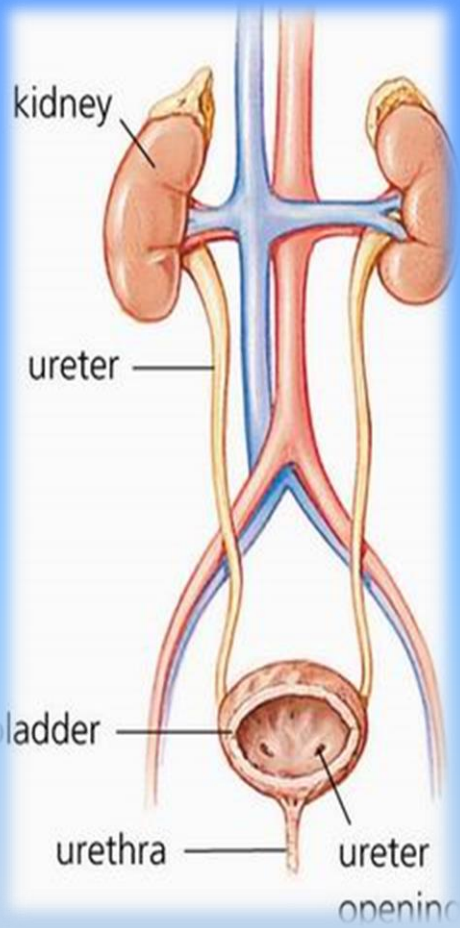
Case -1

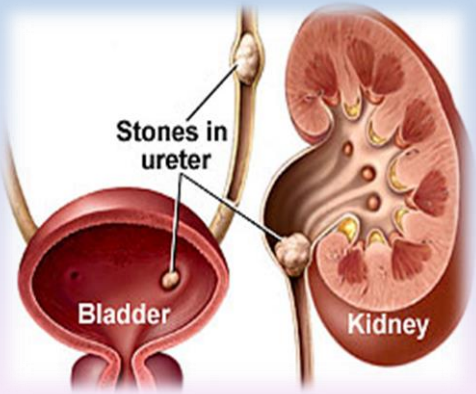
- What do you expect to fined in urine analysis?
  - Normal
- What do you expect urinary Na, osmolality?
  - Urinary Na<10
  - Osmolality > 300
  - Fractional excretion of Na <1%



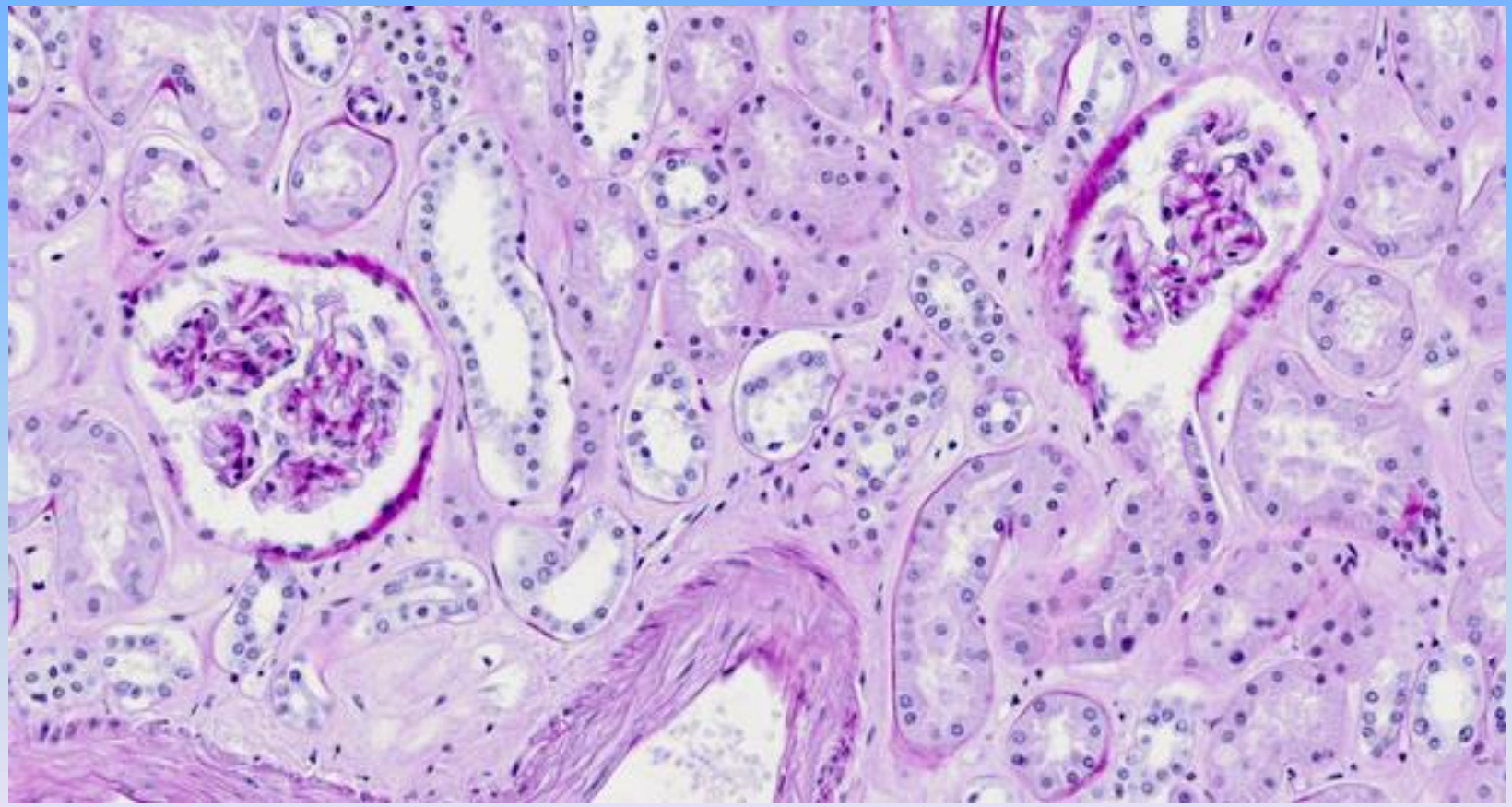
Post-renal AKI

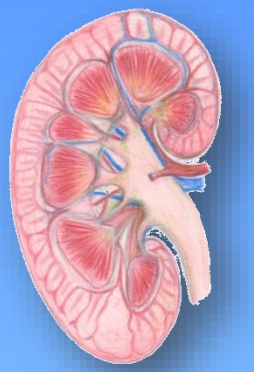
- **Ureteric obstruction**
  - Stone disease,
  - Tumor,
  - Fibrosis,
  - Ligation during pelvic surgery
- **Bladder neck obstruction**
  - Benign prostatic hypertrophy [BPH]
  - Cancer of the prostate
  - Neurogenic bladder
  - Drugs(Tricyclic antidepressants, ganglion blockers,
  - Bladder tumor,
  - Stone disease, hemorrhage/clot)
- **Urethral obstruction** (strictures, tumor)





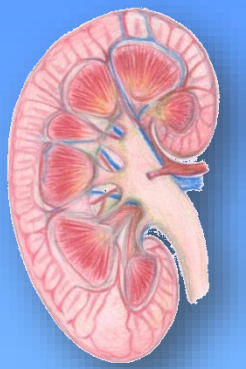
Renal



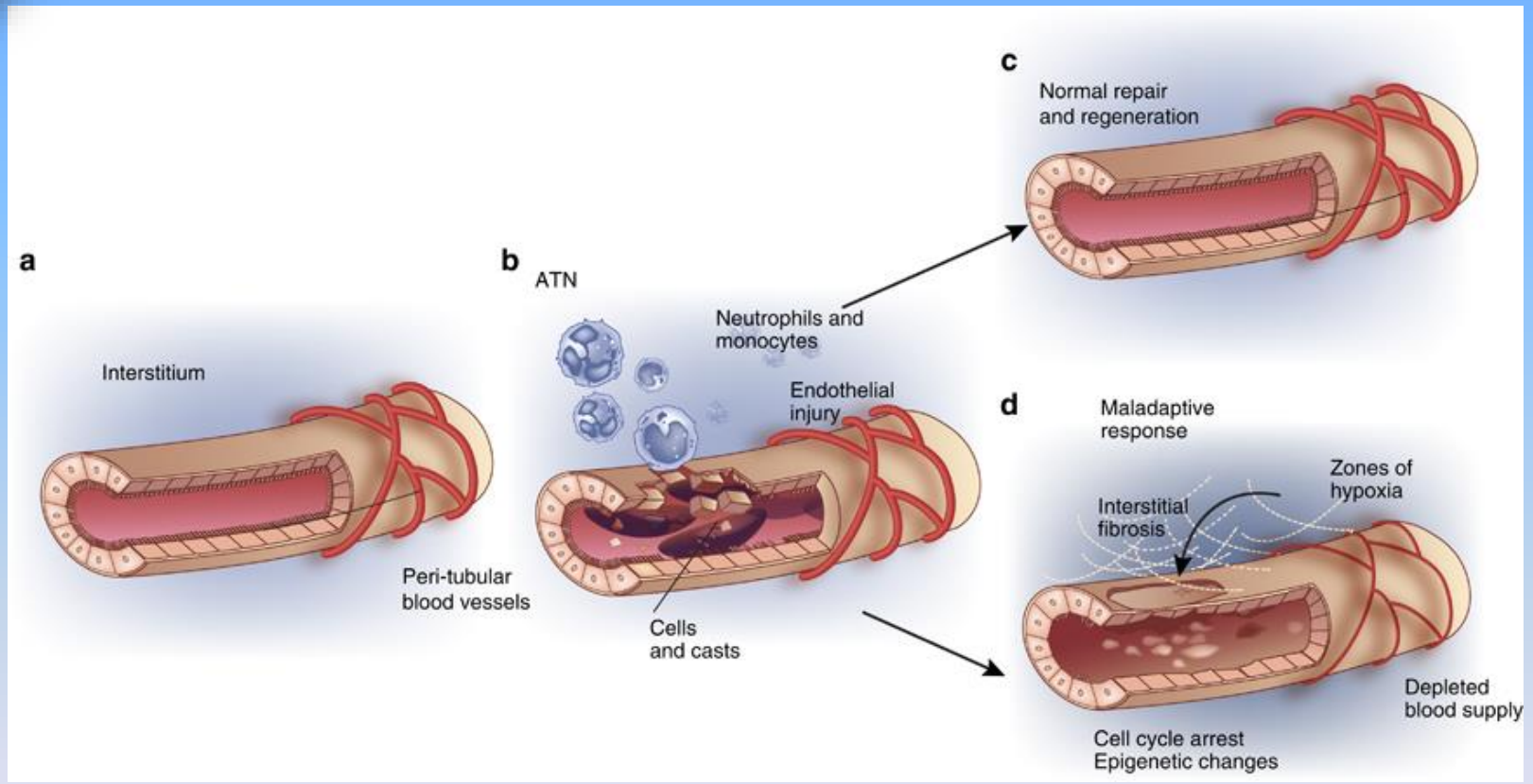


Tubular injury

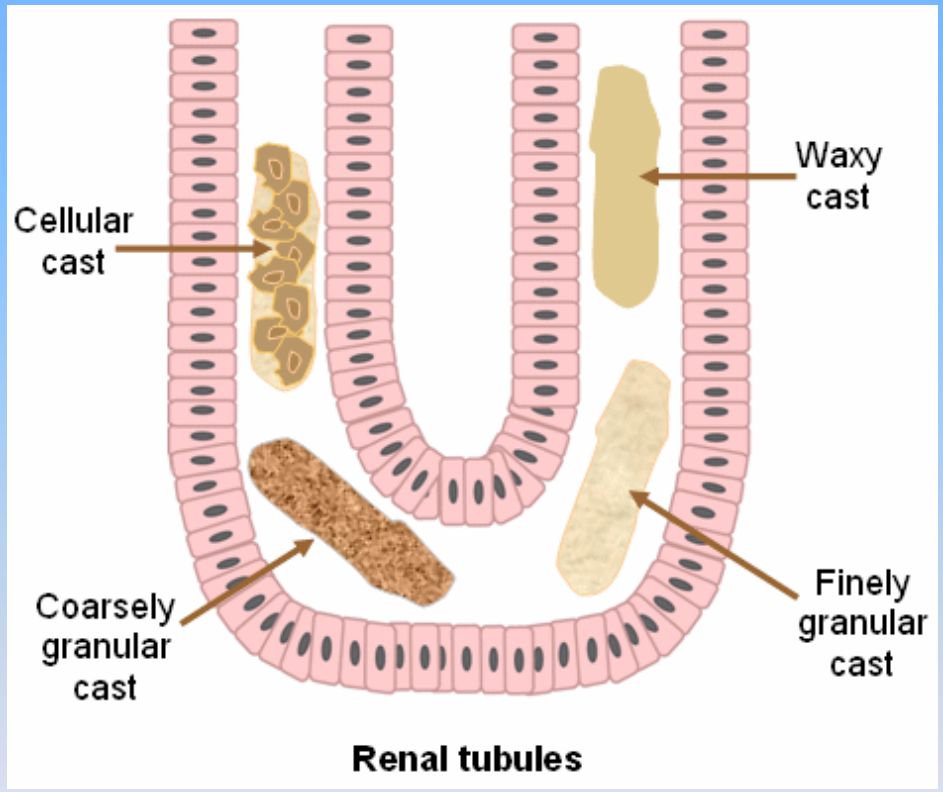
- Ischemia:
  - Hypotension, sepsis, prolonged pre-renal state
- Totoxic
  - Heme pigment (rhabdomyolysis, intravascular hemolysis)
  - Crystals (tumor lysis syndrome, seizures, ethylene glycol poisoning, megadose vitamin C, acyclovir, indinavir, methotrexate)
  - Drugs (aminoglycosides, lithium, amphotericin B, pentamidine, cisplatin, ifosfamide, radiocontrast agents)

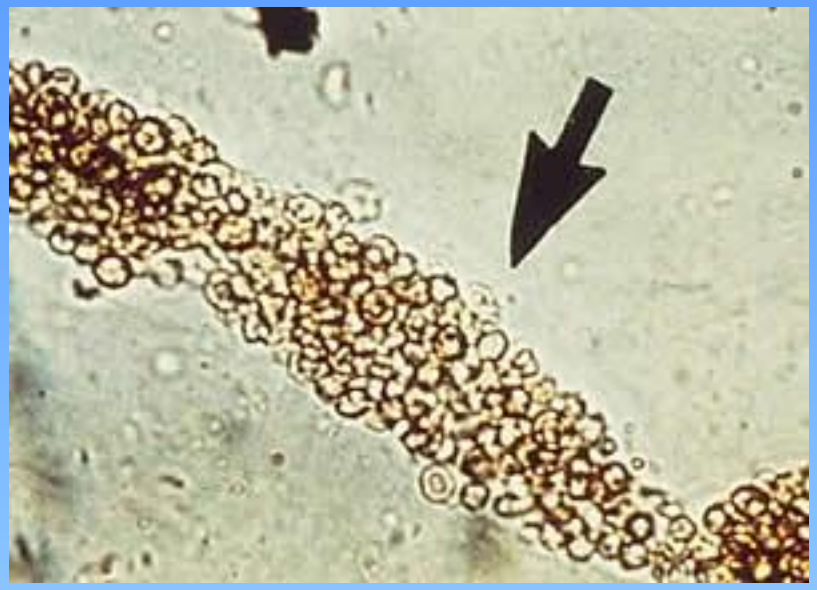


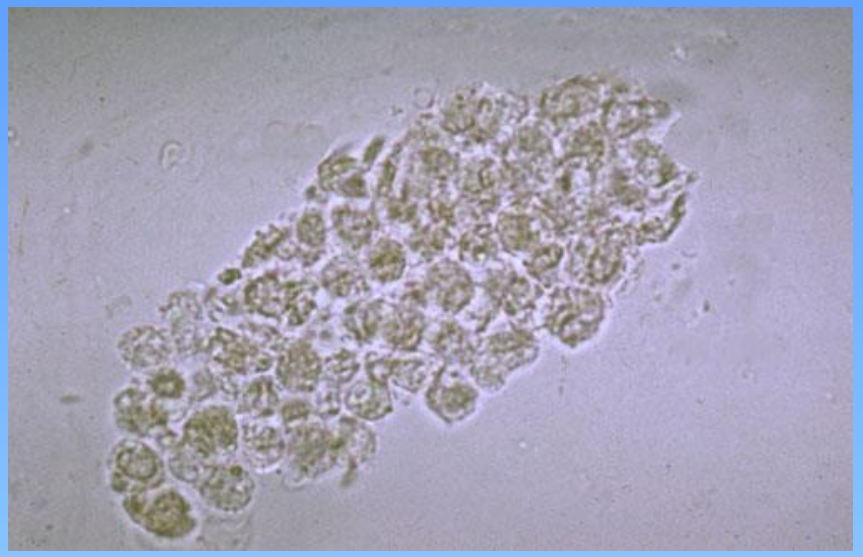
Tubular injury

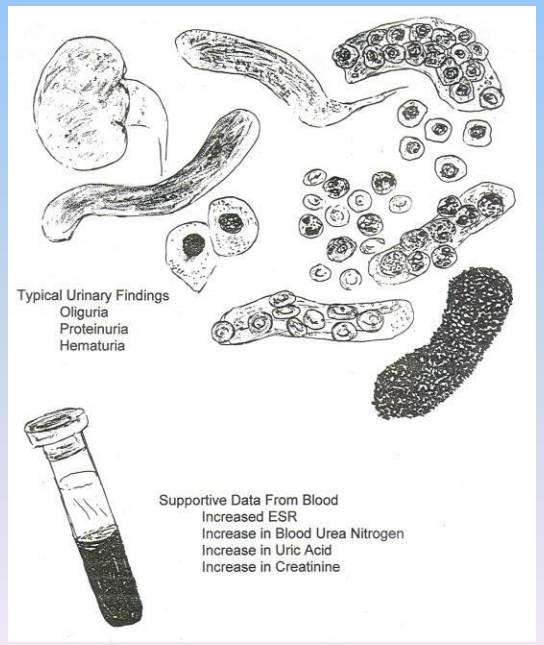


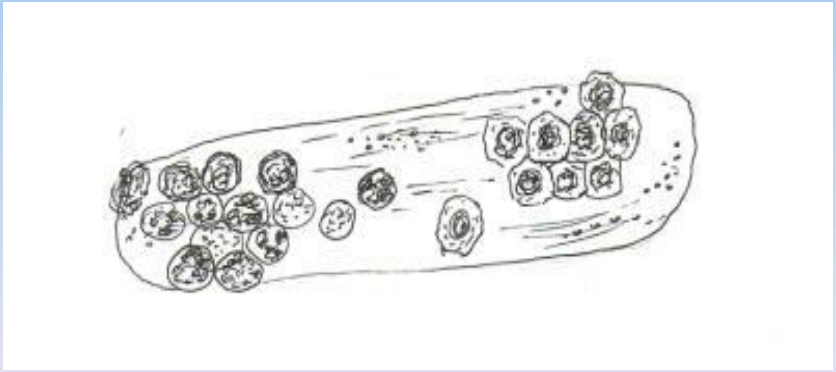
Cast formation

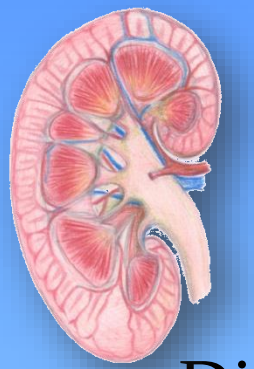






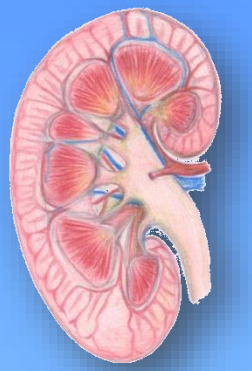

Typical Urinary Findings
Oliguria
Proteinuria
Hematuria
Supportive Data From Blood
Increased ESR
Increase in Blood Urea Nitrogen
Increase in Uric Acid
Increase in Creatinine





Acute Tubular Necrosis

- Diagnose by history, ↑ FE_{Na} (>2%)
- sediment with coarse granular casts, RTE cells
- Treatment is supportive care.
  - Maintenance of euvolemia (with judicious use of diuretics, IVF, as necessary)
  - Avoidance of hypotension
  - Avoidance of nephrotoxic medications (including NSAIDs and ACE-I) when possible
  - Dialysis, if necessary
- 80% will recover, if initial insult can be reversed



Interstitial

Box 1: Common causes* of acute interstitial nephritis[2,4,6]

Drugs

- Antimicrobials (ampicillin, ciprofloxacin, methicillin, penicillin, rifampicin, sulfonamides)
- Nonsteroidal anti-inflammatory drugs (acetylsalicylic acid, fenoprofen, ibuprofen, indomethacin, naproxen, phenylbutazone, piroxicam, tolmetin, zomepirac)
- Acid suppressors (omeprazole, pantoprazole, rabeprazole, cimetidine)
- Others (phenytoin, furosemide, allopurinol, phenindione)

Infections

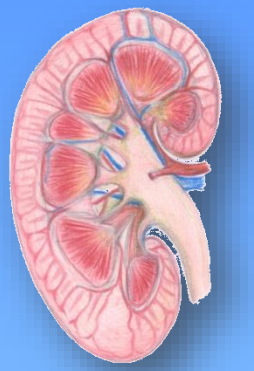
- Direct infiltration (leptospirosis, cytomegalovirus, candidiasis)
- Reactive to systemic infections (streptococcal infection, diphtheria, *Hantavirus*)

Systemic diseases

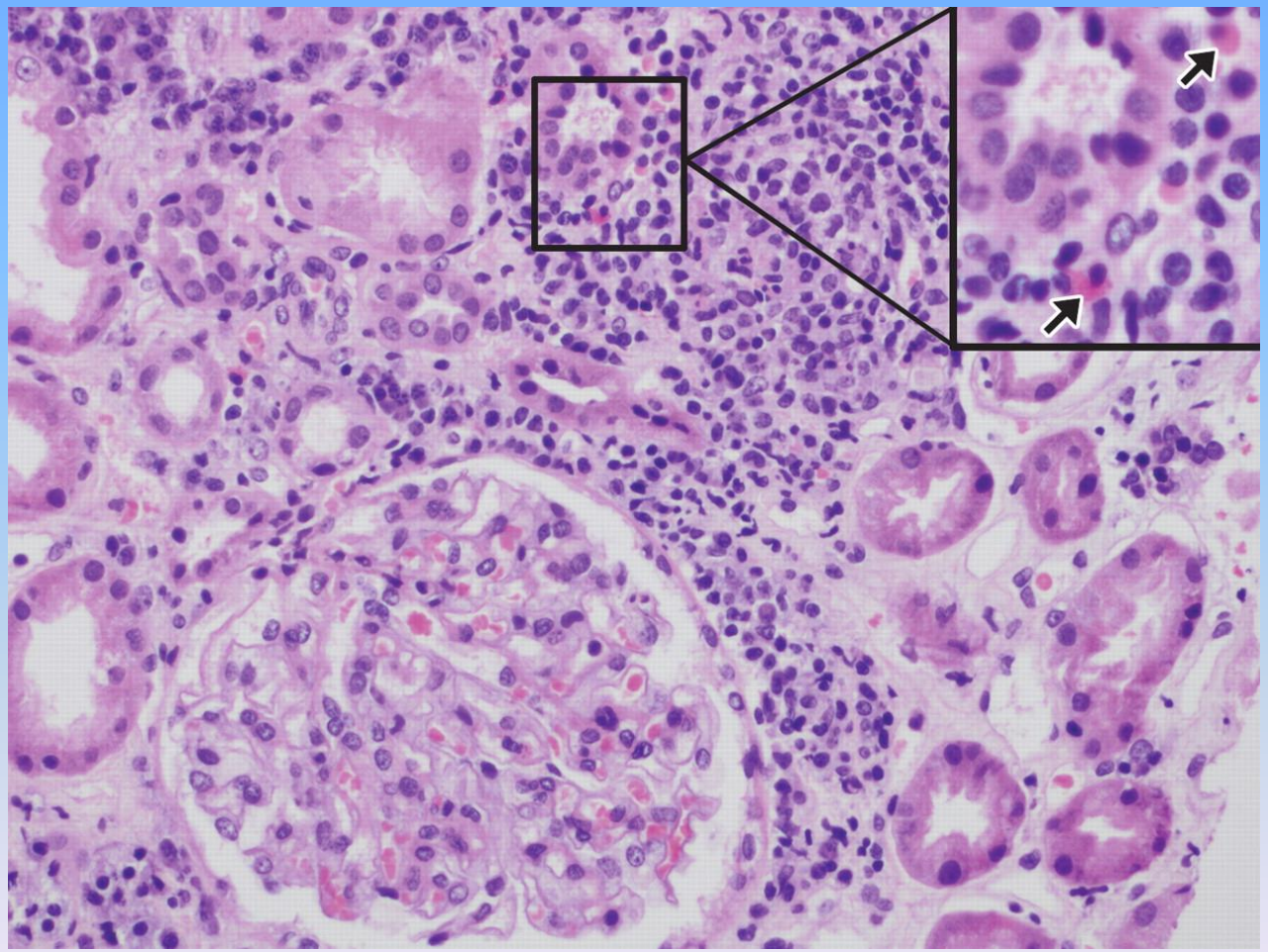
- Metabolic diseases (urate nephropathy, hypercalcemic nephropathy, oxalate nephropathy)
- Immunologic reactions (transplant rejection, systemic lupus erythematosis, sarcoidosis, cryoglobulinemia)
- Neoplastic diseases (lymphoproliferative diseases)

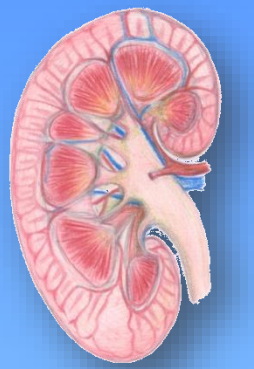
Idiopathic causes

*These are the most common causes of acute interstitial nephritis, but this list is not exhaustive.



Interstitial

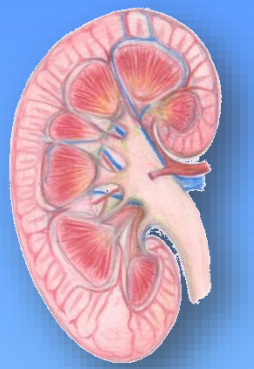




Interstitial

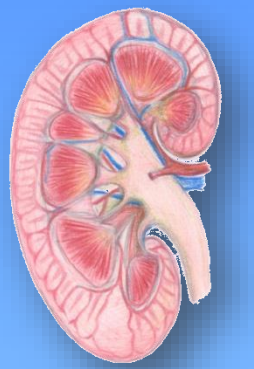
Box 2: Characteristics of acute interstitial nephritis

- Acute elevation in creatinine levels (not caused by pre- or post-renal etiologies)
- General malaise, nausea (caused by buildup of metabolites)
- Normal blood pressure, no edema (distinguishes acute interstitial nephritis from acute tubular necrosis)
- Polyuria and polydypsia (kidneys unable to concentrate urine)
- Maculopapular rash (may be an early indication of drug-induced acute interstitial nephritis)
- Proteinuria (caused by tubular damage)
- Pyuria (occurs in almost all cases)
- Hematuria (occurs in about 90% of cases)
- Eosinophiluria (occurs in 80% of cases of drug-induced acute interstitial nephritis)

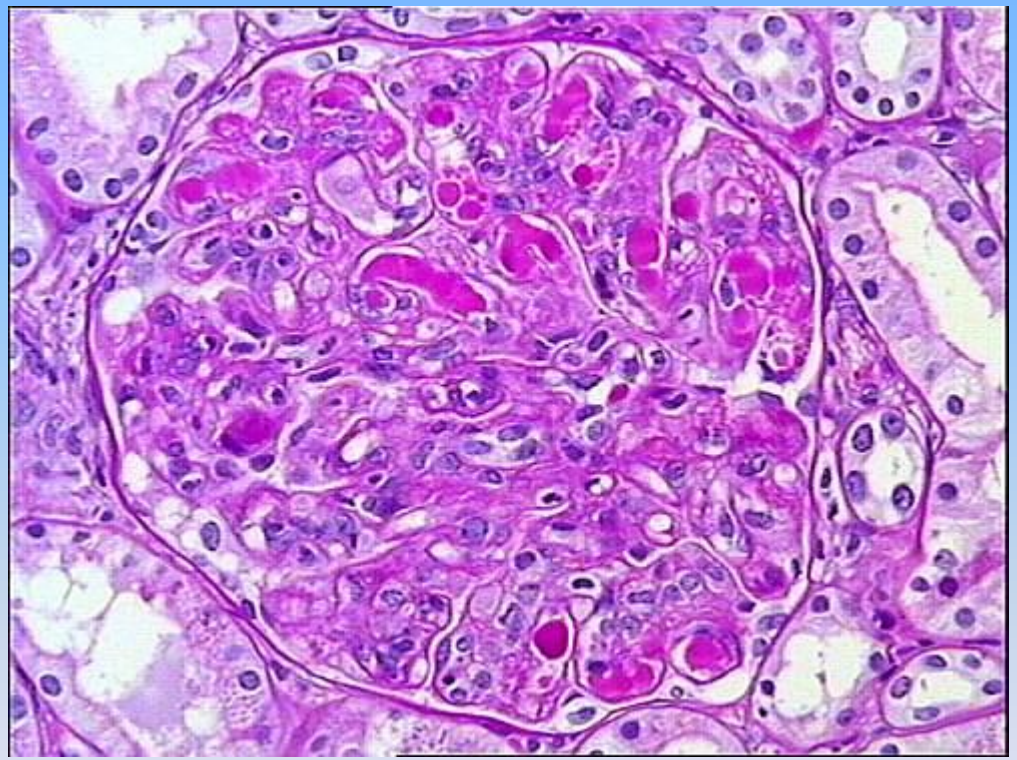


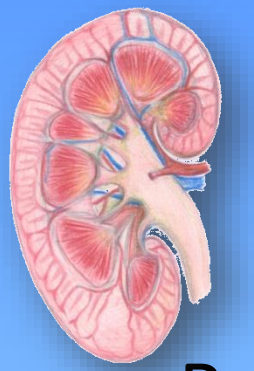
Glomerular

- Anti–glomerular basement membrane (GBM) disease (Goodpasture syndrome)
- Anti–neutrophil cytoplasmic antibody-associated glomerulonephritis (ANCA-associated GN) (Wegener granulomatosis, Churg-Strauss syndrome, microscopic polyangiitis)
- Immune complex GN (lupus, postinfectious, cryoglobulinemia, primary membranoproliferative glomerulonephritis)



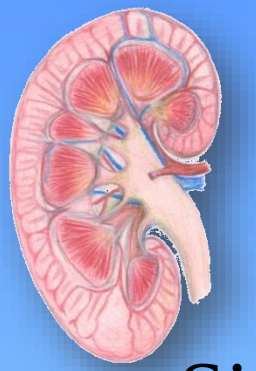
Glomerular





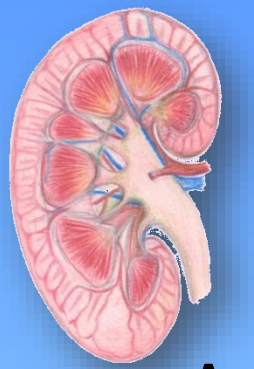
Acute Glomerulonephritis

- Rare in the hospitalized patient
- Diagnose by history, hematuria, RBC casts, proteinuria (usually non-nephrotic range), low serum complement in post-infectious GN), RPGN often associated with anti-GBM or ANCA
- Usually will need to perform renal biopsy



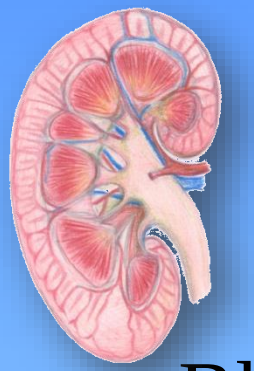
Clinical feature-1

- Signs and symptoms resulting of primary disease
- Signs and symptoms resulting from loss of kidney function:
  - decreased or no urine output, flank pain, edema, hypertension, or discolored urine
  - weakness and
  - easy fatiguability (from anemia),
  - anorexia,
  - vomiting, mental status changes or
  - Seizures
  - edema



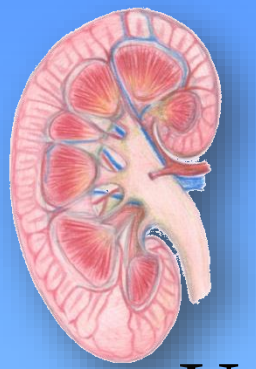
Clinical feature-2

- Asymptomatic
  - elevations in the plasma creatinine
  - abnormalities on urinalysis
- Systemic symptoms and findings:
  - fever
  - arthralgias,
  - pulmonary lesions



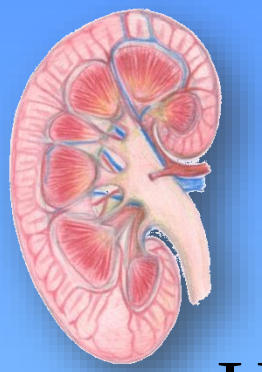
AKI Diagnosis

- Blood urea nitrogen and serum creatinine
- CBC, peripheral smear, and serology
- Urinalysis
- Urine electrolytes
- U/S kidneys
- Serology: ANA,ANCA, Anti DNA, HBV, HCV, Anti GBM, cryoglobulin, CK, urinary Myoglobulin



AKI Diagnosis

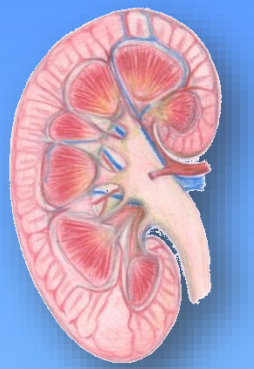
- Urinalysis
  - Unremarkable in pre and post renal causes
  - Differentiates ATN vs. AIN. vs. AGN
    - Muddy brown casts in ATN
    - WBC casts in AIN
    - RBC casts in AGN
  - Hansel stain for Eosinophils



AKI - Diagnosis

- Urinary Indices;
  - $$FENa = \frac{U_{Na} \times P_{Cr}}{P_{Na} \times U_{Cr}} \times 100$$

    FENa < 1% (Pre-renal state)
    - May be low in selected intrinsic cause
      - » Contrast nephropathy
      - » Acute GN
      - » Myoglobin induced ATN
  - FENa > 1% (intrinsic cause of AKI)



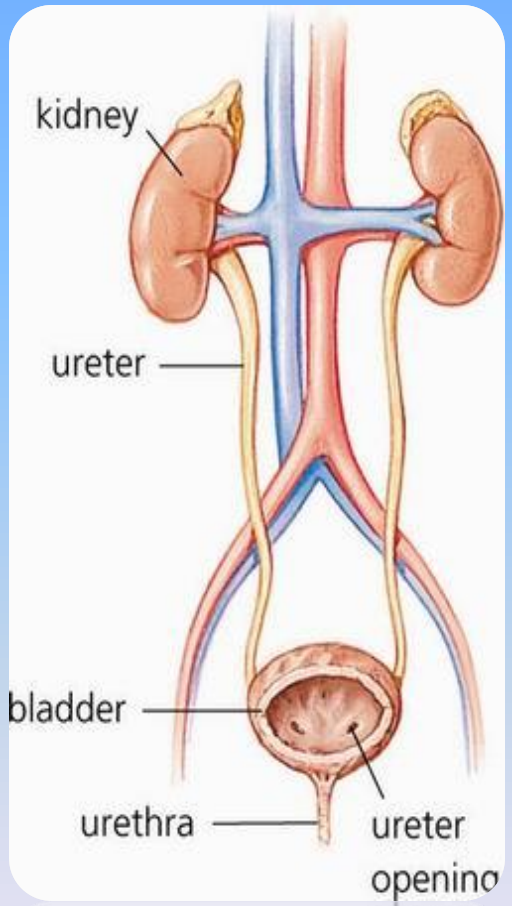
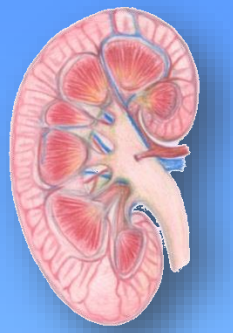

kidney
ureter
bladder
urethra
ureter
opening

TABLE 3-3. Laboratory Tests Useful in the Diagnosis of Acute Renal Failure

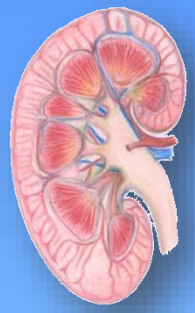
Test	Favors Prerenal Disease	Favors ATN
BUN/P_{cr} ratio	>20:1	10–15:1
Rise in P_{cr}	Variable rate of rise with downward fluctuations in some patients	Progressive increase of ≥0.5 mg/dL per day, particularl oliguric patients
Urinalysis	Normal or near normal; hyaline casts may be seen but are not an abnormal finding	Many granular casts with re tubular epithelial cells an epithelial cell casts
U_{osm}	>500 mosmol/kg	<350 mosmol/kg
U_{Na}	<20 meq/L	>40 meq/L
FE_{Na}	<1 percent	>2 percent



Case -2

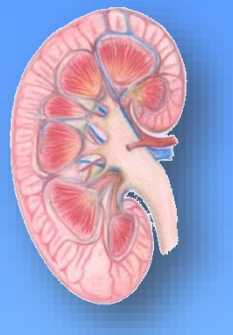
- 16 years old Saudi male,
- s/p road traffic accident developed quadriplegia,
- Creatinine 32 few days ago, now 201
- Urine out put 2 L/day

What is next?



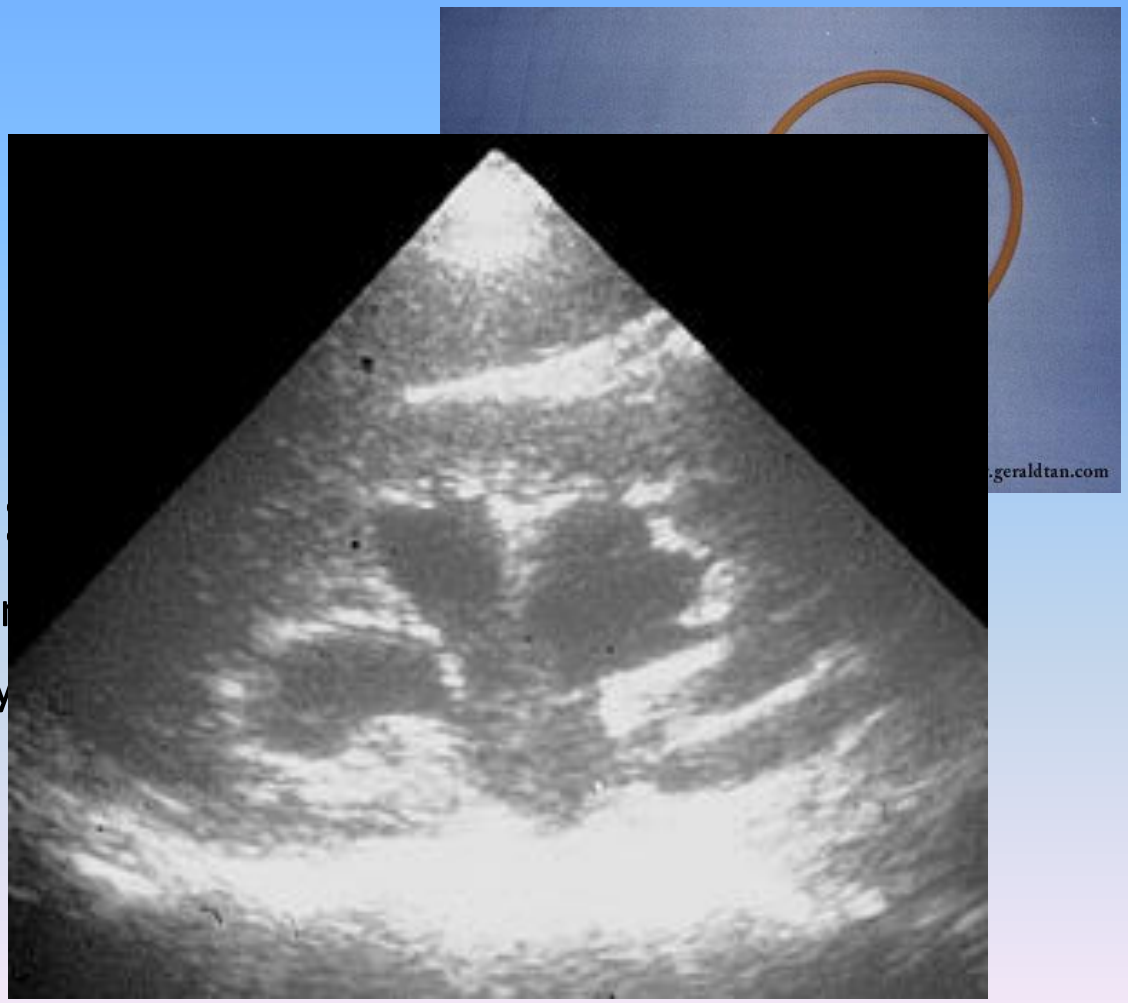
Case -2

- History:
  - No history of vomiting or diarrhea
  - no new medication added
- On examination:
  - BP 123/73 mmHg pulse 78 /min
  - FiO2 saturation is 99% on room air
- Diagnosis:
  - acute
  - Serum creatinine 5 days ago 32

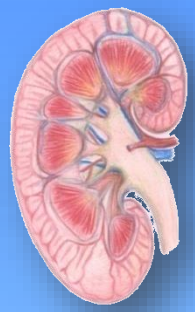


Case-2

- First step:



- Investigations:
  - Urine analysis, Uri
  - Ultra sound kidney

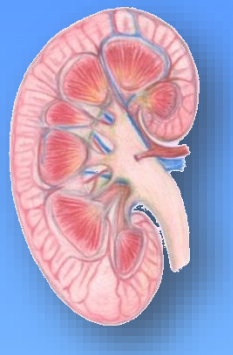


Case-3

- You are working as nephrology resident and ER resident calls you for a consult:
- 25 years old Saudi male sustained Road traffic accident this morning in ER was hypotensive and required 6 units of blood transfusion urine out put decreased significantly serum creatinine 285µmol/l?
- How would you approach this patient?

Case-3

- What other information you need to know?
  - Previously healthy
  - And urine output for the last 3 hours is <10 cc and dark colour



Case-3

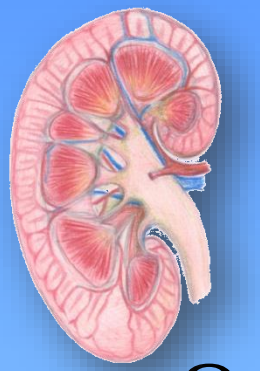
- Physical examination
  - Asses volume status
  - Blood pressure
  - Pulse
  - JVP
  - Urine out put
- Laboratory investigation:
  - K 4.7, Bicarbonate 21, Cl 99, Na 137
  - Urinary Na> 10, Urine osmolality < 350

Case -3

- What is your diagnosis?
  - Acute Kidney Injury
- Where is the etiology?
- Renal?
  - ATN (acute tubular necrosis)
  - AIN (acute interstitial nephritis)
  - GN (glomerulonephritis)

Case-3

- Diagnosis:
  - Acute Kidney Injury secondary to Acute tubular necrosis due to shock

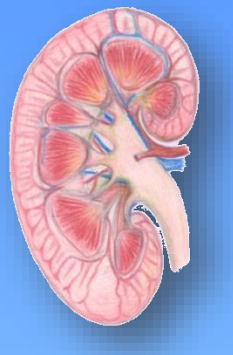


Treatment of AKI

- Optimization of hemodynamic and volume status
- Avoidance of further renal insults
- Optimization of nutrition
- If necessary, institution of renal replacement therapy

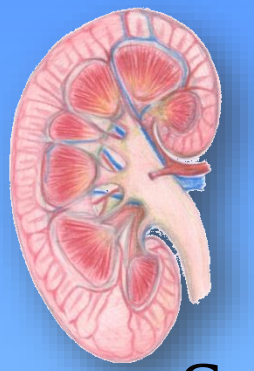
Case-3

- After assessment your staff advise the following:
  - IVF bolus 1 litter then 100 cc/hour, after blood transfusion
- Next day when you came to assess the patient you found him incubated and they told you he went into respiratory distress
  - BP 120/78mmHg
  - Urine output none for the last 3 hours



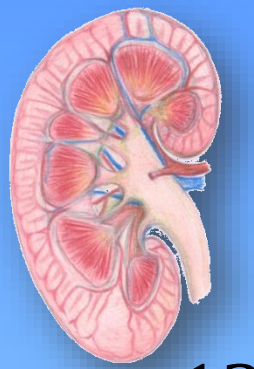
Case-3

- Lab result as follow:
  - K 6.3
  - Creatinine 499µmol/l
  - Bicarbonate 12
- What next:



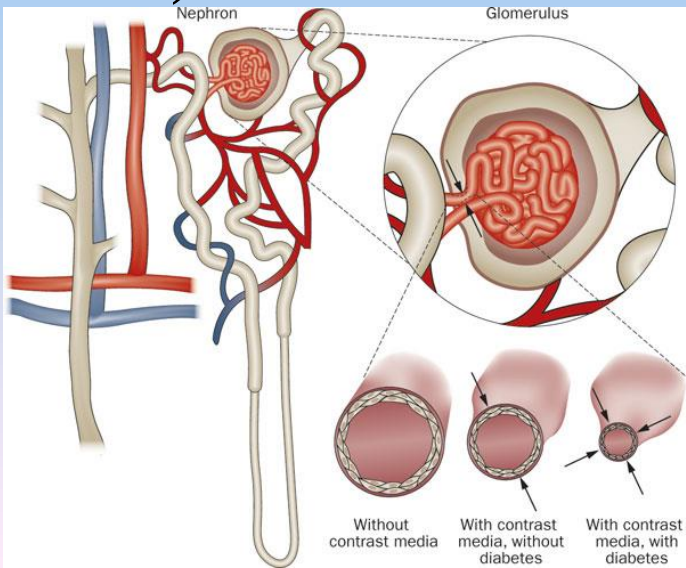
Indication for renal replacement therapy

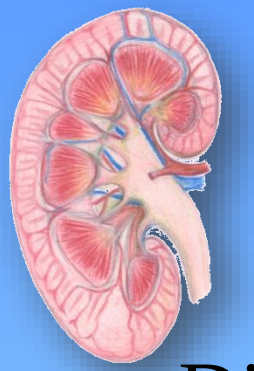
- Symptoms of uremia (encephalopathy,…)
- Uremic pericarditis
- Refractory volume over load
- Refractory hyperkalemia
- Refractory metabolic acidosis



Contrast nephropathy

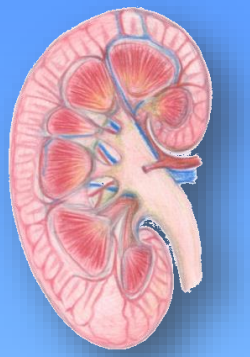
- 12-24 hours post exposure, peaks in 3-5 days
- Non-oliguric, FE Na <1% !!
- RX/Prevention:
  - 1/2 NS 1 cc/kg/hr 12 hours pre/post
  - N-acetyle cystein 600 BID pre/post (4 doses)
- Risk Factors:
  - CKD,
  - Older age
  - Hypovolemia ,DM,CHF





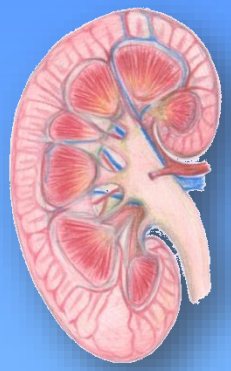
Rhabdomyolysis

- Diagnose with ↑ serum CK (usu. > 10,000), urine dipstick (+) for blood, without RBCs on microscopy, pigmented granular casts
- Common after trauma (“crush injuries”), seizures, burns, limb ischemia occasionally after IABP or cardiopulmonary bypass
- Treatment is largely supportive care. With IVF



Atheroembolic ARF

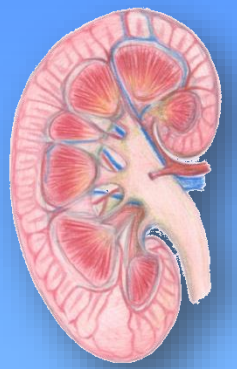
- Associated with emboli of fragments of atherosclerotic plaque from aorta and other large arteries
- Diagnose by history, physical findings (evidence of other embolic phenomena--CVA, ischemic digits, “blue toe” syndrome, etc), low serum C3 and C4, peripheral eosinophilia, eosinophiluria, rarely WBC casts
- Commonly occur after intravascular procedures or cannulation (cardiac cath, CABG, AAA repair, etc.)



Renal failure

Differentiation between acute and chronic renal failure

	Acute	*Chronic*
History	Short (days-week)	Long (month-years)
Haemoglobin concentration	Normal	Low
Renal size	Normal	Reduced
Serum Creatinine concentration	Acute reversible increase	Chronic irreversible



Conclusion

Is this acute or chronic renal failure?	• History and examination • Previous creatinine measurements • Small kidneys on ultrasound (except diabetes)
Has obstruction been excluded?	• Complete anuria • Palpable bladder • Renal ultrasound
Is the patient euvolaemic?	• Pulse, JVP/CVP, postural blood pressure, daily weights, fluid balance • Disproportional increase in urea:creatinine ratio • Urinary sodium concentration (unless on diuretics) • Fluid challenge
Does evidence of renal parenchymal disease exist (other than ATN)?	• History and examination (systemic features) • Urine dipstick and microscopy (red cells, red cell casts, eosinophils, proteinuria)
Has a major vascular occlusion occurred?	• Atherosclerotic vascular disease • Renal asymmetry • Loin pain • Macroscopic haematuria • Complete anuria

Hilton, R. BMJ 2006;333:786-790