AKI Acute Kidney Injury

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Definition

- ***Acute kidney injury (AKI)or Acute renal failure (ARF)*** comprises a family of syndromes that are characterized by an abrupt (over hours to days) decrease in the GFR.
- This decrease in renal renal function can occur in the absence of prior renal dysfunction, or it may represent an acute exacerbation in a patient with known stable chronic kidney disease.
- The primary manifestation of AKI/ARF is the accumulation of nitrogenous waste products, primarily urea and creatinine.

The current diagnostic criteria are a "bump" of serum creatinine of **0.3 mg/dL** or **50% higher** than baseline over a **24-48 hour** period, **OR** a reduction in urinary flow to < **0.5** mL/kg/hr for > 6 hours.

AKI DEFINITION

RIFLE VS AKIN

AKI :RIFLE

- Risk
- Injury
- Failure
- Loss of function
- ESRD

AKI KDIGO 2012 classification

- ***Stage 1***: S Cr 1.5 to 1.9 baseline or 0.3 mg/dl increase ***or***
- Urine output less than 0.5 ml/kg/per hr for 6 -12 hrs
- ***Stage 2***: S Cr 2-2.9 times baseline ***or*** Urine output less than 0.5 ml/kg/per hr for more than 12 hrs
- ***Stage 3:*** S Cr 3 times baseline, or increase in S Cr more than 4 mg/dl or initial of Dialysis ***or***
- Urine output less than 0.3 ml/kg per hr for more than 24 hrs or anuria for 12 hrs

Oliguria

*Although ***oliguria*** (defined as a urine volume of less than 300-400 ml/24 h) may also be a presenting manifestation of AKI/ARF, the urine volume can be variable, ranging from less than 100 ml to greater than 3 L per day.

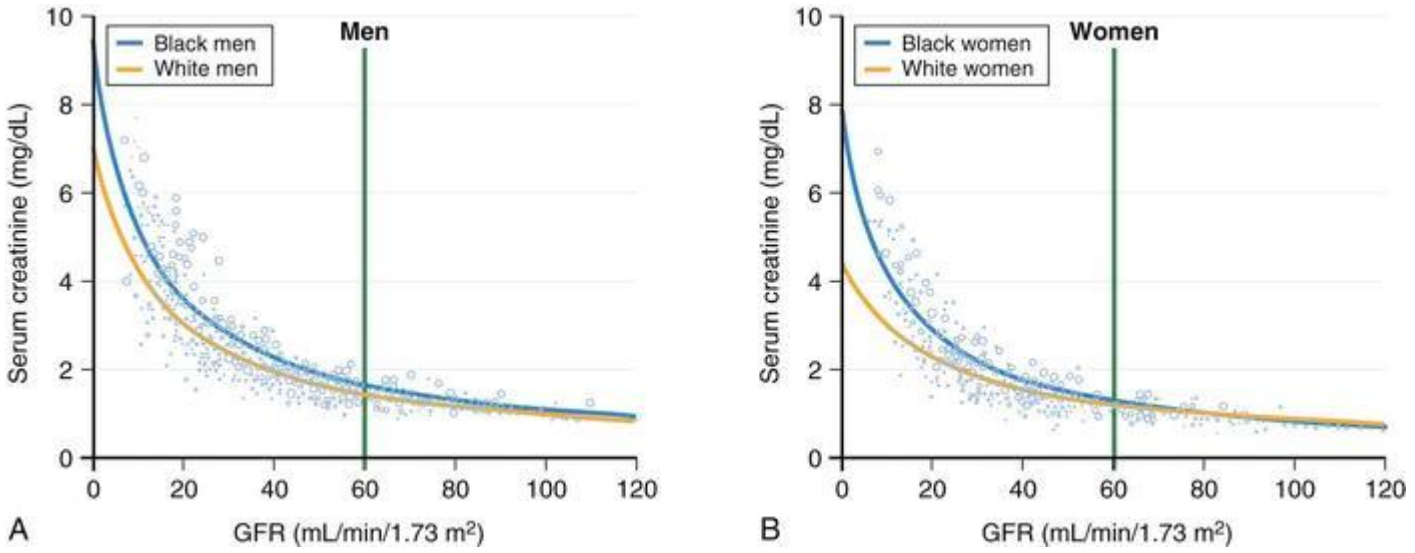
*AKI/ARF is usually diagnosed on the basis of **increases in the serum creatinine and blood urea concentrations**, because direct measurement of GFR in the clinical setting is not practical.

*Although renal function is most commonly assessed on the basis of serum creatinine concentration, a ***precise correlation*** between changes in ***creatinine concentration and GFR*** does not exist.

NEWER markers: not ready for routine clinical use yet

*AKI definitions, based on differing absolute or relative changes in serum creatinine (*e.g.*, an absolute increase in serum creatinine by 0.5 or 1.0 mg/dl, or a relative increase in serum creatinine of 25% to 100%, occurring over 24 to 72 h)

S Cr and GFR


Men
Black men
White men
Serum creatinine (mg/dL)
GFR (mL/min/1.73 m²)
A
Women
Black women
White women
Serum creatinine (mg/dL)
GFR (mL/min/1.73 m²)
B

Syndromes of ARF/AKI

Table 1. Syndromes of acute renal failure

- Prerenal ARF
  - Intravascular volume depletion
  - Decreased effective blood volume
  - Altered intrarenal hemodynamics
    - preglomerular (afferent) vasoconstriction
    - postglomerular (efferent) vasodilation
- Intrinsic ARF
  - Acute tubular necrosis
    - ischemic
    - nephrotoxic
  - acute interstitial nephritis
  - acute glomerulonephritis
  - acute vascular syndromes
- Postrenal ARF

Causes of Increased BUN

- *1.GI bleed*
- *2. Hypercatabolic state*
- *3. Steroid use*
- *4.Tetracycline use*

- *Increase Blood urea concentration in the absence of substantial changes in GFR*

Causes of Lower BUN than expected

- *1. Malnutrition*
- *2. Severe liver disease*

Causes of increase Cr without change in GFR

- 1. Cimetidine
- 2. Trimethoprim

Causes of decreased GFR without change in Cr

- 1. Muscle wasting

The ***non–steady-state*** conditions that prevail in AKI/ARF preclude estimation of GFR using standard formulae derived from patients with chronic kidney disease eg MDRD formula.

CKD stages as per NKF

- *Stage 1*.GFR more than 90,
- *Stage 2*. GFR 60-89.
- *Stage 3*. GFR 30-59. Around 10-12 million in US
- *Stage 4*.GFR 15-29. Around 400,000 pts in US
- *Stage 5*. GFR Less than 15 or on dialysis. 400,000 pts in US

Epidemiology

Hospital-acquired renal insufficiency in a tertiary-care teaching-hospital (using as a definition for AKI/ARF an increase in serum creatinine of 0.5 mg/dl in patients with a baseline serum creatinine of 2 mg/dl, an increase in serum creatinine of 1.0 mg/dl in patients with a baseline serum creatinine of 2 to 4.9 mg/dl, and an increase in serum creatinine of 1.5 mg/dl in patients with a baseline serum creatinine of 5 mg/dl), the **observed incidence of AKI/ARF was 4.9% of hospital admissions**

Prerenal vs ATN

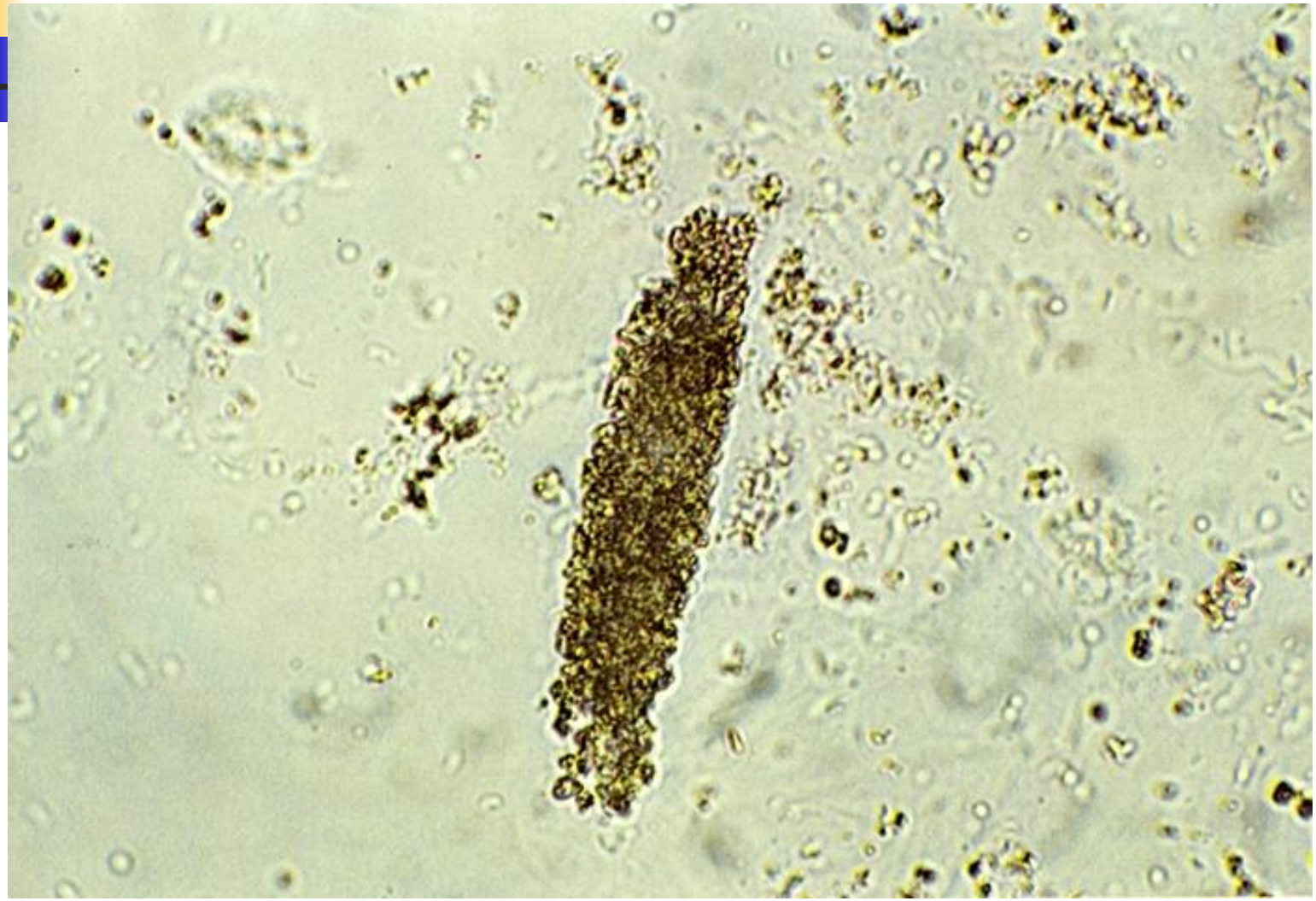
- A. ***Pre-renal azotemia:***
- 1.Urine Sodium less than 20 meq/L
- 2.BUN/P Cr ratio more than 20
- 3.Urine osmolality more than 500 mosmol/L
- 4.FENA less than 1%
- 5. Urine/plamsa Cr more than 40

- ***B. ATN:***
- 1.BUN/Cr ratio: 10-15:1
- 2.Urine sodium more than 40
- 3.Urine osmolality less than 350
- 4.FENA more than 2 %
- 5. Urine/plasma Cr less than 20

Phases

- 1. Prerenal AKI/ARF or Initial Oliguric phase: AKI/ARF potentially reversible
- 2. Maintenance phase: can last for few days to few wks
- 3. Recovery phase or Polyuric phase: GFR returns to normal

This slide illustrates a coarsely granular cast. The granules are likely degenerated cellular debris and may be seen with acute tubular necrosis.. MUDDY BROWN CAST



ATN

- Most common form of intrinsic AKI/ARF
- Etiologies: Ischemic or Nephrotoxic ATN
- Toxic: Exogenous (Aminoglycosides, Radiocontrast agents)
- Endogenous (Rhabdomyolysis)

* Acute tubular necrosis remains a devastating illness that is associated with a high mortality rate.
* During ***World War II***, the mortality rate associated with ARF among combat causalities (predominantly ATN) was ***91%,*** falling to ***68% and 67%,*** respectively, during the ***Korean and Vietnam wars***

Prognosis

*The **outcome** of ATN is highly dependent on the severity of ***comorbid*** conditions.

*For example, **uncomplicated ATN is associated with mortality rates of 7 to 23%,** whereas the mortality of ATN in postoperative or critically ill patients with ***multisystem organ failure*** is ***high as 50 to 80%,*** with mortality rates increasing with the number of failed organ systems

Prognosis

*L***ong-term outcomes** of pts who survive : good.

*Of a population of 979 critically ill patients with ARF who required renal replacement therapy (predominately pts with ATN), **in-hospital mortality was 69%**

*However, of the patients who survived to hospital discharge, 6-mo survival was 77%, 1-yr survival was 69%, and 5-yr survival was 50%

* 90% of surviving patients had no residual renal insufficiency, and **only 10% required chronic dialysis therapy .**

Summary of ATN outcome

The outcome of ATN : high independent risk of in-hospital mortality due to ATN but a reasonable long-term prognosis among survivors.

Management

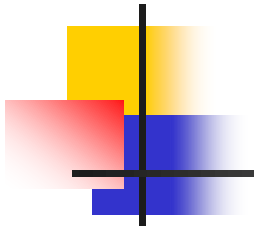
- Fluid Resuscitation
- Management of hyperkalemia
- Mx of Metabolic acidosis
- Mx of Hyperphosphatemia
- Dialysis
- ?Diuretics

Mx

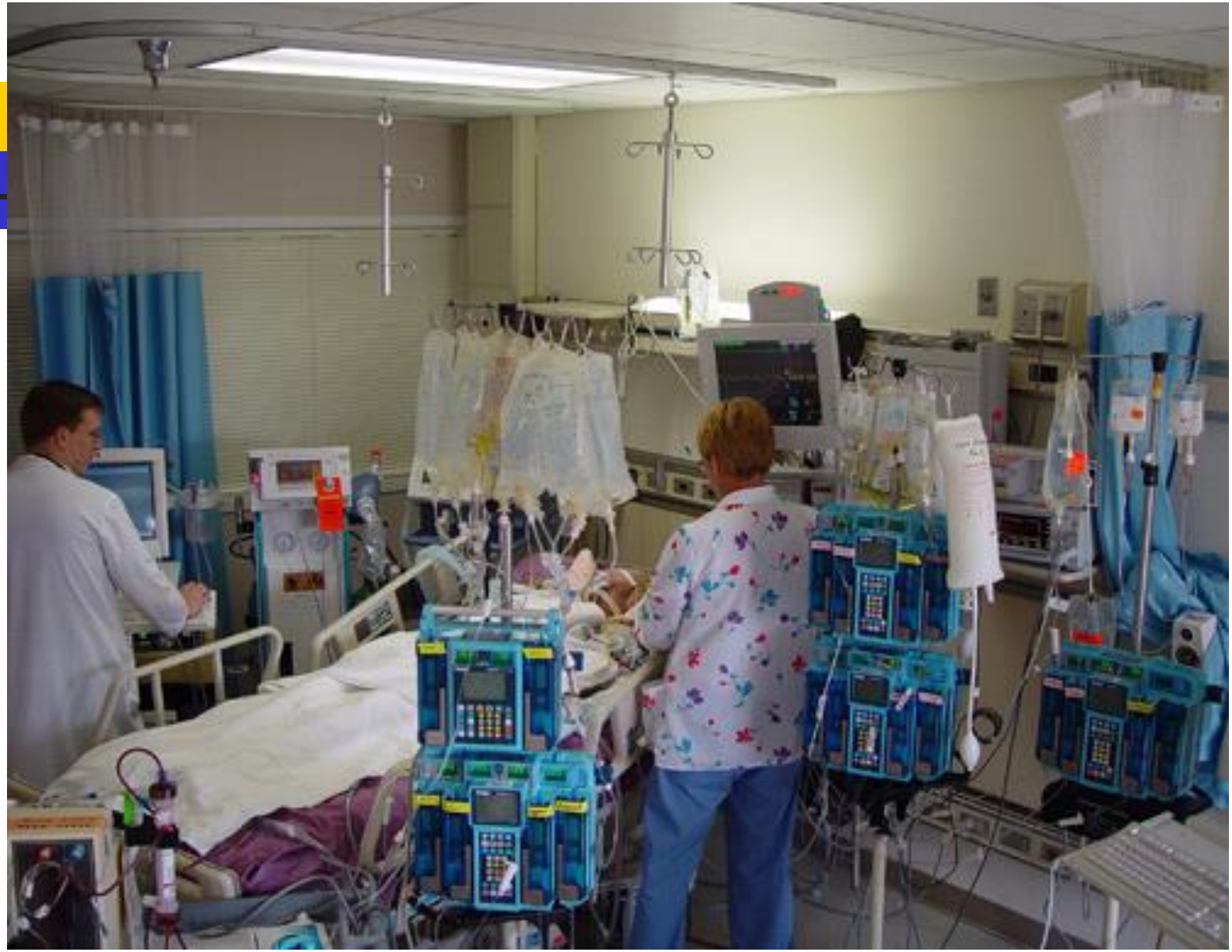
- Mx: avoid nephrotoxins, NSAID,ACEI, Radiocontrast agents
- Drug dosing: adjust to Cr Cl

Indications of Dialysis

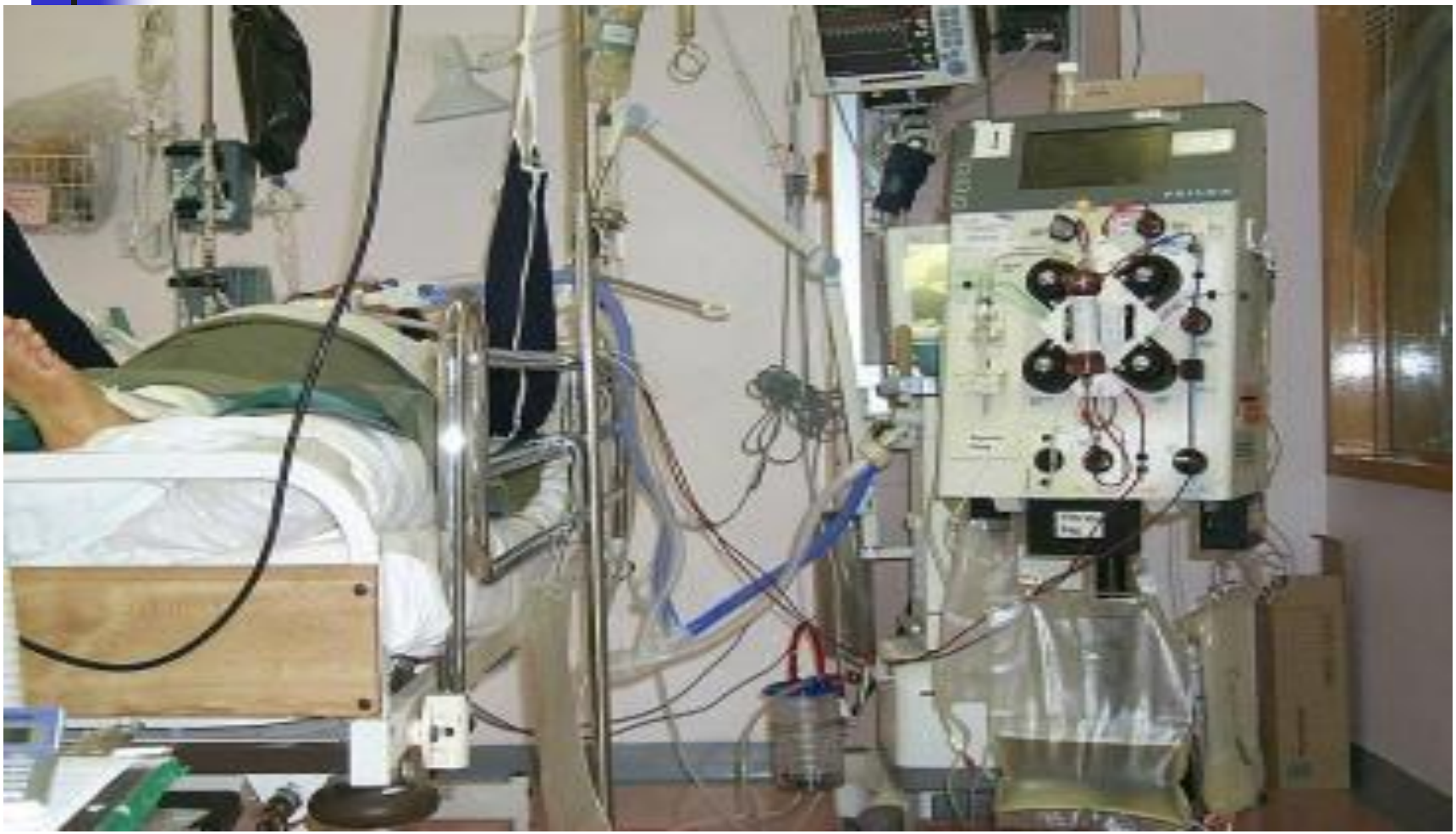
- Mode: HemoDialysis vs Peritoneal Dialysis Vs CVVHD
- ***Acute PD***: almost never done in US,but done sometimes in south-east Asia etc
- ***Absolute Indications***: Refractory hyperkalemia, Pulmonary edema, Refractory acidosis and Uremia
- Relative indications : ?



When to start Dialysis for AKI: controversial



CVVHD pics



Radiocontrast nephropathy

- 10% of all hospital acquired ARF
- Specific risk factors include baseline renal insufficiency, diabetes mellitus, congestive heart failure, and the use of large volumes of contrast media.
- After percutaneous coronary intervention, the incidence ARF (defined as an increase in serum creatinine of 0.5 mg/dl) was 3.3%
- *Contrast nephropaty VS Ac Atheroembolic renal disease: clinical features*

Prevention

- IV Saline: has good evidence based on studies
- ? Bicarb drip:some studies show improvement
- Low osmolal contrast agents
- ? N-acetylcysteine, 600mg PO BID: studies show improvement or no benefit in some
- Not effective: Lasix, Mannitol, Dopamine, Hemodialysis

Cholesterol emboli syndrome

Five weeks after uneventful CABG, an 81-year-old woman presented to the hospital with a serum Cr level of 5.6 mg per deciliter. Her kidney function had remained stable throughout her hospital stay for the surgery, and her serum cr level on discharge had been 1.2 mg per dl, with an eGFR of 46 ml per minute per 1.73 m^2 of body-surface area. Physical examination of her legs and feet now revealed extensive livedo reticularis (Panel A) and cyanosis of the toes (Panel B). A differential blood count was normal, tests for ANCA and cryoglobulins were negative, complement levels were normal, and the results of urinalysis and renal ultrasonography were unremarkable.Percutaneous kidney biopsy revealed obstructive cholesterol crystals within an arcuate artery (Panel C, asterisk; Masson–Goldner trichrome stain), confirming a diagnosis of cholesterol emboli syndrome.

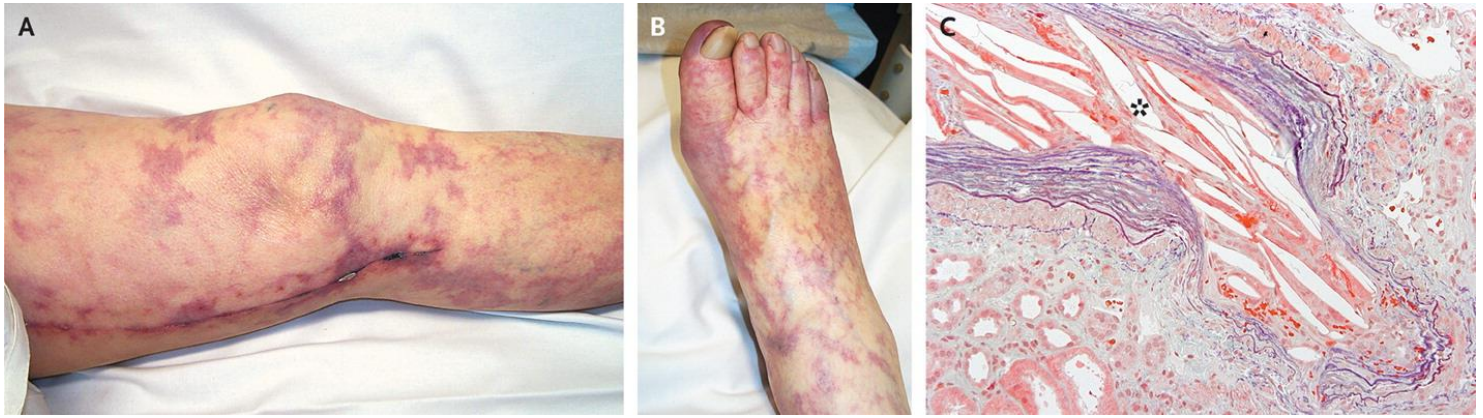
Cholesterol emboli syndrome

It is likely that atheromatous plaques were disrupted at the time of angiographic or surgical arterial manipulation several weeks before the patient's presentation, resulting in progressive subacute renal dysfunction, livedo reticularis, and digital cyanosis. She soon required hemodialysis, had several grand mal seizures, and ultimately died of sepsis.

Cholesterol Emboli after Coronary Bypass Surgery

Rolf Dario Frank, M.D., and Joachim Velden, M.D.

N Engl J Med 2011; 364:265January 20, 2011DOI


A
B
C

Rhabdomyolysis

- *Skeletal muscle injury and myoglobinuric AKI*
- *Clinical syndrome with ARF, elevated CPK and a red/pink urine*
- *Causes: eg Trauma/earthquakes, drugs-cocaine, hypothermia,heat stroke*
- *Mx: early and aggressive volume repletion*
- *Forced alkaline diuresis, bicarb drip*
- *Dialysis*

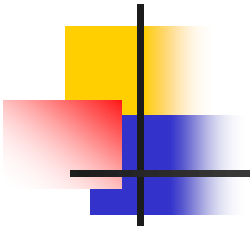
Acute interstitial nephritis (AIN)

*clinical triad of ***fever, rash, and eosinophilia,***

*one or more of these findings is frequently absent.

*majority of cases, AIN results from drug hypersensitivity.

*The clinical features of AIN are best characterized for ***methicillin***-induced AIN.



*Renal symptoms typically developed 2 to 3 wk after the initiation of treatment, including hematuria and pyuria with white blood cell casts. Renal failure developed in only 50% of patients.

*Extrarenal manifestations included fever in patients, eosinophilia in 80% of patients, and rash in approximately 25% of patients

Causes of AIN

- 1.Drugs: NSAID, PCN, Cephalosporins, Sulfa, Quinolones, Omeprazole
- 2.Infections: Bacterial, Strep,Staph, Legionella etc
- 3.Systemic diseases: SLE, Sarcoid, Polyangiitis

Mx AIN

*The mainstay of treatment : supportive care.

*Potentially offending drugs should be discontinued or underlying infections treated.

*In the majority of patients AIN is reversible, with spontaneous recovery of renal function, although it may take weeks for renal function to return to baseline.

*The role of **steroid** therapy in the treatment of AIN has been controversial.

Hepatorenal syndrome

*The renal failure observed in HRS results from ***profound renal vasoconstriction*** in the setting of ***histologically normal kidneys***.

* Although many of the features of HRS resemble prerenal azotemia, the **defining feature** is a **lack of improvement in renal function with volume expansion**.

***Recovery** of renal function is usually observed, however, after restoration of hepatic function after **liver transplantation**

- Two clinical patterns:
- Type 1
- Type 2

- HRS is a ***diagnosis of exclusion***

HRS

Table 5. Diagnostic criteria for hepatorenal syndrome[a]

Major criteria

- Chronic or acute liver disease with advanced hepatic failure and portal hypertension
- Low GFR, as indicated by serum creatinine >1.5 mg/dl or creatinine clearance <40 ml/min
- Absence of shock, ongoing bacterial infection, fluid loss, and current or recurrent treatment with nephrotoxic drugs. Absence of gastrointestinal fluid losses (repeated vomiting or intense diarrhea) or renal fluid losses (as indicated by weight loss >500 g/d for several days in patients with ascites without peripheral edema or >100 g/d in patients with peripheral edema)
- No sustained improvement in renal function (decrease of serum creatinine to 1.5 mg/dl or less or increase in creatinine clearance to 40 ml/min or more) after withdrawal of diuretics and expansion of plasma volume with 1.5 L of isotonic saline
- Proteinuria <500 mg/d and no ultrasonographic evidence of obstructive uropathy or parenchymal renal disease

Other criteria

- Urine volume <500 ml/d
- Urine sodium <10 mEq/L
- Urine osmolality > plasma osmolality
- Urine red blood cells <50 per high-power field
- Serum sodium concentration <130 mEq/L

Arroyo V, Gines P, Gerbes AL, et al. Definition and diagnostic criteria of refractory ascites and hepatorenal syndrome in cirrhosis. *Hepatology*, 23: 164–176, 1996.

Mx

- Mx: Liver transplant is definitive therapy
- HD by itself: no change in prognosis
- ?Combination of oral midodrine (a selective alpha 1 adrenergic agonist) and octreotide (a somatostatin analogue)

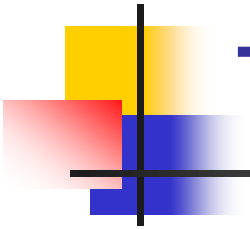
Acute Uric acid Nephropathy

- Case examples

Abdominal compartment syndrome

- Case examples

Cardio-renal syndromes



TTP-HUS

- Examples

Other causes of AKI,discussed elsewhere

- Ac GN
- Rapidly progressive renal failure
- Obstructive uropathy,hydronephrosis : Urology consult

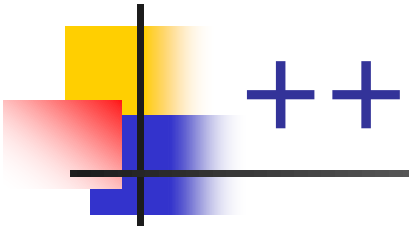
References

- Annals: ATN article,

Diagnosis and Treatment of Acute Tubular Necrosis
Ann Intern Med, Nov 2002; 137: 744 - 752.

* ***Harrison 18th Edition, 2012, Chp 279, AKI, Waikar et al***

- *Cecil*, AKI. 24th ed Cecil
- KDIGO AKI guideline, 2012
- Slides adapted from various resources



- *Thank you*

Richard Hertzler / Lancaster New Era