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Kidney dysfunction

Copotoiu SMa

Functions of the kidneys

- Water and electrolyte homeostasis
- Excretion in the urine of waste products of metabolism
- Excretion of chemicals/drugs
- Hormone production: renin, EPO, active form of vitamin D (1,25 dihydroxyvitamin D_3)
- Gluconeogenesis – during starvation
- Acid-base balance: HCO_3^- & H^+

Clinical assessment of renal function

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- 5-15 % pts in ICU
- Changes in renal function directly affect drug disposition

GFR (Glomerular Filtration Rate) – **standard measure**

RBF – 20 % of CO

AUTOREGULATION

Clinical assessment of renal function
1. Renal Blood Flow **1-1.2l/min**

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- Research studies – PAH Clearance

- Altenatives
  - Selective arteriography
  - Doppler ultrasonography
  - External radionuclide scanning

Clinical assessment of renal function
Renal Blood Flow

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- Research studies – **PAH Clearance**

Almost totally cleared from arterial plasma by filtration & secretion

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PAH Cl approximates RPF

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Renal Blood Flow

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To document renal perfusion

Renal Blood Flow
Clinical correlates

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- **Optimize CO & ECF**

- **Low dose/renal dose dopamine infusion <3 µg/kg/min)→renal vasodilatation**
  - Beneficial effects not documented in
    - NaCl depletion
    - Volume depletion
  - Infusion for 24-36 h

Renal Blood Flow
Clinical correlates

- Optimize CO & ECF
- Low dose/renal dose dopamine infusion <3 µg/kg/min)→renal vasodilatation
- Fenoldopam – selective D1 agonist
  - IV 5-10 µg/min < 48 h (tolerance)

  ↗ urine/Na output

Renal Blood Flow
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  ↑ urine/Na output
- **PG – anecdotal evidence**

Potential vasodilator

2. GFR
Renal clearance

= **Volume of plasma completely cleared of the substance by the kidneys per unit of time**

Glucose
- Normally zero

Inulin
- Freely filtered and not acted upon

Gentamicin Cl

PAH (para-aminohippuric acid)
- Effective renal plasma flow

Creatinine

Urea

2. GFR
Renal clearance

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Glucose
- Normally zero

Inulin
- Freely filtered and not acted upon

Gentamicin Cl

PAH (para-aminohippuric acid)
- Effective renal plasma flow

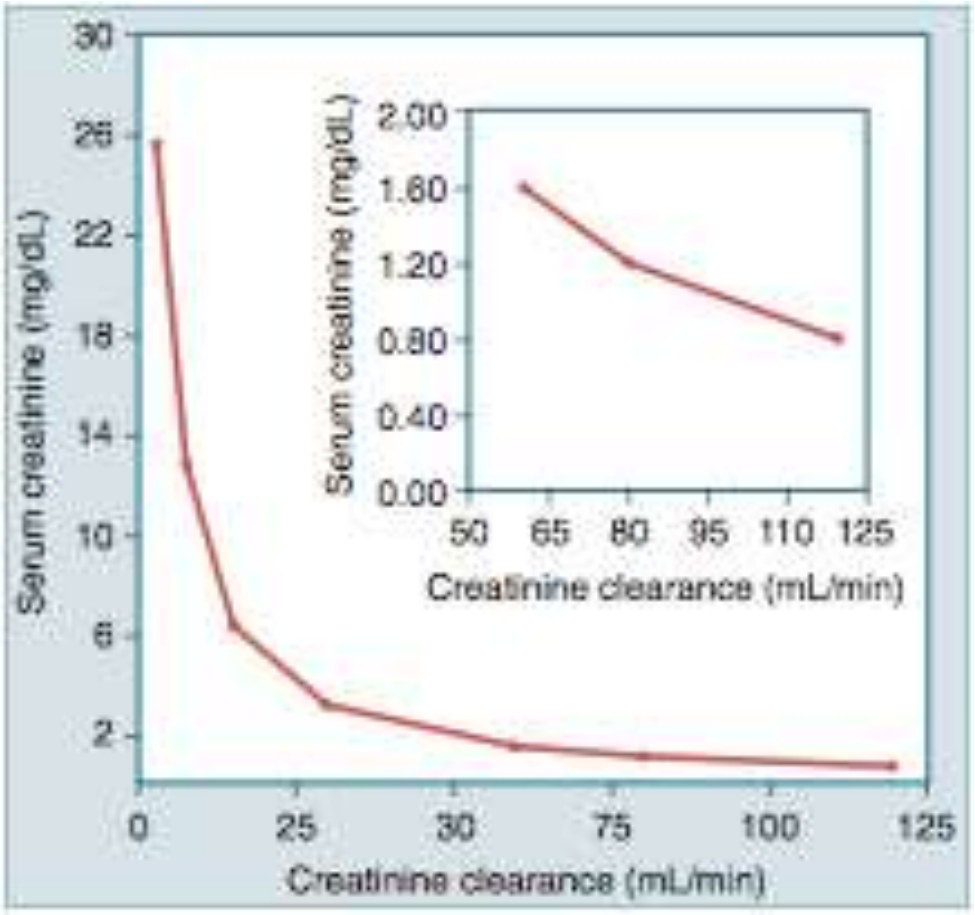
Creatinine ← **Freely filtered, minimally absorbed by the tubules**

Urea ← **!overestimates GFR due to secretion**

Underestimates GFR

Serum creatinine

Insensitive marker of early change
Close estimate of GFR in steady state



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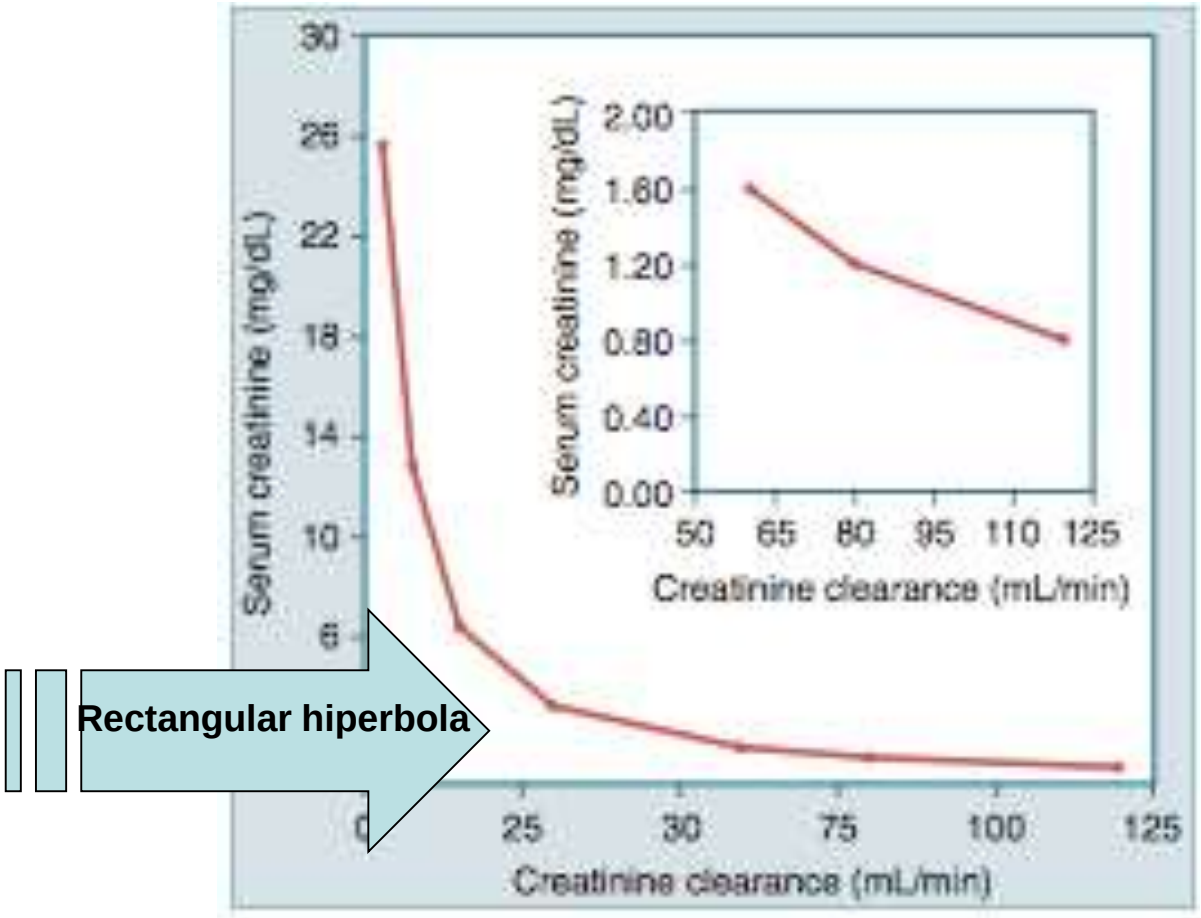

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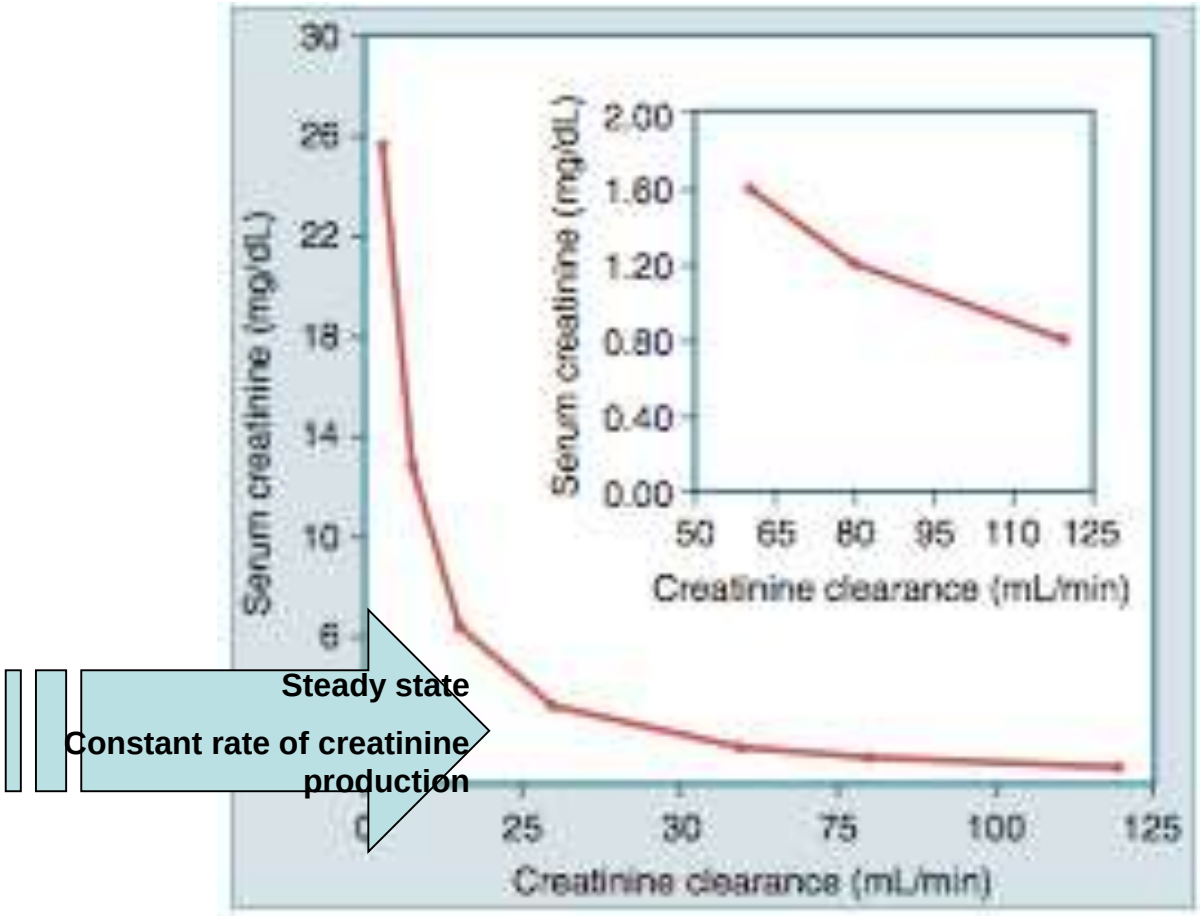

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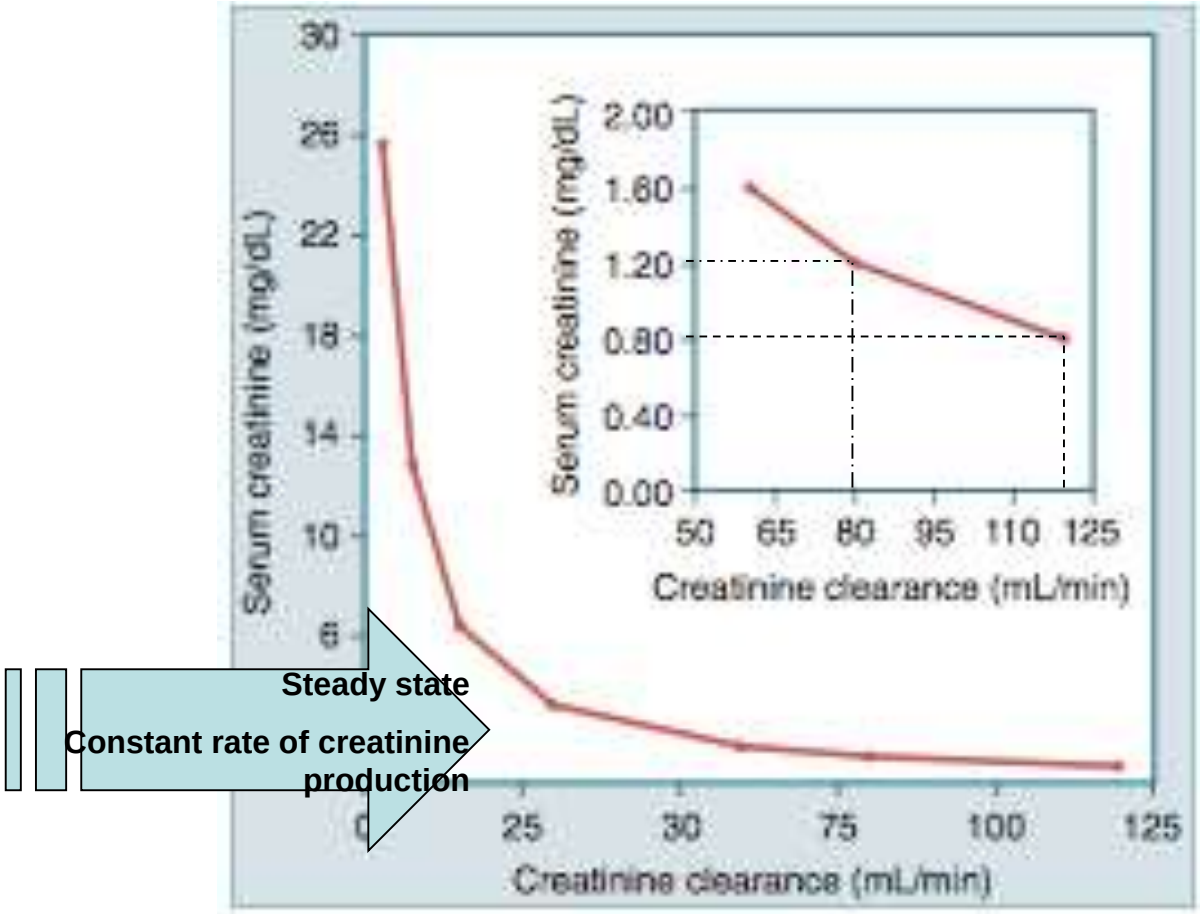

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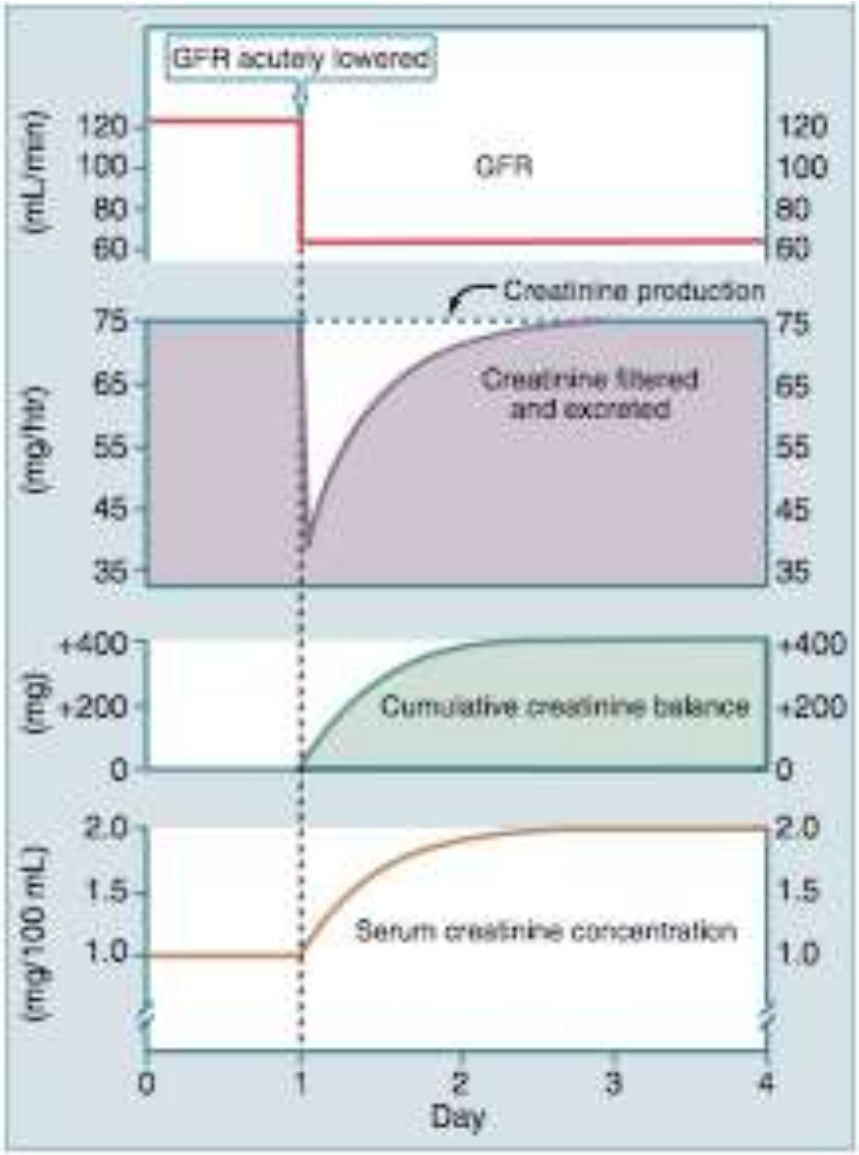


Creatinine clearance estimate

- **Cockroft-Gault**

  C_{Cr} =[(140-age) x lean w in kg]/S_{Cr} x 72 for men

  x 0.85 for women

- **MDRD (Modification of Diet in Renal Disease)**
  - **Clinical laboratories**
  - **Underestimation of GFR at high values**
  - **GFR = 186 x $[S_{Cr}]^{-0.999}$ x $[age]^{-0.203}$ x [0.742 if patient is female] x [1.212 if patient is black]**

Creatinine clearance estimate

- Cock
  C_{Cr} =
  men
  x 0.8
- MDR
  Dise
  - Cl
  - U
  - G
    if
    black]

↓creatinine generation:

- Ageing
- Hepatic diseases
- Excessive muscle wasting
- Severe muscular atrophy or dystrophy
- Hyperthyroidism
- Paralysis
- Chronic glucocorticoid therapy

Serum urea nitrogen SUN = BUN

- Variable production – absorbed Hb from the GI tract in bleeding
- Freely filtered, but reabsorbed

⑩ ↑ by
  - Tetracyclines - antianabolic effect
  - Glucocorticoids
  - Severe illness/trauma

} **Endogenous hipercatabolism, hyperfeeding**

- Marked disproprtion in the elevation of SUN compared with S_{Cr}

Serum urea nitrogen SUN + BUN

- Variable production

⑩ ↑ by
  - Tetracyclines
  - Glucocorticoids
  - Severe illness/trauma

- Marked disproprtion in the elevation of SUN compared with S_{Cr}

Less accurate than Scr for GFR

Na balance and ECF

- 140-142 mmol/L
- ECF 20% TBW, 1/3 total body water
- $FE_{Na} = U_{Na}/S_{Na} \times S_{Cr}/U_{cr}$
- Diuretics

Acute kidney injury (AKI)

Abrupt decrease in GFR ➔ accumulation of nitrogenous waste products

+

Inability to maintain fluid aand electrolyte homeostasis

Medulla = low blood flow and low oxygen tension (10 mmHg) **very susceptible to ischemic injury**

Prerenal causes

- Reduction in renal perfusion without cellular injury
- Reversible process if the underlying cause is corrected
  - Decreased blood volume
    - Vomiting
    - Dehydration
    - Hemorrhage
  - Reduction in the effective arterial blood flow
    - Congestive heart failure
    - Cirrhosis
  - Drugs that interfere with autoregulatory ability
    - NSAIDs
    - ACE

Prerenal causes

Activation of RAA system & ↑ activity of renal adrenergic system
  - Proximal reabsorbtion of Na
  - Distal reabsorbtion of Na (aldosterone)

70% of community-acquired cases of AKI

40% of hospital-acquired cases of AKI

Prerenal causes should be excluded in all cases of AKI

Postrenal causes

- Bilateral
- Unilateral (single kidney)

} Obstruction of urine flow

- Incidence 3-25% AKI
- Community >>>> ICU

- Renal
  - Crystal deposition (ethylene glycol ingestion)
  - Uric acid nephropathy (tumor lysis syndrome)

- Extrarenal
  - Prostatic disease
  - Pelvic malignency
  - Retroperitoneal disorders

Intrarenal causes

Classified according to anatomic location

- Glomerulus
- Tubule
- Vasculature
- Interstitium

Glomerulonephritis/vasculitis

Renal failure

Active urine sediment (red cells, red cells casts)

Acute interstitial nephritis

Pyuria & white cells casts

Drug related (ATB, NSAIDs)

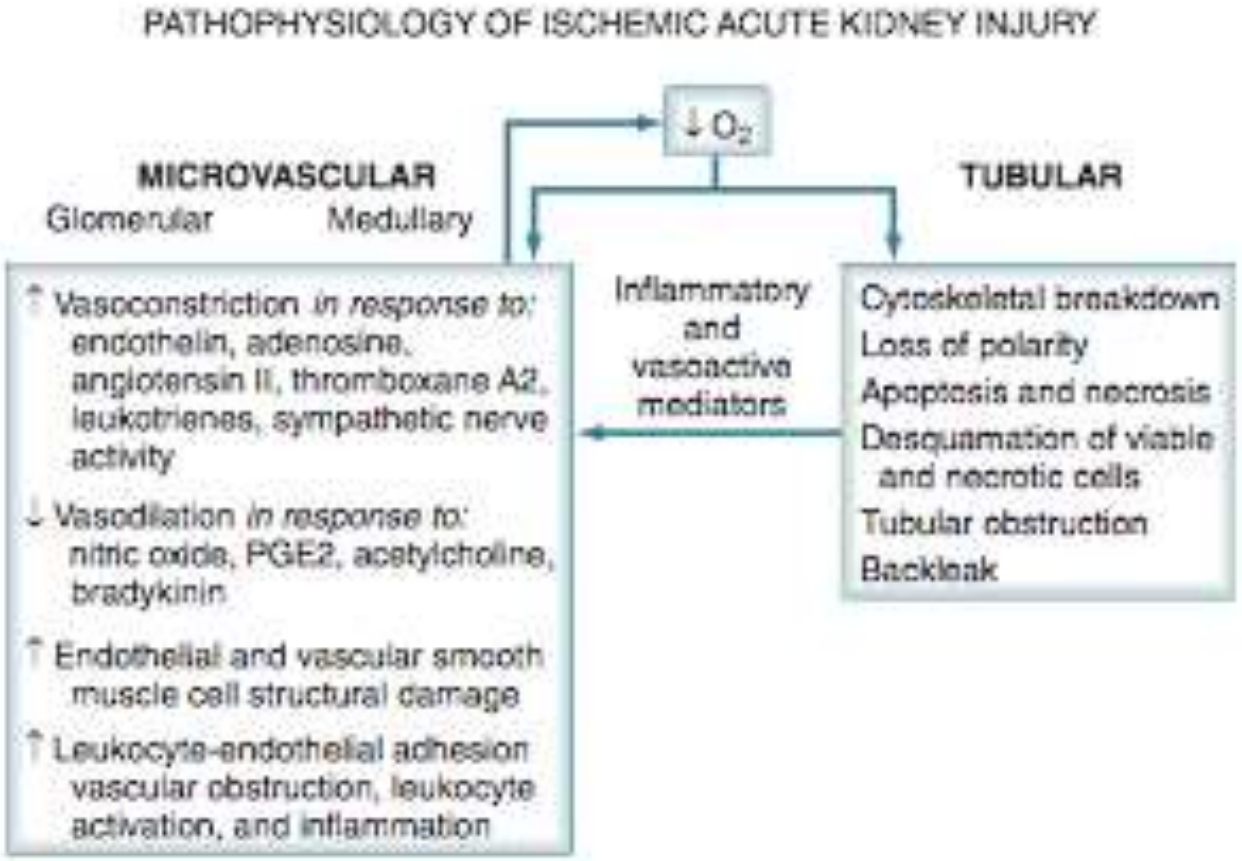
Recovery hastened by short course of steroids: 60-80 mg prednisose for 10 days

Intrarenal causes

ATN (acute tubular necrosis)

ICU most common form of AKI

Tubular & vascular injury



Laboratory and microscopic findings in prerenal azotemia and ATN

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Laboratory test	Prerenal azotemia	Acute Tubular Necrosis
Urine osmolality (mOsm/kg H_2O)	>500	<4400
Urine sodium (mEq/L)	<20	>40
Urine/plasma creatinine ratio	>40 (>15)	<20
FE_{Na} (%)	<1	>2 (exception rhabdomyolisis, myoglobinuria, contrast mediated AKI, sepsis)
Urinary sediment	Normal, occasional hyaline cast	Renal tubular epithelial cells, granular and muddy brown casts
FE_{Urea} for those on diuretics	< 35% No distinction between transient and persistent AKI	

Epidemiology

- RIFLE criteria – 1/3 of ICU pts (manifestation of multiorgan failure syndrome)
  - Multifactorial cause (sepsis)
  - Mortality 40-80%

- Risk factors for developing AKI
  - Age > 65 years
  - Infection on admission
  - Cardiovascular failure
  - Cirrhosis
  - Respiratory failure
  - Chronic heart failure
  - Lymphoma or leukemia

Epidemiology

- Risk factors for mortality
  - Higher severity index score
  - Age > 65 years
  - Male gender
  - Oliguric acute renal failure
  - Sepsis
  - Nonrenal organ failure
  - Thromcytopenia
  - Mechanical ventilation
  - Prior compromised health status

- Low serum cretinine with poor outcome (reflective of poor nutritional status)

- AKI causes mortality vs marker of severly ill patients

Definition

- Lack of a standard one

- AKIN – Acute Kidney Injury Network

- ADQI – Acute Dialysis Quality Initiative
  - Develop consensus & EB guidelines
  - RIFLE criteria

  R - Risk
  I - Injury
  F - Failure
  L - Loss (> 4 weeks)
  E - End stage renal failure (> 3 months)

Better account for small changes (+ anyone who receives acute RRT irrespective of their preceding S_{Cr} increase or urine output)

New staging

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RIFLE stages	RIFLE SCr increase	RIFLE and AKIN urine output	AKIN SCr increase	AKIN stages
Risk	≥150% to 200%	<0.5 ml/kg/h for > 6 h	≥0.3 mg/dL or ≥150% to 200%	1
Injury	>200% to 300%	<0.5 ml/kg/h for > 12 h	>200% to 300%	2
Failure	>300% or Scr> 4mg/dL or ↓ GFR by 75%	<0.3 ml/kg/h for > 24 h or anuria ≥ 12 h	>300% or Acute RRT	3

From baseline to 48 h

Biomarkers under investigation

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- Serum cystatin C
- Urinary IL-18
- Tubular enzymes
  - Intestinal form of alkaline phosphatase
  - N-acetyl-α-glucoseaminidase
  - Alanine aminopeptidase
- **Neutrophyl gelatinase – associated lipocalin (NGAL)**
- Kidney injury molecule 1 (KIM-1)

Treatment

- **No role for dopamine**
- **Diuretics have not been shown to prevent or ameliorate AKI. They can be used in the initial management of AKI to facilitate fluid balance and treat hyperkalemia or hypercalcemia, but their use should not delay commencing RRT when deemed clinically necessary**

  Oliguric ➔ nonoliguric (better outcome)
  No reduction in the need for RRT or mortality.

- **Nesiritide (BNP) – on trial**

Hemodynamic management

- **EGDT may reverse adverse hemodynamics before tissue injury occurs ➔ better outcome**
- **Recognition of pseudo-ARDS (noncardiogenic pulmonary edema in the absence of evidence of decreased pulmonary compliance)**
- **Fluid management to improve organ perfusion**
  Type of fluid???
- **Ne vs dopamine**
- **Vasopressin?**
- **Tight glycemic control? < 150 mg/dL**

Nutritional support

⑩ ↑ protein catabolism (insulin resistance)

- Enteral nutrition recomended
- Caloric supplementation 20-30 kcal/kg/d
  Lipids
  Immuno-enhancing
- No role for protein restriction
  0.8-1.2 g/kg/d AKI without need for RRT
  1-1.5 g/kg/d AKI on RRT

Renal Replacement Therapy (RRT)

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- Early initiation is beneficial

- Clinical context + trends of laboratory tests + metabolic indicators

- IHD – intermittent hemodyalisis
- SLED – slow low-efficiency dialysis
- CRRT – continous RRT
- PD – peritoneal dyalisis

RRT potential indications

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- Nonobstructive oliguria (urine output <200 mL/12 h) or anuria
- Severe acidemia
- Azotemia (blood urea nitrogen >80 mg/dL)
- Hyperkalemia (K^+ >6.5 mmol/L) **IHD**
- Uremia (encephalopathy, pericarditis, neuropathy, myopathy)
- Severe dysnatremia (Na^+ >160 or <115 mmol/L)
- Hyperthermia (temperature >39.5° C)
- Clinically significant organ edema (especially lung)
- Drug overdose with dialyzable toxin
- Coagulopathy requiring large amounts of blood products in a patient at risk for adult respiratory distress syndrome

Note: Any one of these indications is sufficient to consider initiating renal replacement therapy. Two of these indications make renal replacement therapy desirable.

Contrast induced nephropathy (CIN)

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= acute kidney function inpairment within 72 h of intravascular injection of iodinated radiocontrast media in the absence of other ethiology

= 25% ↑ S_{Cr} or
absolute increase of 0.5 mg/dL S_{Cr}

Incidence: 1-30%

Pathogenesis: direct toxic injury to renal tubular cells and medullary ischemic injury (subcoticormedullary congestion)

CIN – Risk factors

- **Preexisting kidney function (C_{Cr} < 47 ml/min)**
- **Type of imaging procedure**
- **Diabetes (nephropathy)**

- **Age> 75 years**
- **Periprocedure volume depletion**
- **Heart failure**
- **Hypotension**
- **Cirrhosis**
- **Proteinuria**
- **Coadministration of nephrotoxins**

Clinical features, diagnosis, prognosis

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- Generally asymptomatic
- Peaks at 3 d, returns to baseline in 10 d

- **Other potential causes must be ruled out**

- < 1% require dialysis (13-50% permanent)
- ??? Casualy linked to early death and adverse cardiovascular events

CIN prevention

1. **Assess risk/benefit of the proposed intervention**
2. **Assess kidney function – eGFR**
3. **Modify correctable risk factors & hold nephrotoxins**
4. **High risk pts, IA contrast – low osmolar or iso-osmolar contrast medium**
5. **Identify patients at risk**
6. **Use the lowest dose of appropriate contrast medium**

CIN prevention

7. **Correct hypovolemia**

   Stop diuretics

   Consider IV fluids (type & quantity ???)

   0.9% saline vs isotonic sodium bicarbonate

   Begin al least 1 h prior to contrast injection

   Continue for at least 6 h (12h before & after – best supported)

   3 m/kg/h x 1h followed by 1ml/kg/h

8. **N-acetylcisteine (NAC)** – higher doses & IA administration

   1200 mg BID PO started Z-1, x 2 d

   Emergent procedure:

   - 1200 mg IV
   - Followed by above 4 doses

9. **Prophylactic RRT**