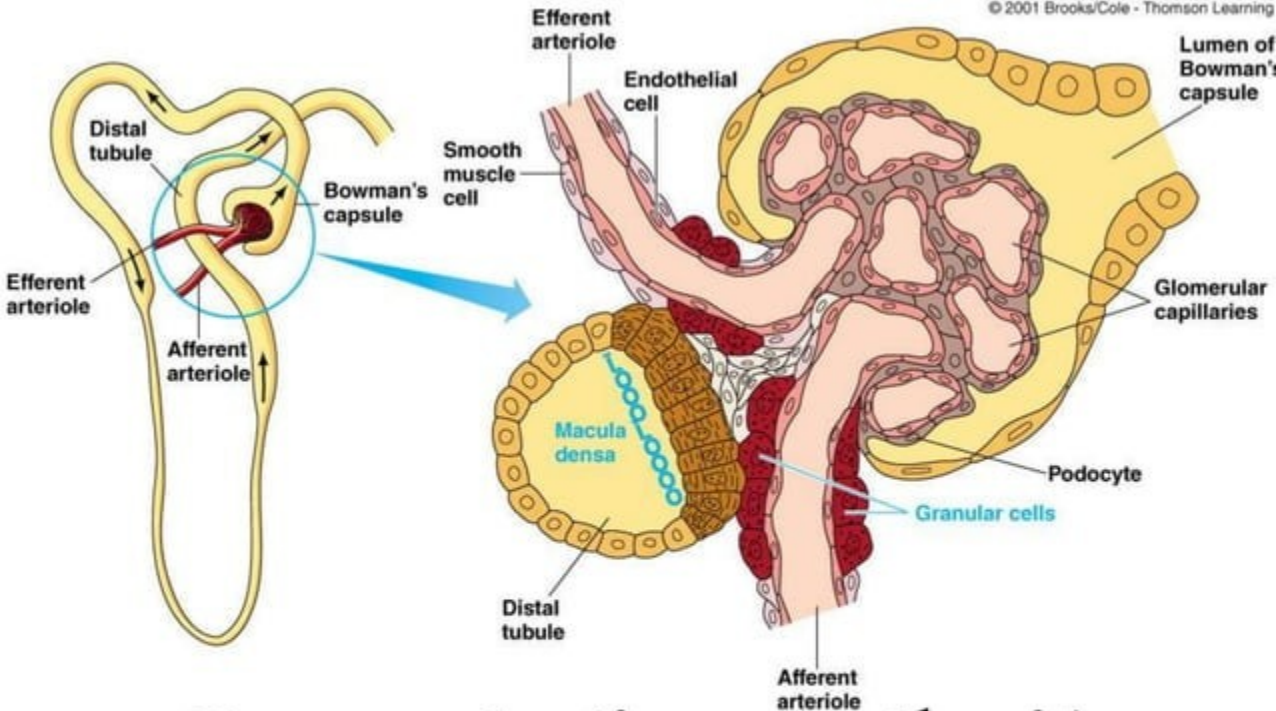




Renoprotective anesthesia

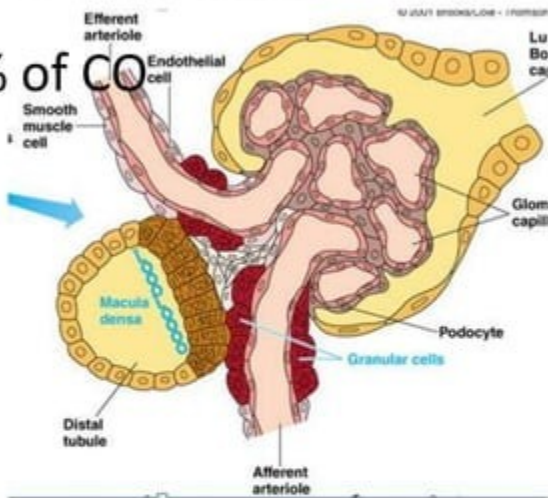
Dr Bikash Subedi
KMCTH, KTM

Statement of the problem

- AKI may occur in 1 % of Gen surg pts & upto 30% of Cardiothoracic & vascular surgeries!
- High mortality of hospital acquired AKI (20-30%)
 - Clinical anesthesiology.Morgan & Mikhail;5th edn

Physiological peculiarities

- Renal blood flow ~20-25% of CO
80% cortical nephrons,
20% medullary
- Autoregulation of RBF @
MAP of 80-180 mm Hg



Physiology & vulnerability

- Kidneys exquisitely sensitive to hypoxic injury
- medullary thick ascending limb have the highest O_2 extraction ratio (80%)!
- Intrinsic vasodilating Prostaglandin synthesis, imp. mechanism during hypotension/ischemia
- Reversible $\downarrow$ in RBF, GFR, urinary flow & Na^+ excretion occur with GA (& RA)

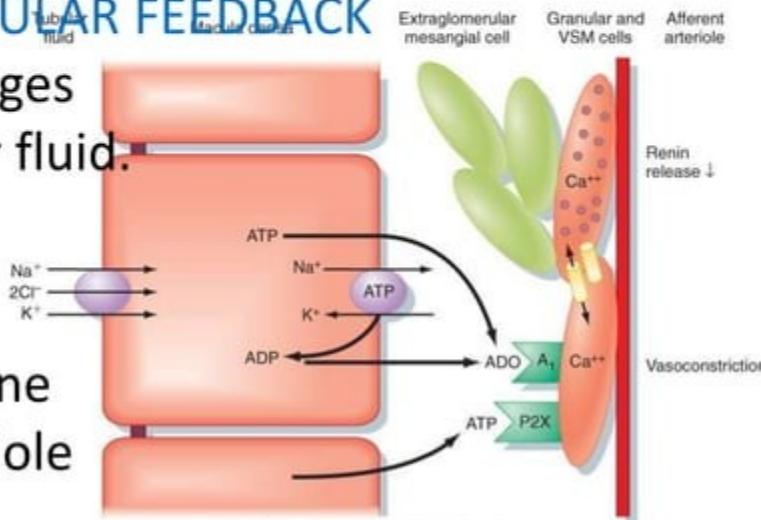
Autoregulation of RBF and GFR

1. **MYOGENIC mechanism** responds to changes in arterial pressure

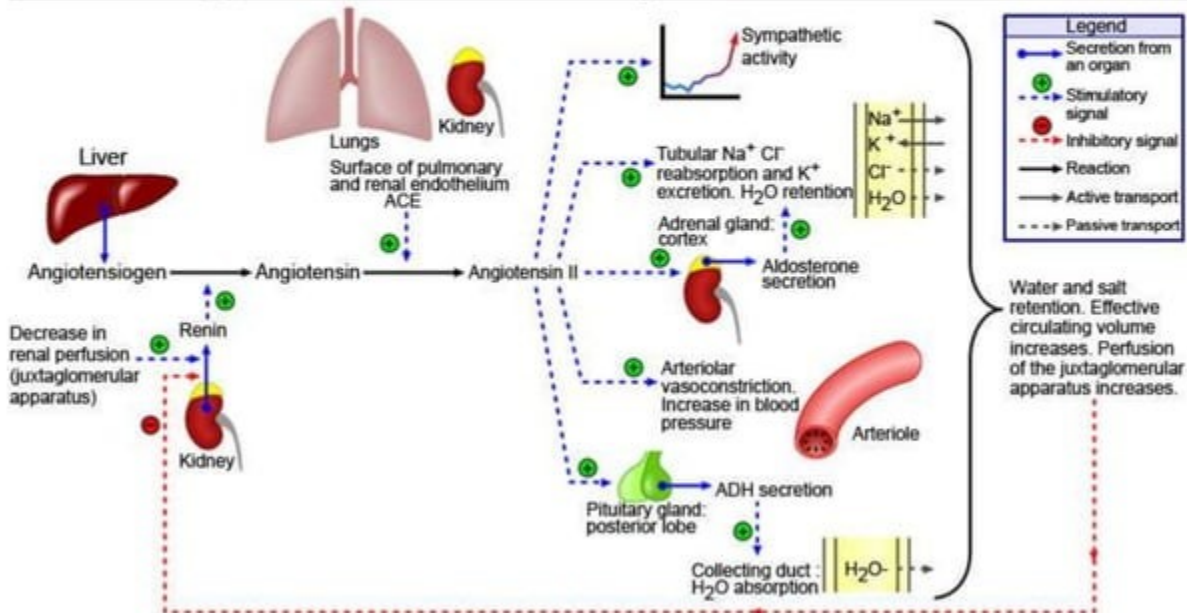
2. **TUBULOGLOMERULAR FEEDBACK**

responds to changes in NaCl in tubular fluid.

Both regulate the tone of the afferent arteriole



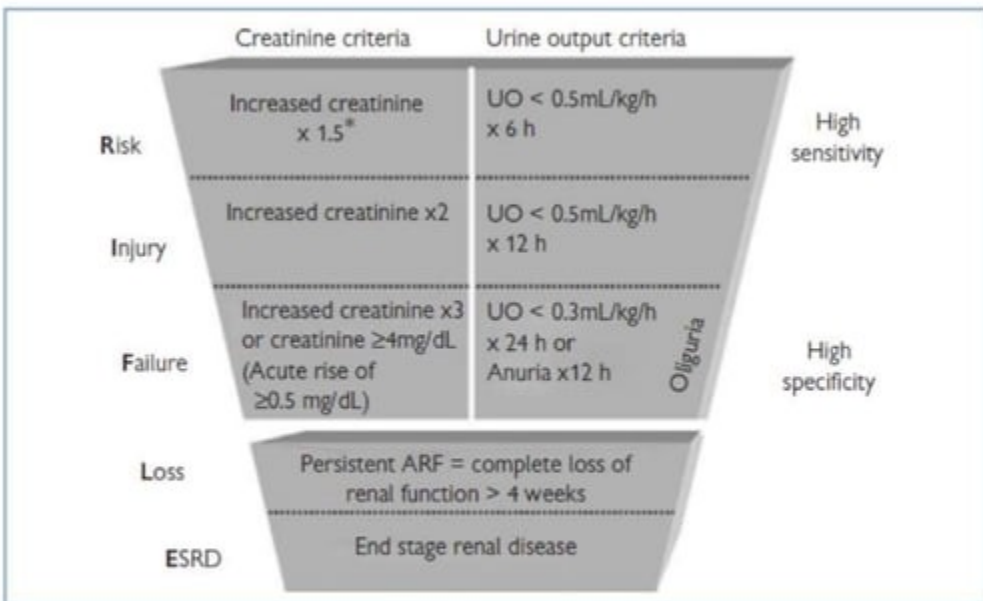
Renin-angiotensin-aldosterone system



AKI

- abrupt and sustained decrease in kidney function
- manifests as ↓UOP followed by ↑ serum creatinine

RIFLE CRITERIA 2004 *Critical Care*



Note: Patients can be classified **either by GFR criteria or by UO criteria**. The criteria that support the **most severe classification should be used**. The superimposition of acute on chronic failure is indicated with the designation RIFLE- F_C ; failure is present in such cases even if the increase in SCr is less than 3-fold, provided that the new SCr is greater than 4 mg/dL (350 $\mu\text{mol/L}$) and results from an acute increase of at least 0.5 mg/dL (44 $\mu\text{mol/L}$).

Acute Kidney Injury Network (AKIN) criteria

- defines AKI as an abrupt (within 48 hours) ↓ in kidney function with an absolute increase in S.creatinine ≥ 0.3 mg/dL (≥ 26.4 $\mu\text{mol/L}$)
- or $\geq 50\%$ (1.5-fold from baseline), or a ↓ in UOP < 0.5 mL/kg per hour for > 6 hrs

Kidney Disease Improving Global Outcome(KIDCO)

- combined rifle and AKIN criteria
- defined AKI as either an
- $\uparrow$ serum creatinine by 0.3 mg/dL within 48 hours or
- an increase of serum creatinine by 1.5 times baseline, which is known/presumed to have occurred within the prior 7 days or
- a decrease of urine volume to less than 0.5 mL/kg per hour for 6 hours

Risk index for developing AKI in the peri-operative patient

- Age >56
- Male
- Active Congestive cardiac failure
- Presence of ascites
- Hypertension
- Emergency Surgery
- Intra-peritoneal surgery
- pre-op renal dysfunction (s.creat>1.2mg/dL)
- Diabetes Mellitus

more than six of the above risk factors have a greater than 10% incidence of developing AKI

Patient factors

- Age
- Gender
- Comorbidities
- Hypovolemia
- sepsis

Anesthetic factors

- hypotension
- Blood products
- Drugs

Surgical

- Prolonged surgery
- Major surg.
- Significant 3rd space loss
- Cardiothoracic/transplant surgery
- Aortic clamping

Assessment of Renal function

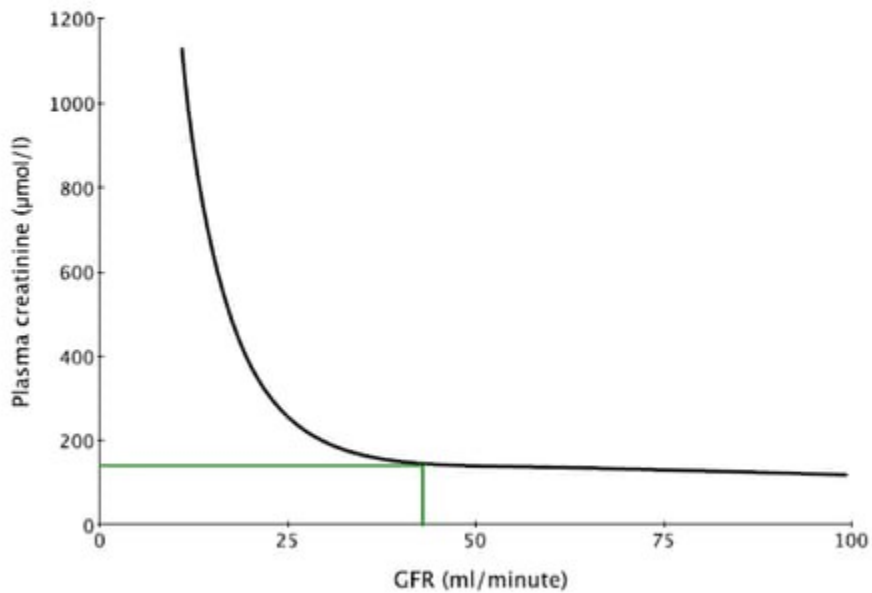
Glomerular filtration Rate (GFR)

- Normally 120 +/- 25 ml/min ($>90\text{ml/min/1.73m}^2$)
- Decreases approx by 1%/decade after 20 yrs
- Direct estimation by Cr^{51} EDTA/ $\text{Tc}^{99\text{m}}$ DTPA
- Approximated by Creatinine clearance
- Uremic symptoms only when $\text{GFR} < 15\text{ml/min/1.73m}^2$

CKD stage	GFR level (mL/min/1.73 m ²)
Stage 1	≥ 90
Stage 2	60 – 89
Stage 3	30 – 59
Stage 4	15 – 29
Stage 5	< 15

Serum Creatinine

- 0.6-1mg/dl (women), 0.8-1.3mg/dl (males)
- Slower to rise with ↓ in GFR
- Affected by age, gender, built, diet
- Creatinine clearance (Cockcroft-gault)
- **(140-Age) X lean body wt. kg**
72 X serum creat.
- Slightly overestimates GFR



Relationship between plasma creatinine and GFR

Blood urea nitrogen (BUN)

- BUN varies with GFR
- But misleading due to change with diet, dehydration, catabolism
- BUN >50mg/dL usu signifies ↓GFR

Urinary Protein

- Excrete 80-150mg/day
- Minimum concentration for dipstick detection 20-30 mg/dl
- Glomerular disease
 - suspected >1g/24 hours
 - certain > 3g/24 hours
- Tubular disease - <3g/24 hours

				Albuminuria categories		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-299 mg/g 3-29 mg/mmol	≥300 mg/g ≥30 mg/mmol
GFR Stages	G1	Normal or high	≥90			
	G2	Mildly decreased	60-90			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

A GFR below 60 for three months or more or a GFR above 60 with kidney damage (marked by high levels of albumin in your urine) indicates chronic kidney disease

Fractional sodium excretion (FENa)

- % of Na filtered by the kidney which is excreted in the urine
- Low FENa indicate renal sodium retention, suggesting pathophysiology extrinsic kidney (volume depletion/↓circulating volume)
- Affected by diuretic use

$$FE_{Na} = 100 \times \frac{\text{sodium}_{\text{urinary}} \times \text{creatinine}_{\text{plasma}}}{\text{sodium}_{\text{plasma}} \times \text{creatinine}_{\text{urinary}}}$$

	Prerenal	ATN
Urinary Na	<20	>40
Urine to plasma creatinine	>30	<20
Renal failure index	<1	>1
FE Na	<1	>1
Urine osmolality	>500	<400

Urinary Neutrophil Gelatinase-Associated Lipocalin and Acute Kidney Injury After Cardiac Surgery.2008

[Gebhard Wagener](#), [Gina Gubitosa](#), [Shuang Wang](#), [Niels Borregaard](#), [Mihwa Kim](#), [H. Thomas Lee](#),

- Serum creatinine–based definition for AKI (increase in serum creatinine from preoperative values by >50% or >0.3 mg/dL within 48 hours).
- Results
- Mean urinary NGAL level was 165 ± 663 (SD) ng/mL preoperatively, peaked immediately after cardiac surgery at $1,490 \pm 102$ ng/mL, and remained significantly higher 3, 18, and 24 hours after surgery. 85 patients (20%) developed AKI. Areas under the receiver operating characteristic curve for urinary NGAL immediately after and 3, 18, and 24 hours later as a predictor for AKI were 0.573 (95% confidence interval [CI], 0.506 to 0.640), 0.603 (95% CI, 0.533 to 0.674), 0.611 (95% CI, 0.544 to 0.679), and 0.584 (95% CI, 0.510 to 0.657), respectively. Urinary NGAL, but not serum creatinine, level correlated significantly with cardiopulmonary bypass and aortic cross-clamp times. Areas under receiver operating characteristic curves for cardiopulmonary bypass time and aortic cross-clamp time to predict AKI were 0.592 (95% CI, 0.518 to 0.666) and 0.593 (95% CI, 0.523 to 0.665), respectively.
- Limitations
- Limited sensitivity of changes in serum creatinine levels for kidney injury.
- Conclusions
- Urinary NGAL has limited diagnostic accuracy to predict AKI defined by change in serum creatinine after cardiac surgery.

Neutrophil Gelatinase Associated Lipocalin (NGAL)

- a protein found excess in the plasma and urine of patients with AKI (up to 48hrs prior to a rise in creatinine)
- The level of NGAL in the urine and plasma increases within 2 hours of kidney injury

Serum Cystatin C

- Protein produced by all nucleated cells; freely filtered but not reabsorbed by kidneys
- serum concⁿ independent of age, sex, muscle mass and diet unlike creatinine

Urine microscopy

- RBCs
 - Infection, glomerular disease, malignancy
- WBCs
 - Infection, glomerulonephritis, malignancy, TB, interstitial nephritis, inflammation
- Crystals
 - Seen with stones, cystinuria, gout
- Casts
 - Hyaline casts (clear and colourless)
 - Seen with exercise, fever, concentrated urine (often in normal subjects)
 - Red cell casts
 - Seen in GN, vasculitis, malignant hypertension
 - White cell casts
 - Pyelonephritis, proliferative glomerulonephritis
 - Epithelial casts
 - Acute tubular necrosis, acute glomerulonephritis
 - Granular casts
 - GN, diabetic nephropathy, amyloidosis, interstitial nephritis

Pre-op

- Delay surgery until recovery of AKI if possible
- Optimize volume status, cardiac output, and systemic arterial pressure
- Withhold nephrotoxic drugs
- glycemic control in diabetic patients

- Correct metabolic and electrolyte disturbances
- Arrange pre-operative dialysis for dialysis-dependent patients
- Administer isotonic i.v. fluids and N-acetylcysteine for prevention of radiocontrast-induced nephropathy

Monitoring

- Strict input/output monitoring
- Invasive hemodynamic monitoring
CVP, IBP as required
- ABGs
- Serial electrolytes

Effects of Anesthetic Agents

Induction

- ↑ sensitivity to barbiturates due to acidosis (↑ non-ionised fraction >> rapid entry)
- all commonly used anesthetic agents decrease SVR (except ketamine)
- Slow, titrated
- ↑ free fraction of drugs due to ↓ albumin

Opioids

- Mostly metabolized in liver, some metabolites excreted in urine
- Morphine & Pethidine metabolites (Morph-6-gluc. & Normeperid.) may accumulate & cause prolonged resp. depression

Volatiles

- Ideal anesthetics (least renal clearance)
- Accelerated induction/emergence with severe Anemia(<5) in CKD
- ? Avoid SEVO flow <2l/min to ↓Comp. A

Muscle relaxants

- Sux safe if K^+ normal range
- Cisatra/atracurium ideal
- Cautious with Vec, Rocuronium, Pancuronium, d-tubocurarine
- Rocuronium although has hepatic elimination prolongation of blockade reported in renal insufficiency

OtherS

- Prolonged elimination of Edrophonium, Pyrido/Neostigmine (recrutarization less likely)
- H₂ blockers (not PPIs) need dose adjustment as well as Metoclopramide

- NSAIDs
- ACE II inhibitor (impairs renal autoregulation)
- Allopurinol
- Aminoglycosides (proximal tubular necrosis)
- Amphotericin B (Glomerulonephritis, ATN)
- Asparaginase
- Cephalosporins (especially with Aminoglycosides)
- Cimetidine (interstitial nephritis)
- Cisplatin (ATN)
- Cyclosporine A, Tacrolimus
- Intravenous radiocontrast (oliguria within 24 h)
- Methotrexate
- Metoclopramide
- Nitrosoureas
- Acetaminophen
- Penicillins, Sulfonamides (interstitial nephritis)

TABLE 17-7 Analgesic dosage adjustments in patients with renal insufficiency

Drug	Adjustment method	GFR > 50 mL/min	GFR 10-50 mL/min	GFR < 10 mL/min
Acetaminophen	↑ Interval	q4h	q6h	q8h
Acetylsalicylic acid	↑ Interval	q4h	q4-6h	Avoid
Alfentanil	↔ Dose	100%	100%	100%
Codeine	↓ Dose	100%	75%	50%
Fentanyl	↓ Dose	100%	75%	50%
Ketorolac	↓ Dose	100%	50%	25%-50%
Meperidine	↓ Dose	100%	75%	50%
Methadone	↓ Dose	100%	100%	50%-75%
Morphine	↓ Dose	100%	75%	50%
Remifentanyl	↔ Dose	100%	100%	100%
Sufentanil	↔ Dose	100%	100%	100%

Adapted from Schrier RW, ed. *Manual of Nephrology*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009.

↑, Increase; ↓, decrease; ↔, no change; GFR, glomerular filtration rate.

Manual of nephrology; Lippincott williams & wilkins: 2009.

Preventive measures

Intraoperative

- Optimize volume status, cardiac output, and systemic arterial pressure
- Avoid $\uparrow$ intra abd. Pressure (Lap.)
compress IVF, $\downarrow$ CO & RBF,
- Avoid nephrotoxic drugs
- Consider maintaining tight glycemic control in all patients
- Use of Mannitol, loop, Dopamine, Ca^{+} channel blockers equivocal

- **Cardiac surgery**
- Maintain adequate flow and mean systemic arterial pressure during CPB
- Limit the duration of CPB
- Avoid excessive haemodilution
- Avoid red cell transfusion
- Consider extra-corporeal leucodepletion
- Consider haemofiltration during CPB
- Consider off-pump coronary artery bypass surgery
- **Vascular surgery**
- Consider abdominal aortic endovascular aneurysm repair

Post-operative

- Avoid nephrotoxic drugs
- Maintain strict glycaemic control in all patients
- Promptly treat acute cardiac dysfunction
- Control haemorrhage
- Manage sepsis aggressively
- Recognize and treat rhabdomyolysis
- Recognize and treat intra-abdominal hypertension
- Provide appropriate organ support for multiple organ dysfunction syndrome
- Consider RRT