ACUTE KIDNEY INJURY:

- An abrupt and sustained decrease in renal function/ GFR (usually reversible) resulting in accumulation of nitrogenous waste compounds
- AKI is usually marked by:
  - Rise in SCr concentration
  - (and/or) Azotemia (a rise in BUN concentration)
  - Decrease in urine output (U/O)
    - Oliguria: U/O < 400 mL/24h or < 0.5 mL/kg/h
    - Anuria: U/O < 50 mL/24h
- AKI = risk factor for nonrecovery of kidney function & progression to CKD/ESRD
- Mortality associated with AKI remains unacceptability high

COMMON RISK FACTORS FOR AKI:

- Age > 75 years
- CKD
- DM
- HF
- Liver disease
- Atherosclerotic PVD
- Nephrotoxic medications
- Dehydration

PRINCIPLES OF THERAPY:

PREVENTION IS VITAL! Once established, there's little that can be done to txt AKI

1. Optimize hemodynamic status
   a. Appropriate fluid therapy
   b. Vasopressors/inotropes
2. Txt of underlying condition
   a. Sepsis, hemorrhage
3. Discontinue nephrotoxic meds
4. Adjust medication dosing

GOALS OF THERAPY:

- Survive the insult
- Prevent further damage
- Prevent/treat complications
- Regain life-sustaining renal function

NORMAL FUNCTIONING OF KIDNEYS (impacts Ddx of AKI):

- Pre-renal: adequate renal blood flow
- Renal: functioning glomeruli & tubule
- Post-renal: clear urinary outflow tract for drainage & elimination of urine

PRE-RENAL AKI: anything that impairs renal perfusion → REVERSIBLE ←

ETIOLOGY:

- Decreased intravascular volume (dehydration – GI/renal losses), hemorrhage, major burns)
- Decreased effective circulating volume (CHF, cirrhosis, sepsis)
- Renovascular occlusion/constriction
  - Large vessel renal vascular disease (renal artery stenosis/thrombosis, arterial cross clamping)
- Impaired renal autoregulation (ACEI/ARB, NSAIDs, calcineurin inhibitors)

CLINICAL DIAGNOSIS:

Patient history	• Prolonged diarrhea, vomiting • Poor oral intake with diuretics • Blood loss

Physical exam	• Signs of volume depletion
	  ○ **Sx:** dry mouth, increased thirst, lightheadedness, syncope, palpitations, muscle cramps, cold extremities, reduced & dark urine
	  ○ **Signs**: tachycardia, weak rapid pulse, orthostatic hypotension, low JVP, poor capillary refill, ↓ skin tugor

Labs	• Elevated SCr and BUN (SCr:BUN ratio)
	  ○ SI units < 12
	  ○ American units > 20:1
	• Electrolyte abnormalities (↑K, Mg, Phos)
	• Urine microscopy & biochemistry
	  ○ Urine Na < 20, Uosm > 500
	  ○ FENa < 1%, FEUrea < 35% (on diuretics)
	  ○ Bland sediment, hyaline or granular casts

FLUIDS MANAGEMENT (pre-renal AKI is volume responsive = reversible)

- Prompt reversal of volume depletion in IVF to prevent progression to ATN
  - Use NS (crystalloid) – confined to ECF compartment = 1/4 in IVF
  - D5W (free water) would be distributed across TBW = 1/12 in IVF
- Fluid challenge when:
  - A clinical hx of fluid loss
  - Physical examination consistent with hypovolemia
- Rapid infusion of NS (1 to 3 L)
  - Total volume administered depends on degree of fluid depletion and on-going loss
  - Optimal infusion rate depends on clinical status & comorbidities
  - Avoid overly aggressive fluid repletion
- Careful & repeated clinical assessment/monitoring
  - Target physiological endpoints (U/O, JVP, MAP, O_2 sat)

AKIN CRITERIA:

	Serum Creatinine	Urine Output Criteria
Stage 1	↑ SCr x 1.5	< 0.5 mL/kg/h x 6 h
	↑ 26 umol/L in SCr over 48h	
Stage 2	↑ SCr x 2	< 0.5 mL/kg/h x 12 h
Stage 3	↑ SCr x 3	< 0.3 mL./kg/h x 24 h
	SCr ≥ 355 umol/L with ↑ 44 umol/L	Anuria x 12 h
Patients who receive RRT are considered to have met stage 3 criteria, irrespective of the stage they are in at the time of RRT		

Even very small incremental increases (>26 umol/L) in SCr could signal significant loss of function and cause increased morbidity & mortality

> Morbidity & mortality increases with each higher degree of impairment
> Early diagnosis is essential
> DO NOT JUST SIT AND WATCH A RISING SCr

CREATININE – AN IMPERFET BIOMARKER:

- Late and indirect reflection of kidney damage
  - Production affected by muscle mass, age, sex, diet, liver disease
  - 10-20% active tubular secretion which can be altered by other compounds (cimetidine, trimethoprim)
  - Altered kinetics of Cr in the setting of AKI (half-life)
  - Dilution during volume overload
- Quest to discover the ideal biomarker that will predict and diagnose AKI

INTRINSIC RENAL AKI: anomaly anywhere inside kidney → SUPPORTIVE TXT

MOST COMMON = ACUTE TUBULAR NECROSIS (ATN):

Ischemic (32%)	• Prolonged pre-renal AKI • Hypotension, hypovolemic shock • Cardiopulmonary arrest or bypass
Sepsis (48%)	• Mortality rates of 50-60%
Direct toxic injury (20%)	• Exogenous (radiocontrast dye, drug-induced ATN) • Endogenous (pigment nephropathy) ○ Rhabdomyolysis
Urinalysis	• Urine Na > 40, Uosm < 300 • FENa > 2%, FEUrea > 35% • Pigmented granular casts, RTE cells

FLUID OVERLOAD = expansion of interstitial space and ↑ venous pressure

- Kidney is sensitive to congestion and ↑ venous pressure
  - ↑ renal subscapsular pressure, ↓RBF and GFR
- F/O is common in ICU pts (hemodynamic instability due to sepsis managed with fluid resuscitation)
  - Exacerbated once AKI and oliguria develop
- F/O correlated adverse outcomes (↑mortality, ↓renal fxn recovery)

LOOP DIURETICS IN AKI:

- Theoretically:
  - Reduce energy requirements of cells of ascending limb of Henle → ameliorate resultant ischemic damage
  - Maintain urine flow, flush out debris, convert pts with oliguric to non-oliguric AKI (better prognosis)
  - Inhibit PG dehydrogenase (↑PG = afferent dilation) – increase RBF
  - Facilitate management of fluid & electrolyte disturbances
- Evidence: loop diuretics can increase U/O without improving renal function or mortality
  - Indications: volume control & maintenance of tubular flow
- Safety: high doses → increased risk of ototoxicity
  - Monitor: hypovolemia, hypotension (can worsen in AKI)

INDICATIONS FOR DIALYSIS: AEIOU

- **A**cidosis (metabolic) – pH > 7.2
- **E**lectrolyte abnormalities (K > 6.5, hypocalcemia)
- **I**ntoxication (salicylates, lithium, methanol, ethylene glycol)
- **O**verload (volume) – pulmonary edema
- **U**remia (encephalopathy, pericarditis, neuropathy)

- Refractory to medical management
- Prolonged time until adequate recovery of renal fxn to keep pace with metabolic/volume demands

POST-RENAL AKI: anything that impairs urinary flow

CAUSES OF POST-RENAL OBSTRUCTION:

Intra-luminal	Extra-luminal
• Stone • Tumor • Abscess • Blood clot	• Vessel • Lymph node • Fluid • Tumor • Abscess

MOST COMMON:
- Prostate enlargement
- Stones
- Urethral stricture or stenosis

Renal stretch → inflammatory response in tubules & interstitium
> Early on → reversible
> With time → tubular atrophy & interstitial fibrosis
  - PERMANENT LOSS in kidney function (chronic obstructive nephropathy) = irreversible loss of kidney fxn

PATIENT HISTORY:
- Urinary symptoms:
  - Hesitancy, frequency, urgency
  - Weak stream, dribbling
  - Feeling of incomplete bladder emptying
  - Flank pain
- History of kidney stones or BPH?
- Spinal cord injury?
- Anticholinergic meds?

MANAGEMENT OF POST-RENAL AKI = DECOMPRESSION:
- Relieve obstruction acutely
  - Foley Catheter: bladder neck (prostate, urethra)
  - Nephrostomy and/or stent: upper tract (ureters)
  - Pharmacotherapy for BPH
  - Urology consult for ultimate management (TURP [transurethral resection of prostate) for BPH)
- Post-obstructive diuresis
  - Follow volume status, K, Mg, Phos, Ca

MAJOR COMPLICATINS OF AKI:
- Fluid overload
- Metabolic acidosis
- Electrolyte disturbances
  - Hyperkalemia
  - Hypocalcemia
  - Hyperphosphatemia
  - Hyperuricemia
  - Hypermagnesemia
- Uremia
  - Encephalopathy/seizures
  - Pericarditis

APPROACH TO ANY PATIENT WITH AKI:
1. Is it post-renal? If so, decompress.
2. Is it pre-renal? If so, reverse the insult quickly, administer fluids, and look for quick improvement
3. If no quick improvement → likely intrinsic AKI. Stop futile and harmful measures (supportive care)
4. Manage complications of AKI & recognize indications for dialysis → call nephrology
5. In all patients with AKI
   a. Identify the etiology and treat the underlying cause
   b. Optimize hemodynamics
   c. Stop/avoid all nephrotic medications
   d. Dosage adjust all renally eliminated medications