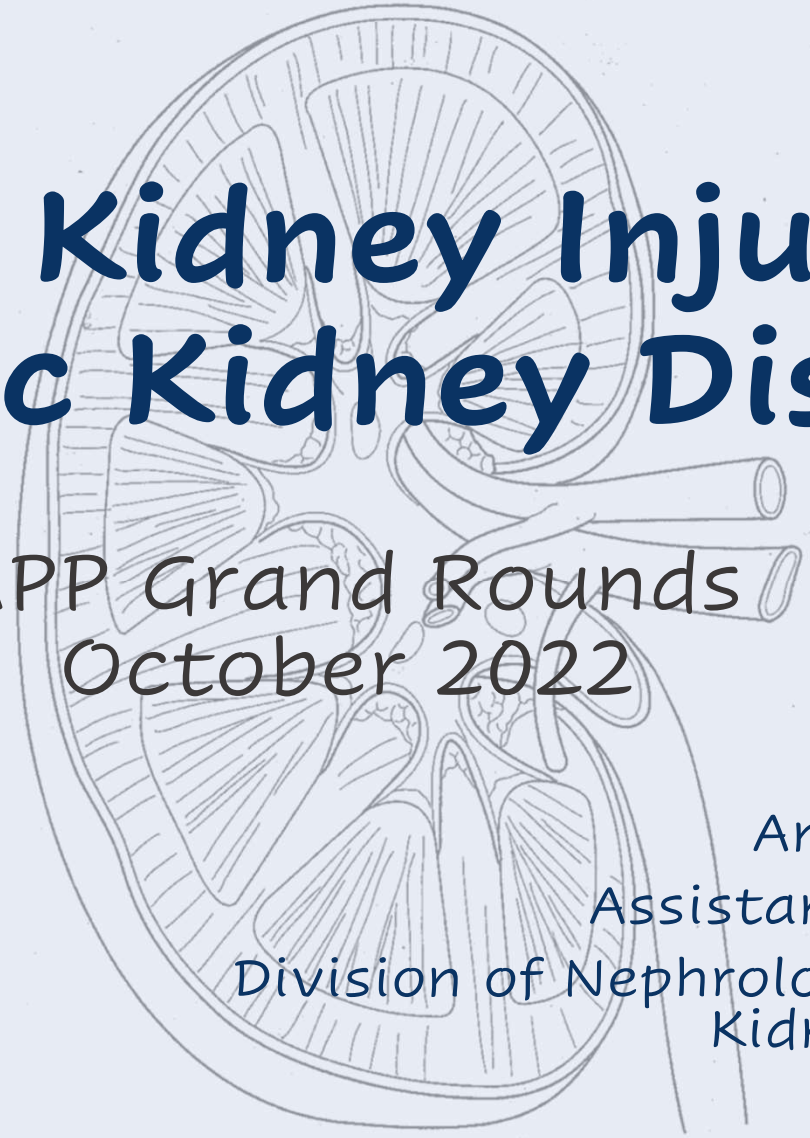
Acute Kidney Injury & Chronic Kidney Disease



APP Grand Rounds
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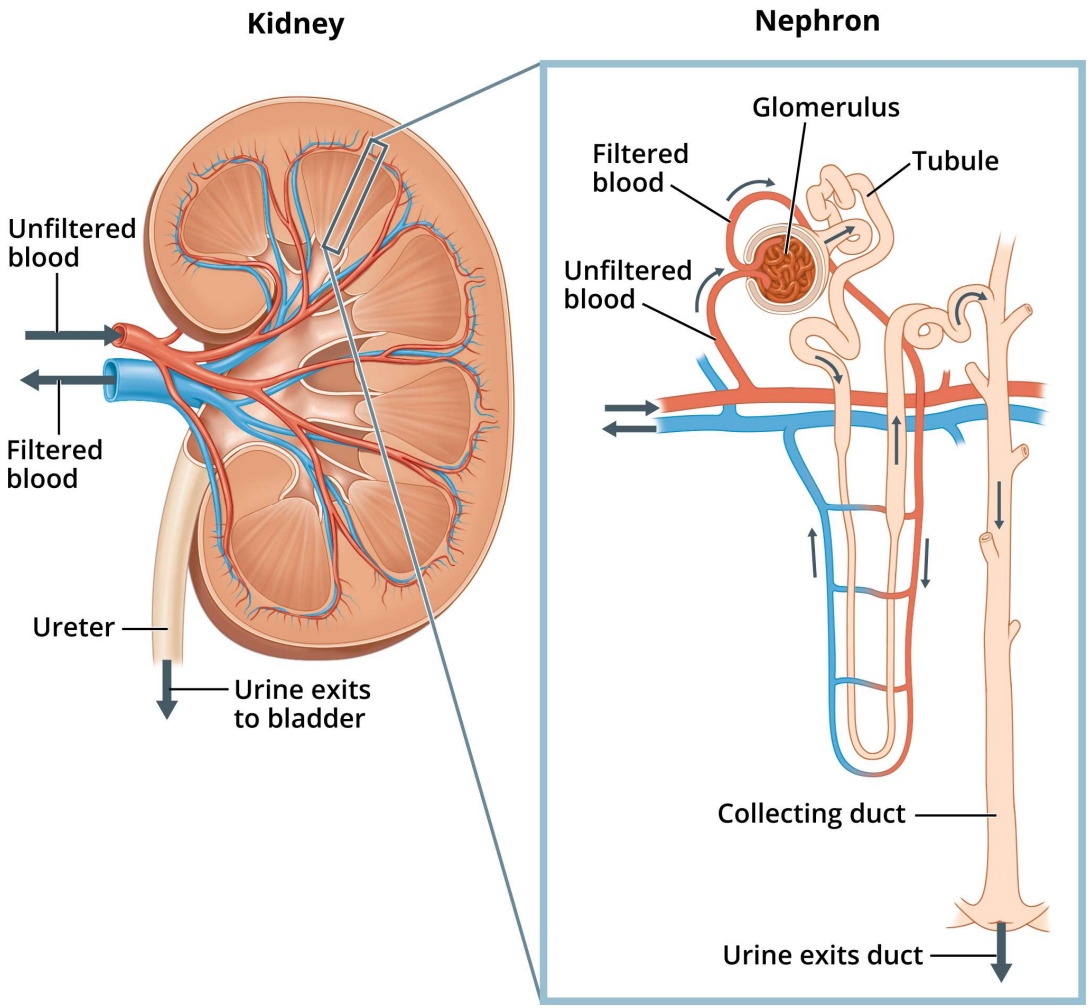
The Kidney

- Filters blood to make urine
  - Waste
  - Water
  - Electrolytes
- Make/ Manage Hormones
  - Blood production
  - BP regulation
    - Volume Status
  - Bone & Mineral Balance
- Acid Base
- Electrolytes



Acute Kidney Injury:
Why do we care?

- Very common:
  - 10% of all hospitalized patients
  - 60% of patients in the ICU
- It is not a single diagnosis but represent a wide range of pathology.
- AKI increases the risk of de novo CKD
  - It maybe the first presentation of intrinsic renal disease
- Associated with CKD progression in patients with CKD
- Even non-dialysis requiring AKI is associated with poorer hospital outcomes and morbidity

Acute Kidney Injury:

Terminology

Sudden decrease in kidney function

- Resulting in dysregulation of electrolytes
- Accumulation of toxins

We don't use "failure" anymore because there is a focus on **Early Recognition and TREATMENT!**

Ideal biomarker for detecting AKI

- Increases in blood or urine within minutes to hours after renal insult
- Remains elevated as l… …is present
- Rise in level correla… …y
- Decreases with rec…

Cr & Cystatin C

NGAL (neutro… …ted lipocali)

KIM-1 (Kidney inj…

TIMP-2 (tissue injury metalloproteinase 2)

IGFBP-7 (insulin-like growth factor binding protein-7)

NephroCheck®

Acute Kidney Injury:
Classification

Research

- Standardize the definition for purpose of research.

Clinically

- Standard definition help early identification.

Many different diagnostic criteria for AKI. (for different target audiences)

RIFLE (2002)

risk → injury → failure → loss of kidney function → end stage renal disease

AKIN (2005)

stages 1 → stage 2 → stage 3

Acute Kidney Injury: Classification

RIFLE *(2002, Acute Dialysis Quality Initiative Group ADQI)*		**AKIN** *(2005, Acute Kidney Injury Network)*		**RIFLE & AKIN**
SCr/eGFR (MDRD) criteria compared to baseline. If baseline not available assume eGFR of 75 mL/min/1.73m²		**SCr criteria: Change in SCr within 48 h following fluid resuscitation**		**Urine Output Criteria**
Risk	↑SCr x 1.5 or ↓eGFR > 25%	Stage 1	↑SCr ≥ 0.3mg/dL or↑ SCr ≥ 1.5-2 x baseline SCr	< 0.5 mL/kg/h for > 6 h
Injury	↑SCr x 2.0 or ↓eGFR > 50%	Stage 2	↑SCr > 2-3x baseline SCr	< 0.5 mL/kg/h for > 12 h
Failure	↑SCr x 3.0 or ↓eGFR > 75% or if baseline SCr ≥ 4mg/dL, ↑ SCr ≥ 0.5 mg/dL	Stage 3	↑SCr > 3x baseline SCr or acute RRT	< 0.3 mL/kg/h for ≥ 24 h or anuria ≥ 12 h
Loss of Kidney Function	Complete loss of function > 4 wk	Remember rule out obstruction, volume evaluation & fluid resuscitation if applicable are important pre-parts of AKIN.		
ESRD	Complete loss of function > 3 mo			
Improves AKI detection at 48 h in the ICU				

Acute Kidney Injury:
Classification

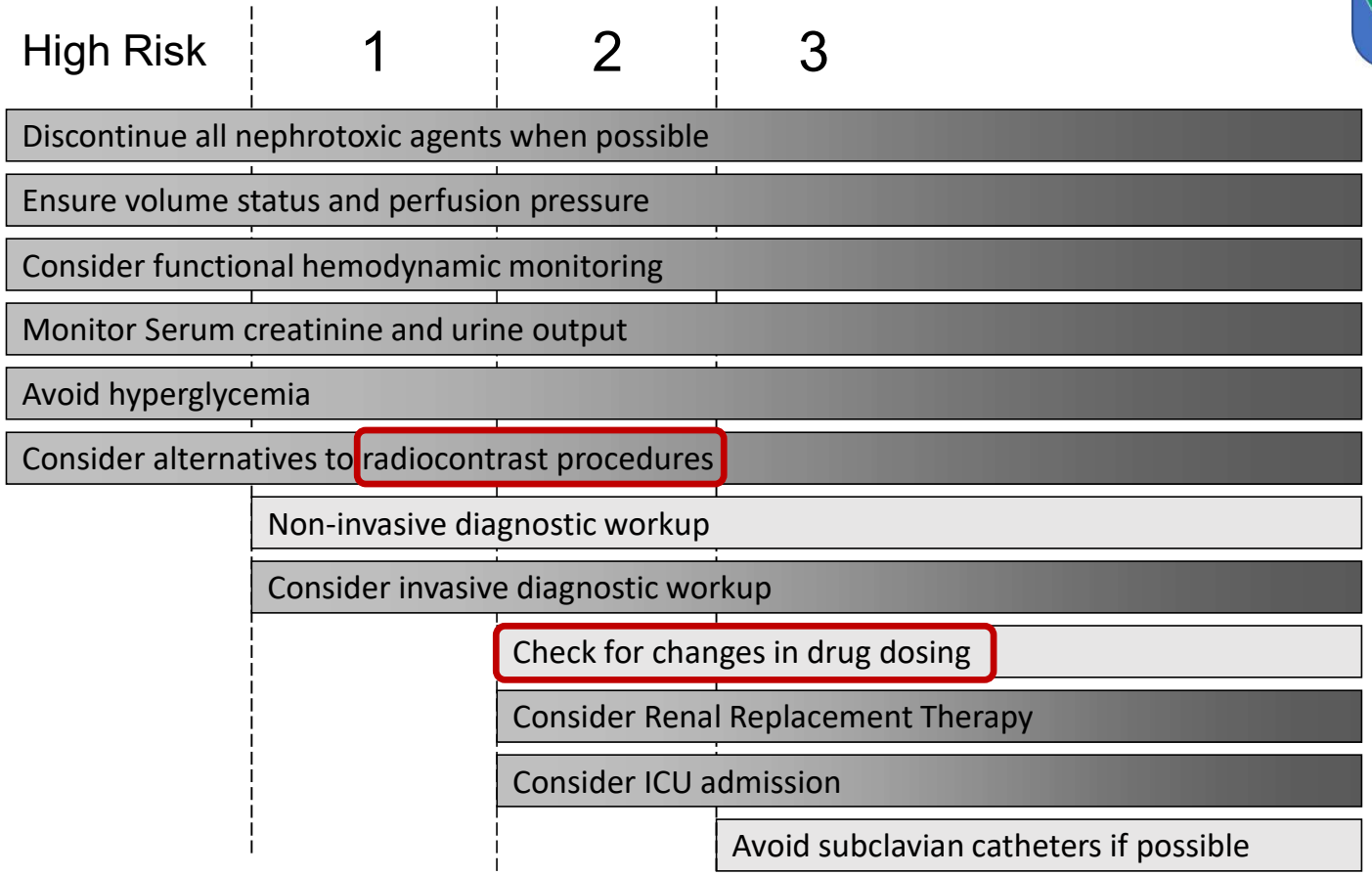
KDIGO

Provides us a **clinically relevant** approach to defining AKI

RIFLE + AKIN

Increase in SCr ≥ 0.3 mg/dL within 48 hours or
increase in SCr by > 1.5 times baseline SCr <u>within prior 7 days</u>
or
Urine Volume < 0.5 mL/kg/h for ≥ 6 hours

AKI Stage


High Risk
1
2
3
Discontinue all nephrotoxic agents when possible
Ensure volume status and perfusion pressure
Consider functional hemodynamic monitoring
Monitor Serum creatinine and urine output
Avoid hyperglycemia
Consider alternatives to radiocontrast procedures
Non-invasive diagnostic workup
Consider invasive diagnostic workup
Check for changes in drug dosing
Consider Renal Replacement Therapy
Consider ICU admission
Avoid subclavian catheters if possible

So we defined AKI (so what?)
What do we do once we have identified it?

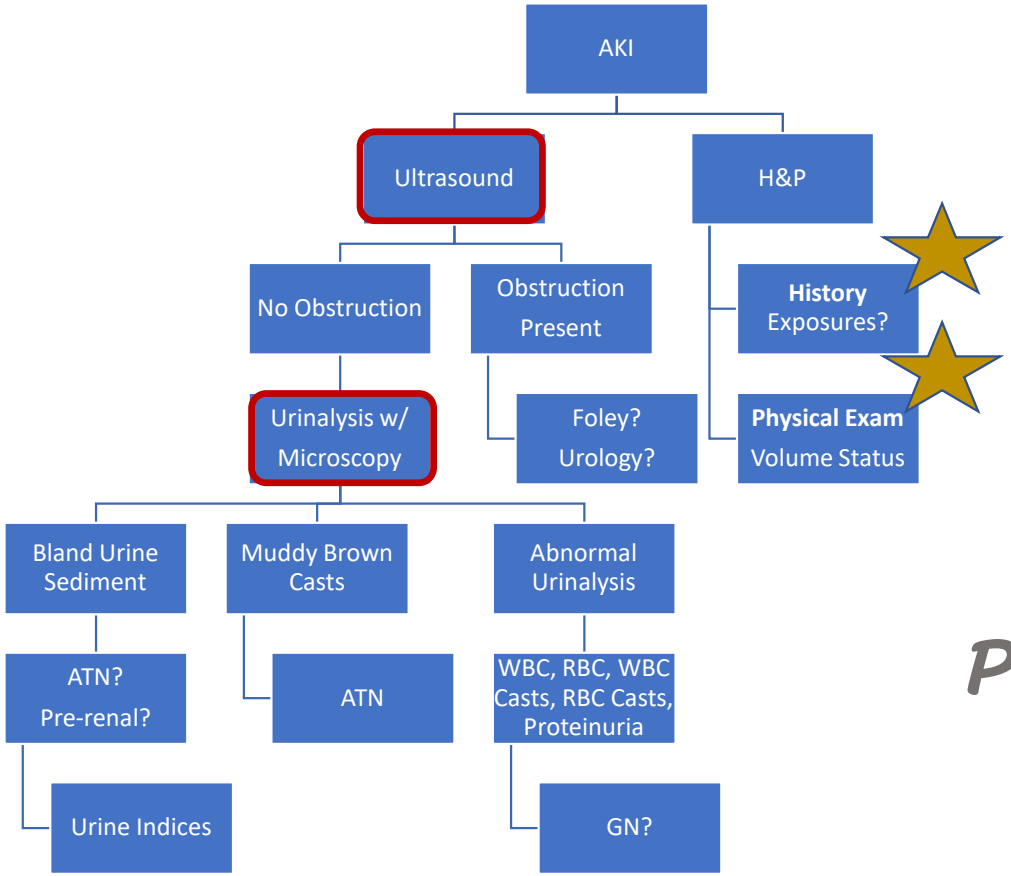
- Test patients at risk for AKI
- Evaluate patients with AKI PROMPTLY
- Determine etiology
- Stratify patient according to exposures and susceptibilities
  - Manage as appropriate
  - Focus on reversible causes
- Follow up patients at 3 months to determine if they have developed CKD

Table 6 | Causes of AKI: exposures and susceptibilities for non-specific AKI

Exposures	Susceptibilities
Sepsis	Dehydration or volume depletion
Critical illness	Advanced age
Circulatory shock	Female gender
Burns	Black race
Trauma	CKD
Cardiac surgery (especially with CPB)	Chronic diseases (heart, lung, liver)
Major noncardiac surgery	Diabetes mellitus
Nephrotoxic drugs	Cancer
Radiocontrast agents	Anemia
Poisonous plants and animals	

Many algorithms for AKI exist

But in the hospital several steps occur simultaneously…



Post-renal

Intrinsic

Pre-renal

Tools for the diagnosis in **AKI**

- History
  - Exposures (hypotension, nephrotoxins, sepsis…etc)
  - Urine Volume
- Physical Exam
- Ultrasound
- Urinalysis
  - Urine Sediment Examination
    - Casts: Cellular (RBC vs WBC), Hyaline Casts, Granular Casts, Muddy Brown Casts, Waxy Casts
    - Cells: RBC vs WBC
- Labs
- Urine Indices
- Kidney Biopsy

History

- Timeline Matter
  - In the hospital regular measurements of Serum Cr and UOP can help identify when the injury occurred.
    - ie: a rising Cr on Hospital Day 7 (should make us look at a Hospital Day 6 or 5 the likely time period when precipitating insult occurred)
    - You may identify multiple insults…

History

- Detailed history, chart review, and physical exam

Hemodynamic **Decreased Kidney Perfusion** **"prerenal"**	**Parenchymal** **Intrarenal** **"intrinsic"**	**Obstructive** **"postrenal"**
Hypovolemia	Vascular (RAS, cross-clamping)	Bladder Outlet
Decreased Cardiac Output	Microvascular TMA, Cholesterol Emboli	Ureteral
Systemic Vasodilation Sepsis, HRS	Glomerular RPGN, AIN Nephrotic Syndrome w/ ATN Myeloma w/ AKI	Renal Pelvis Papillary Necrosis (NSAIDs) Obstructive Stone Disease
Alterations in Glomerular Pressure ie: Meds (NSAIDs, ACEi/ARB, CNI) hypercalcemia, HRS, Abd Compartment Syndrome	Tubulointerstium: AIN ATN	

Medication Review

- Identify nephrotoxic or potentially nephrotoxic medications
- Identify medications which can accumulate when renal function is impaired

Medications Associated with ATN
Aminoglycosides (tobramycin, gentamicin)
NSAIDs
ACEi & ARB
Amphotericin
Cisplatin
Foscarnet
Pentamidine
Tenofovir
Zolendronic Acid
*may not be direct cause but can *predispose patients with volume depletion or simultaneously occurring insult*

Medications requiring dose adjustment
Analgesics (morphine, meperidine, gabapentin, pregabalin)
Antiepileptics (lamotrigine)
Antivirals (acyclovir, ganciclovir, valganciclovir)
Antifungals (fluconazole)
Antimicrobials
Diabetes Medications
Allopurinol
Baclofen
Colchicine
Digoxin
Lithium
Low-molecular-weight heparin / Novel oral anticoagulants

Physical Exam

- Vitals
  - Hypertension and Hypotension
    - Tachycardia (Hemodynamic Instability)
- Volume Status
  - Orthostatic Hypotension
  - Mucous Membranes
  - Skin Turgor
  - Edema
  - Ascites
  - CVP
  - CO, PWCP
- Systemic Illness
  - Rash & Skin Changes
  - Nail bed changes
  - Oral Ulceration
  - Arthralgias
  - Source of Infection
  - Abdominal Distention
- Genito-urinary
  - UOP
    - Foley, Urine Color, Urine Quantity

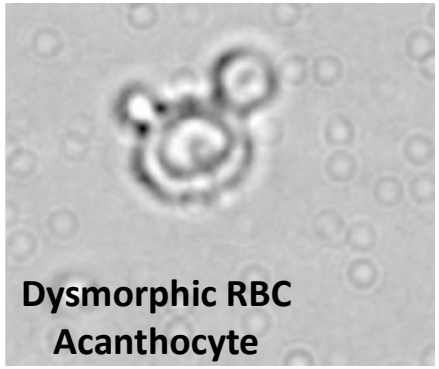
Urinalysis

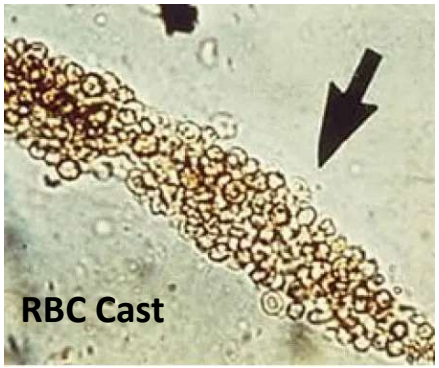
Urine Dipstick & Urine Sediment

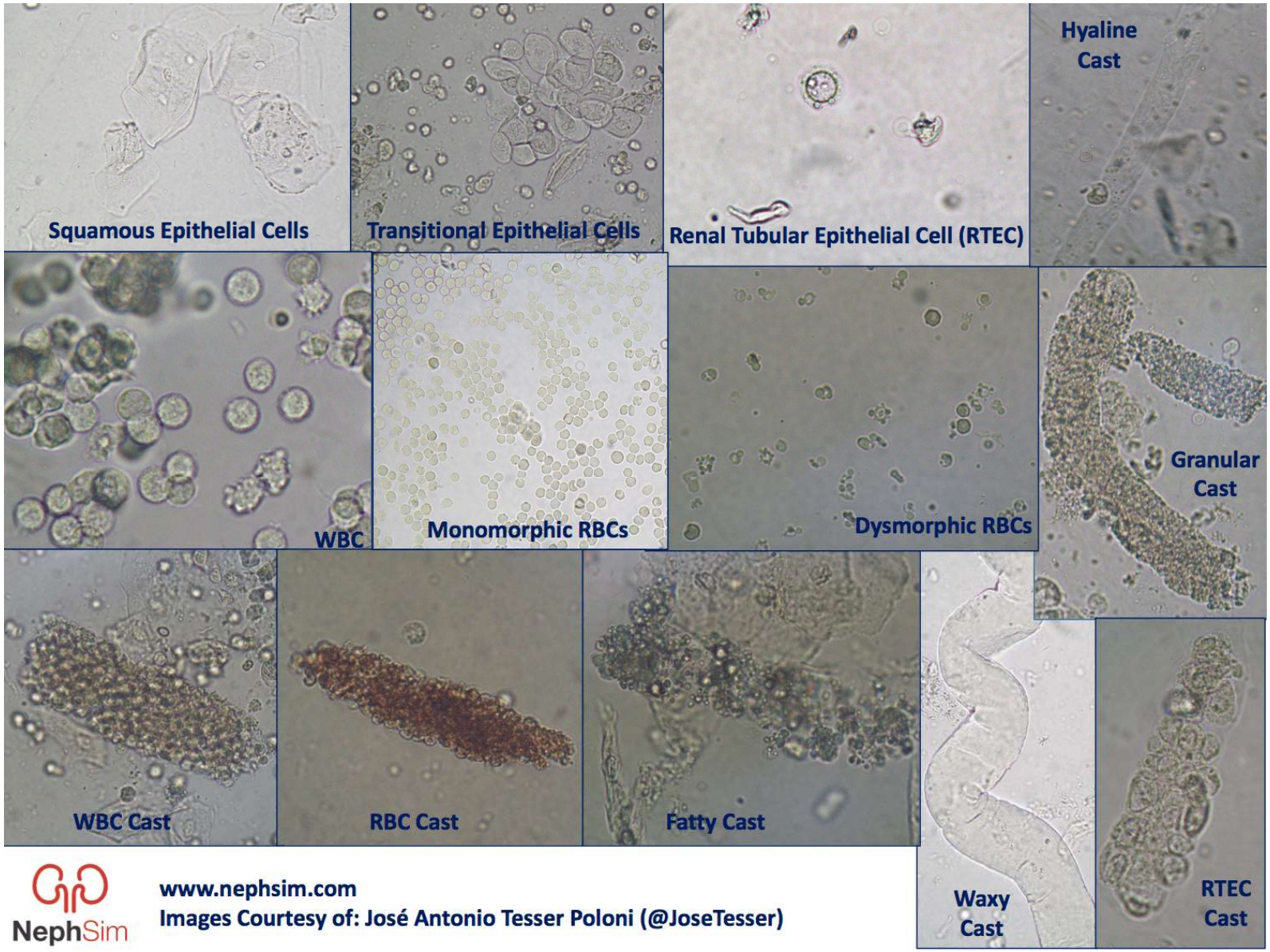
- Urine Sediment (Microscopic Examination)
  - Collected within 2 hours of examination
    - Prolonged standing ↑ urinary alkalization ((urea → ammonia) = dissolves casts & cells lysis
  - Midstream clean catch (ideally) second morning urine
  - ICU: collect fresh from Foley port **NOT Foley bag**

Urine Sediment Evaluation
1. Centrifuge 10 mL aliquot at 1500-3000 rpm *(400-450 g)* for 5 minutes.
2. Remove supernatant
3. Resuspend sediment in remaining supernatant
4. Use pipette and apply one drop to slide & cover with coverslip
5. Examine under phase-contrast light microscopy at increasing magnifications (x160 -> x400).

Urine Sediment	Suggests
RBCs	*dysmorphic = Glomerular Disease*
WBCs	*infection vs inflammation*
Epithelial Cells • Squamous Epithelial Cells • Transitional Epithelial Cells • Renal Tubular Epithelial Cells • Oval fat bodies	*contaminants from distal genital tract* *bladder irrigation vs malignancy (irregular)* *> 15/HPF maybe assoc. w/ tubular injury* *Nephrotic syndrome*
Casts • Hyaline Casts • Granular Casts • Waxy Casts • Fatty Casts • Red Cell Casts • White Cell Casts • Epithelial Cell Casts	*strenuous exercise, dehydration, prerenal* *"muddy brown" ATN* *CKD* *Nephrotic Syndrome, mercury/ethylene glycol poisoning* *Glomerular Disease* *Pyelonephritis*
Crystals *Calcium based, Drug-associated …*	*Some represent disease some are artifacts*
Organisms *Bacteria, Fugus, Parasites*	*Contaminants vs signs of infection*







NephSim

www.nephsim.com

Images Courtesy of: José Antonio Tesser Poloni (@JoseTesser)

Urine Indices

$$\text{FeNa \%} = \frac{\text{UNa} \times \text{SCr}}{\text{SNa} \times \text{UCr}} \times 100$$

Fractional Excretion of Sodium (FeNa)

Measures the percent of filtered sodium excreted in the urine.

Classically: FeNa < 1% suggest prerenal AKI as opposed to ATN.

In patients who have received diuretics classically measure FeUrea and an FeUrea < 35% suggest prerenal AKI as opposed to ATN.

Intrinsic Disease with FeNa < 1%
Early ATN (still have FeNa <1%)
ATN superimposed on chronic prerenal state
AKI with contrast
Acute GN (early course)
Nonoliguric MILD AIN

Be careful! not to base your diagnosis on urine indices alone. There are many situations when urine indices can be misleading.

History and Physical Exam will help you tease these out.

In cirrhosis, FeNa consistently < 1% maybe helpful when attempting to establish a diagnosis of HRS.

Hemodynamic AKI (prerenal)

One of the most common causes of AKI.

- "Decreased renal perfusion"
  - Rapid Decrease in BP (ie: Overcorrection)
  - True Volume Depletion
    - Body Fluid Loss: acute blood loss, decreased access to fluid, fluid shift with paracentesis
    - Reduced Effective Circulating Volume: cirrhosis, heart failure, sepsis, pancreatitis…
  - Acute Cardiopulmonary Event (PE, MI)
  - Intraglomerular hemodynamic compromise
    - Afferent Vasoconstrictors (or Efferent Vasodilation) + Volume Depletion
      - Afferent Vasoconstrictors: NSAIDs, CNI, Contrast Agents, Amphotericin
      - Efferent Vasodilators: ACEi & ARB

"Third Spacing"

Hemodynamic AKI (prerenal)

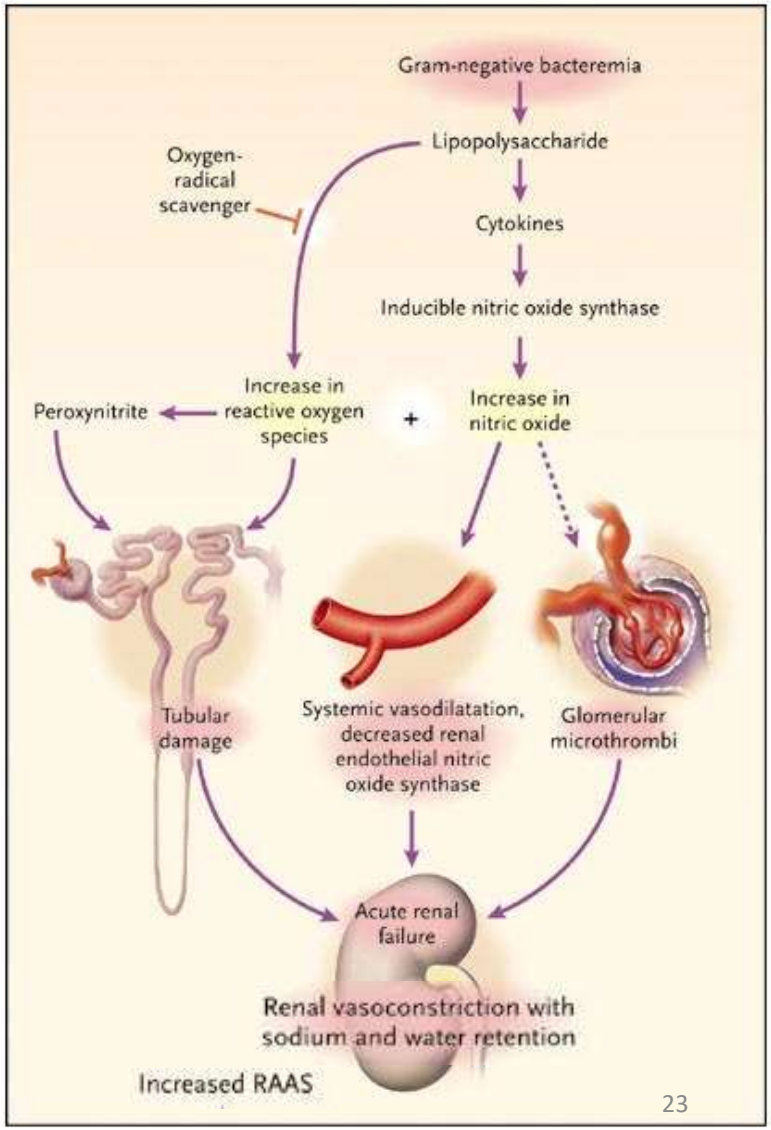
Early Detection → **Appropriate Volume Management** → Prevention of Pre-renal → Intrinsic (ATN)

Hemodynamic AKI (prerenal)

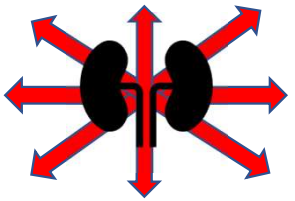
Sepsis Related AKI

- Proinflammatory State
- Systemic Vasodilation
- Impaired Microcirculation
- Cytokine mediated cell injury

- **Intensive Care Unit**
  - Generally have additional nephrotoxic exposure
    - Medication
    - Contrast



Hemodynamic AKI (prerenal)continued…



Poor Effective Circulating Volume

Hepatorenal Syndrome *(functional kidney failure + liver failure)*

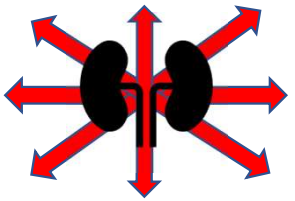
- Portal Hypertension = Increased production of vasodilators (nitric oxide)
- Splanchnic Vasodilation = Splanchnic blood pooling
- Decreased Peripheral Vascular Resistance

Diagnosis
1. Acute Kidney Injury in patient with underlying cirrhosis
2. NO improvement following diuretic withdrawal & volume expansion *Typical Volume Expansion: Albumin 1g/kg/24hrs (up to 100 g/day)*
3. No other cause for AKI - No shock - No nephrotoxins - No intrinsic renal disease *(ie: proteinuria > 500 mg/24hr, hematuria, ATN, abnormal renal ultrasound)*

Prevention	
SBP	IV Albumin 1.5 g/kg at time of diagnosis & 1 g/kg 48 hours later.

Therapeutic Option
Vasopressor + Albumin +/- Octreotide (USA) NE or Midodrine ↑ *MAP by 10-15 mmHg*

Hemodynamic AKI (prerenal)continued…



Poor Effective Circulating Volume

Cardiorenal Syndrome *(one organ dysfunction leading to another)*

- CKD in Heart Failure 20-70%

Cardiorenal Syndrome Classification	
CRS Type 1	ACUTE (Acute HF → AKI)
CRS Type 2	CHRONIC (Chronic HF → Progressive CKD)
CRS Type 3	acute renocardiac (AKI → HF exacerbation)
CRS Type 4	chronic renocardiac (CKD → volume overload/ stress → HF develops
CRS Type 5	Systemic → simultaneous kidney & heart disease

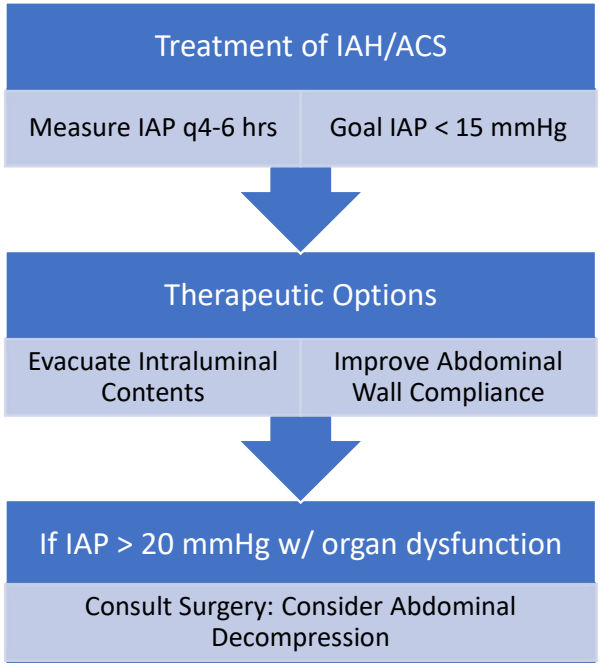
Stepped pharmacologic therapy with diuretics is generally the optimal treatment strategy.

Hemodynamic AKI (prerenal)continued…

Intrabdominal Hypertension (IAH)

- "Abdominal Compartment Syndrome" (ACS)
  - IAP > 12 mmHg.
  - ACS > 20 mmHg + new or worsening organ dysfunction

Risk Factors fo IAH → ACS
Abdominal surgery, Trauma, Burn, Prone Positioning *(doesn't allow flexibility in abdominal wall)*
Gastroparesis, Gastric Distention, Ileus, Pseudo-obtrucition, Volvulus Pancreatitis, hemo-pneumonperitoneum, tumors, **cirrhosis w/ ascites** *(anything that over fills the abdomen)*
Acute Illness: Acidosis, hypothermia, massive fluid resuscitation, polytransfusion
ICU Pt: Mechanical Ventilation (PEEP > 100 mmHg), peritonitis, shock



Parenchymal AKI (intrarenal, “intrinsic”)

Many Causes…

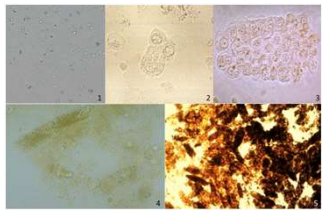
- Ischemic Injury
  - Most common in hospital setting
- Vascular AKI
  - Thrombotic Microangiopathies (TMA)
    - TTP, HUS, Complement Mediated HUS, etc.. Scleroderma Renal Crisis, Malignant HTN
  - Atheroembolic Disease
    - Cholesterol Emboli (following procedure)
    - Infection, Endocarditis
  - Large Vessel Disease
    - Aortic dissection extending to renal artery
- Glomerular Disease
- Tubulointerstitial Disease
  - Hemolysis, Rhabdomyolysis, Hyperbilirubinemia, Contrast Induced AKI

Parenchymal AKI (intrarenal, “intrinsic”)

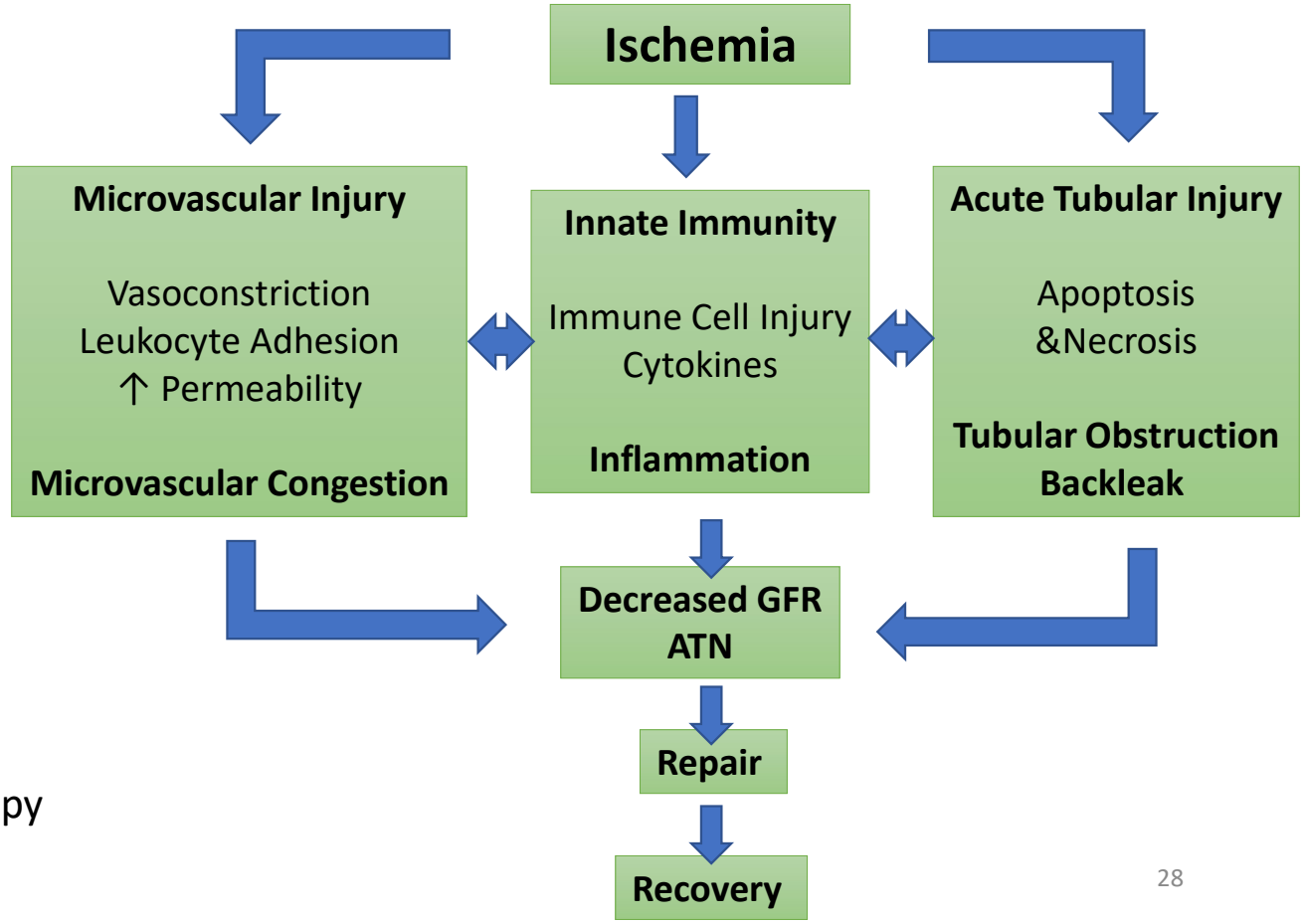
Ischemic Injury

Acute Tubular Necrosis

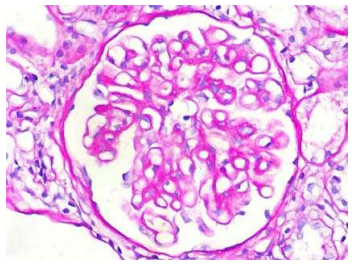
Urine Sediment Evaluation



- Prevention
- Supportive Care
  - Volume Management
    - Diuretic
    - Renal Replacement Therapy



Glomerular Injury



Heterogenous collection of inflammatory and noninflammatory insults to the filtering unit of the kidney.

- Clinical presentation will be key in helping you identify these patients

Signs of Glomerular Injury
Proteinuria
Hematuria (absence of urologic cause)
Dysmorphic RBCs, RBC Casts
Nephrotic Syndrome
Hypertension
Acute Oliguria (in some cases)

Serologies to Consider
ANA, anti-dsDNA, C3, C4, CH50
Cryoglobulins, RF
Anti-GBM Ab
ANCA
ASO, anti-DNAse-B
Hep B & Hep , HIV
SPEP, UPEP, IFE, Kappa/Lambda
PLA2R Ab

Renal Biopsy

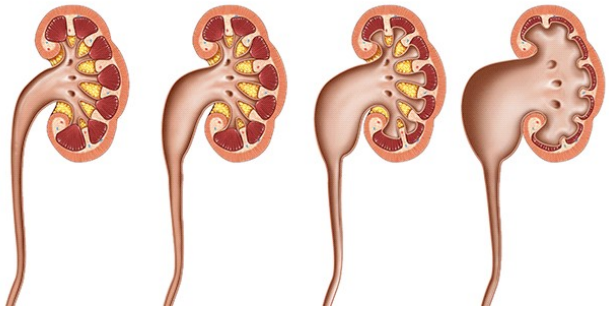
Postrenal AKI (obstructive)

Obstructive Uropathy

Etiologies

- Intrinsic
  - **Stones**, Papillary Necrosis (NSAIDs, Sickle Cell Disease) Renal TB, Fungus Balls, Drug Crystals (acyclovir, sulfonamides, sulfadiazine, ethylene glycol, methotrexate, indinavir)
  - Warfarin Related Kidney Injury (suspect related to RBC casts causing tubular obstruction.
- Extrinsic
  - **Cancer** (female pelvic malignancies)
  - Retroperitoneal Fibrosis
  - Neurogenic Bladder (diabetes, anticholinergics, NSAIDS…)
  - *Pregnancy may begin in first trimester, typically right sided obstruction resolves 2-3 weeks postpartum*

Postrenal AKI (obstructive)



Obstructive Uropathy

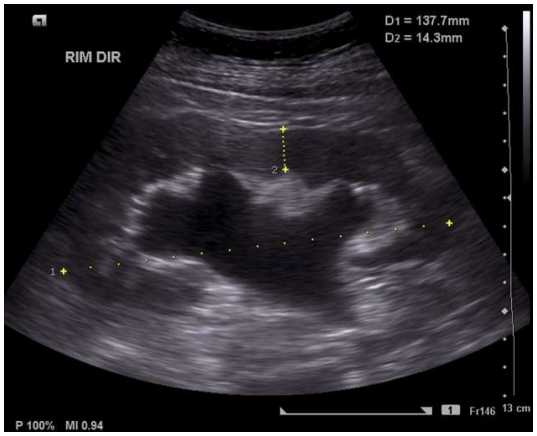
Presentation

- Decreased UOP
  - Anuria (think lower tract obstruction ie: bladder neck, urethral)
- Pain (kidney stones)
- Urinary Symptoms (incomplete emptying, frequency, overflow incontinence)
- Suprapubic Tenderness

Labs

- ↑Cr (if bilateral); ↑ BUN (tubular stasis and re-absorption)
- Hyperkalemia, Metabolic Acidosis (generally out of proportion to AKI)

Postrenal AKI (obstructive)



Obstructive Uropathy

Evaluation

- Ultrasound
  - Inexpensive & readily available. (*false negative if volume depleted & retroperitoneal fibrosis*)
- CT Urogram
  - Great for stone evaluation
  - Avoid in pregnant women

  MRI poor stone visibility

Findings

- Cortical Thinning: implies longstanding obstruction (reduced recovery potential)
- Empty bladder: think ureteral obstruction

Postrenal AKI (obstructive)

Obstructive Uropathy

Treatment

- Decompression
  - Foley
  - Urology / IR consultation depending on level of obstruction & etiology
- **Post Obstructive Diuresis**
  - Monitor and replace electrolytes

Typical Fluid & Electrolyte Replacement

Initially: 0.5mL for every 1mL of urine output above 100 mL/hr with 1/2NS.

Replace potassium and magnesium losses

Monitor Labs: q8 hours (adjust based on severity of diuresis)

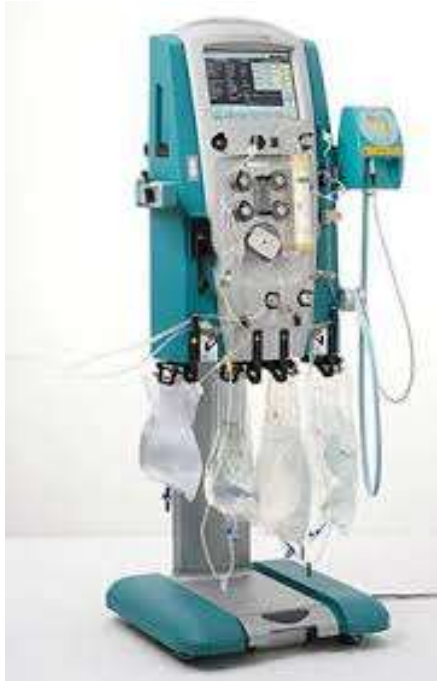
Fluid Management in AKI

- Caution with Excessive Volume Overload
  - Delay the diagnosis of AKI
  - Associated with worse outcomes
  - Fluid overload at time of diagnosis of AKI NOT associated with recovery of kidney function.
- IV fluids should be reviewed regularly in ICU patients.
  - Select the fluid that is appropriate to the clinical setting.
    - LR is hypotonic and contains almost negligible amount of potassium
    - NS & ½NS are chloride rich solutions
- Diuretics, acceptable for volume management of patient with AKI.
  - Data does not support the notion that diuretics improve chance of renal recovery. ***May cloud our interpretation of UOP as marker of recovering renal function***

Renal Replacement Therapy in AKI

Available to support renal function when native function is absent or insufficient to avoid additional complications.

- Ask yourself what are you trying to prevent or accomplish with introduction of therapy?



Indications

- Metabolic Acidosis
- Hyperkalemia
- Volume Overload
- Uremia
- Intoxication (ethylene glycol, methanol, lithium, theophylline, barbiturates …)

Renal Replacement Therapy in AKI

Early vs Late

There is extensive variability in the timing of renal replacement therapies between institutions and even among nephrologists with similar practice patterns at the same institution.

- As a result there have been many studies trying to determine the best time to institute replacement therapy.

STARRT, HEROICS, AKIKI, ELAIN, IDEAL-ICU, FST, HYPERDIA…

Timing of Initiation of Renal Replacement Therapy in AKI (NEJM 7/16/2020)

In general the timing of initiation of renal replacement therapy **does not affect survival in critically ill patients** with acute kidney injury. Data **does not** support the notion that early renal replacement therapy **improves chances of renal recovery.**

Renal Replacement Therapy in AKI

Start when there is an indication whether it be early or late.

Choose the modality that is right for the clinical setting with which you are faced.

- Intermittent HD — Rapid Clearance (decreased treatment time) → Requires some degree of **Hemodynamic Stability**
- Continuous Renal Replacement Therapy — Steady solute control (at the expense of 24 hour treatment) → **Hemodynamically Unstable Patients**
- SLED
- PD

Remember

- AKI is common
- AKI is associated with increased LOS, morbidity, & mortality
- Early detection and volume management are key

- Very satisfying when you can act early to prevent hemodynamic injury from extending to an intrinsic injury.

- Don’t forget to get the history, a little work up front, will save you time and help predict your patient’s course/ treatment
- Urinalysis and Urine Sediment are part of your exam
- AKI is not a single diagnosis… so think outside the box

CKD is a MAMMOTH issue

- ESRD (Medicare HMO costs for ESRD are several billion dollars annually).
  - Hemodialysis costs on average $ 90,000 per person per year
  - Peritoneal dialysis costs on average $ 75,000 per person per year

- Today MORE than 26 million Americans have CKD.
  - Perhaps fortunately the need for treatment of CKD with dialysis or transplant arises in only 1-2% of individuals with CKD.
    - It remains the most expensive chronic disease in the United States.
    - 5% of the annual FEDERAL budget is consumed by less than 1% of the population.
    - Need for renal replacement therapy is associated with reduced life span and reduction in quality of life.

Early recognition of CKD

- There are interventions to lower risk of progression of early CKD to ESRD.
  - Screening is particularly important for high risk populations.
    - Individuals with Hypertension - Prevalence of CKD is 27.5%
    - Individuals with Diabetes – Prevalence of CKD is 34.5%
    - Family history of CKD
      - African Americans & Native Americans
      - Hispanics

3-4 x more likely to progress to ESRD than Caucasians

2 x more likely to progress to ESRD than Caucasians

- Individuals with CKD are susceptible to Acute Kidney Injury
  - AKI accelerates progression of underlying CKD

Chronic Kidney Disease Defined

Reduced Glomerular Filtration Rate
GFR < 60 mL/min/1.73m^2 for
at least 3 months

or

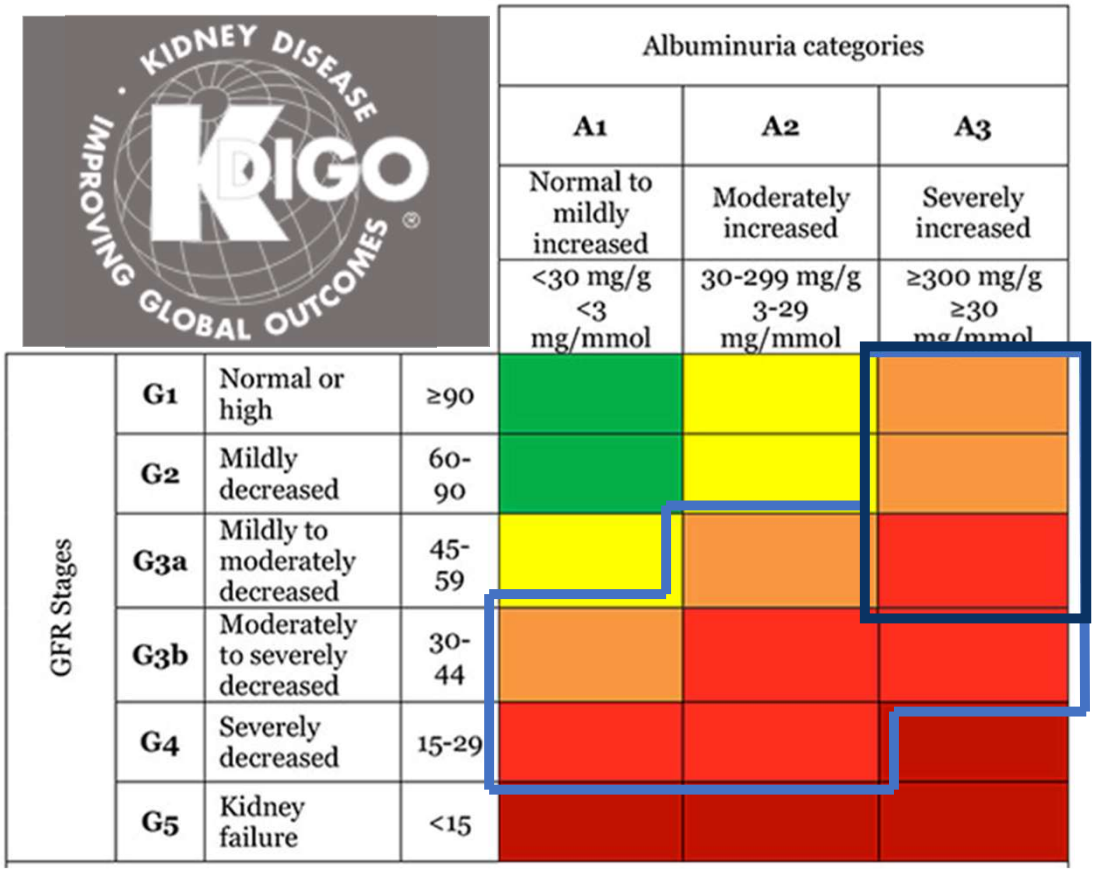
Kidney Damage
Any of the following…
1.Albuminuria or Proteinuria
- Microalbmin: Cr (ACR) > 30 mg/g
- Protein: Cr (UPC) > 0.2

2.Structural Renal Disease
- Abnormal Imaging

3.Abnormal Kidney Biopsy

Understanding the etiology of chronic kidney disease helps predict the rate of progression of CKD and how to best optimize medical management to alter the natural history of the disease.

Staging CKD



GFR Stages				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
	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			

High and Very High risk for progression of CKD

Degree of albuminuria is important and may help us focus in on some patients which we might not have realized were at risk for more rapid progression.

Chronic Kidney Disease Stage G1 & G2

			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
G1	Normal or high	≥90			
G2	Mildly decreased	60-90			

Stages 1 & 2

Remember these individual with GFR>60 **don't** have CKD unless they have evidence of **functional** or **structural** disease.

ie: abnormal urine sediment, abnormal renal biopsy, proteinuria or abnormal renal imaging

Treatment/ Monitoring:

Yearly Labs :
(CMP, UPC or ACR & UA with micro)

1. **BP Goal <140/90 or <130/80**
2. **UPC < 0.2 or ACR < 0.3**

Immunizations: All CKD 2+ pts should have PPV 13, PSV 23, HBV, TdaP, VZ, Flu, and COVID

Chronic Kidney Disease Stage G3a & G3b

			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
G3a	Mildly to moderately decreased	45-59			
G3b	Moderately to severely decreased	30-44			

Stages 3a & 3b

Treatment/ Monitoring:

Labs 2-3x per year

(BMP, Phos, iPTH, CBC, UPC or ACR & UA with micro)

1. **BP Goal < 140/90 almost always**
2. **UPC < 0.2 or ACR < 0.3**
3. **Hbg > 9.0 mg/dL**
4. **PTH is 130-500 pg/mL**
5. **CO_2 is between 22-26 mEq/L**
6. **PHOS in normal Range for Lab**

Immunizations: All CKD 2+ pts should have PPV 13, PSV 23, HBV, TdaP, VZ, Flu, and COVID

Chronic Kidney Disease Stage G4 & G5

			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
G4	Severely decreased	15-29			
G5	Kidney failure	<15			

Stages 4 & 5

Generally already co-managed with nephrologists and already preparing for renal replacement therapy exploring options or already on some form of ESRD therapy.

General Management Guidelines

Glycemic Control

- Goal A1C < 7%
    - Metformin is contraindicated for eGFR <30
- **Metformin** use is controversial if GFR is < 45
    - eGFR 30-45 don't go above 1 gram per day
    - eGFR <30 generally contraindicated
- SGTL2 inhibitors!

Table 2. Dosing recommendations for noninsulin antihyperglycemic agents currently available in the United States in the setting of CKD[19,37,38]

Medication	Recommended Dosing with Impaired GFR, ml/min per 1.73 m^2
Biguanides	
Metformin	No dose adjustment if eGFR>45
	Do not initiate or assess risk/benefit if currently on metformin if eGFR=30–45
	Discontinue if eGFR<30
Second generation sulfonylureas	
Glipizide	No dose adjustment required
Glimepiride	Initiate conservatively at 1 mg daily
Glyburide	Avoid use
Meglitinides	
Repaglinide	Initiate conservatively at 0.5 mg with meals if eGFR<30
Nateglinide	Initiate conservatively at 60 mg with meals if eGFR<30
Thiazolidinediones	
Pioglitazone	No dose adjustment required
Rosiglitazone	No dose adjustment required
α-Glucosidase inhibitors	
Acarbose	Avoid if eGFR<30
Miglitol	Avoid if eGFR<25
GLP-1 RAs	
Exenatide	Not recommended with eGFR<30
Liraglutide	No dose adjustment recommended by manufacturer
Lixisenatide	No dose adjustment required for eGFR=60–89
	No dose adjustment required for eGFR=30–59, but patients should be monitored for AEs and changes in kidney function
	Clinical experience is limited with eGFR=15–29; patients should be monitored for AEs and changes in kidney function
	Avoid if eGFR<15
Albiglutide	No dose adjustment required for eGFR=15–89 per manufacturer
Dulaglutide	No dose adjustment recommended by manufacturer

Hypoglycemia more common in CKD

Neumiller, Joshua J., et al. "Therapeutic Considerations for Antihyperglycemic Agents in Diabetic Kidney Disease." Journal of the American Society of Nephrology, vol. 28, no. 8, 2017, pp. 2263–2274., doi:10.1681/asn.2016121372.

Table 2. Dosing recommendations for noninsulin antihyperglycemic agents currently available in the United States in the setting of CKD[19,37,38]

Medication	Recommended Dosing with Impaired GFR, ml/min per 1.73 m^2
DPP-4 inhibitors	
Sitagliptin	100 mg daily if eGFR>50 50 mg daily if eGFR=30–50 25 mg daily if eGFR<30
Saxagliptin	5 mg daily if eGFR>50 2.5 mg daily if eGFR≤50
Linagliptin	No dose adjustment required
Alogliptin	25 mg daily if eGFR>60 12.5 mg daily if eGFR=30–60 6.25 mg daily if eGFR<30
Amylinomimetic	
Pramlintide	Specific guidelines for dosage adjustment in CKD are not available
SGLT-2 inhibitors	
Canagliflozin	No dose adjustment required if eGFR≥60
Dapagliflozin	eGFR 30-60 100mg daily eGFR < 30 can continue 100 mg daily if already taking it
Empagliflozin	No dose adjustment needed No dose adjustment for eGFR > 30 Probably okay when eGFR < 30

AE, adverse event.

Neumiller, Joshua J., et al. "Therapeutic Considerations for Antihyperglycemic Agents in Diabetic Kidney Disease." Journal of the American Society of Nephrology, vol. 28, no. 8, 2017, pp. 2263–2274., doi:10.1681/asn.2016121372.

General Management Guidelines

Blood Pressure

- Goal < 130/80 while avoiding hypotension
  - If ACR (Microalbumin:Cr) > 30 mg/g
    - Consider <130/80 if this can be safely achieved.
    - **Ace inhibitor or ARB** (but not both) should be part of management strategy and the goal would be to reduce ACR to < 30 mg/g (or UPC < 0.2) or lowest achievable level.

Ace inhibitor or ARB should be part of antihypertensive regimen for CKD patients with:

- Proteinuria > 300mg/day ***with or without*** HTN
- All diabetics with CKD

General Management Guidelines

Underappreciated fact is the risk of having an MI with CKD is equivalent to that of diabetes …

CKD Lipid Management (not transplanted or on dialysis)

- Secondary Prevention: (prior history of CAD, CVA, or PAD)
  - Maximally tolerated statin therapy (same as non CKD)
    - *Atorvastatin commonly used because it does not require any dose adjustment*
- Primary Prevention
  - Adults >50 years and eGFR of <60ml
    - Moderate intensity statin or statin/ezetimibe combination.
  - Adults >50 with CKD and eGFR ≥60
    - Moderate intensity statin.
  - Adults 19-49 with CKD
    - Many would treat with **Moderate Intensity Statin**
    - Others would only treat if 10 year cardiovascular risk is > 7.5 – 10%.

**Moderate-intensity statins that have shown benefit in CKD include atorvastatin 20 mg daily, fluvastatin 80 mg daily, pravastatin 40 mg daily, rosuvastatin 20 mg daily, and simvastatin 40 mg daily.*

General Management Guidelines

- **Anemia in CKD**
  - In advanced CKD 70% of pre-dialysis patients will have a Hb <10 and ½ of those will have a Hb < 9.
  - All patients with CKD should have age appropriate malignancy screening.
  - GOAL Hb 9-11 g/dL
    - Iron deficiency is common in CKD
      - Many won't respond to oral iron therapy
    - Many will eventually require Erythropoietin Stimulating Agents

Early management of anemia in CKD slows the progression, avoids the need for blood transfusion (reduces Ab formation for patients who will eventually benefit from solid organ transplantation), and reduces hospitalizations.

General Management Guidelines

Remember susceptibility to Acute Kidney Injury…

- **Sick day medication list**
  - On days when the patient is tolerating solids and fluids poorly due to acute illness (viral syndrome, etc.) they should hold ACEi/ARB, SGLT2i, and diuretics.
  - Consider giving them a list of approved medications for viral illness and avoiding NSAID

- **Pain**
  - Avoid NSAIDs in CKD (except 81mg ASA for CV reduction)
  - Tylenol for mild pain control
  - Patients should be given a list of brand and generic NSAIDs to avoid and to prevent accidental over-the-counter purchase.

Radiology Considerations

- **CT Scans** with contrast
  - Consider alternative non-contrast imaging study
  - If no other alternative in patients with eGFR >30, then:
    - Hold ACE/ARB and diuretics the day before the study. Repeat eGFR in 3-5 days to be sure it is safe to restart.
    - Hold Metformin 2 days before the study. Repeat eGFR in 3-5 days to be sure it is safe to restart.
    - Have patient drink to thirst on day of procedure *(or a little extra if they can tolerate it)*

Radiology Considerations

- MRI with Gadolinium Group 1 & 3 Agents
  - DO NOT administer gadolinium for the following circumstances
    - CKD with eGFR ≤30 or during AKI
    - CKD due to hepatorenal syndrome or Peri-operatively post liver transplant
    - *If gadolinium must be administered, consult nephrology prior*
- MRI with Gadolinium Group 2 Agents

There is emerging body of literature to support the use of Group II Gadolinium (Macrocyclic chelate GBCA preparations) in these cases with very low risk of NSF. These agents are safer and being used at our hospital now routinely.

Verify with radiology the gadolinium used for your study is appropriate.

GFR declining, when to worry

- General considerations:
  - Stable GFR between **45-59** mL/min/1.73 m^2 generally do not presage future kidney failure (in the absence of albuminuria).
  - When GFR drops below **45** mL/min/1.73 m^2 there is a significant increase in cardiovascular disease risk.
  - GFR that falls by > **4** mL/min/1.73 m^2**/year** is considered rapid progression of CKD.
    - GFR calculated in the setting of AKI is unreliable and should not be used to determine stage of CKD.
  - Normal age-related decline in renal function is a drop in GFR by **0.8-1** mL/min/1.73 m^2**/year.**

Follow serum Cr in your aging population alongside GFR. If the Cr stays about the same as the GFR slowly drifts down you can be more reassured that this is age related change.

Renal "Kidney" Replacement Therapies

- Conversation historically has started CKD stage 4-5
  - Options include
    - Peritoneal Dialysis (home therapy)
    - Hemodialysis (in center and home therapy available)
      - Access maturation can take over 3 months
    - Kidney Transplant (preferred but limited by organ availability)
    - No RRT
      - Patients over 80 have recently been the fastest growing population of new dialysis patients.
        - Though dialysis can prolong survival in elderly patients with ESRD ***(some doing very well)*** this survival advantage diminishes in individuals with high comorbidity scores.
        - Individualized approach to each patient.