Acute Kidney Injury Cases

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Disclosures

- None. (Well, I am not a Nephrology PA).

- This presentation has no current affiliation or financial arrangements and does not cover any off-label uses of products.

Objectives

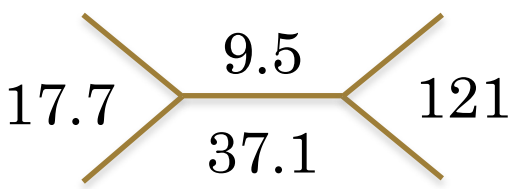
- Recognize the stages of kidney disease and the signs and symptoms that accompany them
- Define acute kidney injury (AKI), its different causes and treatment options
- Determine the desired goals of therapy for patients with progressive kidney disease
- Identify the indications for dialysis in a hospitalized patient with ESRD or AKI

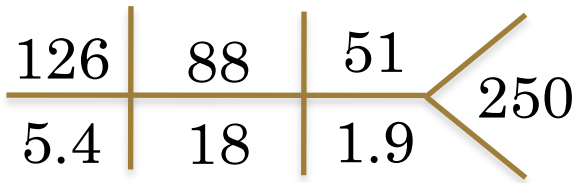
Captain O’Hagen

- 66 y/o male who is a recently retired state trooper
- PMH
  - HTN on HCTZ and Lisinopril
  - Previous bladder CA status post resection and BCG
  - UTI one week ago treated with Bactrim
- Presents to ED with c/o fever, chills and worsening dysuria for the last 24 hours

Captain O’Hagen

- VS: T 39.2 BP 90/45 P 115 R 26 Sat 96%





(Cr last week 1.1)

- UA: Large leukocytes, WBC: TNTC, RBC: Few
- EKG: Sinus tachycardia

Audience Response

- What is the most likely cause of Captain O'Hagen's renal failure?

A. Hypertensive nephropathy secondary to non-compliance

B. Acute tubular necrosis secondary to sepsis

C. Obstructive uropathy secondary to bladder CA

D. Prerenal azotemia secondary to dehydration

E. Interstitial nephritis secondary to Bactrim

Acute Kidney Injury

- Incidence
  - 3-7% of hospitalized patients.
  - 25-30% of ICU patients

- Sudden decline in renal function (GFR)
  - Failure to excrete metabolic waste products
  - Inability to maintain fluid and electrolyte balance
  - Impaired acid-base regulation

Cost of AKI in the Hospital

- When adjusted for severity, Acute Kidney Injury:
  - Increased the costs of hospitalization by $1795
  - Increased LOS by 1.1 days

- In patients with AKI requiring dialysis
  - Increased the cost of hospitalization by $42,077
  - Increased LOS by 11.5 days

Journal of Hospital Medicine.2017

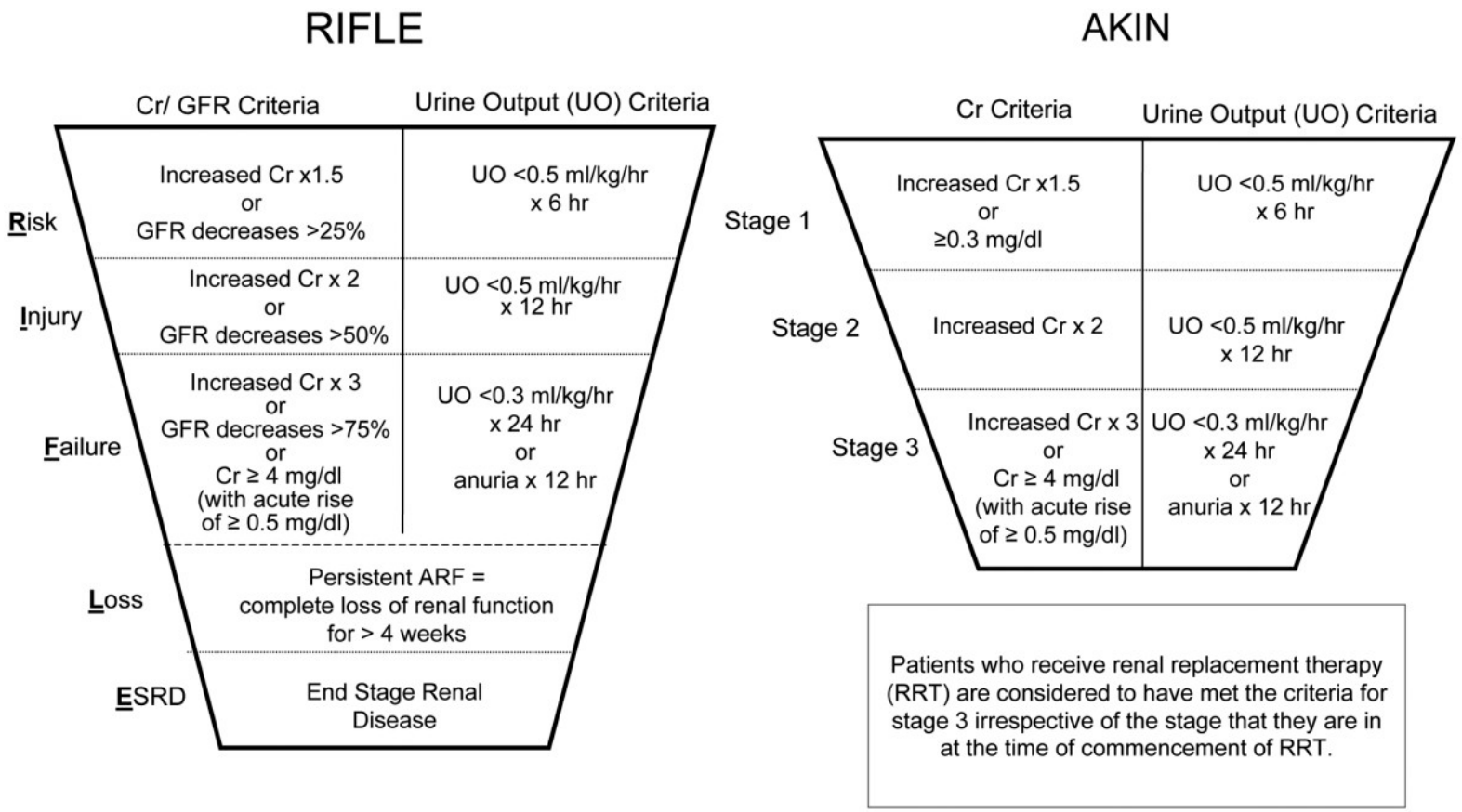
Criteria

- RIFLE
  - System for classification of severity/staging and outcome
    - Spectrum of kidney impairment/injury
  - Based on changes in serum creatinine or urine output
  - Severity classes: Risk, Injury, Failure
  - Outcome classes: Loss, ESRD

Criteria

- Acute Kidney Injury Network (AKIN)
  - Modification of RIFLE to include diagnostic criteria and staging of disease
  - Risk category
    - Addition of a 0.3mg/dL or higher increase in serum creatinine level
  - Better capture of I and F classes in RIFLE

Diagnostic Criteria



Kidney International Supplements; 2012.

Diagnostic Criteria

- Kidney Disease: Improving Global Outcomes (KDIGO)
  - Combination of RIFLE and AKIN

Criteria	KDIGO
Diagnostic	Increase in serum creatinine of ≥0.3 mg/dL within 48 hours or ≥50% within 7 days OR Urine output of <0.5 mL/kg/hour for >6 hour
Stage 1	Increase in serum creatinine of ≥0.3 mg/dL or 50 to 99% OR Urine output of <0.5 mL/kg/hour for 6 to 12 hours
Stage 2	Increase in serum creatinine of 100 to 199% OR Urine output of <0.5 mL/kg/hour for 12 to 24 hours
Stage 3	Increase in serum creatinine of ≥200% OR Increase in serum creatinine of ≥0.3 mg/dL to ≥4.0 mg/dL OR Urine output of <0.3 mL/kg/hour for ≥24 hours or anuria for ≥12 hours OR Initiation of renal replacement therapy

Staging

- Staging
  - Risk RRT
  - Mortality
  - Long-term risk (after resolution)
    - Chronic kidney disease
    - Cardiovascular disease
  - RIFLE or AKIN acceptable
    - Highest stage

Criteria Limitations

- Limitations
  - Need serum creatinine level
  - May underestimate fast progressing disease
  - Correlation between serum creatinine level and urine output not established
  - Poor correlation between AKI stage and GFR
  - Relies on relative changes in serum creatinine
  - Independent of cause of AKI

Audience Response

- If it was reported that Captain O’Hagens urine output for the first 24 hours of hospitalization was 90mL, what would be the most appropriate classification of his kidney injury?

A. Oliguric
B. Non-oliguric
C. Anuric
D. End stage

Classification

- Urine output
  - How much urine is produced
    - Nonoliguric: >400mL/24 hour
    - Oliguric: <400mL/24 hour
    - Anuric: <100mL/24 hour
- Source of injury
  - Prerenal
  - Intrarenal
  - Postrenal

Prerenal

- Inadequate perfusion to the kidneys
  - True
    - Vascular depletion
  - Effective
    - Low cardiac output
    - Change in vascular resistance

True Volume Depletion

- Hemorrhage
- GI
  - Vomiting
  - Diarrhea
  - NG tube
  - Pancreatitis
- Renal
  - Diabetic ketoacidosis
  - Addison’s disease
- Cutaneous
  - Burns
  - Sweating

Effective Volume Depletion

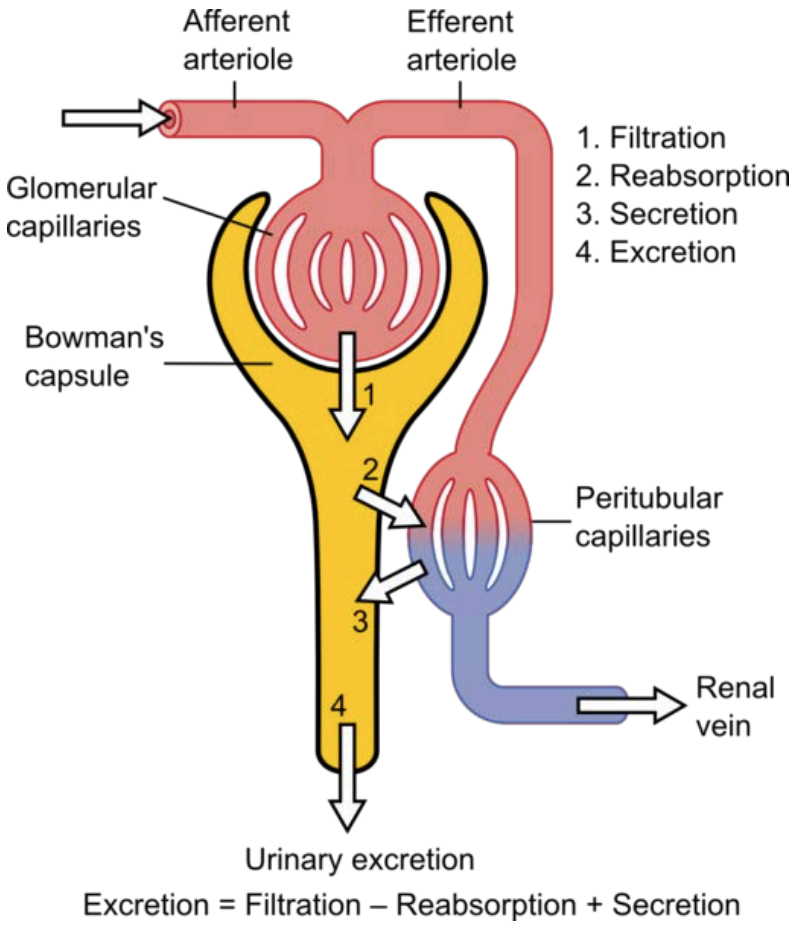
- Decreased effective circulating volume
  - Vasodilation
    - Sepsis
    - Cirrhosis
    - Anaphylaxis
  - Reduced cardiac output
  - Renal vasoconstriction

Vasoconstriction

Often medication induced

NSAIDs: Afferent arteriole

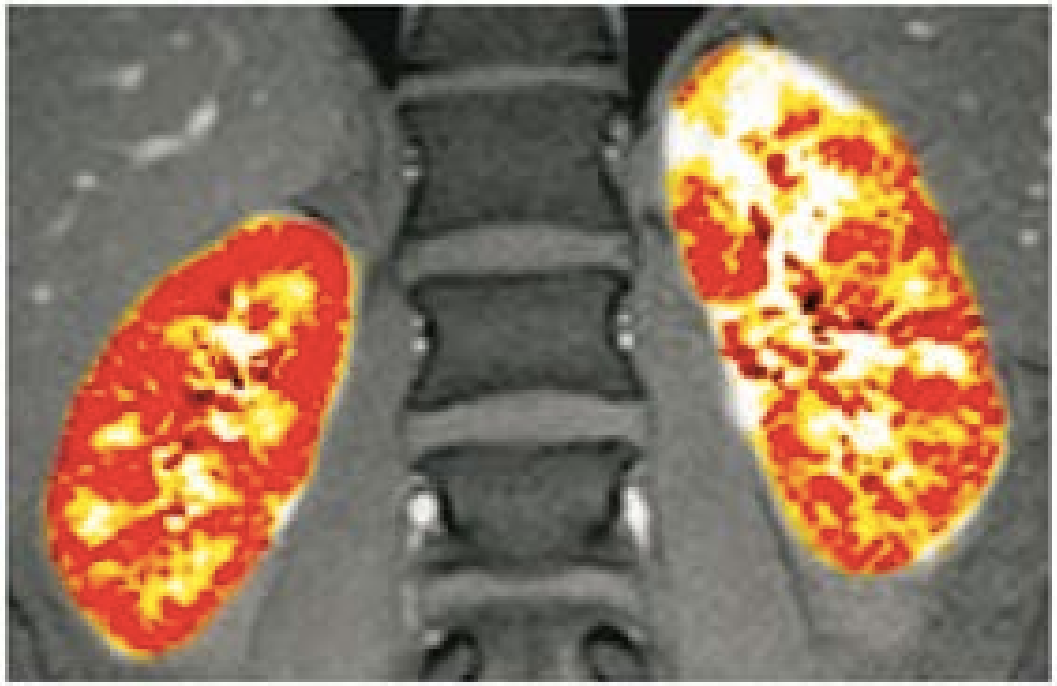
ACE-I/ARBs: Efferent arteriole



Dr. Reem Al-Quadah, 2011

Intrarenal

- Glomerular
- Interstitial
- Vascular
- Tubular
  - Most common: 85%



“Bold MRI” *Kidney International* 2006

Tubular

- Ischemic
  - Hypotension
  - Sepsis
- Nephrotoxic
  - Medications
    - Aminoglycosides, Amphotericin B, Cisplatin, Contrast
  - Cast nephropathy
    - Multiple myeloma
  - Rhabdomyolysis

Bracco.com. 2018

Contrast Nephropathy

- Renal tubular epithelial cell toxicity and renal medullary ischemia
- Second leading cause of acute kidney injury in hospitalized patients
- Risk factors
  - Age
  - **Preexisting renal disease**
  - Volume depletion
  - Comorbid conditions: Diabetes, CHF
  - **Repeated doses of contrast**

Contrast Nephropathy

- Prevention
  - Hydration is key
  - Acetylcysteine
  - Sodium bicarbonate

Postrenal

Obstruction

- Retroperitoneal fibrosis
- Bladder outlet obstruction
- Stones
- Crystals
- Tumors
- Clots
- BPH

NEJM. 2006

Back to Captain O'Hagen

Acute Tubular Necrosis

Metastasis

Hypotension

Possible causes of AKI in this patient?

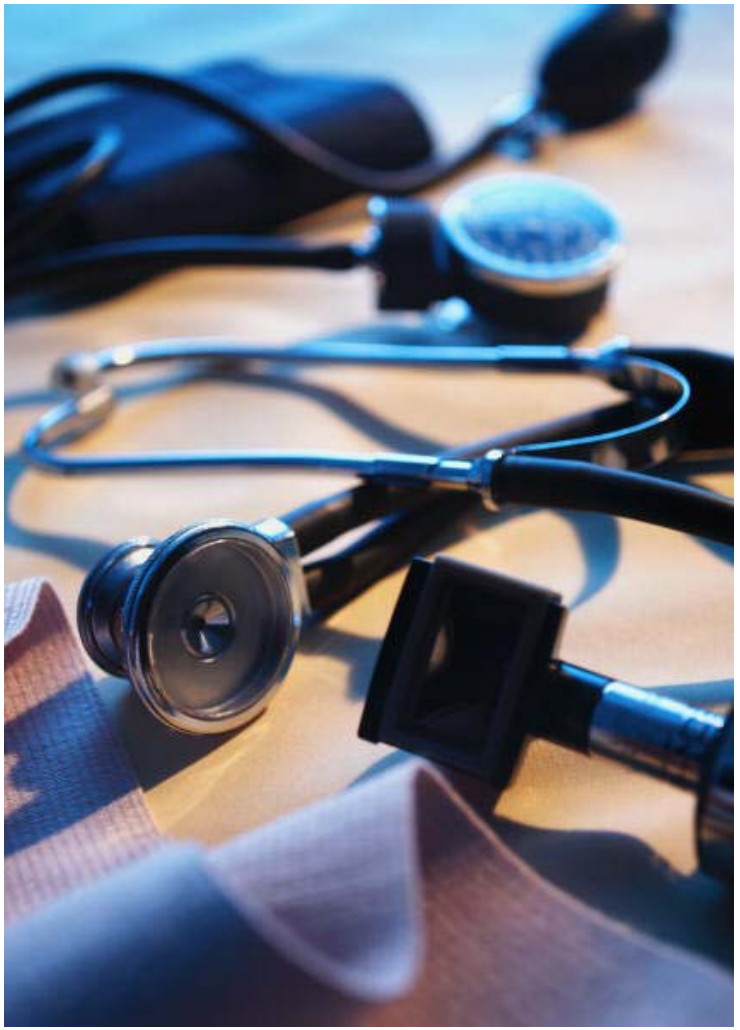
Effective volume depletion

Acute Interstitial Disease

Pyelonephritis

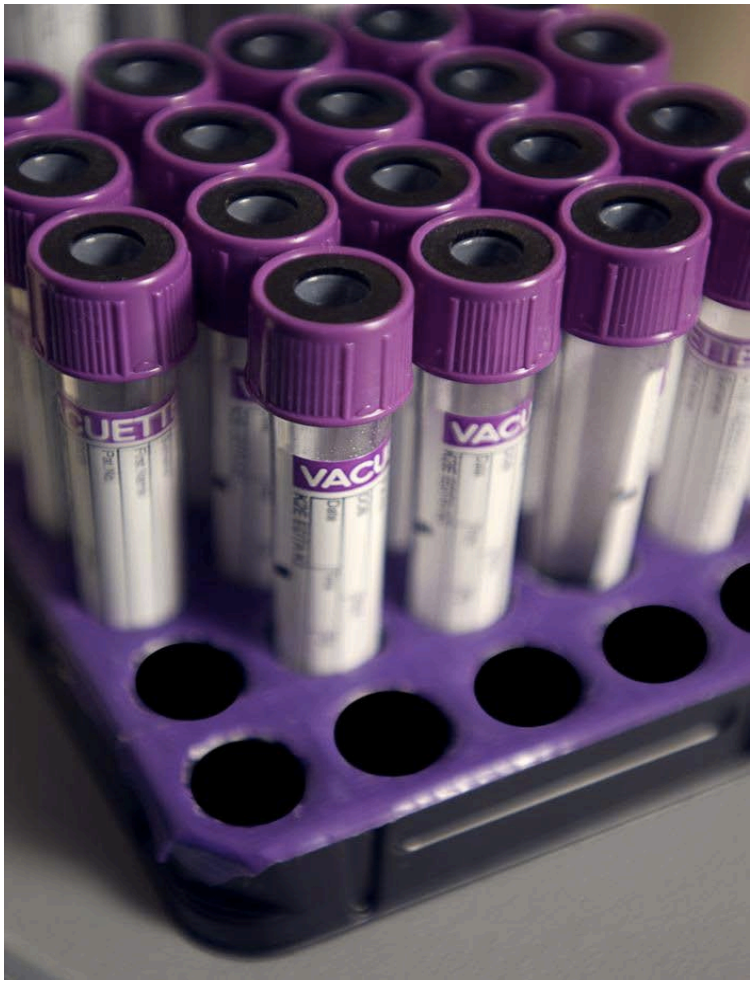
Evaluation

- History and Physical
- Laboratory exams
  - Blood
  - Urinalysis
- Imaging
  - US
  - CT
  - MR
- Biopsy



Primary Blood Exams

- BUN
- Electrolytes
- CBC with differential
  - Eosinophils
- Phosphorus
- Uric acid



CDC.org

Evaluation

- Serum Creatinine
  - Normal range (Adult)
    - Male: 0.6 – 1.2 mg/dL
    - Female: 0.5 – 1.1 mg/dL

Creatinine	GFR
2 X normal	1/2 normal
3 X normal	1/3 normal
4 X normal	1/4 normal
5 X normal	1/5 normal

  - NKF- CKDEPI Creatinine Equation

Calculating GFR

- Cockcroft-Gault

$$eC_{Cr} = \frac{(140\text{-Age}) \times \text{Mass(kg)} \times (0.85 \text{ if female})}{72 \times \text{Serum Creatinine(mg/dL)}}$$

- Modification of Diet in Renal Disease (MDRD)
  - More accurate
  - $eGFR = 186 \times \text{Serum Creatinine}^{-1.154} \times \text{Age}^{-0.203} \times (1.210 \text{ if Black}) \times (0.742 \text{ if Female})$

Secondary Blood Exams

- Albumin
- ANA
- Anti-DS DNA Ab
- Cryoglobulins
- Complement
  - Low C3; Normal C4
- ANCA
- Anti-GBM
- Antistreptolysin O titer
- Hepatitis B & C Ab

CDC.org

Urine

- Urinalysis
- Urinary sediment
  - Muddy brown casts:
    - *Pathognomonic of tubular injury*
- Random electrolytes
- Eosinophils

Azoproducts.com

Urine

- Urine protein/Urine creatinine ratio
  - Normal: <30 mg/g
  - 24 hour urine collection versus spot
    - In previous healthy individuals, 24 hour collection better but spot analysis nearly as accurate in predicting outcomes
    - Mixed evidence in patients with chronic kidney disease
    - Early morning sample best

International Journal of Nephrology. 2015

FENa

Fractional Excretion of Sodium (FENa)

$$\text{FENa \%} = \frac{\text{UNa} \times \text{PCr}}{\text{PNa} \times \text{UCr}} \times 100$$

Interpretation:
<1% suggests prerenal etiology
>3% more suggestive of intrarenal (ATN)

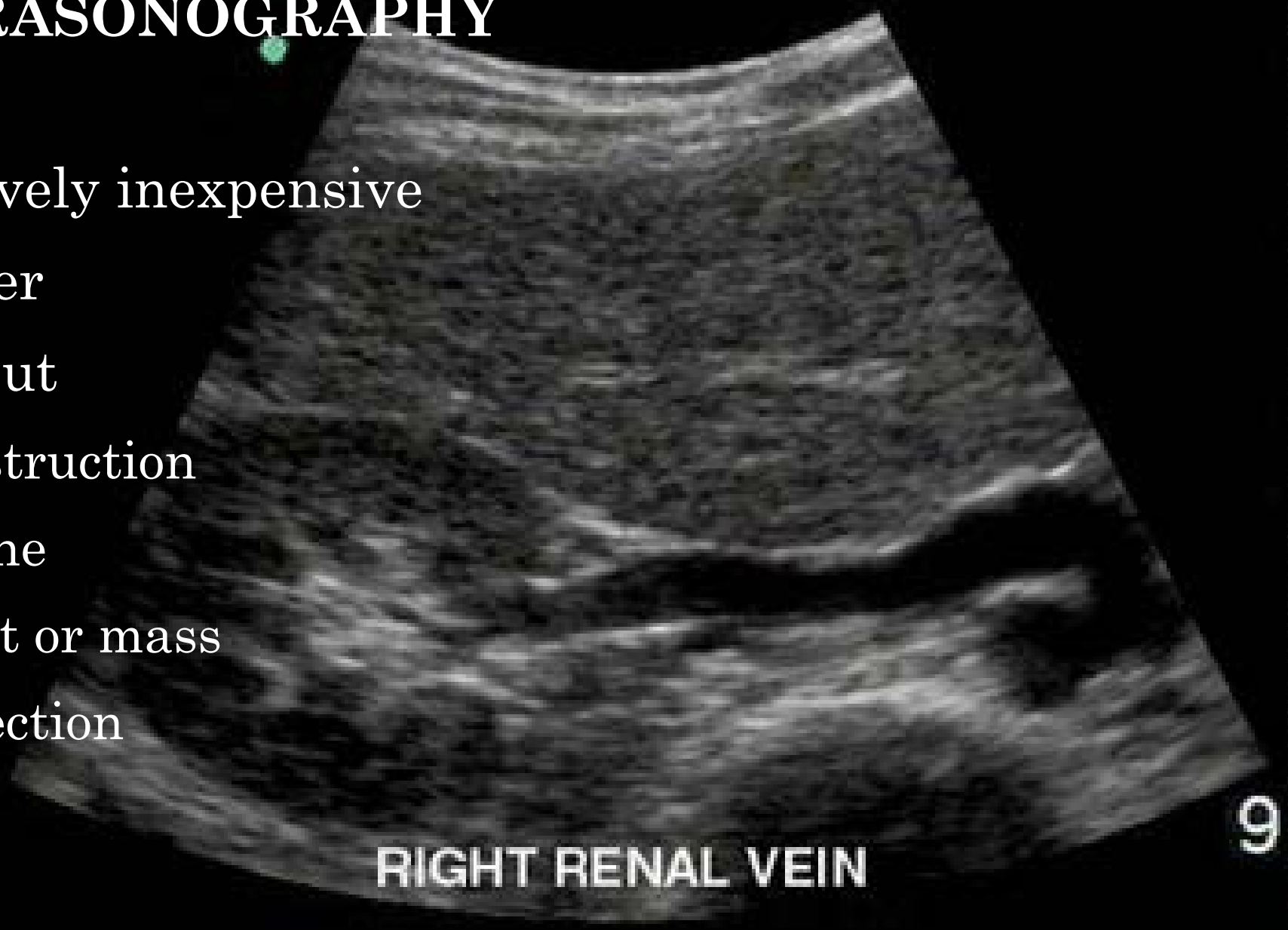
Blood and Urine Studies

Type of kidney injury	BUN/ Creat ratio	Urine Osmolality	Urinalysis	Urine Volume	Proteinuria	Urine Na+	Fractional excretion Na+
Prerenal	>20:1	>500 mOsm/kg	Normal	Decreased	Trace	< 20 MEq/dL	<1%
Intrinsic	<20:1	250-300 mOsm/kg	Dark granular casts	Oliguric or nonoliguric	2+ - 4+	>30 MEq/dL	>3%
Postrenal	<20:1	> 400 mOsm/kg	Hyaline casts	Absent*	0 - Trace	< 20 MEq/dL	

Captain O’Hagen

ULTRASONOGRAPHY

- Safe
- Relatively inexpensive
- Doppler
- Rule out
  - Obstruction
  - Stone
  - Cyst or mass
  - Infection



Sonosite.com

Radiology

- Little value in CT or MRI
  - CT may be useful if retroperitoneal fibrosis or stone suspected
  - No gadolinium with GFR <30

Role of Biopsy

- Indications
  - Unexplained CKD
  - Unexplained worsening AKI
  - Nephrotic syndrome
  - Acute nephritic syndrome
- Contraindications
  - Solitary native kidney
  - Bleeding diathesis
  - Hydronephrosis
  - Pyelonephritis
  - Renal tumor

Rarely needed to diagnose AKI

Practical Approach

- Detailed history and Physical
- Careful review of medical record
  - Medications
  - Procedures
- Labs
  - U/A, Urine electrolytes
  - CBC, Electrolytes
- Bladder scan
- +/- Ultrasound

Captain O’Hagen

- Diagnosis: Sepsis secondary to urinary tract infection
- Volume resuscitation
  - Improved BP and HR
- Creatinine hospital day #3: 2.2

Captain O’Hagen

- Phosphorus, Uric acid, LDH WNL
- Urinary sediment shows muddy brown granular casts
- FENa 4%
- Renal US negative for pyelonephritis

MANAGEMENT

CDC.org 20

Management

- Optimization volume status, hemodynamics
- Avoidance nephrotoxins
  - Renal dosing of medications
- Nutritional support
- Complication management
  - Uremic complications
- Renal replacement

Medication Pearls

- Traditional medication concerns
  - Discontinue diuretics/ACE/ARD
    - Consider clonidine 0.1 mg PO 2–3 times a day or may use hydralazine 25 mg PO 2–3 times a day (if no other contraindications, i.e. reflex tachycardia) for high BP
  - Vancomycin, Gentamycin, Potassium supplements
  - Don’t forget about OTC medications or supplements
  - Avoid contrast studies

Medication Pearls

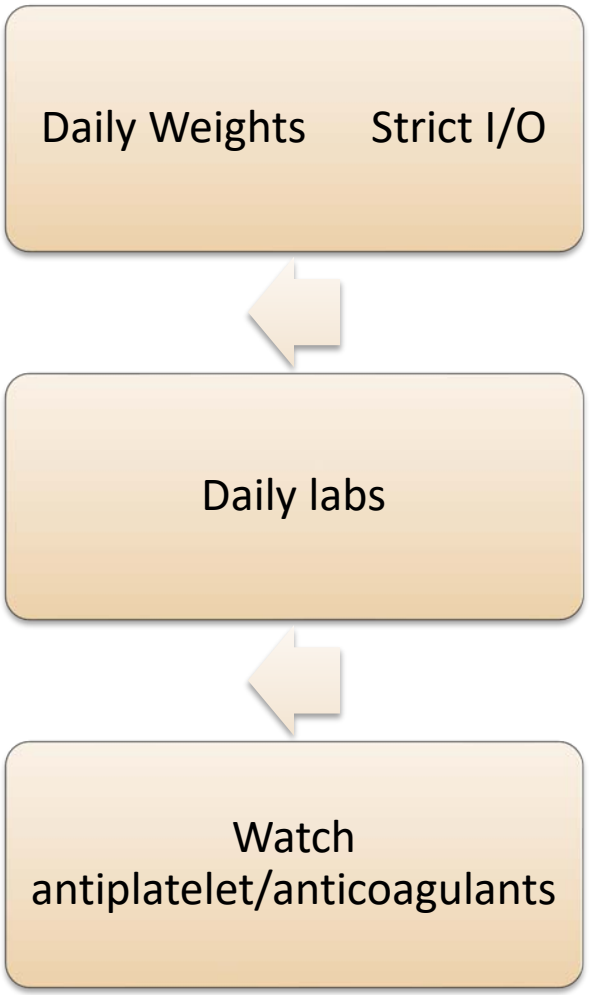
- Some medications can cause a false positive rise in creatinine
  - Interfere with creatinine secretion
  - Interfere with assay
  - Examples
    - Cimetidine
    - Trimethoprim
    - Cefoitin
    - Flucytosine

Nutrition Support

- Conflicting opinions
- Calorie maintenance historically ignored
- Protein restriction is controversial as acutely ill patients often run a protein deficit
  - Data lacking either way
  - Uremia may contribute to feeding challenges
- Most agree:
  - *Low potassium*
- Fluid restriction depends on fluid status
- May need tube feeding to provide calories

Complication Management

- Volume issues
  - Volume depletion
  - Volume overload
- Electrolytes
  - Hyperkalemia
  - Hypocalcemia
  - Hyperphosphatemia
- Metabolic acidosis
- Uremic complications

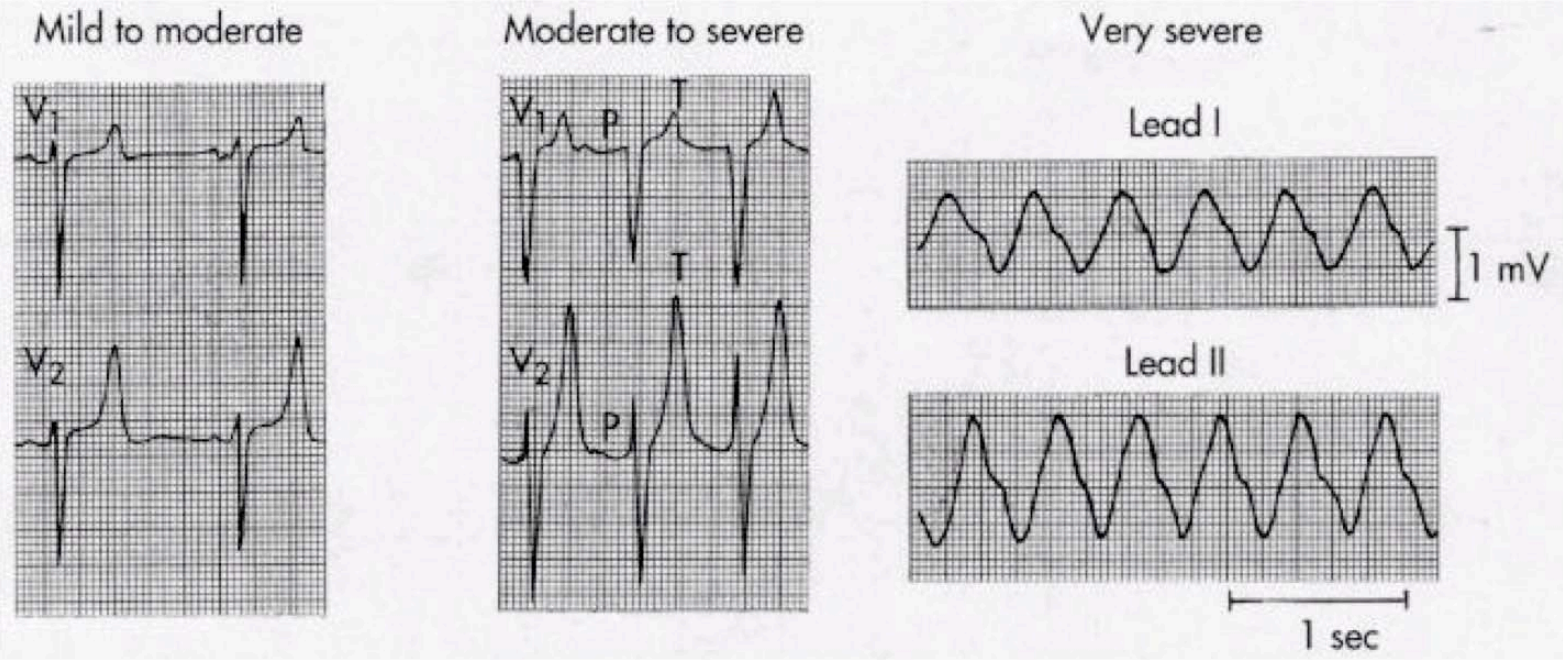


Hyperkalemia

- Normal range varies
- When to treat?
  - Based on clinical findings
  - EKG findings determine urgency

- Three treatment principles:
  - Stabilize cardiac membranes
  - Drive extracellular potassium into cells
  - Remove excess potassium from body

Hyperkalemia



Peaked T waves

Flattened P wave

Widened QRS complex

Sine-wave pattern

Audience Response

- Which of the following treatments for hyperkalemia acts by enhancing potassium uptake by cells?

  A. Calcium gluconate

  B. Furosemide (Lasix)

  C. Albuterol (Proventil)

  D. Sodium polystyrene sulfonate (Kayexalate)

Hyperkalemia

- Stabilize cardiac membranes
  - IV Calcium
- Drive extracellular potassium into cells
  - Insulin
  - Beta 2- adrenergic agonist
  - Sodium bicarbonate (Controversial)
- Remove excess potassium from body
  - Diuretics
  - Cation exchange resins
  - Dialysis

Audience Response

- Which of the following is NOT a recognized indication for emergent hemodialysis?

  A. Hyperkalemia

  B. Treatment refractory fluid overload

  C. Hyponatremia

  D. Metabolic acidosis

  E. Uremic pericarditis

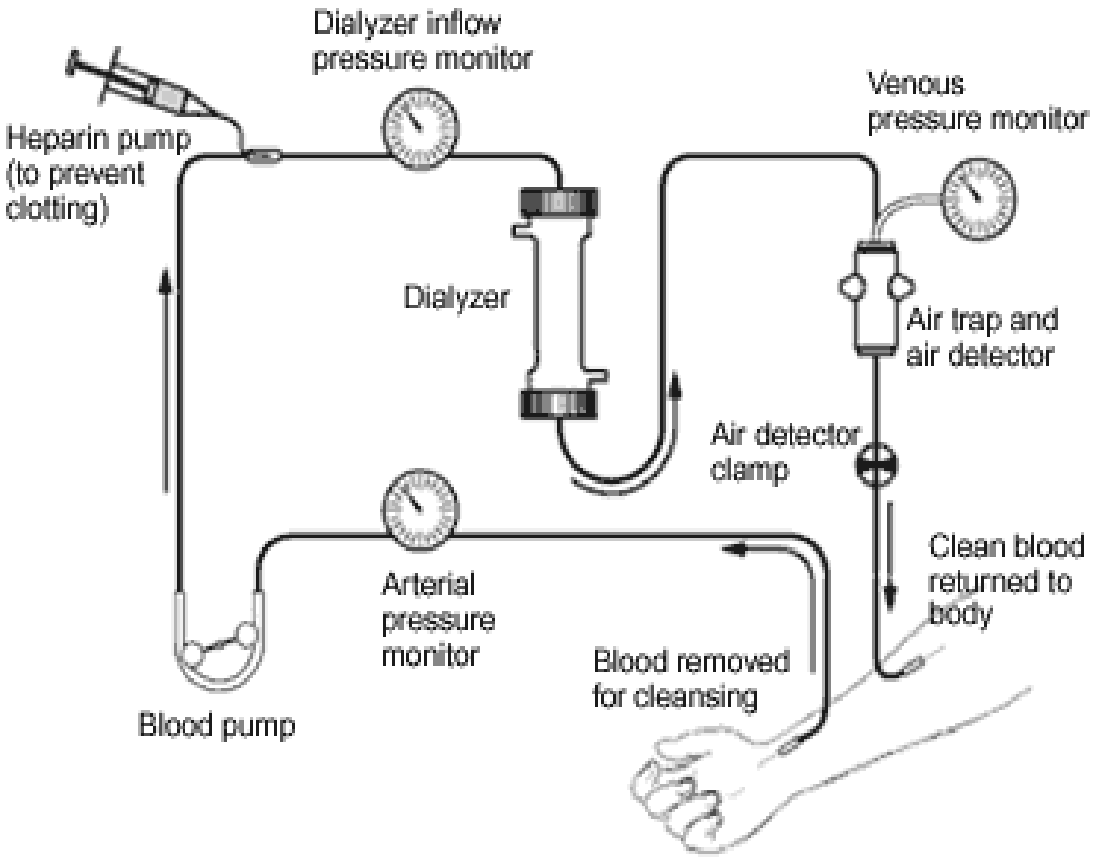
Indications for Dialysis

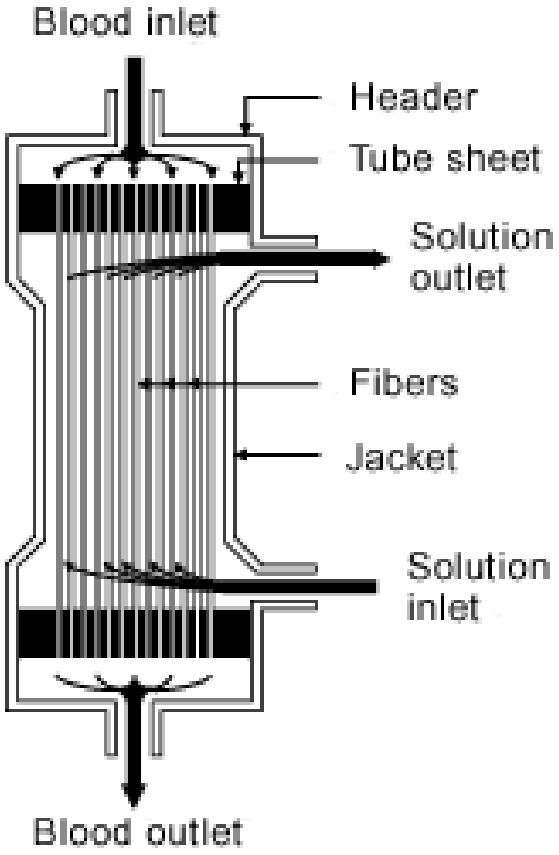
- **A**cid-base disturbance
  - Metabolic acidosis
- **E**lectrolyte abnormalities
  - Hyperkalmia with EKG changes
- **I**ngested toxins
- **O**verload refractory to diuretics
- **U**remia
  - AMS, Seizure, Pericarditis

What is Dialysis

- Diffusion of small molecules down their concentration gradient across a semi-permeable membrane.
  - Diffusion: Movements of small particles down their gradients
  - Ultrafiltration: Removal of water from a patients circulation

Standard Hemodialysis





Role of Nephrologist in Management of AKI in the Hospital

- In general earlier is better
  - CKD model
- ICU patients
- Considering dialysis
- Possible need for renal biopsy

Outcomes

- Strong association of AKI with hospital mortality
  - Overall mortality 20-90%
  - 33-66% of critically ill patients who develop AKI done survive to discharge
- Near linear increase in hospital mortality with increasing RIFLE class
  - R: 3x mortality of patients without AKI
  - I: 2x mortality of R
  - F: 10x mortality of patients without AKI

Outcomes in AKI

- 28% of patients admitted with AKI died within the subsequent 12 months
  - Causes CV (28%) and Cancer (28%)
  - Associated with age, cancer, chemotherapy and nursing home residence
- Increased cost
- Increased LOS

Journal of the American Society of Nephrology. 2017

Audience Response

- What is the most likely cause of death in a patient with acute kidney injury?

  A. Hyperkalemia

  B. Myocardial infarction

  C. Infection

  D. Stroke

  E. Dialysis related complication

Death in Acute Kidney Injury

- Infections (30-70%)
- Cardiovascular events (5-30%)
- GI, pulmonary or neurologic complications (7-30%)
- Hyperkalemia or Dialysis related (1-2%)

Prevention of AKI in the Hospital

- Avoid hypotension
- Maintain fluid balance
  - Selection of fluid (NEJM 2018)
  - Watch the I/O
- Avoid nephrotoxins

NEJM. March 2018; June 2018.

Hospitalized patients with ESRD

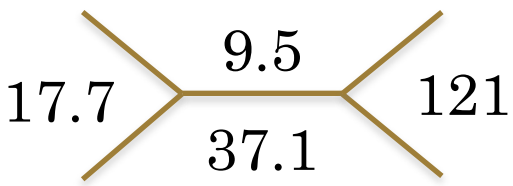
Mr. Farva

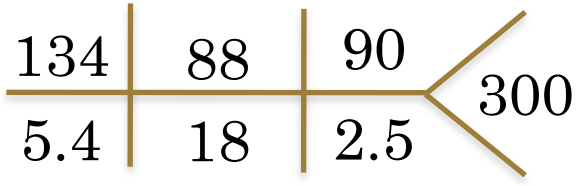
- 50 y/o male who is a country western signer
- PMH
  - History of Type 1 DM and HTN
  - Progressive CKD
  - Started dialysis 8 months ago with a M,W,F schedule, still has left chest catheter for dialysis
  - Makes little/no urine

- Presents to ED with c/o fever, chills and cough for the last 3 days. Fever in dialysis today, sent to ER.

Mr. Farva

- VS: T 39.2 BP 100/45 P 95 R 26 Sat 90%





- UA: Unable to obtain
- EKG: Sinus tachycardia, no acute CT Changes
- CXR: RLL infiltrate

Mr. Farva

- Patient started on piperacillin-tazobactam, levaquin and vancomycin for healthcare associated pneumonia.
- Nursing asks about timing of the antibiotics in relation to patients dialysis in the morning.
- What would you recommend?

Hospitalized Patients With ESRD

- On average, patients with ESRD are admitted twice a year
- 30% will be readmitted within 30 days of a discharge
- Hospitalization accounts for 40% of all spending on ESRD patients
- Age-adjusted life expectancy in patients with ESRD lower then the general population

USRDS. 2016

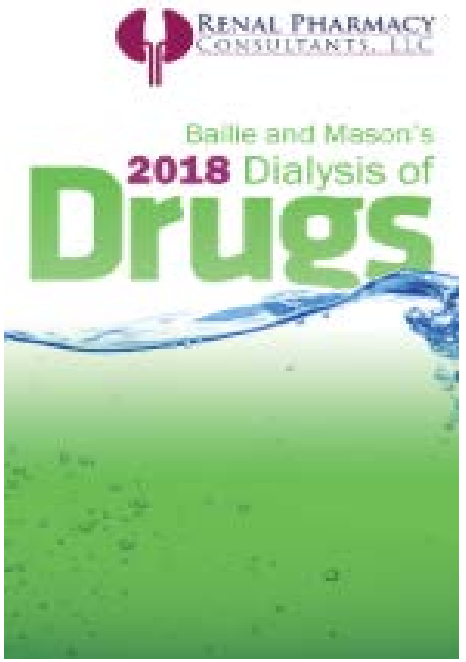
Hospitalized Patients With ESRD

- Three types of patients with Renal Replacement Therapy (RRT)
  - Hemodialysis
  - Peritoneal Dialysis
  - Renal Transplant

USRDS. 2016

Hemodialysis

- Dialysis access
  - Temporary access/ lines- source of infection?
  - IV access
- Fluid status and electrolytes
- Bleeding diathesis
- Drug dosing
- Timing of procedures
- Timing of medications



USRDS. 2016

Peritoneal Dialysis

- Timing of dialysis
- Infection, infection, infection
- Dialysis solutions
  - Nephrology typically involved
- Electrolytes

USRDS. 2016

Transplant Patient

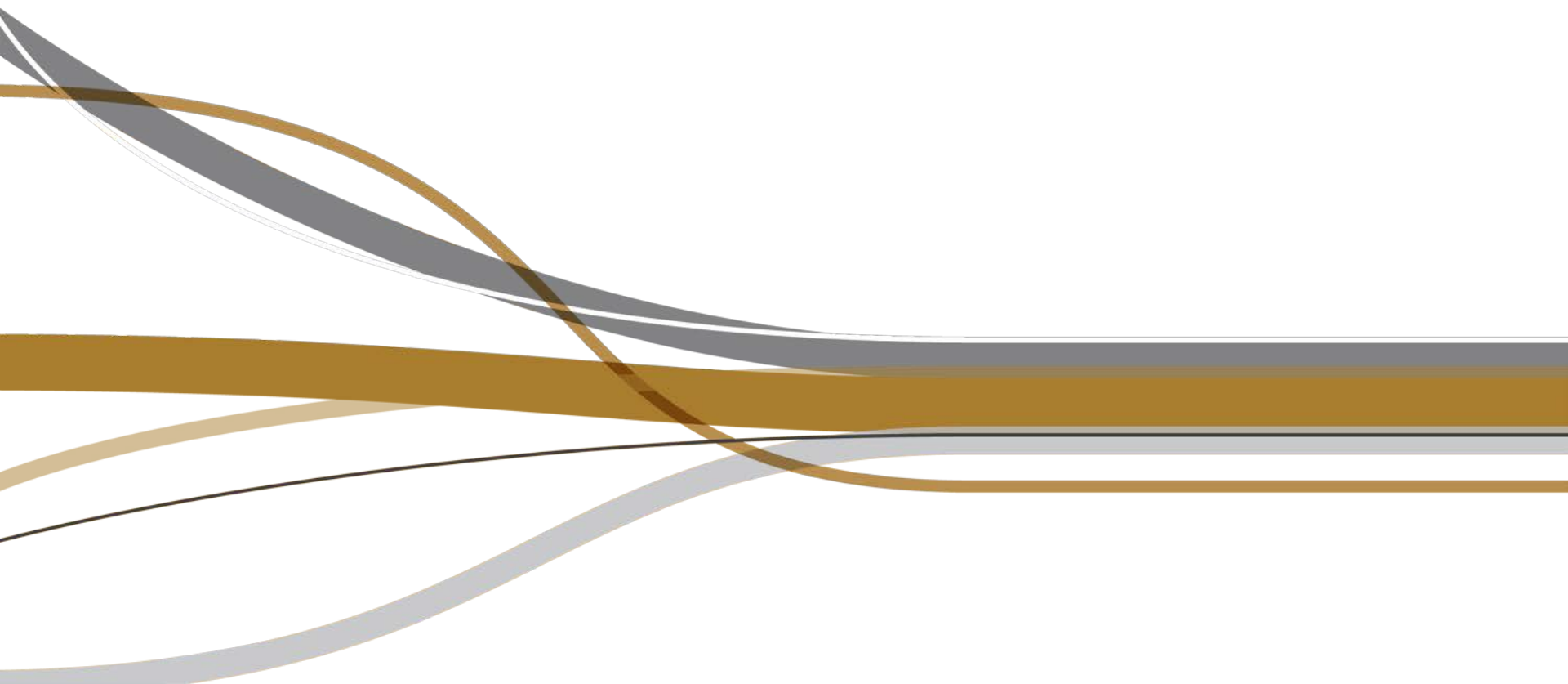
- Immunosuppressants
  - Don’t miss doses*
  - Drug levels/ dose timing
  - Drug/ drug interactions
- Infection, infection, infection

USRDS. 2016

Take Home Points

- Acute Kidney Injury (AKI) is associated with significant increased cost and morbidity/mortality in the hospitalized patient.
- Careful history and physical are often the key to diagnosis.
- Remember to adjust medications based on renal function.
- The vowels can help you remember the indications for acute dialysis (*A,E,I,O,U*).
- Timing of medications around hemodialysis is crucial to achieve therapeutic levels.

Questions?



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