Renal Disease 1

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Continuing Medical Education
Disclosure

Gary Levine, MD, returned disclosures indicating that indicating that he has no affiliation or financial interest in any organization(s).

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Special Thanks

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Learning Objectives

1. Cite the causes and explain the management of acute kidney injury.

2. Discuss the common metabolic issues seen in the critically ill patient as a result of renal compromise.

3. Discuss the principles of neurohormonal antagonism and the role of the kidney in the management of heart failure.
Functions of the Kidney

Maintenance of the extracellular fluid environment

- Excretion of metabolic waste products
  - Urea
  - Creatinine
  - Uric acid
- Water balance
- Electrolyte balance
- Acid-base balance
Functions of the Kidney

Hormone secretion

• Regulation of systemic and renal hemodynamics
  • Renin
  • Angiotensin II
  • Prostaglandins
  • Bradykinin

• Red blood cell production
  • Erythropoietin

• Calcium/phosphorus regulation
  • 1,25-dihydroxycholecalciferol; calcitriol
1. The most cost effective test in evaluating renal disease is?

A. Urine analysis
B. Ultrasound
C. 24-hour urine for CrCL
D. Complete metabolic panel
1. The most cost effective test in evaluating renal disease is?

- A. Urine analysis [74%]
- B. Ultrasound [1%]
- C. 24-hour urine for CrCL [10%]
- D. Complete metabolic panel [14%]
Urinalysis

- The most cost-effective test in evaluating renal disease
- Always perform your own microscopic exam
Urinalysis

- If there is a positive dipstick test for blood
  - But few RBCs
    - Hemolysis
    - Rhabdomyolysis
- Urinary dipstick for protein only measures albumin
  - Bence Jones protein will be missed
  - Urinary protein also varies with the hydration status of the patient
Urinalysis

• Positive leukocyte esterase dipstick test
  – Usually indicates UTI
  – If WBCs and no bacteria, think urethritis
• Large numbers of WBC may not always indicate a UTI
  – Glomerular disease
  – Interstitial nephritis
    • NSAIDs
  – Chronic cystitis
Urinalysis

• Hyaline and granular casts can be normal
• RBC and WBC casts are always abnormal
  – Glomerulonephritis
  – Pyelonephritis
2. The Cockroft-Gault and MDRD formulas both use age, creatinine, and which of the following variables in determining GFR?

A. Sex
B. Ethnicity
C. Microalbumin
D. Actual body weight
2. The Cockroft-Gault and MDRD formulas both use age, creatinine, and which of the following variables in determining GFR?

A. Sex
B. Ethnicity
C. Microalbumin
D. Actual body weight

- A. Sex: 34%
- B. Ethnicity: 29%
- C. Microalbumin: 5%
- D. Actual body weight: 32%
Glomerular Filtration Rate (GFR) Assessment

- Two common calculations
  - Cockroft-Gault estimated CrCl
  - Modified MDRD (Modification of Diet in Renal Disease) formula
- 24-hour urine creatinine clearance
Formulas to Assess Renal Function

- **Cockcroft-Gault** (really CrCl, not GFR)
  \[ e\text{CrCl (cc/min)} = (140 - \text{age yrs}) \times \text{IBW kg/SeCr mg/dl x 72)} \times (0.85 \text{ if female}) \]

- **MDRD**
  \[ e\text{GFR} = 186 \times \text{(SeCr mg/dl)} - 1.154 \times \text{(age yrs)} - 0.203 \times (0.742 \text{ if female}) \times (1.212 \text{ if African Am}) \]
Acute Kidney Injury

- Creatinine is a metabolic waste product excreted by the kidneys
  - Filtered through the glomerulus into the tubules then excreted
  - It is also secreted by tubular cells
    - Certain medications can inhibit tubular secretion and falsely elevate the serum creatinine level: trimethoprim, sulfamethoxazole, cimetidine
Protein Excretion

- 24-hour urine collection
- Random spot urine protein excretion
  - Normal
    - < 150 mg/24 hour in the non-pregnant patient
    - < 300 mg/24 hour in the pregnant patient
    - 3 grams/24 hr = nephrotic syndrome
- Urine microalbumin/creatin
  - < 30 mg/g – normal
  - 30-300 mg/g - microalbuminuria
  - > 300 mg/g - macroalbuminuria
Acute Kidney Injury (AKI)
3. An 70 y/o, 70 kg man is admitted to the hospital with pyelonephritis. His admission creatinine is 1.5 mg/dL. The following morning, his creatinine is 2.8 mg/dL. He has voided 300 ml of urine over the past 10 hrs. According to KDIGO criteria, he has which one of the following:

A. Stage 1 AKI
B. Stage 2 AKI
C. Stage 3 AKI
D. Stage 4 AKI
E. Unstageable AKI
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A. Stage 1 AKI
B. Stage 2 AKI
C. Stage 3 AKI
D. Stage 4 AKI
E. Unstageable AKI
Acute Kidney Injury

• Acute kidney injury
  – Historically referred to as acute renal failure
  – Early recognition facilitates interventions
    • Prevent worsening
    • Prevent multi-organ system failure (SOR C)
Acute Kidney Injury

- Prevalence in US
  - 1% (community-acquired)
  - Up to 7.1% (hospital-acquired) of all hospital admissions
  - Non-ICU mortality rate is ~10%

- Affects 15-20% of pts in ICUs
  - Reported mortality rates > 50%; up to 80% if renal replacement therapy (RRT) or dialysis required

- Most common causes of death are
  - Infectious complications
  - Cardiorespiratory complications
Acute Kidney Injury

• Dx based on
  – Changes in GFR
  – Changes in serum creatinine
  – Urine output
  – Need for renal replacement therapy (dialysis)
Kidney Disease: Improving Global Outcomes (KDIGO)

KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease

Acute Kidney Injury

- KDIGO criteria for AKI
  - Kidney Disease: Improving Global Outcomes (KDIGO)
    - Increase in serum creat of $\geq 0.3$ mg/dL) within 48 hours OR
    - Increase in serum creat of $\geq 1.5$ times baseline within the prior 7 days OR
    - Urine volume $< 0.5$ mL/kg per hour for more than 6 hours
Acute Kidney Injury

• KDIGO severity of AKI
  – Stage 1 AKI
    • (1.5 - 1.9) x baseline increase in serum creat OR
    • ≥ 0.3 mg/dL increase in the serum creat OR
    • Urine output < 0.5 mL/kg per hour for 6 to 12 hrs
  – Stage 2 AKI
    • (2.0 - 2.9) x baseline increase in the serum creat OR
    • Urine output < 0.5 mL/kg per hour for ≥ 12 hours
Acute Kidney Injury

- KDIGO severity of AKI
  - Stage 3 AKI
    - 3 x baseline increase in the serum creat OR
    - Increase in serum creat to $\geq 4.0$ mg/dL OR
    - Urine output of $< 0.3$ mL/kg per hour for $\geq 24$ hours OR
    - Anuria for $\geq 12$ hours OR
    - Initiation of renal replacement therapy OR
    - Decrease in estimated GFR to $< 35$ mL/min in children $< 18$ y/o
4. The most common cause of acute kidney injury is which of the following?

A. Ureteral calculus with hydronephrosis
B. Dehydration
C. Acute tubular necrosis
D. Acute interstitial nephritis
4. The most common cause of acute kidney injury is which of the following?

A. Ureteral calculus with hydronephrosis
B. Dehydration
C. Acute tubular necrosis
D. Acute interstitial nephritis

Correct answer: C. Acute tubular necrosis
Causes of AKI

- Prerenal
- Intrarenal
  - Tubular
  - Glomerular
  - Interstitial
  - Vascular
- Postrenal

Account for 75% of all AKI
Causes of AKI

- Acute tubular necrosis (ATN) - 45%
- Prerenal disease - 21%
- Acute on chronic kidney disease - 13%
  - ATN with prerenal disease
- Urinary tract obstruction - 10%
  - BPH
- Glomerulonephritis or vasculitis - 4%
- Acute interstitial nephritis - 2%
- Thromboembolic disease - 1%
Causes of AKI
Prerenal Azotemia

- Actual intravascular volume depletion
- Diseases that lead to decreases in the effective arterial blood volume
- Medications that reduce renal perfusion
Prerenal Causes of AKI

• Volume depletion
  – Bleeding
  – Dehydration
    • Gastrointestinal volume loss
    • Urinary volume loss
    • Cutaneous losses
Prerenal Causes of AKI

• Decreased effective renal perfusion
  – Shock
  – CHF
    • Effective circulating volume depletion
      – Cardiorenal syndrome
  – Cirrhosis
    • Hepatorenal syndrome
  – Thromboembolic disease
Prerenal Causes of AKI

Medications

• NSAIDs
  – Block cyclo-oxygenase $\rightarrow$ increase thromboxane $A_2$ $\rightarrow$
    afferent vasoconstriction $\rightarrow$ decreased glomerular perfusion

• ACE inhibitors
  – Block production of angiotensin II $\rightarrow$ vasodilation of
    postglomerular efferent vessels $\rightarrow$ decreased glomerular pressure $\rightarrow$
    may cause azotemia
5. Which of the following drugs is commonly associated with allergic interstitial nephritis?

A. Carbamazepine  
B. Allopurinol  
C. Omeprazole  
D. Fluoxetine
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A. Carbamazepine
B. Allopurinol
C. Omeprazole
D. Fluoxetine

Correct Answer: B. Allopurinol
Causes of AKI

Intrarenal

• Tubular/interstitial
• Glomerular
• Vascular
Intrarenal Causes

**Tubular**

- Injury most often caused by
  - Ischemia and/or
  - Nephrotoxins
Renal Causes of AKI

- Tubulointerstitial diseases (acute)
  - Acute tubular necrosis (ATN)
  - Acute interstitial nephritis (AIN)
    - Usually drug-induced
  - Multiple myeloma
  - Hypercalcemia
  - Tumor lysis syndrome
  - Acute phosphate nephropathy
    - Following a phosphate-containing bowel preparation prior to colonoscopy or surgery
Intrarenal Causes

• Acute tubular necrosis ATN
  – Initiation phase (initial insult)
  – Maintenance phase (1-2 wks)
  – Recovery phase (marked diuresis and slow return of kidney function)
  – No therapy has been shown to hasten recovery
Intrarenal Causes
Acute Interstitial Nephritis (AIN)

• Causes
  – Allergic reaction to a drug
  – Autoimmune diseases
  – Infection
  – Infiltrative diseases

• Symptoms
  – Fever
  – Rash
  – Elevated serum and urine eosinophils

• Immediate withdrawal of drug and supportive care are essential
  – Corticosteroids may be beneficial
Drugs Commonly Associated with AIN

- Allopurinol
- Cimetidine
- Thiazides
- Furosemide
- Cephalosporins
- Ciprofloxacin
- Penicillin
- Rifampin
- Sulfonamides
- NSAIDs
- Phenytoin
Renal Causes of AKI

• Tubulointerstitial diseases (chronic)
  – Polycystic kidney disease
  – Nephrocalcinosis
    • Hypercalcemia and/or hypercalciuria
  – Sarcoidosis
  – Sjögren's syndrome
  – Reflux nephropathy
    • Children/adolescents
  – Medullary cystic kidney disease
    • Autosomal dominant
Intrarenal Causes

Glomerular

- An uncommon cause of AKI
- Systemic manifestations
  - Fever
  - Rash
  - Arthritis
- Urine findings
  - RBC casts
  - Hematuria
  - Proteinuria
- Renal consult and biopsy may be required
Renal Causes of AKI

- Glomerular diseases (nephritic)
  - Postinfectious glomerulonephritis
  - IgA nephropathy
  - Thin basement membrane disease
  - Hereditary nephritis
  - Henoch-Schönlein purpura
  - Mesangial proliferative glomerulonephritis
  - Rapidly progressive glomerulonephritis
  - Fibrillary glomerulonephritis
  - Membranoproliferative glomerulonephritis
  - Vasculitis
    - Mixed cryoglobulinemia
Renal Causes of AKI

- Glomerular diseases (nephrotic)
  - Minimal change disease
  - Focal glomerulosclerosis
  - Mesangial proliferative glomerulonephritis
  - Membranous nephropathy
  - Diabetic nephropathy
  - Preeclampsia
  - IgA nephropathy
  - Primary amyloidosis
  - Light chain deposition disease
  - Benign nephrosclerosis
  - Postinfectious glomerulonephritis (later stage)
Intrarenal Causes

Vascular

- **Microvascular**
  - Presents as microangiopathic hemolytic anemia and ARF
  - Secondary to small vessel thrombosis or occlusion

- **Macrovascular**
  - Renal artery stenosis or thrombosis
  - Atheroembolism secondary to:
    - Atrial fibrillation
    - Aortic disease
    - Acute dissection
Renal Causes of AKI

• Vascular disease (acute)
  – Vasculitis
    • Wegener's granulomatosis
  – Thromboembolic disease
  – Hemolytic-uremic syndrome/thrombotic thrombocytopenic purpura
  – Malignant hypertension
  – Scleroderma
Renal Causes of AKI

- Vascular disease (chronic)
  - Hypertensive nephrosclerosis
  - Renal artery stenosis
  - Atheroembolic disease
Causes of AKI
Postrenal

- Obstruction of the outflow tracts of the kidneys
- Most are readily reversible
- Recovery of renal function is directly proportional to the duration of the obstruction
- Renal US recommended to assess for hydronephrosis
Postrenal Causes of AKI

- Obstructive uropathy
  - Anatomic abnormalities
    - Urethral valves
    - Ureterovesical or ureteropelvic junction stenosis
  - Stricture
  - Renal/ureteral calculi
  - BPH
  - Prostate cancer
  - Retroperitoneal or pelvic neoplasms
6. You are reviewing the lab findings of a 64 y/o male hospitalized with AKI, who has no h/o of any long-term medication use. Renal function has been normal, but now the Cr = 2.8 mg/dL, BUN = 60 mg/dL and FENa = 0.75%, urine sp gr = 1.025, and urine sediment shows only hyaline casts. Based on these findings, which one of the following conditions is most likely?

A. Hypovolemia due to vomiting
B. Acute pyelonephritis
C. Interstitial nephritis
D. Hypovolemia due to diuretics
E. Obstruction due to BPH
6. You are reviewing the lab findings of a 64 y/o male hospitalized with AKI, who has no h/o of any long-term medication use. Renal function has been normal, but now the Cr = 2.8 mg/dL, BUN = 60 mg/dL and FENa = 0.75%, urine sp gr = 1.025, and urine sediment shows only hyaline casts. Based on these findings, which one of the following conditions is most likely?

- A. Hypovolemia due to vomiting (35%)
- B. Acute pyelonephritis (2%)
- C. Interstitial nephritis (24%)
- D. Hypovolemia due to diuretics (11%)
- E. Obstruction due to BPH (28%)
FENa

- Fractional excretion of sodium
  - \( \text{FENa} = 100 \times \frac{(U \text{ Na} \times \text{Plasma Creat})}{(\text{Plasma Na} \times U \text{ Creat})} \)
- FENa interpretation
  - < 1% = prerenal
  - 1% - 2% = renal
  - > 2% = ATN
FENa

• Limitations
  – May be < 1% if ATN superimposed on chronic prerenal disease (CHF, cirrhosis)
    • Can occur with certain types of kidney injury including contrast induced nephropathy
  – May not be < 1% in prerenal states in patients with preexisting CKD
  – Can be > 1-2% if diuretics used even in prerenal
  – Can be < 1% in early obstruction, > 1 with chronic obstruction
Renal Biopsy in AKI

- Prerenal and postrenal causes of acute kidney injury have been excluded
- Cause of intrinsic renal injury is unclear
- Clinical assessment and laboratory investigations suggest a diagnosis that requires confirmation before disease-specific therapy is instituted
  - Immunosuppressants
- May need to be performed urgently
  - Oliguria who have rapidly worsening acute kidney injury, hematuria, with RBC casts.
## Drugs Associated with Nephrotoxicity

**Analgesics**
- Acetaminophen
- ASA
- NSAIDS

**Antidepressants**
- Amitriptyline
- Doxepin
- Fluoxetine
- Lithium

**Antihistamines**
- Diphenhydramine, doxylamine

**Antimicrobials**
- Acyclovir
- Aminoglycosides
- Amphotericin B
- Beta-lactams
- Foscarnet
- Ganciclovir
- Pentamidine
- Quinolones
- Rifampin
- Sulfonamides
- Vancomycin
- Adefovir
- Cidofovir
- Tenofovir
- Indinavir
- Calcineurin inhibitors
  - Cyclosporine
  - Tacrolimus

**Antimicrobials (cont)**
- Beta-lactams

**Antimicrobials (cont)**
- Foscarnet
- Ganciclovir
- Pentamidine
- Quinolones
- Rifampin
- Sulfonamides
- Vancomycin

**Antiretrovirals**
- Adefovir
- Cidofovir
- Tenofovir

**Benzodiazepines**
- Benzodiazepines

**Cardiovascular agents**
- ACE -I
- ARB
- Clopidogrel
- Ticlopidine
- Statins

**Chemotherapeutics**
- Carmustine
- Cisplatin
- Interferon-alfa
- Methotrexate
- Mitomycin-C

**Contrast dye**
- Loops
- Thiazides
- Triamterene

**Diuretics**
- Loops
- Thiazides
- Triamterene

**Calcineurin inhibitors**
- Cyclosporine
- Tacrolimus

**Contrast dye**
- Indinavir

**Others**
- Allopurinol
- Gold therapy
- Haloperidol
- Pamidronate
- Phenytoin
- Quinine
- Ranitidine
- Zoledronate

**Drugs of abuse**
- Cocaine
- Heroin
- Ketamine

**Drugs of abuse (cont)**
- Methadone
- Methamphetamine

**Herbals**
- Chinese herbals with aristolochic acid

**Proton pump inhibitors**
- Lansoprazole
- Omeprazole
- Pantoprazole

**Others**
- Chinese herbals with aristolochic acid
Nephrotoxic Meds

- NSAIDs
- Lithium
- Antibiotics
  - Aminoglycosides
  - Vancomycin
  - Amphotericin B
  - Acyclovir
Nephrotoxic Meds

- ACE/ARB
- Diuretics
- Methotrexate
- Cisplatin
Other Important Medications in Renal Disease

• Metformin
  – Should not be used if creatinine
    • ≥ 1.5 (men)
    • > 1.4 (women)
    • CC < 60 mL/min
  – Increased risk of lactic acidosis
Other Important Medications in Renal Disease

- **Enoxaparin**
  - Don’t use if creat > 2 mg/dL

- **Nitrofurantoin**
  - Needs CC > 60 mL/min for clinical effectiveness & avoid toxicity

- **Allopurinol**
  - Adjust dose for CC
7. An 81 y/o male is scheduled to have a CT of his abdomen with contrast to assess for a tumor. He has COPD, type II DM, with a serum Cr of 1.5mg/dL (nl = 0.6-1.5) Which one of the following would decrease the likelihood of contrast-related nephropathy?

A. Oral acetylcysteine BID 24 hr prior to the procedure and the day of it
B. Oral prednisone on the morning of the procedure
C. Oral enalapril (Vasotec) 24 hrs prior to the procedure
D. Use of a hyperosmolar contrast medium
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78%  A. Oral acetylcysteine BID 24 hr prior to the procedure and the day of it

12%  B. Oral prednisone on the morning of the procedure

3%   C. Oral enalapril (Vasotec) 24 hrs prior to the procedure

7%   D. Use of a hyperosmolar contrast medium
Contrast-Induced Nephropathy

- Due to iodinated contrast agents
- 3rd leading cause of AKI in hospitalized patient
  - Increases mortality, morbidity, and length of hospitalization
- Rapid and often irreversible decline in renal function
  - Inc in serum creat ≥ 0.5 mg/dL
  - Inc > 25% above baseline
- Follows a predictable time of onset
- Potentially preventable
Contrast-Induced Nephropathy

• Radiocontrast media
  – Best avoided in patients with, or at risk for, AKI
    • CKD
    • DM
      – Metformin
    • SS disease
    • Dehydration
    • Elderly
Management of At-Risk Patients

BEFORE a Dye Study

- Stop all diuretics, ACE-I/ARB, & metformin
- Isotonic solution IV hydration
  - Favored over hypotonic solutions & oral hydration
- Alkalinize the urine
  - D5W with 3 amps NaHCO3 1cc/kg/hr at least 4-6 hrs prior to exam
  - 1/4NS with 2 amps NaHCO₃ (patients with diabetes)
- Acetylcysteine 1200 mg bid the day before and the day of the exam
  - Lower risk of CIN, compared with 600-mg doses (3.5% versus 11%).
8. Systemic manifestations of acute kidney injury include which of the following biochemical disturbances?

A. Hypokalemia
B. Metabolic acidosis
C. Peripheral insulin resistance and glucose intolerance
D. Decreased BUN
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## Systemic Manifestations of AKI

<table>
<thead>
<tr>
<th>Fluid, electrolyte, &amp; serum biochemical disturbances</th>
<th>Gastrointestinal disturbances</th>
<th>Hematological disturbances</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anuria, oliguria, polyuria/polydipsia</td>
<td>Anorexia</td>
<td>Platelet function defect/bleeding tendencies</td>
</tr>
<tr>
<td>Dehydration</td>
<td>Vomiting and diarrhea</td>
<td>Blood loss anemia</td>
</tr>
<tr>
<td>Azotemia: increased urea and creatinine</td>
<td>Halitosis</td>
<td>Lymphopenia</td>
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<tr>
<td>Metabolic acidosis</td>
<td>Oral ulceration/stomatitis</td>
<td>Neutrophilia</td>
</tr>
<tr>
<td>• Hyperphosphatemia</td>
<td></td>
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- Azotemia: increased urea and creatinine
- Metabolic acidosis
  - Hyperphosphatemia
  - Hyperkalemia
  - Hypercalcemia/hypocalcemia
- Peripheral insulin resistance and glucose intolerance
- Dehydration
- Anuria, oliguria, polyuria/polydipsia
- Anorexia
- Vomiting and diarrhea
- Halitosis
- Oral ulceration/stomatitis
- Gastropathy, gastritis, gastric and duodenal ulceration and bleeding
Systemic Manifestations of AKI

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<tr>
<th>Cardiovascular and pulmonary disturbances</th>
<th>Neuromuscular disturbances</th>
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<tbody>
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<td>Systemic arterial hypertension</td>
<td>Weakness</td>
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<tr>
<td>Uremic pneumonitis</td>
<td>Lethargy</td>
</tr>
<tr>
<td></td>
<td>Depression</td>
</tr>
<tr>
<td></td>
<td>Uremic encephalopathy</td>
</tr>
<tr>
<td></td>
<td>Coma/death</td>
</tr>
</tbody>
</table>
Management of AKI

• Patients with AKI generally should be hospitalized – Unless mild and clearly resulting from an easily reversible cause
• Close collaboration among primary care physicians, nephrologists, hospitalists, and other subspecialists is essential
• Management is primarily supportive
Management of AKI

• Treat underlying cause if identified
  – Sepsis, CHF, DKA, other catastrophic illness
• Treat reversible causes
  – Volume depletion
• Avoid exposure to aggravating factors
  – Contrast studies
  – Toxic medications/NSAIDs
  – ACE-inhibitors/ARB (rare)
Treatment of AKI

• Assure adequate renal perfusion
  – Achieve and maintain hemodynamic stability
    • Goal is mean arterial pressure $>65 \text{ mm Hg}$
  – Avoid hypovolemia
  – Isotonic solutions are preferred over hyperoncotic solutions
    • NS $> \text{ dextrans, hydroxyethyl starch, albumin}$
Treatment of AKI

• Volume overload
  – Furosemide IV q 6 hrs is the initial Rx
    • 20-100 mg initially
    • If inadequate response after 1 hr, double the dose
    • Repeat process until adequate urine output
  – Ultra-filtration via dialysis (last resort)
Treatment of AKI

• Correct
  – Electrolyte abnormalities
  – Symptomatic uremia

• Prevent complications
  – Including nutritional deficiencies
Hyperkalemia Rx (Initial Rx)

- Calcium
  - Calcium gluconate 10% solution – 10 mL IV
    - Cardio protective/membrane stabilizer
    - Temporarily reverses the neuromuscular effects of hyperkalemia
- Insulin*
  - 10 units IV and glucose 25 gm
- Inhaled beta-agonists*
- Sodium bicarbonate*
  - 3 ampules in 1 L of 5% dextrose

*Temporarily shift K⁺ intracellularly
Hyperkalemia Rx—(K+ Elimination)

• Sodium polystyrene sulfonate (Kayexalate)
  – Orally
    • 25-50 g mixed with 100 mL of 20% sorbitol
  – Rectally
    • 50 g in 50 mL of 70% sorbitol and 150 mL of tap water
Acidosis

• Sodium bicarbonate (if serum level < 15 mEq/L or pH < 7.2)
  – Given IV or PO
  – Amount based on Bicarb deficit equation
    – Bicarb deficit (mEq/L) = 0.4*wt(kg) * (24 – pt’s serum bicarb level)
  – Arm and Hammer baking soda provides approx 50 mEq of sodium bicarb per rounded tsp
Acute Kidney Injury (AKI)

- Nonoliguric renal failure patients fare better than those with oliguria
- Use of diuretics to stimulate urine output actually increases mortality and does not promote recovery of renal function (SOR B)
Acute Kidney Injury (AKI)—Rx

- Dopamine (low-dose)
  - No benefit (SOR A).
    - Preventing AKI
    - Need for dialysis
    - Reduce hospital or ICU lengths of stay
    - Mortality
9. In patients with AKI, urgent dialysis is **not** indicated in which of the following situations?

A. Hyperkalemia refractory to medical therapy  
B. Volume overload unresponsive to diuretics  
C. Metabolic acidosis with pH = 7.25  
D. Lithium overdose  
E. Uremic pericarditis
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- C. Metabolic acidosis with pH = 7.25
- D. Lithium overdose
- E. Uremic pericarditis

A. Hyperkalemia refractory to medical therapy (2%)
B. Volume overload unresponsive to diuretics (2%)
C. Metabolic acidosis with pH = 7.25 (76%)
D. Lithium overdose (12%)
E. Uremic pericarditis (8%)
Acute Kidney Injury

- Indications for dialysis in patients with AKI
  - Metabolic acidosis
    - pH < 7.1
    - Administration of bicarbonate is not indicated or effective
      - Volume overload
      - Ketoacidosis
  - Uremia
    - Pericarditis/pleuritis
    - Neuropathy
    - Encephalopathy/altered MS
Acute Kidney Injury

- Indications for dialysis in patients with AKI
  - Fluid overload refractory to diuretics
  - Hyperkalemia
    - K+ > 6.5 or rapidly rising
    - Refractory to medical therapy
- Poisonings and intoxications
  - Ethylene glycol, lithium
AKI—Prevention

• Vasopressors are recommended for persistent hypotension despite fluid resuscitation

• Hepatic failure/cirrhosis
  – Avoid hypotension/GI bleeding
  – Albumin infusion during large volume paracentesis
AKI—Prevention

• Cancer chemotherapy
  – Hydration and allopurinol (Zyloprim) administration a few days before chemotherapy initiation
• Avoid nephrotoxic medications
• Exposure to radiographic contrast agents
  – Optimize volume status
  – Isotonic normal saline or sodium bicarbonate in high-risk patients who are not at risk of volume overload
  – N-acetylcysteine
AKI—Prevention

- Rhabdomyolysis
  - Maintain adequate hydration
  - Alkalization of the urine with intravenous sodium bicarbonate
- Surgery – Preop
  - Adequate volume resuscitation/prevention of hypotension
  - Consider holding ACE/ARB/aldosterone blockers
  - Treat sepsis
AKI—Prognosis

- Patients with acute kidney injury
  - More likely to develop chronic kidney disease
  - Higher risk of end-stage renal disease
  - Higher risk of premature death
Neurohormonal Antagonism &
The Role of the Kidney in Heart Failure
10. Which of the following statements is true?

A. ACE inhibitors enhance angiotensin 2 vasoconstriction of efferent arterioles
B. Angiotensin 2 inhibits secretion of aldosterone and vasopressin
C. ACE-I therapy should be stopped if a 20% increase in serum creatinine is noted
D. Type 1 cardiorenal syndrome is defined as AKI resulting from acute CHF
10. Which of the following statements is true?

A. ACE inhibitors enhance angiotensin 2 vasoconstriction of efferent arterioles  
   20%

B. Angiotensin 2 inhibits secretion of aldosterone and vasopressin  
   9%

C. ACE-I therapy should be stopped if a 20% increase in serum creatinine is noted  
   59%

D. Type 1 cardiorenal syndrome is defined as AKI resulting from acute CHF  
   12%
Neurohormonal Renal Effects

• Renin
  – Released by renal juxtaglomerular apparatus
  – In response to
    • Fall in BP
    • Decreased blood volume
    • Decreased sodium concentration in the distal tubule
    • Sympathetic stimulation

• Angiotensin 1
  – Formed from renin-induced conversion of angiotensinogen
Neurohormonal Renal Effects

• Angiotensin 2
  – Formed from angiotensin 1 via ACE
  – Direct arterial vasoconstriction
    • Constriction of efferent arterioles
  – Results in aldosterone secretion from adrenal gland
    • Sodium retention
  – Results in vasopressin release from posterior pituitary
    • H2O retention at distal tubule
Diuretic Effects

Volume Depletion → JG Cells

↑ Renin Release → Renin

Renin → Angiotensin I

Angiotensin I → ACE Inhibitor

ACE Inhibitor → Angiotensin II

Angiotensin II → AT₁ Receptor

AT₁ Receptor → Vasoconstriction

Distal Tubule

Na⁺ Diuresis

Less Na⁺ Reabsorbed
Renal Autoregulation

- Enables the kidney to maintain fairly constant renal blood flow and GFR as mean arterial pressure varies between 80 and 160 mm Hg.
- Myogenic reflex causes afferent arteriole to constrict or dilate in response to changes in intraluminal pressure.
- Angiotensin II – mediated efferent arteriole constriction provides support for GFR when renal perfusion pressure decreases.
Renal Autoregulation in Chronic Hypertension

- As systolic pressure rises above 160 mm Hg, constriction of preglomerular vessels is overcome by high pressure.
- With progressive renal injury, autoregulation is impaired and intraglomerular (IG) pressure begins to vary directly with systemic pressure.
- High intraglomerular pressure can lead to injury and rapid loss of renal function.
1. Filtration
2. Reabsorption
3. Secretion
4. Excretion

Excretion = Filtration – Reabsorption + Secretion

Source: KH Maen/Wikipedia
Treatment-Induced Decline in Renal Function

- ACE-I/ARB dilate efferent arteriole, exaggerating decline in IG pressure.
- A 20-30% increase in creatinine, which then stabilizes, represents a *hemodynamic* change, and *not* a structural change.
- 1997 study following GFR after initiation of ACE-I
  - Those with *largest* initial increase in creatinine had most *stable* renal function over time
  - Creatinine reversed with discontinuation of drug

Treatment-Induced Decline in Renal Function

• If creatinine increases by *more than 30%*, agent (ACE-I or ARB) should be discontinued and other causes of renal dysfunction should be evaluated.
Causes of > 30% ACE-I/ARB-Induced Decline in Renal Function

- Bilateral renal-artery obstruction (usually > 70%)
- Absolute or effective reduction in intravascular volume:
- Aggressive diuresis
- Poor oral intake
- Moderate-to-severe congestive heart failure
- Renal vasoconstriction:
  - NSAIDs
  - Early sepsis
Heart Disease and Kidney Disease

- Acute or chronic dysfunction of the heart or kidneys can induce acute or chronic dysfunction in the other organ.
- Mortality is increased in patients with heart failure (HF) who have a reduced glomerular filtration rate (GFR)
  - Mortality increased by approximately 15% for every 10 mL/min reduction in estimated GFR
- Patients with chronic kidney disease have an increased risk of both atherosclerotic cardiovascular disease and heart failure
- Cardiovascular disease is responsible for up to 50 percent of deaths in patients with renal failure
Cardiorenal Syndrome (CRS)

• National Heart, Lung, and Blood Institute definition

• Type 1 (acute)
  – Acute HF results in acute kidney injury (AKI).

• Type 2
  – Chronic cardiac dysfunction (chronic CHF) causes progressive chronic kidney disease (CKD)
Cardiorenal Syndrome (CRS)

- **Type 3**
  - Abrupt and primary worsening of kidney function causes acute cardiac dysfunction
    - Renal ischemia or glomerulonephritis
    - May be manifested by CHF

- **Type 4**
  - Primary CKD contributes to cardiac dysfunction
    - Manifested by coronary disease, HF, or arrhythmia.

- **Type 5 (secondary)**
  - Acute or chronic systemic disorders cause both cardiac and renal dysfunction
    - Sepsis, diabetes
Cardiorenal Syndrome (CRS)

• Possible mechanisms by which acute HF leads to worsening kidney function (type 1 & 2 CRS)
  – Neurohumoral adaptations - result in vasoconstriction
    • Activation of the sympathetic nervous system
    • Renin-angiotensin-aldosterone system
    • Release of vasopressin
  – Reduced renal perfusion
  – Increased renal venous pressure
    • Reduces GFR
  – Right ventricular dysfunction
ACE-Inhibitors

- Block the conversion of angiotensin I to angiotensin II
- Lower arteriolar resistance
- Increase venous capacity
- Decrease cardiac output/stroke work
- Increase sodium excretion
- Increase levels of renin, angiotensin 1, and bradykinin
ACE-Inhibitors

- Cause a central enhancement of parasympathetic activity
  - Break cycle of sympathetic system activation
  - Reduce plasma norepinephrine levels in CHF
    - May reduce the prevalence of malignant cardiac arrhythmias
    - Reduction in sudden death
    - Interrupt the downward spiral in cardiac function in congestive heart failure
Cardiorenal Syndrome (CRS)

- Possible mechanisms by which AKI & CKD lead to worsening cardiac function (type 3 & 4 CRS)
  - Volume overload
  - Hypertension
  - Acidosis
  - Electrolyte abnormalities
  - Anemia
Answers

1. A
2. A
3. A
4. C
5. B
6. A
7. A
8. B
9. C
10. D