Learning Objectives

1. Cite the causes and management of acute renal failure.
2. List the risk factors for and prevention of chronic renal disease.
3. Summarize the management principles of the patient with chronic renal 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

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

Other

- Gluconeogenesis in starvation
- Catabolism of peptide hormones

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 (75%)
- B. Ultrasound (5%)
- C. 24-hour urine for CrCL (2%)
- D. Complete metabolic panel (8%)

**Urinalysis**

- The most cost-effective test in evaluating renal disease
- Always perform your own microscopic exam
- If there is a positive test for blood but few RBCs
  - Hemolysis
  - Rhabdomyolysis

**Urinalysis**

- Urinary dipstick for protein only measures albumin
  - Bence-Jones protein will be missed
  - Urinary protein also varies with the hydration status of the patient
- Hyaline and granular casts can be normal
- RBC and WBC casts are always abnormal

2. GFR estimation formulas may be used in place of 24-hr urine collection. The Cockroft-Gault and MDRD formulas use the following variables EXCEPT?

- A. Age
- B. Weight
- C. Total protein
- D. Creatinine

**Urinalysis**

- Large numbers of WBC may not always indicate a UTI
- Glomerular disease
- Interstitial nephritis
- Drugs: NSAIDS
- Chronic cystitis

2% 6% 31% 64%

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Glomerular Filtration Rate Assessment (GFR)

- Two Common Calculations
  - Cockcroft-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)
  \[ e\text{CrCl} \text{(cc/min)} = \left(140 - \text{age yrs}\right) \times \text{IBW kg/SeCr mg/dl} \times 72 \times (0.85 \text{ if female}) \]
- MDRD
  \[ e\text{GFR} = 186 \times \left(\frac{\text{SeCr mg/dl}}{1.154 \times \text{age yrs} - 0.203 \times (0.742 \text{ if female}) + 0.0412 \times \text{if African Am}}\right) \]

Protein Excretion

- 24-hour urine collection
- Estimated protein excretion
  - Normal
    - <150mg / 24 hour in the nonpregnant patient
    - <300 mg / 24 hour in the pregnant patient

Acute Renal Failure (ARF)

3. You are reviewing the lab findings of a 64 yo male hospitalized with ARF, 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
B. Acute pyelonephritis
C. Interstitial nephritis
D. Obstruction due to BPH

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Acute Renal Failure Defined

- Accepted diagnostic criteria include:
  - Increase in serum creatinine level of 0.5 mg/dl or
  - 50% increase in the creatinine level above baseline value, or
  - 50% decrease in the baseline-calculated GFR, or
  - The need for acute kidney replacement therapy

Acute Renal Failure

- 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
  - Infection complications
  - Cardiorespiratory complications

Acute Renal Failure Pathophysiology

- Creatinine is a metabolic waste product excreted by the kidneys
- Normal GFR
  - 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 (ie, trimethoprim, sulfamethoxazole, cimetidine)

Risk Factors for ARF

<table>
<thead>
<tr>
<th>Concurrent Nephrotoxic Drugs</th>
<th>Concurrent Disease States</th>
<th>Patient Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Furosemids</td>
<td>Neoplasia</td>
<td>Advanced age</td>
</tr>
<tr>
<td>Hypercalcemia</td>
<td>Hemoscytic anemia</td>
<td>Advanced age</td>
</tr>
<tr>
<td>Chemotherapeutic agents</td>
<td>Hemolysis</td>
<td>Advanced age</td>
</tr>
<tr>
<td>NSAIDS</td>
<td>Dehydration</td>
<td>Advanced age</td>
</tr>
<tr>
<td>Liver failure</td>
<td>Pre-existing renal</td>
<td>Insufficiency</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>Shock; decreased</td>
<td>Cardiac output</td>
</tr>
<tr>
<td>Heart failure</td>
<td>Trauma</td>
<td>Advanced age</td>
</tr>
<tr>
<td>Fever</td>
<td>Electrolyte abnormalities</td>
<td>Advanced age</td>
</tr>
<tr>
<td>Sepsis</td>
<td>Metabolic acidosis</td>
<td>Advanced age</td>
</tr>
</tbody>
</table>

4. Common causes for acute renal failure include all Except?

A. Urinary tract infection
B. Dehydration
C. Rheumatoid arthritis
D. Obstruction by a urinary stone

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Causes of ARF

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

Account for 75% of all ARF

Prerenal Azotemia

- Intravascular volume depletion
  - Fever, vomiting, and diarrhea can lead to decreased kidney perfusion
  - Dehydration from any cause (diuretics) can precipitate ARF
- Diseases that lead to decreases in the effective arterial blood volume
  - Heart failure
  - Liver failure
  - Nephrotic syndrome

Prerenal Azotemia (cont.)

- NSAIDS
  - Block cyclo-oxygenase → increase thromboxane A₂ → afferent vasoconstriction → decreased glomerular perfusion
- ACE inhibitors
  - Block production of angiotensin II → vasodilation of postglomerular efferent vessels → decreased glomerular pressure → may cause azotemia
- Large vessel disease
  - Thrombosis, embolus, and dissection can lead to reduced renal perfusion

Intrarenal Causes

- Tubular
  - Injury most often caused by
    - Ischemia and/or
    - Nephrotoxins
  - 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

- Glomerular
  - An uncommon cause of ARF
  - Systemic manifestations
    - Fever
    - Rash
    - Arthritis
  - Urine findings
    - RBC casts
    - Hematuria
    - Proteinuria
  - Renal consult and biopsy may be required
5. Which of the following drugs is commonly associated with Allergic Interstitial Nephritis?

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

Intrarenal Causes

Acute Interstitial Nephritis [AIN]
- 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
- Cephalosporins
- Ciprofloxacin
- Penicillin
- Rifampin
- Thiazides
- Furosemide
- Cimetidine
- NSAIDs
- Phenytoin
- Sulfonamides

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

Causes of ARF

Postrenal
- Obstruction of the outflow tracts of the kidneys
- Prostatic hypertrophy
- Catheters
- Tumors
- Most are readily reversible
- Recovery of renal function is directly proportional to the duration of the obstruction
- Renal US recommended to assess for hydronephrosis
Alternatively…

- ARF can be classified as,
  - Nephrosis
  - Renal ischemia
  - Nephrotoxicosis
  - Nephritis

An Alternative Approach to ARF - Nephrosis

- Renal ischemia*
- Dehydration
- Hypovolemic shock
- Sepsis, burns, heat-stroke: DIC
- Decreased CO: HF, tamponade, dysrhythmias
- Thromboembolism, vasculitis, HTN
- Hyperviscosity: multiple myeloma, polycythemia
- Pigments: hemoglobinuria, myoglobinuria
- NSAIDs
- Acute decompensation of CRF*  
  * Most frequently encountered causes of nephrosis

An Alternative Approach to ARF – Nephrosis

- Nephrotoxicosis
  - Ethylene glycol*
  - Antibiotics: aminoglycosides, sulfonamides, IV tetracyclines, cyclosporin
  - Chemotherapeutics: amphotericin B, cis-platinum, doxorubicin
  - Anesthetics: methoxyflurane
  - Heavy metals: lead, thallium, zinc, arsenic, mercury
  - Hypercalcemia: malignancies, hyperparathyroid, vitamin D toxicity
  - Other causes: carbon tetrachloride, chloroform, iodinated radio contrast media
  * Most frequently encountered causes of nephrosis

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
- Antimicrobials (cont)
- Adefovir
- Cidofovir
- Tenofovir
- Antiretrovirals
- Indinavir
- Benzodiazepines
- Calcineurin inhibitors
- Cyclosporine
- Tacrolimus
- Cardiovascular agents
- ACE –I
- ARB
- Co-enzymes
- Statins
- Chemotherapeutics
- Carmustine
- Cisplatin
- Interferon-alfa
- Methotrexate
- Mitomycin-C
- Contrast dye
- Drugs of abuse (cont)
- Cocaine
- Methadone
- Methamphetamine
- Herbals
- Chinese herbals with aristolochic acid
- Proton pump inhibitors
- Lansoprazole
- Omeprazole
- Pantoprazole
- Others
- Allopurinol
- Gold therapy
- Haloperidol
- Methotrexate
- Quinine
- Ritalin
- Zidovudine

6. Systemic manifestations of Acute Renal Failure include which of the following biochemical disturbances?

A. Hypokalemia
B. Metabolic alkalosis
C. Peripheral insulin resistance and glucose intolerance
D. Decreased BUN
6. Systemic manifestations of Acute Renal Failure include which of the following biochemical disturbances?

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Systemic Manifestations of ARF

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

<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 defects/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>
</tr>
<tr>
<td>Metabolic acidosis</td>
<td>Oral ulceration/stomatitis</td>
<td>Neutrophilia</td>
</tr>
<tr>
<td>Hyperkalemia/hypocalcemia</td>
<td>Gastropathy, gastritis, gastric and duodenal ulceration and bleeding</td>
<td></td>
</tr>
<tr>
<td>Peripheral insulin resistance and glucose intolerance</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Treatment of ARF

Therapy is directed at treating the underlying cause

- Correcting
  - Fluid imbalance
  - Electrolyte abnormalities
  - Uremia
- Preventing complications
  - Including nutritional deficiencies

- Volume depletion
- Volume overload (more common)
  - Resuscitate with saline
  - Furosemide IV q 6 hrs is the initial Rx
    - 20-100mg initially
    - If inadequate response after 1 hr, double the dose
    - Repeat process until adequate urine output
  - Ultra-filtration via dialysis (last resort)

Electrolyte disturbances

- Hyperkalemia
  - Aggressiveness of Rx depends on severity of hyperkalemia and EKG changes seen
  - Acidosis
Hyperkalemia

- Calcium
  - Calcium gluconate 10% solution – 10ml IV
    - Cardio protective
    - Temporarily reverses the neuromuscular effects of hyperkalemia
- Insulin*
  - 10 units IV and glucose 25gm
- Inhaled Beta agonists*
- Sodium bicarbonate*
  - 3 ampules in 1 L of 5% dextrose
  - Temporarily shift K⁺ intracellularly

*Temporarily shift K⁺ intracellularly

Hyperkalemia

- Sodium polystyrene sulfonate (Kayexalate)
  - Orally
    - 25-50g mixed with 100ml of 20% sorbitol
  - Rectally
    - 50g in 50ml of 70% sorbitol and 150ml of tap water
- Dialysis
  - If none of the above measures is successful, dialysis should be initiated

Acidosis

- Sodium bicarbonate
  - (if serum level <15mEq/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 50mEq of sodium bicarb per rounded tsp
- Dialysis
  - Required for irretactable acidosis
  - 20-60% of pts when BUN>100 or Cr=5-10

Acute Renal Failure

Reversible causes of ARF

- Contrast studies
- Volume depletion, diuretics
- Toxic medications/NSAIDs
- ACE-inhibitors/ARB (rare)
- Sepsis or other catastrophic illness
- ATN (acute tubular necrosis)
- Acute interstitial nephritis

Evidence-Based Medicine

Clinical Recommendations for ARF

- Use of Mucomyst (acetylcysteine) prophylactically may be considered to decrease the incidence of renal insufficiency in radiocontrast-media procedure (SOR C)
  - Studies showing improved outcomes are needed
- Dopamine should NOT be used to prevent ARF (SOR A)
- Diuretics should NOT be used to treat oliguria in patients with ARF (SOR B)

Chronic Kidney Disease (CKD)
Definition of CKD
- Kidney damage for >3 mo
  - Structural or functional abnormalities
  - With or without decreased GFR manifested by either
    - Pathological abnormalities or
    - Markers of kidney damage, including abnormal blood, urine, or imaging tests
- GFR <60ml/min/1.73 for >3 mo with or without kidney damage

7. Stage 2 Chronic Kidney Disease is defined as an estimated GFR of?
   A. >90
   B. 60-90
   C. 30-60
   D. 15-30

Renal Disease Staging
- Stage I GFR > 90
  - Dx and Tx of comorbid conditions, slowing progression, CV risk reduction
- Stage II GFR 60-90
  - Estimating progression
- Stage III GFR 30-60
  - Evaluating and Tx of complications
- Stage IV GFR 15-30
  - Prep for kidney replacement
- Stage V GFR < 15 (ESRD)
  - Replacement

Causes of CRF that Lead to ESRD and Transplant
- Chronic glomerulonephritis
- Diabetic nephropathy
- HTN nephropathy
  - ~25% of cases
- Polycystic kidney disease
- Chronic pyelonephritis
- Renal calculi

Chronic Renal Disease
- Evaluation should include:
  - Diagnosis (type of RD)
  - Comorbid conditions
  - Severity, assessed by level of kidney function
  - Complications, related to level of kidney function
  - Risk for loss of kidney function
  - Risk for cardiovascular disease
8. Measures that help slow the progression of CKD include all Except?

A. Use of ACE-I and/or ARB antihypertensive agents
B. Tight glucose control in diabetics
C. Tight BP control
D. High dose NSAIDS

9. Which of the following statements are true about CKD and Hypertension?

A. Most pts with elevated Cr levels should avoid ACE-I or ARB antihypertensives
B. Pts with CKD should strive for a SBP <140
C. Pts with CKD should not have their SBP <130
D. HTN in pts with CKD is typically not responsive to sodium reduction

10. For CKD patients whose protein excretion exceeds 1 g/24 hr, the National Kidney Foundation’s Kidney Disease Outcomes Quality Initiative (KDOQI) recommends a BP goal of?

A. <140/90 mm Hg
B. <135/85 mm Hg
C. <125/75 mm Hg
D. <110/60 mm Hg
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Blood Pressure Goals

<table>
<thead>
<tr>
<th>Population</th>
<th>Blood Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>&lt;140/90</td>
</tr>
<tr>
<td>CKD stages 1-4 with proteinuria &gt;1g/d</td>
<td>&lt;125/75</td>
</tr>
<tr>
<td>CKD stages 1-4 without proteinuria &lt;1g/d</td>
<td>&lt;135/85</td>
</tr>
<tr>
<td>CKD stage 5</td>
<td>&lt;140/90</td>
</tr>
</tbody>
</table>

Non-Pharmacologic Rx of BP

<table>
<thead>
<tr>
<th>Population</th>
<th>Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>Reduce dietary salt and exercise</td>
</tr>
<tr>
<td>CKD stages 1-4 with proteinuria &gt;1g/d</td>
<td>Reduce dietary salt</td>
</tr>
<tr>
<td>CKD stages 1-4 without proteinuria &lt;1g/d</td>
<td>Reduce dietary salt</td>
</tr>
<tr>
<td>CKD stage 5</td>
<td>Reduce dietary salt and fluid intake in HD pt</td>
</tr>
</tbody>
</table>

Pharmacologic Rx of BP

<table>
<thead>
<tr>
<th>Population</th>
<th>Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>Beta Blockers, diuretics</td>
</tr>
<tr>
<td>CKD stages 1-4 with proteinuria &gt;1g/d, and CKD stages 1-4 without proteinuria &lt;1g/d</td>
<td>ACE-I, ARB, diuretics or CCBs in kidney transplant</td>
</tr>
<tr>
<td>CKD stage 5</td>
<td>Any except diuretics in HD pts</td>
</tr>
</tbody>
</table>

Chronic Renal Disease

Review of Medications at all visits for:
- Dosage adjustment based on level of CKD
- Detection of potentially adverse effects on KF or complications of CKD
- Detection of drug interactions
- Therapeutic drug monitoring, if possible

Renal Disease

Evaluation of CKD
- Laboratory evaluation
- Radiology evaluation
- GFR assessment
- Protein excretion
- Kidney biopsy
Laboratory Evaluation for CKD

- UA with microscopic exam
- CMP & uric acid level
- Calcium and phosphorous level
- CBC
- ANA
- Serum protein electrophoresis (SPEP)
- 24-hour urine CrCl and protein
- Estimated GFR and protein excretion
- HepBsAg, Hepatitis C antibody; HIV
- ANCA
- C3, C4, & CH50
- Anti-GBM antibody

Radiology Evaluation for CKD

- Renal ultrasound
- Mag3 renal scan
- Renal angiogram
- Voiding cystourethrogram
- CT scan of the kidneys and liver
- MRI of the kidneys

Indications for a Renal Biopsy

- Hematuria with a low GFR or proteinuria
- Nephrotic range proteinuria
- CKD of unknown cause and normal or large kidneys on US
- ARF of unknown cause
- Patient wants/needs to know

Contraindications to Renal Biopsy

- Uncorrectable bleeding tendency
- Small kidneys <9cm
- Single (functioning) kidney
- Severe HTN
- Multiple large cysts
- Hydronephrosis
- Active infection
- Uncooperative patient

Monitoring CKD

- eGFR should be obtained at least yearly in CKD, and more often in patients with:
  - GFR <60 mL/min/1.73 m²
  - Fast GFR decline in the past
  - Risk factors for faster progression
  - Ongoing treatment to slow progression
  - Exposure to risk factors for acute GFR decline

Guideline 3

11. An 81 yo 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. Fluid loading this patient prior to the procedure
C. Oral enalapril (Vasotec) 24 hrs prior to the procedure
D. Use of a hyperosmolar contrast medium
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Management of Patients with CRF BEFORE a Dye Study

- Stop all diuretics and ACE-I/ARB
- D5W with 3 amps NaHCO3 1cc/kg/hr at least 4-6hrs prior to exam
- 1/4NS with 2 amps NaHCO3 (patients with diabetes)
- Mucomyst 1200mg bid the day before and the day of the exam

Answers

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