Chronic Kidney Disease

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Physiology
Main Kidney Functions
- Balancing solute and water transport
- Excreting metabolic waste products
- Conserving nutrients
- Regulate acid base balance
Endocrine Function

Secretion of:

1. Renin (regulation of blood pressure)
2. Erythropoietin (erythrocyte production)
3. Vitamin D3 (calcium metabolism)
Structure
Major components:
1. Outer Renal Cortex
   • Contains all glomeruli and portions of the tubules
2. Inner Renal Medulla
   • Formed by segments of the proximal and distal tubules, as well as the collecting ducts
   • Consists of renal pyramids
Nephron Function

- Filters plasma at the glomerulus and then reabsorbs and secretes different substances

- Function = form a filtrate of protein free plasma

- Regulates filtrate to maintain:
  1. body fluid volume
  2. electrolyte composition
  3. pH
Filtration Membrane
- Separates the blood within the glomerular capillaries from the filtered fluid in Bowman’s Space

- The glomerular filtrate passes through the 3 layers of the glomerular membrane and forms the primary urine
Renal Blood Flow

- The kidneys are highly vascular, receiving 1000-1200 ml of blood per minute
- Regulated by
  1. Autoregulation
  2. Neural Regulation
  3. Hormonal Regulation

- If mean arterial pressure decreases OR vascular resistance increases, renal blood flow decreases
- Low blood pressure causes NE release which constricts arterioles, leading to decreased secretion of water and salt which increases blood volume and pressure
- Hormonal regulation through the renin angiotensin system
Regulation of Filtrate

- Occurs through two processes:

1. Tubular reabsorption
   • Movement of fluids and solutes from nephron tubules to the blood

2. Tubular secretion
   • Movement of substances from the blood into the nephron tubules

Excretion = elimination of final urine
Figure 35

water, glucose, urea and calcium, potassium, sodium and chloride ions

filtration

hydrogen ions

potassium

secretion

reabsorption

glucose

amino acids

potassium ions

calcium ions

water

concentration

water

sodium

urine
Urine Formation

- From the proximal tubules, Na and glucose are reabsorbed into peritubular capillaries by active transport.

- Water reabsorption follows by osmosis.

- From the distal tubules Na is reabsorbed by active transport.

- Osmotic reabsorption of H2O occurs when ADH is present.

- Secretion of ammonia and hydrogen occurs from peritubular capillaries into distal tubules by active transport.
Helpful Clips

- [http://www.youtube.com/watch?v=uo-NOr-P49I](http://www.youtube.com/watch?v=uo-NOr-P49I)

- [http://www.youtube.com/watch?v=aQZaNXNroVY&feature=related](http://www.youtube.com/watch?v=aQZaNXNroVY&feature=related)

- [http://www.youtube.com/watch?v=AdlfxBooqIA&feature=related](http://www.youtube.com/watch?v=AdlfxBooqIA&feature=related)
Vitamin D

- Inactive vitamin D (from diet or sunlight) require two hydroxylations to become metabolically active

- The first hydroxilation occurs in the liver, the second occurs in the KIDNEY

- This process is stimulated by parathyroid hormone

- End result = active vitamin D₃
Pathophysiology
The progressive loss of renal function associated with systemic disease such as hypertension and diabetes mellitus or intrinsic kidney disease including glomerulonephritis, chronic pyelonephritis, obstructive uropathies, or vascular disorders
Definitions

**Chronic Pyelonephritis** – persistent or recurrent infection of the kidney leading to kidney scarring

**Glomerulonephritis** – inflammation of the glomerulus caused by factors such as infection, immunologic abnormalities, ischemia, free radicals, drugs, toxins, vascular diseases, and systemic diseases such as diabetes mellitus and lupus erythematosis

**Obstructive uropathies** – anatomic changes in the urinary system cause by an obstruction
CKD

- CKD decreases GFR and tubular functions with changes manifested in ALL organ systems

- Kidney damage is defined as GFR less than 60 ml/min/1.73m$^2$ for 3 months or more, irrespective of cause

- Other terms: Renal Insufficiency Chronic Renal Failure
Pathophysiology

- Kidneys can adapt to loss of nephron mass

- Symptomatic changes resulting from increased creatinine, urea, potassium, and alterations in salt and water balance do not become apparent until renal function declines to less than 25% of normal when adaptive renal reserves are exhausted
Intact Nephron Hypothesis

- Loss of nephron mass causes remaining nephrons to hypertrophy/hyperfunction their rates of filtration, reabsorption, and secretion in order to maintain a constant rate of excretion and normal kidney function in the presence of overall declining GFR

- This explains the adaptive changes in solute and water regulation that occur with advancing renal failure
Trade Off Hypothesis

- The continual loss of functioning nephrons and the adaptive hyperfiltration/increased glomerular pressure causes glomerulosclerosis which contributes to uremia and end stage renal failure.
Location of Kidney Damage

- The location of kidney damage influences the loss of kidney function

- Tubular interstitial diseases damage the tubular or medullary parts of the nephron
  - causing renal tubular acidosis, salt wasting, and difficulty and diluting or concentrating urine

- Vascular or Glomerular damage
  - Proteinuria, hematuria, and nephrotic syndrome
Progression
Progression of CKD

- Progression of CKD is thought to be associated with common pathogenic processes regardless of the initial disease
  1. Glomerular hypertension, hyper-filtration, and hypertrophy
  2. Glomerular-sclerosis
  3. Tubulo-interstitial inflammation and fibrosis
Progression of CKD

- Two factors are consistently recognized with advanced renal disease
  - Proteinuria
  - Elevated angiotensin II
Proteinuria

- Glomerular hyper-filtration and ↑’d glomerular capillary permeability
- Protein excreted into the urine (proteinuria)

Tubulo-interstitial injury by activation of complement proteins, macrophages, and pro-inflammatory factors
Elevated Angiotensin II

- Angiotensin II is elevated with progressive nephron injury
- Efferent arteriolar vasoconstriction
- Glomerular hypertension and hyper-filtration
- Systemic hypertension
Angiotensin II

- This high intra-glomerular pressure can cause proteinuria as well
- may also promote pro inflammatory cells the cause fibrosis and scarring of the tissue.
Risk Factors
Risk Factors

1. **Diabetes Mellitus**
   - 33% of CKD is due to diabetes mellitus

2. **Hypertension**

3. **Family History of CKD**
Risk Factors Cont.

- Ethnicity
  - African Americans: 3.8x
  - Native Americans: 2.0x
  - Asians: 1.3x
  - Others: Hispanics and Pacific Islanders
  - Due to higher rates of developing diabetes mellitus and hypertension

- Age

- Polycystic kidney disease
Risk Factors - Polycystic Kidney Disease

• An inherited disorder
• Causes large cysts to form on the kidneys
• Leads to kidney damage and lower GFR
  ▫ Leads to chronic kidney disease
Signs and Symptoms
Signs and Symptoms

• Change in urination
  ▫ Pressure during urination
  ▫ More frequently
  ▫ At night
  ▫ Foamy or bubbly

• Swelling
  ▫ In hands, feet, ankles, legs, or face
  ▫ Kidney can’t filter fluid properly so more gets retained
Signs and Symptoms Cont.

- Skin rashes and itching
- Metallic taste in mouth
- Nausea and vomiting
  - Due to the build up of urea and other waste products in the blood
Signs and Symptoms Cont.

- Fatigue
- Feeling cold
- Dizziness
- Shortness of breath
  - Due to the reduced amount of erythropoietin being produced by the kidney
  - Can lead to anemia
Diagnosis and Staging
Diagnosis – Glomerular Filtration Rate

- Kidneys’ rate of fluid filtration of the blood
  - Regulated by:
    - Hydrostatic pressures in blood and Bowman’s space
      - Pulls water out of the blood
    - Oncotic pressures in blood and Bowman’s space
      - Pressure from protein – pulls water into the blood
    - Thickness of glomerular membrane
    - Area of glomerular membrane
Diagnosis - GFR cont.

- Normal GFR: 125 mL/min
- Kidney dysfunction: <60 mL/min
- Kidney failure: <15 mL/min
Diagnosis - GFR cont.

• Measuring GFR
  ▫ Inulin clearance rate
    • Not widely used – too time and labor intensive
  ▫ Plasma and urine creatinine
    • Metabolic waste – increases during kidney dysfunction
    • Over estimates, but used more often
Diagnosis - Urinalysis

- Tests for different products in urine
  - Protein, glucose, RBCs, WBCs, bacteria, etc
- Urine albumin levels are most important
  - Normally, no measurable albumin
  - In CKD, kidney can’t filter albumin so in urine
- If small amounts detected, another urinalysis
- If large amounts detected, 24-hour urine collection
Diagnosis - Urinalysis cont.

- Urine albumin to urinary creatinine ratio
  - If above 30 mg albumin/creatinine - kidney dysfunction
- Using urinary protein along with GFR is more indicative of severity of kidney dysfunction than GFR alone
Diagnosis - Serum Markers

- Serum creatinine and blood urea nitrogen (BUN)
  - Both are metabolic waste products
    - Build up in blood during CKD
- Creatinine
  - 10-12 mg/dL
    - Normal is 0.5-1.2 mg/dL
- BUN
  - Above 100 mg/dL
    - Normal is 5-20 mg/dL
- Not only diagnosis of CKD, but can help
Terms

• Azotemia: when nitrogenous waste products build up in the blood
  ▫ Urea, creatinine, etc
• Uremia: when waste products build up in blood and cause clinical side effects
  ▫ Itching, rashes, metallic taste in food, etc
Staging

- Based on GFR

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR, mL/min per 1.73m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Kidney damage with normal or increased GFR</td>
<td>≥90</td>
</tr>
<tr>
<td>II</td>
<td>Kidney damage with mildly decreased GFR</td>
<td>60–89</td>
</tr>
<tr>
<td>III</td>
<td>Moderately decreased GFR</td>
<td>30–59</td>
</tr>
<tr>
<td>IV</td>
<td>Severely decreased GFR</td>
<td>15–29</td>
</tr>
<tr>
<td>V</td>
<td>Kidney failure</td>
<td>&lt;15 (or dialysis)</td>
</tr>
</tbody>
</table>

**NOTE.** Adapted from [5]. Chronic kidney disease is defined as either kidney damage or glomerular filtration rate (GFR) <60 mL/min per 1.73m² for ≥3 months. Kidney damage is defined as pathologic abnormalities or markers of damage, including abnormalities in urine test results or the findings of imaging studies.
Comorbidities
Comorbidities - Diabetes

- Diabetes is the leading cause of chronic kidney disease
- ~1/3 of diabetes pts. develop CKD
Diabetes

• Earliest sign of kidney damage from diabetes: albumin in the urine.
• Other signs include
  ▫ HBP
  ▫ Swelling in ankles and legs
  ▫ Increased urination
Diabetes - Mechanism

- High blood glucose causes damage to blood vessels in the kidney.
- This decreases kidney function
- Buildup of waste products in the blood (they aren’t excreted in the urine)
- Changes in the kidney affect blood vessels and protein is excreted into the urine.
- Damage to nerves (from high glucose) can damage nerves- making it harder to empty the bladder.
- Pressure from this can cause infection or injure the kidney further
Anemia and CKD

- Normally...
  - Low O2 content of kidney cells stimulate them to produce erythropoietin (EPO)
  - Erythropoietin signals the bone marrow to produce mature red blood cells.
    - Without EPO, the ability of the body to produce RBC is greatly decreased
Anemia & CKD

- In kidney disease...
  - Damage to the kidney can result in scar tissue buildup within the cells that produce EPO
  - Because these cells are not able to function properly, EPO is not produced as steadily
  - Bone marrow can’t produce mature RBC
  - Body has a hard time receiving enough oxygen
Anemia and CKD

- Anemia is usually evident in the 3rd stage of kidney disease—long before dialysis is needed.
- As kidney disease gets worse, so does anemia.
- Symptoms:
  - Fatigue, weakness
  - Less energy and enthusiasm
  - Harder to concentrate
  - Dizziness— if anemia is severe
  - Pale skin
Anemia & CKD

• Usual cause of anemia in CKD is lack of EPO
  ▫ Normochromic, normocytic
• Anemia can also result from
  ▫ Low iron
  ▫ Chronic inflammation
  ▫ Blood loss from GI tract (ulcers, tumors, gastritis)
  ▫ Menstruation
  ▫ Other uterine bleeding
• Blood tests can determine cause
Anemia Therapy

- Injections of synthetic EPO
- Can be given every week, 2 weeks, or month
Heart Disease and CKD

Heart disease is the major cause of morbidity and mortality for patients with CKD
Heart Disease - Manifestations

• Manifestations:
  ▫ Left ventricular hypertrophy
  ▫ Cardiomyopathy
  ▫ Ischemic heart disease
    • Hypertension
    • Dysrhythmias
    • Accelerated atherosclerosis
    • Chest pain
Heart Disease - Mechanisms

- Hypersecretion of renin and angiotensin II cause blood volume to increase causing HBP
- Anemia increases cardiac workload
- Hyperlipidemia promotes atherosclerosis
Medical Nutrition Therapy in CKD
PRO Restriction and Kidney Function

- Studies determined protein restriction may decrease renal decline
  - Modification of diet in renal disease study
  - Protein increases glomerular pressure
- Prompted conference with National Institute of Diabetes and Kidney and Digestive National Institutes of Health to determine protein recommendations
Current PRO Recommendations

- Results of conference:
  - Determined by GFR
  - GFR >55 ml/min - .8 g/kg
  - GFR 25-55 ml/min - .6 g/kg
  - GFR <25ml/min - .6 g/kg & 35 kcals/kg

- If .6 g/kg is inadequate, intake may be increased to .75 g/kg
Protein Restriction vs. Malnutrition

• Despite conference, protein recommendations are controversial
  ▫ Benefits in renal function are seen with PRO restriction
  ▫ High PRO contributes to the health of patient by preventing PRO malnutrition
  ▫ Balance must be found between PRO restriction and PRO malnutrition
    • Current recommendations restrict PRO
  ▫ If the benefits of PRO restriction outweigh malnutrition risk, PRO is restricted
    • Patient must be carefully monitored
Effective PRO Restriction

- Hypertension must be controlled as it also contributes to renal decline
- In patients with DM, blood glucose control is more important than PRO restriction in preventing renal decline
High Biological Value Protein

• Needed with intake less than .8 g/kg
• 50 % of intake should be HBV
• Provides all of the essential amino acids
• Sources:
  ▫ Animals products such as meat, poultry, fish, eggs, cheese, yogurt, milk
• Plant sources such as grains, legumes, and nuts are considered low biological value
Na+ and Fluid Recommendations

- Sodium intake is reduced to decrease thirst, fluid gain, and hypertension
- 2,000 – 3,000 mg/day
- No...
  - Added salt in cooking or at the table
  - Convenience/processed foods
  - Cured meats
- There is rarely a fluid restriction pre-dialysis
K+ Recommendations

• Reduced to 2.3 – 3.1 g/day
  ▫ Normal intake for most Americans is 3 – 4 g/day
• Avoid foods high in K+ such as avocado, banana, cantaloupe, spinach, tomato, milk chocolate
  ▫ Fruits and vegetables may be leached to lower K+ content
• Avoid potassium chloride as a salt substitute in low sodium foods
Phosphorus Recommendations

• Limit intake to 17 mg/kg or 1200 mg/day
• Processed foods and metabolically active foods
  ▫ Metabolically active foods contain ATP
• High phosphorus foods include fast food pancakes and hamburgers, mac’n cheese, 2% milk, cheese, meats
• Intake of PRO contributes to the intake of P
  ▫ The following equation estimates the PRO impact
    • $128 + 14 \times g \text{ of PRO in diet} = \text{mg P/day}$
Phosphate Binders

- Usually dietary restrictions is not enough
- Calcium carbonate, acetate, lactate, gluconate
  - Risk of hypercalcemia
  - Used in lower amounts along with aluminum binders Basaljel and Amophojel, although aluminum toxicity is a risk
- Renagel
  - Phosphate binding resin
  - Does not raise calcium levels
  - High dosage puts pill burden on patients
- Fosrenol is also used
Side Effects of Phosphate Binders

- GI distress
- Constipation
  - Can lead to intestinal impaction
  - Important to treat constipation so patients will stay on binders
Anemia

- Treated with recombinant human EPO (rHuEPO)
  - Given when serum ferritin <100 ng/ml
- Initial treatment can cause a rise in K+
- Treatment should cause a rise in hematocrit
  - Increased need for iron
  - Cochrane review: Effective in pre dialysis patients
Iron Supplementation

• Iron is usually replaced IV or intramuscularly
• Oral iron is not sufficient to replenish stores
• Iron dextran, iron gluconate, iron sucrose are available to patients with an allergy to IV iron
  ▫ Oral iron is available for the small minority of patients who can’t tolerate any other form
  ▫ Should be taken between meals and w/o large amounts of Vit C to avoid kidney stone formation
Blood Transfusions

• NOT recommended for the following reasons:
  ▫ Depresses EPO levels in bone marrow
  ▫ Risk of over expanding blood volume
  ▫ Risk of blood borne pathogens
  ▫ The additional K+ load
  ▫ Risk of hemochromatosis and hemosiderosis
Incidence & Prevalence

• Incidence:
  ▫ 111,000 U.S residents began new CKD treatment in 2007

• Prevalence:
  ▫ 26 million people in the US have CKD
  ▫ Millions more at increased risk
Quality of life

- Depends on stage of CKD and presence of comorbidities
- Knowledge and awareness of CKD will help patients cope
- Self-empowerment: a positive attitude can help patients feel better and reduce complications
- Proper care and self management slow progression of disease
  - Good blood glucose control
  - Maintaining blood pressure
Case Study
Assessment

- Age: 24
- Height: 5’0
- Weight: 140#
- BMI: 27 (overweight)
- Ideal body weight: 100# (140%)
Biochemical

- Albumin: 3.2 (low)
- BUN: 80 (high)
- Creatinine: 1.5 (high)
- Uric acid: 6.2 (high)
- Cholesterol: 443 (high)
  - HDL: 37 (low)
  - TG: 300 (high)
Biochemical

- Glucose: 205 (high)
- HbA1c: 8.2 (high)
- HGB: 9.7 (low)
- HCT: 28.4 (low)
- All other labs normal
Clinical

- Overweight Native American female
- Appears her age (24)
- BP: 140/80
- 1+ pitting generalized edema
- Dry skin
- Lungs: rhonchi with rales- mild
Dietary- recall

- Usual dietary intake around 2850 kcals
- 50% calories from fat
  - Hyperlipidemia
  - Hypertension
  - Chronic Kidney Disease
Dietary

• Previous MNT- 1200 kcal/day (reservation health service)
• Current diet order
  ▫ 35 kcal/kg = \textbf{2240 kcal}
  ▫ 0.8 g/kg protein= \textbf{51 g}
  ▫ 8-12 mg/kg phosphorus= \textbf{640 mg}
  ▫ 2-3 g Na
Genetics & Histories

- Mother and father both diagnosed with DM II
- Diabetes Type II (diagnosed at age 13)
- Pt. reports she is poorly compliant with diabetes diet
- GFR has been declining over past year
- Meds
  - Glucophage 850 mg bid
PES Statement

Limited adherence to nutrition-related recommendations related to patient report of poor compliance to diabetes diet as evidenced by declining GFR
Intervention

• Educate patient about diet changes and importance of how diet affects quality of life.
  ▫ Less fat, more carbs, protein around the same
  ▫ Carb counting
  ▫ Sodium restriction

• Hypertension may cause heart failure (comorbidity of both DM and CKD)
  ▫ Abnormal triglyceride profile
Monitoring & Evaluation

- Monitor labs
  - BUN, creatinine, triglycerides, glucose, HbA1c
- Monitor weight
- Evaluate adherence to dietary changes