Chronic Kidney Disease and New Biomarkers of Kidney Injury

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Disclaimer

• I have no conflicts of interest
• I do not speak for any pharmaceutical companies
Chronic Kidney Disease

- EPIDEMIOLOGY
- Pathogenesis
- Diagnosis
- Treatment
- Prognosis
<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR ml/min/1.73m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>1(p)</td>
<td>Kidney damage with normal or raised eGFR</td>
<td>≥90</td>
</tr>
<tr>
<td>2(p)</td>
<td>Kidney damage with mild decreased eGFR</td>
<td>60–89</td>
</tr>
<tr>
<td>3A(p)</td>
<td>Moderate decreased eGFR</td>
<td>45–59</td>
</tr>
<tr>
<td>3B(p)</td>
<td>Moderate decreased eGFR</td>
<td>30–44</td>
</tr>
<tr>
<td>4(p)</td>
<td>Severe decreased eGFR</td>
<td>15–29</td>
</tr>
<tr>
<td>5(p)</td>
<td>Kidney failure</td>
<td>&lt;15 or dialysis</td>
</tr>
</tbody>
</table>
Epidemiology

• One in 10 American adults has some level of chronic kidney disease (CKD)
• Ninth leading cause of death in the United States
• 20 million have some stage of CKD

• 398,861 patients on dialysis in 2009
• Incidence of ESRD
  – 350 per 1 million

Kidney Disease Statistics for the United States.
September, 2012
NIDDK, November 2012
Percent of Population with New Cases of CKD, by Age Group

*MarketScan represents data from employer group health plans.
Percent of Population with Stage 3 CKD, by Age Group

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Ages 20–39</td>
<td>0.1%</td>
<td>0.3%</td>
<td>0.1%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Ages 60+</td>
<td>18.8%</td>
<td>24.2%</td>
<td>24.5%</td>
<td>26.0%</td>
</tr>
</tbody>
</table>
Annual ESRD Treatment Costs per Patient for HD, PD, Transplantation (Tx), and all ESRD

Year

2006 2007 2008 2009

Cost

$100,000 $90,000 $80,000 $70,000 $60,000 $50,000 $40,000 $30,000 $20,000 $10,000 $0

HD PD Tx All ESRD
Causes of Chronic Kidney Disease

- Type 2 diabetes: 42%
- High blood pressure: 28%
- Glomerular diseases: 6%
- Miscellaneous: 6%
- Unknown: 4%
- Type 1 diabetes: 4%
- Cystic/Hereditary: 3%
- Nephritis: 3%
- Tumors: 3%
- Other: 7%
Chronic kidney disease

- Epidemiology
- PATHOGENESIS
- Diagnosis
- Treatment
- Prognosis
# Pathogenesis of the Uremic Syndrome

<table>
<thead>
<tr>
<th>Major “Toxins”</th>
<th>Hormone</th>
<th>Derangements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea</td>
<td>EPO</td>
<td><strong>Deficiencies</strong></td>
</tr>
<tr>
<td>Polyamines</td>
<td>1,25-(OH)$_2$D$_3$</td>
<td></td>
</tr>
<tr>
<td>Guanidines</td>
<td>Testosterone</td>
<td>PTH</td>
</tr>
<tr>
<td>Myo-inositol</td>
<td>FSH</td>
<td><strong>Excesses</strong></td>
</tr>
<tr>
<td>Homocysteine</td>
<td>Insulin</td>
<td>Prolactin</td>
</tr>
<tr>
<td>B$_2$-microglobulins</td>
<td></td>
<td>Growth hormone</td>
</tr>
<tr>
<td>PTH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trace metals</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Altered Extracellular Environment**
- Metabolic acidosis
- $\uparrow K^+, PO_4^-, Mg^{++}, \downarrow Ca^{++}$

**Altered Intracellular Environment**
- $\uparrow Ca^{++}, K^+$
- $\downarrow$ Resting membrane potential
- $\downarrow Na^+-K^+-ATPase, Ca^{++}ATPase$
Pathogenesis of chronic kidney disease

Once half of the total nephrons are lost, CKD progresses similarly regardless of etiology. Initial hyperfiltration activates RAAS and causes proteinuria. Angiotensin II and protein uptake at the tubules causes inflammation and fibrosis of the glomerulus and tubules. Progressive decline in GFR and systemic complications occurs.

FSGS Focal segmental glomerulosclerosis
SNGFR Single nephron GFR
RAAS Renin angiotensin aldosterone system

↓ nephron number

Adaptive hyperfiltration at glomerulus

↑ glomerular permeability

↑ RAAS

↑ filtration of proteins and macromolecules

Proteinuria

Dyslipidemia

Hypertension

Nephrotoxic inflammation/remodelling

Tubulointerstitial fibrosis and 2° FSGS

↓ GFR

↓ Urine output

Systemic complications

LATE IN COURSE

EARLY IN COURSE
Primary Renal Disease

- Excess Ang II

- Glomerular pressure

- Glomerular damage

- Nephrons

Hypertension

- Renal excretion ability

Diabetes

- Afferent arteriolar resistance

Obesity

Chronic kidney disease

- Epidemiology
- Pathogenesis
- DIAGNOSIS
- Treatment
- Prognosis
### Clinical Manifestations of Chronic Kidney Disease

<table>
<thead>
<tr>
<th>Cardiovascular</th>
<th>Hematologic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid overload</td>
<td>Anemia</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Platelet dysfunction</td>
</tr>
<tr>
<td>Electrolyte &amp; Acid-Base</td>
<td>Neurologic</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>Peripheral neuropathy</td>
</tr>
<tr>
<td>Metabolic acidosis</td>
<td>Encephalopathy</td>
</tr>
<tr>
<td>Endocrine</td>
<td>Rheumatologic</td>
</tr>
<tr>
<td>Calcium, phosphorus,</td>
<td>Crystal-induced arthritis</td>
</tr>
<tr>
<td>Vit. D abnormalities</td>
<td>Amyloid deposition</td>
</tr>
<tr>
<td>Gonadal dysfunction</td>
<td></td>
</tr>
</tbody>
</table>
Factors Suggesting Chronic Kidney Disease

Duration of symptoms for months
Nocturia
Absence of acute illness with very high BUN and creatinine
Anemia of chronic disease
Bone disease
Sexual dysfunction
Skin disorders, nail changes, pruritus
Neurological complications
Echogenic kidneys with sonography
Potentially Reversible Problems Contributing to Chronic Kidney Disease

- Dehydration
  - Diarrhea, Vomiting
  - Excess diuretics & salt restriction, Fever
- Urinary tract infection
- Obstructive uropathy
  - Tract obstruction, papillary necrosis, crystal deposits
- Uncontrolled hypertension
- Catabolism

- Impaired cardiac function
  - CHF, Arrhythmia, 3rd Space of Fluids
- Nephrotoxicity of drugs
- Nephrotoxicity of contrast media
- Renal vein thrombosis
- Hypercalcemia
- Complication of pregnancy
Anemia in CKD

- Parameter to assess
  - Hemoglobin

- If Hemoglobin abnormal
  - RBC indices
  - Retic count
  - Iron Studies (ferritin, Serum iron, TIBC, %transferrin saturation)
  - Hemoccult stools
  - Medical eval for comorbid conditions
Anemia of CKD

- Erythropoietin deficiency is primary cause in CKD
- Associated with worse outcomes
- Functional or absolute iron deficiency
- Blood loss
- Presence of uremic inhibitors (PTH)
- Deficiencies of folate, B12
Differential Diagnosis of Anemia with Chronic Kidney Disease

GI bleeding - iron deficient  Microangiopathic anemia
Defective erythropoiesis  Malignant hypertension
Mallory-Weiss syndrome  HUS
Uremic gastritis  Folate deficiency
Uremic colitis  Bone marrow infiltration
Autoimmune hemolysis  Underlying myeloma
in SLE  Myelodysplasia - fibrosis
Malnourishment  Splenomegaly
Uremia: Gastrointestinal and Other Manifestations

- Esophagitis
- Anorexia
- Nausea
- Vomiting
- Diarrhea
- Constipation
- Abdominal Distention
- Muscle and bone pain
- Muscle weakness
- Cheilitis
- Glossitis
- Stomatitis
- Halitosis
- Amenorrhea
- Loss of Libido, Infertility
- Impotence
- Arthralgias
- Gout
- Pseudogout
- Abdominal Distention
Malnutrition

• Parameters to assess
  – Weight
  – Serum Albumin
  – Dietary history
  – Subjective global assessment

• If malnourished
  – 24 hour urine for urea nitrogen excretion
  – Food recall/records for protein and total energy intake (kcal)
  – Medical eval for comorbid conditions
Protein Energy Malnutrition (PEM)

- 50-70% of dialysis patients
- Associated with worse outcomes
- Pathophysiology
  - Decreased appetite
  - Metabolic acidosis – increased protein catabolism, suppresses albumin synthesis
  - Resistance to insulin, IGF (anabolic hormones)
  - Chronic inflammatory state – anorexia, increased muscle breakdown, increased whole body protein catabolism
Uremia: Dermatologic Manifestations

- Uremic frost (hair stubs)
- Pruritus
- Scratches
- Excoreation
- Pallor
- Conjunctival irritation (red eye syndrome)
- Ecchymoses
- Purpura
- Conjunctival irritation (red eye syndrome)
- Pallor
- Pruritus
- Scratches
- Excoreation
Uremia: Neurologic Manifestations

Vertigo Ataxia

Organic psychoses
Memory defects
Drowsiness
Sluggishness

Amnesia
Depression

Asterixis
Generalized convulsions

Bladder atony

Abnormal gait

Burning foot syndrome

Foot flap
Foot drop

Restless leg syndrome

Fasciculations
Twitchings

Coma may supervene
Bone Disease

- Parameters to assess
  - Serum PTH
  - Serum calcium
  - Serum phosphorus
  - Calcium X Phosphorus product

- If abnormal
  - Consider Vitamin D Levels
  - Consider bone X-ray
  - Consider DEXA scan
  - Ca x Phos > 55
    - Calcification of vessels and cardiac muscles
    - Calciphylaxis
Pathophysiology of Secondary Hyperparathyroidism

- Decreased kidney function leads to decreased phosphorus excretion (hyperphosphatemia)
- Elevated phosphorus suppresses calcitriol production
- Reduced kidney mass decreases calcitriol production
- Reduced calcitriol decreases calcium absorption from GI tract – leads to hypocalcemia
- Hypocalcemia, low calcitriol, and high phosphorus all stimulate PTH production
- High PTH – stimulates osteoblasts – high bone turnover
- Hallmark lesion of secondary hyperparathyroid is osteitis fibrosa cystica
Renal Osteodystrophy

Chronic renal disease

- Reduction in functioning nephron ➔ Acidoses
- Acidosis ➔ Bone resorption
- 1,25(OH)_2D_3 ➔ Phosphate retention ➔ Metastatic calcification
- Metastatic calcification ➔ Skeletal calcium
- Skeletal calcium ➔ Renal PTH degradation
- Renal PTH degradation ➔ Skeletal resistance
- Skeletal resistance ➔ Hypocalcemia
- Hypocalcemia ➔ Ca absorption
- Ca absorption ➔ Increased PTH secretion & circulatory levels
- Increased PTH secretion & circulatory levels ➔ Osteomalacia ➔ Osteodystrophy
Bone disease in CKD

- High bone turnover
  - High PTH
  - Osteitis fibrosa cystica

- Low bone turnover
  - Low to normal PTH levels
  - Osteomalacia
    - Vitamin D deficiency
    - Excess aluminum
    - Metabolic acidosis
  - Adynamic bone disease
    - Oversuppression of PTH with Vitamin D analogs
X-Ray Features of Renal Osteodystrophy

A - Osteolysis/osteosclerosis of diploë - “Pepper pot skull”,

B - Busal - soft tissue calcification

C - Vascular calcification - “Mönckeberg” type & periosteal neostosis,

D - Vertebral sclerosis - “Rugger jersy-spine”
Cardiovascular Manifestations in Chronic Renal Failure

- Myocardial calcification
- Uremia
- Acidosis
- Anemia
- Electrolyte disturbances (K, Ca, Mg)
- Hypertension
- Carbohydrate intolerance
- Hyperlipidemia
- Atherosclerosis
- Coronary disease
- Congestive heart failure
- Arrhythmias
- Cardiomyopathy
- Functional murmurs

From Eknoyan in *Pathophysiology of the kidney* 1997
Uremic Pericarditis: Effusion & Fibrin Strand
Subcostal Four Chamber View
## Renal and Extrarenal Factors that Predispose to Hyperkalemia

<table>
<thead>
<tr>
<th>Increased intake</th>
<th>Decreased Renal excretion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diet</td>
<td>K sparing diuretics</td>
</tr>
<tr>
<td>Salt substitutes</td>
<td>Trimethoprim</td>
</tr>
<tr>
<td>Redistribution - cells to ECF or reduced cell uptake</td>
<td>Hypoaldosteronism</td>
</tr>
<tr>
<td>Insulin deficiency</td>
<td>Idiopathic, Type IV RTA</td>
</tr>
<tr>
<td>Acidosis</td>
<td>Drug induced</td>
</tr>
<tr>
<td>Nonselective beta-blockade</td>
<td>ACE-Is</td>
</tr>
<tr>
<td>Digitalis</td>
<td>NSAIDs</td>
</tr>
<tr>
<td></td>
<td>Heparin</td>
</tr>
</tbody>
</table>
Urine Sediment

- **RBCs**
  - Cystic kidney disease, Alports, IGA Nephropathy, Thin basement membrane disease, kidney neoplasms, Other UT disorders
- **RBCs and RBC casts**
  - Proliferative GN, Hereditary nephritis
- **Proteinuria >1000mg/g**
  - Diabetic nephropathy, FSGS

- **RBCs, tubular cells, Granular casts**
  - Hereditary nephritis, microangiopathy
- **RBCs, WBC, WBC casts, <1000mg/g proteinuria**
  - Tubulointersitial nephritis
- **Tubular casts, Cellular casts, granular casts**
  - ATN
Ultrasonography

• **General appearance**- Nephrocalcinosis, stones, hydronephrosis, cysts or mass

• **Increased echogenecity**- Cystic disease or “medical renal disease”, Small, “hyperechoic” kidneys-indicates CKD

• **Large kidneys**- Indicate tumors, infiltrative diseases (lymphoma), diseases causing nephrotic syndrome (diabetes)

• **Size disparity**- Vascular, urologic or tubulointerstitial disease due to stone/infections

• **Doppler** – venous thrombosis, arterial stenosis
Radiology studies

- **Intravenous pyelography (IVP)**
  - Reveal asymmetry of size or function
  - Presence of obstructive stone, tumors, scars
  - Dilated collecting ducts in medullary sponge kidney

- **Computed tomography (CT)**
  - Obstruction
  - Tumors
  - Cysts
  - Ureteral calculi
  - CTA – renal artery stenosis
Interpretation of Abnormalities on Imaging Studies as Markers of Kidney Damage

- Ultrasonography
- Intravenous Pyelography (IVP)
- Computed Tomography (CT)
- Magnetic resonance imaging (MRI)
- Nuclear scans
  - Captopril renography
  - Mercaptoacetyltriglycine (MAG3)
Radiology studies

- Magnetic resonance imaging (MRI)
  - Avoid gadolinium with advanced disease
  - Masses
  - Renal vein thrombosis
  - Cysts

- Nuclear scans
  - Captopril renography
  - Mercaptoacetyltriglycine (MAG3)
  - Asymmetry of kidney size or function
  - Functional evidence of renal artery stenosis, obstruction
  - Acute pyelonephritis
## Diagnostic Approach to Chronic Kidney Disease

### Glomerular Disease

**Diagnostic features:** RBC casts >3.5 g protein excretion, or systemic disease with glomerulopathy

- **Primary:** GN, MN, MPGN
- **Secondary:** DM, SLE, amyloid

### Interstitial or Vascular Disease

**Diagnostic features:** Bland UA, <2-3 g protein, no systemic disease associated with glomerulopathy

**Anatomic abnormalities:** PCKD, Obstructive nephropathy

**Other Diseases:** Hypertensive NS, Analgesic abuse, Ischemic, Nephrolithiasis, Idiopathic
Chronic kidney disease

- Epidemiology
- Pathogenesis
- Diagnosis
- TREATMENT
- Prognosis
<table>
<thead>
<tr>
<th>Stage/Description</th>
<th>GFR (mL/min/1.73 m²)</th>
<th>Action*</th>
</tr>
</thead>
<tbody>
<tr>
<td>At increased risk</td>
<td>≥ 90 with CKD risk factors</td>
<td>Screening CKD risk reduction</td>
</tr>
<tr>
<td>1 Kidney damage with normal or ↑ GFR</td>
<td>≥ 90</td>
<td>Diagnosis and treatment, Treatment of comorbid conditions, Slowing progression CVD risk reduction</td>
</tr>
<tr>
<td>2 Kidney damage with Mild ↓ GFR</td>
<td>60–89</td>
<td>Estimating progression</td>
</tr>
<tr>
<td>3 Moderate ↓ GFR</td>
<td>30–59</td>
<td>Evaluating and treating complications</td>
</tr>
<tr>
<td>4 Severe ↓ GFR</td>
<td>15–29</td>
<td>Preparation for kidney replacement therapy</td>
</tr>
<tr>
<td>5 Kidney failure</td>
<td>&lt; 15 or dialysis</td>
<td>Replacement, if uremia present</td>
</tr>
</tbody>
</table>

GFR, glomerular filtration rate; CKD, chronic kidney disease; CVD, cardiovascular disease.

*Includes actions from preceding stages.

Management of the Patient with Chronic Kidney Disease

• Control progression rate of renal disease
  ‒ Treatment of hypertension
  ‒ Dietary protein and phosphate restriction
  ‒ Reduction of proteinuria
  ‒ Management of diabetes
  ‒ Control acidosis

• Avoid further kidney damage

• Manage the individual complications of uremia
Decline in GFR Over 3 Years vs Mean Blood Pressure and Urine Protein Excretion Rate

## JNC 8 Recommendations

<table>
<thead>
<tr>
<th>Patient Subgroup</th>
<th>Target SBP (mm Hg)</th>
<th>Target DBP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 60 years</td>
<td>&lt;150</td>
<td>&lt;90</td>
</tr>
<tr>
<td>&lt; 60 years</td>
<td>&lt;140</td>
<td>&lt;90</td>
</tr>
<tr>
<td>&gt; 18 years with CKD</td>
<td>&lt;140</td>
<td>&lt;90</td>
</tr>
<tr>
<td>&gt; 18 years with diabetes</td>
<td>&lt;140</td>
<td>&lt;90</td>
</tr>
</tbody>
</table>

CKD = chronic kidney disease; DBP = diastolic blood pressure; SBP = systolic blood pressure

JNC 8 Recommendations (continued)

- General nonblack population
  - Thiazides, CCB, ACEI, or ARB initially
- General black population
  - Thiazides or CCB initially
- CKD
  - Treatment should include ACEI or ARB
- Up-titrage or add therapy after 1 mo if BP goal not achieved
  - Don’t use ACEI and ARB together
  - If > 3 drugs needed, refer to hypertension specialist

<table>
<thead>
<tr>
<th>CKD Stage GFR (mL/min/1.73 m²)</th>
<th>Calcium</th>
<th>Phosphorus</th>
<th>PTH</th>
<th>Alkaline Phosphatase</th>
<th>25 (OH)D (Calcidiol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 30-59</td>
<td>Every 6-12 months</td>
<td>Every 6-12 months</td>
<td>Based on baseline level and CKD progression</td>
<td>NA</td>
<td>Measure with repeated testing determined by baseline values</td>
</tr>
<tr>
<td>4 15-29</td>
<td>Every 3-6 months</td>
<td>Every 3-6 months</td>
<td>Every 6-12 months</td>
<td>Every 12 months, or more frequently in the presence of elevated PTH</td>
<td>Measure with repeated testing determined by baseline values</td>
</tr>
<tr>
<td>5 or 5D &lt; 15</td>
<td>Every 1-3 months</td>
<td>Every 1-3 months</td>
<td>Every 3-6 months</td>
<td>Every 12 months, or more frequently in the presence of elevated PTH</td>
<td>Measure with repeated testing determined by baseline values</td>
</tr>
</tbody>
</table>

Phosphorus Management

- CKD 3 and 4 - Goal range 2.7-4.6mg/dl
- CKD 5 - goal 3.5-5.5mg/dl
- Ca X Phos < 55 at all times
- Restrict phosphorus to 1000mg/day if phosphorus or PTH elevated
- Phosphate binders
  - Calcium based (calcium carbonate or calcium acetate)
  - Non–calcium based (lanthanum carbonate, sucroferric oxyhydroxide, and sevelamer)
**PTH and Vitamin D**

**PTH**
- CKD 3 – 30-70pg/ml
- CKD 4 – 70-110pg/ml
- CKD 5 – 150-300pg/ml
- Vitamin D suppresses PTH
- Don’t oversuppress

**Vitamin D**
- Goal level >30ng/ml (use 25-OH vit D levels)
- Use ergocalciferol if 25-OH <30
- Use calcitriol if Vit D >30 (patient likely has secondary hyperparathyroidism)
Anemia

- CKD 3 and 4 - Goal Hemoglobin 9-11
- CDK 5 – Goal hemoglobin 10-12
- Tsat >20%
- Ferritin needs to be < 800
- Erythropoietin/darbepoietin (ESA – erythropoietin stimulating agents)
Stage 1 Management

- GFR ≥ 90 with hematuria or proteinuria
- A1c goal ≈ 7
- BP goal < 140/90
- LDL < 100mg/dl
- Add ACE or ARB if urine microalbumin ≥ 30mg/g creatinine
Stage 2 Management

- GFR 60-89 with hematuria or proteinuria
- A1c goal ≈ 7
- BP goal < 140/90
- LDL goal < 100mg/dl

- ACE or ARB recommended for all patients

J Clin Endocrinol Metab, July 2010, 95(7):3103-3110
Stage 3 Management
Moderate

- GFR 30-59
- A1c goal ≈ 7
- BP goal < 140/90
- LDL goal < 100mg/dl
- Refer patients not meeting treatment goals to nephrology for preparation of impending renal failure
- Monitor for anemia
- Monitor for secondary hyperparathyroidism

- ACE or ARB recommended to all patients
- Discontinue metformin, all sulfonylureas except glipizide, nateglinide, α-glucosidase inhibitors, GLP-1 analogs
- Reduce doses of DDP-4 inhibitors
- Add erythropoietin if Hgb <9mg/dl
- Add calcitriol when 1,25 dihydroxyvitamin D is low or when PTH > 70
Stage 4 Management
Severe

- GFR 15-29
- A1c goal ≈ 7
- BP goal < 140/90
- LDL goal < 100mg/dl
- Refer patients to nephrology for preparation of impending renal failure
- Consider AV Fistula placement
- Monitor for anemia
- Monitor for secondary hyperparathyroidism and hyperphosphatemia
- Monitor for acidosis

- ACE or ARB recommended to all patients with careful monitoring of serum K (stop if >5.5)
- Insulin therapy recommended for most patients with diabetes
- Add erythropoietin if Hgb <9mg/dl
- Add calcitriol when 1,25 dihydroxyvitamin D is low or when PTH > 110
- Low phosphorus diet and phosphate binders
- Sodium bicarbonate. Goal >24
- Transplant referral when GFR<20 if candidate
Stage 5 Management
ESRD

- GFR <15 or dialysis
- A1c goal ≈ 7
- BP goal < 140/90
- LDL goal not known
  - Statins do not reduce cardiovascular mortality in ESRD
- Monitor for signs and symptoms of uremia

- ACE/ARB/Renin inhibitors/aldosterone antagonists should be held if not on dialysis
- AV fistula should be in place
- Place PD catheter 4 weeks prior to needing dialysis
- Renal diet
- Goal Hemoglobin – 10-12mg/dl
- Goal PTH – 150-300
- Goal Phosphorus 3.5-5.5
- Sodium bicarbonate – Goal >24
Indications for Dialysis Initiation in ESRD

- Absolute
  - Pericarditis
  - Encephalopathy
  - Neuropathy
  - Pulmonary edema
  - Bleeding diathesis
  - N/V, Anorexia
  - Cr>12
  - Psychosis
  - Malnutrition

- Relative
  - Disturbed Sleep
  - Memory, cognitive disorder
  - Peripheral Neuropathy
  - Peripheral edema
  - Incipient Nausea, Anorexia
  - Pruritus
  - Poorly control Ca++ or PO₄=
  - Anemia, poor EPO response
  - Depression
Summary

- Know stages of CKD
- Monitor for symptoms
- Routine labs depending on stages
- Control BP, DM, Cholesterol
- Follow electrolytes, anemia, phosphorus, calcium, PTH, Vitamin D, proteinuria
- Institute fluid restrictions and dietary restrictions when appropriate
- Plan dialysis access/transplant evaluation when eGFR <20
New Biomarkers for Kidney Injury

- Mounting evidence of connection between AKI and risk of future deterioration of kidney function, manifesting as CKD
- CKD major contributing factor in cardiovascular diseases
- Need to find predictive and prognostic biomarkers for transitions from AKI to CKD and CKD to CVD
Cystatin C

- Low molecular weight basic protein, freely filtered and metabolized in the kidney
- Production less influenced by age, gender, body size, cigarette smoking than creatinine
- Reflect GFR better than creatinine
- May provide accurate estimates of GFR among stages 1 and 2 CKD and not misdiagnosing normal patients with CKD
- PETIA (Particle Enhanced Turbidometric Immunoassay) - Cystatin C reference range
  - Adults (Mayo study 2010)-0.488 to 1.134 mg/L (Mean – 0.71 mg/L)
Cystatin C

- REGARD S study
  - Persons with increased Cystatin C and urinary albumin creatinine ratio at baseline had much higher rates of subsequent CKD
  - Persons with elevated creatinine and Cystatin C had much higher rates of CKD than either marker alone
  - Persons with normal eGFR by MDRD but an increased Cystatin C level had a 2-fold increased risk of mortality over the 7 years of the study
Cystatin C

• MESA and CHS
  – Cystatin C predicted all cause mortality and cardiovascular disease, while creatinine alone did not
  – much stronger predictor of future kidney failure than creatinine alone
  – An increase in creatinine and cystatin C – 24X risk of kidney failure
New Markers in Acute Kidney Injury

- **Proteinuria**
  - Elevated protein content in urine is sensitive marker of kidney injury and monitoring for recovery
  - Not very specific
  - Not helpful with determining etiology of injury

- **Urinary NGAL – neutrophil gelatinase-associated lipocalin**
  - Rise within 2-4 hours following AKI
  - Independent risk factor for CKD
New markers in AKI

• **KIM-1 (kidney injury molecule 1)**
  – Also known as TIM-1
  – Transmembrane tubular protein promising early–stage urinary biomarker of AKI
  – Undetectable at the gene level in normal kidneys
  – Rapidly and highly upregulated in ischemic kidneys and toxic injury

• **L-FABP (liver type fatty acid-binding protein)**
  – Cardiac bypass surgery
Chronic Kidney Disease and New Biomarkers

• References
  – KDOQI guidelines
  – J Clin Endocrinol Metab, July 2010, 95(7):3103-3110
QUESTIONS?

Chronic Kidney Disease
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