CHRONIC KIDNEY DISEASE IN PRIMARY CARE

JENNIFER SEBES DNP, APRN, FNP-C
**CKD AS A PUBLIC HEALTH ISSUE**

- 26 million American affected
- Prevalence is 1 out of 9 people
- 28% of Medicare budget in 2013, up from 6.9% in 1993
- $>50 billion in 2016
- Increases risk for all-cause mortality, CV mortality, kidney failure (ESRD), and other adverse outcomes.
- 6 fold increase in mortality rate with DM + CKD
- Disproportionately affects African Americans and Hispanics

Table 6.3  Adjusted survival (%) by treatment modality and incident cohort year (year of ESRD onset): Dialysis

<table>
<thead>
<tr>
<th></th>
<th>3 months</th>
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<td><strong>Peritoneal dialysis</strong></td>
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<td>2001</td>
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<td>51.4</td>
</tr>
</tbody>
</table>

COSTS OF CKD IN 2013 DOLLARS
USRDS REPORT

- 678,383 pts ESRD (10,000 pts 1972)
- 17,600 transplanted patients 2013
- CKD 10% medicare pop., 20% cost
- ESRD 1% medicare pop., 7% cost
- ESRD $85,578/yr Hemodialysis
- ESRD $69,919/yr Peritoneal dialysis
- Transplant $29,920/yr/$75,000-150,000 for actual transplant and 3 months of followup

USRDS, 2016
STEPS TO CKD PATIENT CARE

1. CKD definition and risks
2. Assess GFR, albuminuria
3. Determine etiology
4. Slow progression
5. Assess for associated complications
6. Discuss dialysis/transplantation
RENNAL ANATOMY AND PHYSIOLOGY

• Each kidney has 1 million nephrons-slow loss may not be noticeable.
  • Person with CKD may not feel different until >3/4 of nephrons are lost
• Blood supply per gram
  • ~3.5mL/g/min vs ~0.07mL/g/min for most organs except lungs
  • Accepts 25% of resting cardiac output
  • Increased circulating agents/toxins (nephrotoxic meds)

(Matovinović, 2009)

By Artwork by Holly Fischer
DEFINITION OF CHRONIC KIDNEY DISEASE

• Kidney damage for > 3 months
  • Structural or functional abnormalities of the kidneys, with or without decreased GFR, manifest by *either*
    • Pathological abnormalities
    • Markers of kidney damage, including abnormalities in the composition of the blood or urine, or in imaging tests
  • GFR < 60 ml/min/1.73 m² for > 3 months, with or without kidney damage as defined above

(Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group, 2013)
CKD RISK FACTORS*

**Modifiable**
- Diabetes
- Hypertension
- History of AKI
- Frequent NSAID use
  - Obesity ?
  - Hyperuricemia ?
  - Smoking ?
  - Sedentary lifestyle ?
  - Dietary Protein Intake ?

**Non-modifiable**
- Family history of kidney disease, diabetes, or hypertension
- Age 60 or older (GFR declines normally with age)
- Race/U.S. ethnic minority status

*Partial list
AKI, acute kidney injury

(Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group, 2013)
Improved Diagnosis...

Studies demonstrate that clinician behavior changes when CKD diagnosis improves. Significant improvements realized in:¹⁻³

- Increased urinary albumin testing
- Increased appropriate use of ACEi or ARB
- Avoidance of NSAIDs prescribing among patients with low eGFR
- Appropriate nephrology consultation

STEPS TO CKD PATIENT CARE

1. CKD definition and risks
2. Assess GFR, albuminuria (knowing the labs)
3. Determine etiology
4. Slow progression
5. Assess for associated complications
6. Discuss dialysis/transplantation
CREATININE

• Creatinine is derived from the metabolism of creatine in skeletal muscle and from dietary meat intake.

  creatinine secretion by the renal tubules
  + creatine intake (ie, diet)
  + creatinine pool size (ie, muscle mass) all remain constant

= plasma creatinine concentration remains constant.

(Inker, Perrone, Sterns, & Forman, 2017)
GLOMERULAR FILTRATION RATE

- GFR is equal to the sum of the filtration rates in all of the functioning nephrons
- Glomeruli filter 180L/day (125mL/min) of plasma
- Normal GFR depends on age, sex, body size and is approximately 130mL/min for men, and 120mL/min for women—with considerable variation
- CKD-EPI equation (estimated GFR in mL/min/1.73m²) is most accurate
<table>
<thead>
<tr>
<th>Age</th>
<th>Gender</th>
<th>Race</th>
<th>SCr (mg/dL)</th>
<th>eGFR (mL/min/1.73 m²)</th>
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<tbody>
<tr>
<td>20</td>
<td>M</td>
<td>B</td>
<td>1.3</td>
<td>91</td>
</tr>
<tr>
<td>20</td>
<td>M</td>
<td>W</td>
<td>1.3</td>
<td>75</td>
</tr>
<tr>
<td>55</td>
<td>M</td>
<td>W</td>
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</tr>
<tr>
<td>50</td>
<td>F</td>
<td>W</td>
<td>1.3</td>
<td>46</td>
</tr>
</tbody>
</table>

B = black; W = all ethnic groups other than black; *With evidence of kidney damage.

(Duncan, Heathcoat, Djurdjev, & Levin, 2001)
(National Kidney Foundation, 2002)
The “e” in eGFR Stands for “Estimated”.....

True GFR could be > 70 mL/min.1.73m²

or < 15 mL/min.1.73m²

(Levey, et al. 2009)
USE THESE EQUATIONS CAUTIOUSLY IF AT ALL IN ....

- Patients who have/are:
  - Poor nutrition/loss of muscle mass
  - Amputation
  - Chronic illness
  - Not African American or Caucasian
  - Changing serum creatinine
  - Obese
  - Very elderly, young

(National Kidney Foundation, 2014)
LAB: ALBUMIN CREATININE RATIO

- Urinary albumin-to-creatinine ratio (ACR) is calculated by dividing albumin concentration in milligrams by creatinine concentration in grams.
- Creatinine assists in adjusting albumin levels for varying urine concentrations, which allows for more accurate results versus albumin alone.
- Spot urine albumin-to-creatinine ratio for quantification of proteinuria
  - New guidelines classify albuminuria as mild, moderately or severely increased
- First morning void preferable
- 24hr urine test rarely necessary
<table>
<thead>
<tr>
<th>GFR categories (ml/min/1.73 m²)</th>
<th>Description and range</th>
<th>Persistent albuminuria categories</th>
<th>A1</th>
<th>A2</th>
<th>A3</th>
</tr>
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<tbody>
<tr>
<td>G1</td>
<td>Normal or high</td>
<td>≥90</td>
<td>Normal to mildly increased</td>
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<tr>
<td>G2</td>
<td>Mildly decreased</td>
<td>60-89</td>
<td></td>
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</tr>
<tr>
<td>G3a</td>
<td>Mildly to moderately decreased</td>
<td>45-59</td>
<td>Moderately increased</td>
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<tr>
<td>G3b</td>
<td>Moderately to severely decreased</td>
<td>30-44</td>
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<tr>
<td>G4</td>
<td>Severely decreased</td>
<td>15-29</td>
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<td>G5</td>
<td>Kidney failure</td>
<td>&lt;15</td>
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</table>
STEPS TO CKD PATIENT CARE

1. CKD definition and risks
2. Assess GFR, albuminuria
3. Determine etiology- what is going on here??
4. Slow progression
5. Assess for associated complications
6. Discuss dialysis/transplantation
KIDNEY INVOLVEMENT IN SYSTEMIC DISEASES

- Hypertension
- Diabetes
- Amyloidosis
- Sickle cell diseases
- Immune complex GN
- Illicit drugs – cocaine, heroin
- Cholesterol emboli
- HIV
- Liver Failure
- Congestive heart Failure
- Systemic vasculitis
- Lupus
- Hemolytic Uremic syndrome
- interstitial nephritis
- Allergic reactions- drugs

(Vasudev & Vasudev, 2012)
New CKD

Obtain ultrasound, UA, microscopy, albumin/cr ratio

Ultrasound shows obstruction?

- Yes: Relieve obstruction
- No: Is there albuminuria or glomerular bleeding? (eval for glomerulonephritis)

Fatehi & Chi-yuan, 2016
If red cells have their typical shape and color, this indicates **extra glomerular hematuria**.

Examples: kidney stone disease, UTI, cystitis, bleeding from collecting duct, ureters, bladder or urethra.

(Vasudev & Vasudev, 2012)
DYSMORPHIC/RENAL HEMATURIA

• This hematuria is characterized by:
  • a great variation in the size of the cells and by a high percentage of dysmorphocytosis/casts (>20%).

• Hematuria is usually related to glomerular bleeding.

• It is typically accompanied by variable levels of albumunuria

(Vasudev & Vasudev, 2012)
Urine Microscopy can be helpful in work up of chronic kidney disease

In GN’s the red blood cells leak from the glomerulus into the tubules. As they traverse through the tubules, they can form cylindrical casts called RBC casts.

Image retrieved on 05 October 2010 from: http://commons.wikimedia.org/wiki/File:Redbloodcells.jpg
This image is a work of the National Institutes of Health, part of the United States Department of Health and Human Services. As a work of the U.S. federal government, the image is in the public domain.

(Vasudev & Vasudev, 2012)
IF YOU HAVE ALBUMINURIA OR HEMATURIA-ORDER THE FOLLOWING LABS:

<table>
<thead>
<tr>
<th>Tests of autoimmunity</th>
<th>Hepatitis serologies</th>
<th>&gt;40 years- paraprotein assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANA</td>
<td>Hepatitis B serology (HBsAG)</td>
<td>Serum protein electrophoresis (SPEP)</td>
</tr>
<tr>
<td>RF/anti-ccp</td>
<td>Hepatitis C serology (HCV antibody)</td>
<td>Urine protein electrophoresis (UPEP)</td>
</tr>
<tr>
<td>Complement C3, C4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANCA</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

National Kidney Disease Education Program, 2014, NIH
UPTODATE LAB RECOMENDATIONS

• Lab to order: cbc, cmp, urine albumin/cr ratio, urine microscopy

• Nephrotic pattern (protein >3.5g/day): ANA, anti DS DNA, C3 and C4 antibodies, HIV, HBV, HCV, serum/urine immunofixation (amyloidosis), free light chain analysis (light chain deposition disease)

• Nephritic pattern (red cells, white cells, casts, variable protein): C3, C4, ANA, dsDNA, antineutrophil cytoplasmic antibody (ANCA) titers, a streptozyme test, HBV and HCV serologies, HIV, and in some cases, blood cultures, anti-glomerular basement membrane (GBM) antibodies, and cryoglobulins

• Renal biopsy

(Hebert & Parikh, 2014)
EVALUATION OF NEW CKD

NO OBSTRUCTION

NO EVIDENCE OF GLOMERULAR BLEEDING
High risk for multiple myeloma? (>40, no NSAIDs, no contrast)

- SPEP, UPEP with immunofixation, serum free light chains

Evaluation depends on UA

- Sterile pyuria?
- Normal urinalysis?

- Eval for interstitial nephritis
- High risk for renovascular disease

- Eval for renovascular disease
- Follow serum creatinine—does it remain stable?

(Fatehi & Chi-yuan, 2016)
POSSIBLE INVESTIGATIONS...

Acute interstitial nephritis

- Drugs are the most common cause of AIN. (antibiotics, NSAIDs PPI’s)
- Autoimmune disorders (Sjogren, lupus, Wegeners)
- Infections (legionella, CMV, Strep)
- Sarcoidosis

- ?renal biopsy?

Renovascular disease risk

- Cr elevation 30% after starting ACE
- Mod-severe htn in pt with atherosclerosis, unilateral small kidney, or asymmetry more the 1.5cm
- Onset of stage II htn after 55 years
- Normal UA, no proteinuria, or use of nephrotoxic drug
- Hyperlipidemia, smoking, CAD, PAD
- DX: duplex Doppler ultrasonography, CTA, or MRA
Creatinine remains stable

Evidence of chronicity on imaging?

Yes: No further evaluation, follow closely, prepare for renal replacement therapy

No: Kidney biopsy

(Fatehi & Chi-yuan, 2016)
STEPS TO CKD PATIENT CARE

1. CKD definition and risks
2. Assess GFR, albuminuria
3. Determine etiology
4. **Slow progression**
5. Assess for associated complications
6. Discuss dialysis/transplantation
POTENTIALLY MODIFIABLE CKD PROGRESSION RISK FACTORS

- Diabetes/glucose control
- Hypertension
- Albuminuria/Proteinuria
- Metabolic acidosis
- Obesity ?
- Hyperuricemia ?
- Smoking ?
- Sedentary lifestyle ?
- Dietary Protein Intake ?
DIABETIC NEPHROPATHY #1 CAUSE OF CKD

• Clinical syndrome
• Albuminuria >30 mg/24 hrs
• Proteinuria >500 mg/24 hrs
• Hypertension develops
• Progressive increase in proteinuria
• Progressive decline in glomerular filtration rate

• Chronic kidney disease should be attributed to diabetic nephropathies in most patients with diabetes if albuminuria and diabetic retinopathy are both present; other causes of CKD should be entertained if diabetic retinopathy is absent. (KDIGO, 2007)
DIABETIC NEPHROPATHY MORTALITY

• After 40 yrs of DM
  • 10% alive if proteinuria is present
  • 70% alive if proteinuria is absent
• Heart Disease is 15 times higher risk in those with proteinuria
• Proteinuria = death in this population

Dunkler, et al, 2015
GOALS OF CARE IN CKD: GLUCOSE CONTROL

• Target HbA1c ~7.0% (<6.95% greatest chance of reducing albuminuria)
• Can be extended above 7.0% with comorbidities or limited life expectancy, and risk of hypoglycemia
• Risk of hypoglycemia increases as kidney function becomes impaired
• Declining kidney function may necessitate changes to diabetes medications and renally-cleared drugs

HYPERTENSION #2 CAUSE OF CKD

• Just having HTN can cause proteinuria
• Usually 1-2 gms of protein a day
• Treat them like a diabetic with ACEI or ARBS and tight blood pressure control
• JNC-8 goal <140/90 for pt’s with CKD
• National kidney foundation: <140/90 if ckd and no proteinuria, <130/80 if proteinuria present

(James, Ortiz, & Et Al., 2014)
TREATING HYPERTENSION/PROTEINURIA: ACEI OR ARB

- Risk/benefit should be carefully assessed in the elderly and medically fragile
- Check labs after initiation
  - If less than 30% SCr increase, continue and monitor
  - If more than 30% SCr increase, stop ACEi and evaluate for renal artery stenosis
- Continue until contraindication arises, no absolute eGFR cutoff
- Better proteinuria suppression with low Na diet and diuretics
- Avoid volume depletion
- Avoid ACEi and ARB in combination\(^1,2\)
  - Risk of adverse events (impaired kidney function, hyperkalemia)

(Kunz, Friedrich, Wolbers, & Mann, 2008)
(Mann, Schmieder, & McQueen, 2008)
HYPERTENSIVE NEPHROPATHY

Nonproteinuric CKD

- With edema:
  1. Loop diuretic
  2. ACE inhibitor
  3. Dihydropyridine calcium channel blocker (amlodipine)

- Without edema:
  1. ACE inhibitor
  2. Dihydropyridine CCB (amlodipine)
  3. Diuretic

- 4th line: spironaldactone

Proteinuric CKD

1. ACE or ARB
2. Diuretics
3. Non dihydropyridine CCB (diltiazem, verapamil)

Mann, 2016
MODIFICATION OF OTHER CVD RISK FACTORS IN CKD

- Smoking cessation
- Exercise
- Weight reduction to optimal targets
- Lipid lowering therapy
  - In adults >50 yrs, statin when eGFR $\geq 60$ ml/min/1.73m$^2$; statin or statin/ezetimibe combination when eGFR < 60 ml/min/1.73m$^2$
  - In adults < 50 yrs, statin if history of known CAD, MI, DM, stroke
- Aspirin is indicated for secondary but not primary prevention

STATINS-RENO PROTECTIVE?/CONTROVERSY

• HMG-CoA reductase inhibitors (statins) in high doses can cause proteinuria
• Possibly associated with less inflammation, endothelial dysfunction, and scarring in the kidney because they also block inflammatory cytokines
• Use statins for CV disease, not to treat proteinuria

(Afzali and Goldsmith, 2016)
MEDICINE CAUTION

- Hold metformin when GFR <35 ml/min
- GFR <50 ml/min should alert to check all doses of meds
- No bisphosphonates <35 ml/min
- No NSAIDS/cox 2 inhibitors <60 ml/min
- Atenolol –renal excretion
- BACTRIM!!!! A lot of AKI!!!
MEDICINE CAUTION

• Lovenox-use subcut heparin
• Apixiban
• Dabigatran
• Rivaroxiban
• Lithium
• GABAPENTIN (ckd 4 max 300mg qd, ckd 5 max 300mg qod)
STEPS TO CKD PATIENT CARE

1. CKD definition and risks
2. Assess GFR, albuminuria
3. Determine etiology
4. Assess for evidence of progression
5. **Assess for associated complications**
6. Discuss dialysis/transplantation
CKD-CVD-DIABETES LINK: CKD IS A DISEASE MULTIPLIER

National kidney foundation, 2014
Chronic Kidney Disease–Mineral & Bone Disorder (CKD-MBD)
Pathophysiology of Secondary Hyperparathyroidism in CKD

- **Systemic Toxicity**
  - Cardiovascular Disease
  - Hypertension
  - Inflammation
  - Calcification
  - Immunological Disorders

- **Mineral & Bone Disease**
  - Fractures
  - Bone Pain
  - Marrow Fibrosis
  - Erythropoietin Resistance

- **PTH**
  - $\downarrow$ PTH $\rightarrow$ $\downarrow$ VDR $\rightarrow$ $\downarrow$ CaR $\rightarrow$ $\downarrow$ PTH

- **Ca$^{2+}$**
  - $\downarrow$ Ca$^{2+}$ $\rightarrow$ PTH $\rightarrow$ $\downarrow$ VDR $\rightarrow$ $\downarrow$ CaR $\rightarrow$ $\uparrow$ PTH

- **25(OH) Vit D**
  - $\downarrow$ 25(OH) Vit D $\rightarrow$ $\downarrow$ 1,25(OH)$_2$ Vit D $\rightarrow$ PTH $\rightarrow$ $\downarrow$ VDR $\rightarrow$ $\downarrow$ CaR $\rightarrow$ $\uparrow$ PTH

- **1,25(OH)$_2$ Vit D**
  - $\downarrow$ 1,25(OH)$_2$ Vit D $\rightarrow$ PTH $\rightarrow$ $\downarrow$ VDR $\rightarrow$ $\downarrow$ CaR $\rightarrow$ $\uparrow$ PTH

- **FGF23**
  - $\uparrow$ FGF23 $\rightarrow$ $\downarrow$ PTH $\rightarrow$ $\downarrow$ VDR $\rightarrow$ $\downarrow$ CaR $\rightarrow$ $\uparrow$ PTH

- **PO$_4$**
  - $\uparrow$ PO$_4$ $\rightarrow$ $\downarrow$ VDR $\rightarrow$ $\downarrow$ CaR $\rightarrow$ $\uparrow$ PTH

- **1-α hydroxylase**
  - $\downarrow$ 1-α hydroxylase $\rightarrow$ $\downarrow$ PTH $\rightarrow$ $\downarrow$ VDR $\rightarrow$ $\downarrow$ CaR $\rightarrow$ $\uparrow$ PTH

- **Nephron number**
  - $\downarrow$ Nephron number $\rightarrow$ $\downarrow$ Net renal PO$_4$ clearance $\rightarrow$ $\downarrow$ VDR $\rightarrow$ $\downarrow$ CaR $\rightarrow$ $\uparrow$ PTH

- **PTH Effects**
  - $\leftarrow$ PTH Effects $\rightarrow$ CKD Effects

- **CKD Effects**
  - $\leftarrow$ CKD Effects $\rightarrow$ PTH Effects

- **Renal PO$_4$ clearance**
  - $\uparrow$ Renal PO$_4$ clearance $\rightarrow$ $\downarrow$ VDR $\rightarrow$ $\downarrow$ CaR $\rightarrow$ $\uparrow$ PTH
CKD-MINERAL BONE DISORDERS

- As kidneys fail they:
  - Stop activating calcitriol (the active form of Vit D)—causing calcium imbalance
  - Do not remove phosphorus from blood—leading to phosphorus retention.
    - The extra phosphorus pulls calcium out of bones, causing them to weaken
    - High phosphorus stimulates PTH release
  - These changes (plus others) cause the start of secondary hyperparathyroidism

- Labs:
  - eGFR
  - Calcium
  - Phos
  - Vit D
  - iPTH

(Qunibi & Henrich, 2017)
PREVALENCE OF ABNORMALITIES OF MINERAL METABOLISM, PTH IN CKD

<table>
<thead>
<tr>
<th>CKD Stage 3</th>
<th>CKD Stages 4 and 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of Patients</td>
<td></td>
</tr>
<tr>
<td>eGFR (mL/min/1.73 m²)</td>
<td></td>
</tr>
</tbody>
</table>

- iPTh >65 pg/mL
- Phosphorus >4.6 mg/dL
- Calcium <8.4 mg/dL

MANAGING CKD-MBD COMPLICATIONS

• Treat with D3 as indicated to achieve normal serum levels
  • Goal is 25 OH >30
• 2000 IU po qd is cheaper and better absorbed than 50,000 IU monthly dose.
• Limit phosphorus in diet (CKD stage 4/5), with emphasis on decreasing packaged products - Refer to renal dietician
• May need phosphate binders (when phos >5.5)
• All-cause and CV mortality increase 30-60% with each 1 mg/dL higher phosphorus level above normal

(Qunibi & Henrich, 2017)
## CKD-MBD TESTING

<table>
<thead>
<tr>
<th>CKD Stage</th>
<th>Calcium, Phosphorus</th>
<th>PTH</th>
<th>25(OH)D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 3</td>
<td>Every 6-12 months</td>
<td>Once then based on CKD progression</td>
<td></td>
</tr>
<tr>
<td>Stage 4</td>
<td>Every 3-6 months</td>
<td>Every 6-12 months</td>
<td></td>
</tr>
<tr>
<td>Stage 5</td>
<td>Every 1-3 months</td>
<td>Every 3-6 months</td>
<td>Once, then based on level and treatments</td>
</tr>
</tbody>
</table>
ANEMIA BECOMES MORE COMMON AS KIDNEY FUNCTION DECLINES

![Image showing the percentage of patients with Hgb ≤12 g/dL across different stages of CKD](image)

- Stage 1/2: 26.7%
- Stage 3: 41.6%
- Stage 4: 53.6%
- Stage 5: 75.5%

DETECT AND MANAGE CKD COMPLICATIONS

• Anemia
  
  • Initiate iron therapy if TSAT $\leq 30\%$ and ferritin $\leq 200 \text{ ng/mL}$ (-Oral for non-dialysis CKD)
  
  • Individualize erythropoiesis stimulating agent (ESA) therapy: Start ESA if Hb $<10 \text{ g/dl}$, and maintain Hb $<11.5 \text{ g/dl}$. Ensure adequate Fe stores.
  
  • Appropriate iron supplementation is needed for ESA to be effective
  
  • MAKE SURE ANEMIA IS from CKD!!

(Berns, 2017)
COMPLICATIONS-METABOLIC ACIDOSIS

• Usually occurs later in CKD
  o Serum bicarb >22mEq/L
  o Correction of metabolic acidosis may slow CKD progression and improve patients functional status\(^1,2\)

• Goal CO2 22-26
• Sodium Bicarb 650 1-2 bid to tid
• Bicitra 30 ml daily to bid

(Mahajan, et al., 2010)
(de Brito-Ashurst, Varagunam, Raftery, & Yagoob, 2009)
COMPLICATIONS-VASCULAR CALCIFICATION

• Lateral abdominal radiograph can be used to detect vascular calcification
• Echocardiogram can be used to detect presence or absence of valvular calcification

KDIGO, 2017
HYPERKALEMIA MANAGEMENT

• Hyperkalemia
  • Reduce dietary potassium
  • Stop NSAIDs, COX-2 inhibitors, potassium sparing diuretics (aldactone)
  • Stop or reduce beta blockers, ACEi/ARBs
  • Avoid salt substitutes that contain potassium

Rosenberg, 2016
Hyperuricemia can develop due to decreased urinary excretion.

Several studies show hyperuricemia may contribute to CKD progression - longer term studies are needed to confirm.

Can treat with use of allopurinol max dose is 900 mg/day, Uloric 80 mg also can be used.

(Gaffo & Saag, 2008)
CKD MONITORING, LEVELS 3,4,5

- PTH intact
- Complete blood count (CBC)
- Lipids
- 25-OH vitamin D levels
- Uric acid
- Urinalysis with microscopy
- Urine prot/creat ratio
- Complete metabolic panel (CMP)
- Phosphate

- Get a renal sono at least once
<table>
<thead>
<tr>
<th>GFR Categories (mL/min/1.73 m²)</th>
<th>Stage, Description, and Range</th>
<th>Normal to mildly increased</th>
<th>Moderately increased</th>
<th>Severely increased</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Normal or high</td>
<td>≥90</td>
<td>1 if CKD</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>Mildly decreased</td>
<td>60–89</td>
<td>1 if CKD</td>
<td>1</td>
</tr>
<tr>
<td>3a</td>
<td>Mildly to moderately decreased</td>
<td>45–59</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>3b</td>
<td>Moderately to severely decreased</td>
<td>30–44</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>Severely decreased</td>
<td>15–29</td>
<td>3</td>
<td>4+</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure</td>
<td>&lt;15</td>
<td>4+</td>
<td>4+</td>
</tr>
</tbody>
</table>

**Persistent Albuminuria Categories, Description and Range**

- **Normal to mildly increased**: <30 mg/g (<3 mg/mmol)
- **Moderately increased**: 30-300 mg/g (3-30 mg/mmol)
- **Severely increased**: >300 mg/g (>30 mg/mmol)
WHEN TO REFER TO A NEPHROLOGIST

- CKD stages 3-5
- Progression of disease – declining eGFR, increasing proteinuria
- Degree of proteinuria: nephrotic syndrome, > 0.5-1.0 g/d on ACEi or ARB therapy
- Etiology of CKD not certain
- Need help with disease management
- Indications for kidney biopsy

Rosenberg, 2016
### WHEN TO REFER

<table>
<thead>
<tr>
<th>Persistent albuminuria categories</th>
<th>A1</th>
<th>A2</th>
<th>A3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description and range</td>
<td>Normal to mildly increased</td>
<td>Moderately increased</td>
<td>Severely increased</td>
</tr>
<tr>
<td>GFR categories (ml/min/1.73 m²)</td>
<td>Normal or high ≤90</td>
<td>Monitor</td>
<td>Refer*</td>
</tr>
<tr>
<td>G2</td>
<td>Mildly decreased 60–89</td>
<td>Monitor</td>
<td>Refer*</td>
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<td>G3a</td>
<td>Mildly to moderately decreased 45–59</td>
<td>Monitor</td>
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<tr>
<td>G3b</td>
<td>Moderately to severely decreased 30–44</td>
<td>Monitor</td>
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<tr>
<td>G4</td>
<td>Severely decreased 15–29</td>
<td>Refer*</td>
<td>Refer*</td>
</tr>
<tr>
<td>G5</td>
<td>Kidney failure &lt;15</td>
<td>Refer</td>
<td>Refer</td>
</tr>
</tbody>
</table>
STEPS TO CKD PATIENT CARE

1. CKD definition and risks
2. Assess GFR, albuminuria
3. Determine etiology
4. Assess for evidence of progression
5. Assess for associated complications
6. Discuss dialysis/transplantation
KIDNEY TRANSPLANTATION

• Treatment of choice for ESRD
• Improves quality of life
• Waiting list time varies-3-5 years
• 3 year survival rate after transplantation is 83-94%
• Increased risk of cancer
STARTING DIALYSIS IN THE ELDERLY...OR NOT?

• Among patients > 75 yrs with stage 5 CKD who chose to NOT start dialysis:
  • Overall, more likely to die over next 1-2 years
  • But if they had ischemic heart disease or other significant comorbidity \(\rightarrow\) NO DIFFERENCE in survival

• Active disease management and supportive care may be appropriate without starting dialysis in the ill elderly
  • Palliative care does not mean “no care”

• Must have end-of-life discussions!

(Murtagh, et al. 2007)
CKD MANAGEMENT

• Diagnose cause and treat underlying condition
• Stage per guidelines
• Slow progression of kidney disease (ACE inhibitors)
• Monitor for complications—volume overload, hyperkalemia, metabolic acidosis, hyperphosphatemia, anorexia, fatigue, htn, bone disease
• Labs: cmp, cbc, phos, Vit D 25OH, iPTH, urine microscopy, uric acid, urine protein/cr ratio-frequency based off heat map. Get sono at least once
• Vaccinate: influenza, hep B, pneumococcal
• Eval ASCVD risk-likely needs statin
• Possible dexa (don’t give bisphosphonates if GFR<35, let specialist manage)
• Refer to nephrology when eGFR is <30 (sometimes if higher risk-refer earlier)
CASE 1

- 55 year old man with past medical history of headaches presents to your office for his first time visit to a PCP in over 30 years.

- He has no past history of being admitted to the hospital and he does not take any OTC meds/NSAIDs/herbal meds. He has no history of ETOH abuse, smoking or drug use.
• Vitals: BP 180/100 mmHg, pulse 80, R 18

• Exam: No JVD, S1S2 regular, PMI shifted to the left, no gallop, no abdominal bruit, pulses bilaterally equal and regular, no leg edema.

• What would you order?

• EKG, cbc, cmp, ua, urine protein/cr ratio lipid
LAB RESULTS

- Labs reveal a creatinine of 2.2 mg/dL, eGFR 33. Urine shows no blood or casts. Urine/protein ratio shows 1 gm protein/24 hrs. EKG shows LVH
- Next step in workup?
  - Renal ultrasound 1st, then SPEP, UPEP with immunofixation, serum free light chains
- Additional labs neg, Renal ultrasound shows that both kidneys are slightly reduced in size and are mildly echogenic with no mass or hydronephrosis.
- What is your diagnosis?
Main complications of persistent High blood pressure

**Brain:**
- Cerebrovascular accident (strokes)
- Hypertensive encephalopathy:
  - confusion
  - headache
  - convulsion

**Retina of eye:**
- Hypertensive retinopathy

**Heart:**
- Myocardial infarction (heart attack)
- Hypertensive cardiomyopathy:
  *heart failure*

**Blood:**
- Elevated sugar levels

**Kidneys:**
- Hypertensive nephropathy:
  *chronic renal failure*
HYPERTENSIVE NEPHROPATHY WITH PROTEINURIA

- Dual therapy-Lisinopril, diltiazem f/u 1 week, ASCVD risk calculator-statin, aspirin
- Can we officially diagnosis CKD?
- 3 months. However—we have evidence of structural abnormalities Could potentially stage at G3b, A3 (red on the heat map)
- Goal blood pressure?
- JNC 8: 140/90, NKF: 130/80
- Additional lab needed for progression monitoring?
- Cbc, renal panel, phos, Vit D, iPTH, uric acid, urine micro (we already have the renal sono, and urine protein/cr ratio, and lipid)
Secondary Hypertension

Selective renal angiography (left lower renal artery) after successful percutaneous balloon dilatation of the stenotic lesion. Fibromuscular dysplasia in an accessory renal artery causing renovascular hypertension.

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O.S. is a 64-year-old Hispanic female in for DM check. She has had DM for 15+ years, and is currently taking metformin 1000mg bid, Lisinopril 10mg a day, atorvastatin 40mg a day. Labs today showed the following:

- Hgba1c 8.6%, cmp: eGFR 50, lipid WNL, protein/cr ratio 650mg. These results are similar to her last visit.
- Upon further hx-you find that she had a recent eye exam, and has mild nonproliferative retinopathy. She does not have neuropathy or other s/s.
- What further workup do you need?
- Renal sonogram, urine micro, iPTH, vit D (25 OH), phos, uric acid
- Dx stage:
  - G3a A3
- What further treatment do you need?
- Improve glycemic control, Increase Lisinopril to 20mg, with a goal of 40mg. Avoid NSAIDs, or other nephrotoxic agents, make sure meds are renally dosed, monitor 3x/year, nephro referral?
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# MANAGEMENT OF CKD IN DIABETES

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<th>eGFR</th>
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<td>All patients</td>
<td>Yearly measurement of creatinine, urinary albumin excretion, potassium</td>
</tr>
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<td>45-60</td>
<td>Referral to a nephrologist if possibility for nondiabetic kidney disease exists</td>
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- Consider dose adjustment of medications
- Monitor eGFR every 6 months
- Monitor electrolytes, bicarbonate, hemoglobin, calcium, phosphorus, parathyroid hormone at least yearly
- Assure vitamin D sufficiency
- Consider bone density testing
- Referral for dietary counselling

CASE 3

- 19 year old African American woman presents to your clinic with complaints of fatigue, joint pains, a new rash on her face, oral ulcer.

- On exam: BP 150/80 P 88 Afebrile 96% O2 sats on RA
- GEN: No respiratory distress at rest
- HEENT: painless oral ulcer, flat rash over malar eminences sparing the nasolabial fold, pallor +
- Lungs: CTA
- CVS: S1S2 regular
- Abdomen: soft, NT
- Ext: left elbow joint and bilateral wrist joints are swollen and tender

- What would you order?
- CBC, CMP, ua, urine microscopy, (microalbumin or urine protein/cr ratio), ANA, esr, RF, anti-ccp, uric acid, TSH
CASE 3

• Working dx: fatigue, oral ulcer, joint pain

• Basic Labs: Na 135, K 5.5, Bicarb 18, BUN 50, Cr 3.5, eGFR 22, Ca 9.0, ANA +, titer 1:640

• UA: 3+ blood, 3+ protein, RBC casts +

• Given these results, what is the most likely diagnosis?

• What would you do?
SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)


- Production of autoantibodies and immune complexes formation.

- There is renal involvement in the great majority of patients with SLE at some time of the evolution: 66-90%.
SLE – LUPUS NEPHRITIS

- Race: SLE is more common/severe in African americans than Caucasians.

- Gender: female-to-male ratio of 9:1

- Age: Most patients develop lupus nephritis early in their disease course. SLE is more common among women in the third decade of life, and lupus nephritis occurs in patients aged 20-40 years.

- Kidney Biopsy: For staging lupus nephritis (Class 1-5).
CASE 5

- A 80 year old man who has not seen a PCP in many years presents to your clinic for weakness for the past few months. On further questioning he tells you that his bones also have been hurting lately and he has developed leg swelling in the past month or so.

- On exam:
  - BP: 160/90 P 88  Afebrile
  - GEN: Thin built man
  - HEENT: pallor present
  - Lungs: clear
  - CVS: S1S2 regular, no rub or gallop
  - Abdomen: soft, NT
  - Ext: 2 + edema
CASE 5

- Differentials:
  - CHF, MI, Cancer, arthritis
- Labs:
  - CBC, CMP, urine microscopy, urine protein/cr ratio, ESR, TSH, EKG, BNP, pa and lat CXR
LABS: Urine dipstick negative for protein or blood

Basic chem:
- Na 136 (135-145), K 5.1 (3.5-5.5), Chloride 108 (96-106), Bicarb 25 (20-29), BUN 40, Creatinine 2 (0.6-1.2), eGFR 31, Glucose 78 (70-100), Calcium 10.5 (7.8-9.0), WBC 8, Hgb 9, Hct 28, Plat 200
- ?anion gap? 3 (3-11)

Given this presentation and the labs (low anion gap and elevated calcium, anemia, kidney failure), what will you think of? What will you order next?

Serum and urine protein electrophoresis
Kidney Biopsy

Intratubular refractile casts with surrounding syncytial giant cell reaction with chronic tubulointerstitial nephritis and fibrosis, characteristic of myeloma cast nephropathy.
CASE STUDY

• A 35 year old African American woman was seen in the clinic for chronic cough and dyspnea on exertion. She gave history of vague symptoms of fatigue and weight loss of 20 lbs over the last six months.

• List some differentials
  • TB, sarcoid, lupus, thyroid problems, PE
  • What would you order?
  • PPD, cbc, cmp, UA, TSH, ANA, pa and lat cxr
• Her labs were significant for mildly elevated calcium level and a creatinine of 2.0 mg/dL, eGFR 37

• She had 750 mg of proteinuria/day
• PPD neg, ANA neg, TSH and other labs WNL
• Assuming this is present more than 3 months.......what is her ckd stage?
  • G3b, A3
  • What do we still need?
CXR – HILAR LYMPHADENOPATHY

CT scan of chest

Image retrieved on 05 October 2010 from: http://commons.wikimedia.org/wiki/File:Anterior Mediastinal mass thymoma.jpg
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WHAT'S NEEDED NEXT?

- Biopsy of hilar lymphadenopathy or renal biopsy
- DX: sarcoidosis
NEWLY DX CKD

- 1) urinalysis, microscopy, ultrasound, protein/cr ratio
- If obstruction-treat
- No obstruction:
  - Hx critical (consider myeloma if high risk)
    - glomerular bleeding or albumin in urine?
      - Yes: workup for glomerular causes (ANA, rf, hep B, C, upep, spep ANCA, complement C3, C4)
      - No: sterile pyuria-consider interstitial nephritis.
  - High risk renovascular disease? Evaluate renovascular disease
  - Follow creatinine-if stable, monitor. Consider renal biopsy

Refer to nephrology
Additional Online Resources for CKD Learning

- National Kidney Foundation: [www.kidney.org](http://www.kidney.org)
- United States Renal Data Service: [www.usrds.org](http://www.usrds.org)
- CDC’s CKD Surveillance Project: [http://nccd.cdc.gov/ckd](http://nccd.cdc.gov/ckd)


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