NEPHROLOGY

Care of the CKD Patient: A Collaborative Effort

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Our Case

• A 54 yo African American man presents to establish care after recently relocating to your area ~

• PMH
  ~HTN x10 yrs, under fair control on HCTZ with last BP reading 144/92
  ~DM type II for 8 yrs, on metformin over the last 5 yrs ~ last HgbA1c was 8.1%; eye check 10 months ago revealed some mild neovascularization on the right 'being monitored'
  ~Gout for which he takes indomethacin episodically (average use 3-4 days at a time, 4-5x/yr)
  ~30 pkyr smoker who has cut down to <10 cigarettes/day over last 4 months
Our Case

- **ROS** ~ benign except for +nocturia, +foamy urine

- **FMH** ~ +DM, HTN on paternal side of family; father was on dialysis due to diabetic nephropathy and HTN; mother had hypothyroidism and rheumatoid arthritis; 2 siblings, one with HTN, DM, CAD and CKD and the other with HTN

- **Meds** ~ HCTZ 25 mg QD, Metformin 1000mg BID, indomethacin 25 mg q 6hrs prn for joint pain

- **Social** ~ Married, 3 grown children, works as insurance adjuster; no alcohol, no illicit drugs, no allergies, no high risk behaviors except for smoking but trying to quit
Our Case

- **Exam**: BP 150/96, HR 80, BMI 31

- Pertinent findings include: +S4 gallop, slight displacement of PMI to the left; soft left carotid bruit, soft right femoral bruit; DP/PT pulses easily palpable bilaterally; fundoscopic exam with some AV nicking, arteriolar narrowing and a single flame hemorrhage noted on right; lung and abd exams benign; feet in good condition; trace LE edema

- **Old records** ~ disappointing! No EKG, no lipid panel, no urinalysis; last HgbA1c 8.1% 1 year ago, last creat 0.9 mg/dl 2 yrs ago, last Hgb 14.9 gm/dl also 2 yrs ago
Does this patient have risk factors for CKD?

A better question might be “Which risk factors does he NOT have?”
Risk Factors for developing CKD

**Modifiable**
- Obesity
- Smoking
- Drugs

**Modifiable with Active Management**
- Diabetes
- Hypertension
- Autoimmune diseases
- Frequent UTI
- Obstruction
- Stones
- Systemic Infections
- Primary glomerular diseases
- Heart Failure
- Hereditary renal diseases
- Proteinuria

**Non-Modifiable**
- Family history of CKD
- Older age (>60)
- African American, Hispanic, Asian race
- Genetic diseases (e.g., PCKD)
Screening for CKD

3 simple tests for anyone at risk:

1. BP check
2. Serum creatinine (with calculated eGFR)
3. Urinalysis and measurement of proteinuria (urine PCR)
NKF K/DOQI Definition of Chronic Kidney Disease

• Structural or functional abnormalities of the kidneys for >3 months, as manifested by either:

  1. Kidney damage, with or without decreased GFR, as defined by
     * Pathologic abnormalities
     * Markers of kidney damage
     * Urinary abnormalities (proteinuria)
     * Blood abnormalities (renal tubular defects)
     * Imaging abnormalities (polycystic kidneys)
     * Kidney transplantation

  2. GFR <60 ml/min/1.73 m²
Treatment of Hypertension in CKD: Goals of Therapy

• Reduce progression of disease
• Reduce cardiovascular risk
• Prevent other end-organ damage
• Multitasking is ideal*

• Target < 130/80
Multitasking is preferred ~
eg, HTN treatment in diabetics

**ACE inhibitors**

![Graph showing percentage with doubling of baseline creatinine vs years of follow-up. Placebo and Captopril data points are shown.](image)

- Placebo: 202, 184, 173, 163, 142, 99, 75, 45, 22
- Captopril: 207, 199, 190, 180, 167, 120, 82, 50, 24

*P = 0.007*

*N Engl J Med 1993; 329:1456-1462*

**ARBs**

![Graph showing end-stage renal disease or death (%) vs months of study. Losartan and Placebo data points are shown.](image)

- Losartan: 702, 715, 714, 713, 712, 710, 708, 706, 704, 702
- Placebo: 751, 749, 747, 745, 743, 741, 739, 737, 735, 733

*Risk reduction, 20%; P = 0.01*

Estimating GFR: MDRD and Cockcroft-Gault

**Abbreviated MDRD Equation**

\[
GFR \text{ (mL/min/1.73 m}^2) = 186 \times (SCr)^{-1.154} \times (age)^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if African American})
\]

**Cockcroft-Gault Equation**

\[
C_{cr} \text{ (mL/min)} = \frac{(140 - \text{age [y]} \times \text{weight [kg]})}{72 \times SCr \text{ (mg/dL)}} \times 0.85 \text{ if patient is female}
\]

\[C_{cr} = \text{creatinine clearance; MDRD = Modification of Diet in Renal Disease.} \]

Progression of CKD
Measurement of Proteinuria

Spot Urine protein = 200 mg/dL = 4 grams proteinuria/day
Spot Urine creatinine = 50 mg/dL

Ginsberg. NEJM 1983;309:1543-6
The importance of proteinuria.

Associated with faster progression of kidney disease

Reduction in proteinuria helps slow the loss of kidney function

Associated with the development of cardiovascular disease

Guide to therapy (ACE-I and/or ARB)

Those with higher levels of proteinuria have more benefit than those with lower levels
Our Case: Lab evaluation

BUN/creat 30/1.6, eGFR 50 ml/min
[Na+] 131 meq/l, [K+] 5.1 meq/l, bicarb 21 meq/l
Albumin 3.4 gm/dl
HgbA1c 8.9%
Hgb 11.8 gm/dl
Lipid panel: Tchol 288, HDL 41, LDL 164, Tgl 220
UA with 3+ protein, 1+ glucose, pH 5.5, SG 1.022; micro ~ 3-5
OFB/HPF, some fatty casts, few fine and coarse granular casts, rare nondysmorphic RBC
Urine protein:creatinine ratio = 3.8
**Interpretation? Stage 3 CKD**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR (mL/min/1.73 m²)</th>
<th>Action*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>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</td>
<td>Kidney damage with mild ↓ GFR</td>
<td>60–89</td>
<td>Estimating progression</td>
</tr>
<tr>
<td>3</td>
<td>Moderate ↓ GFR</td>
<td>30–59</td>
<td>Evaluating and treating complications</td>
</tr>
<tr>
<td>4</td>
<td>Severe ↓ GFR</td>
<td>15–29</td>
<td>Preparation for kidney replacement therapy</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure</td>
<td>&lt;15 (or dialysis)</td>
<td>Replacement (if uremia present)</td>
</tr>
</tbody>
</table>

CKD is defined as either kidney damage or GFR <60 mL/min/1.73 m² for ≥3 months. Kidney damage is defined as pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.

* Includes actions from preceding stages.

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Let’s customize an action plan for our patient ~

BP control not optimal
Definite stage 3 CKD by eGFR
Nephrotic range proteinuria
Modest hyponatremia
Modest hyperkalemia
Modest acidosis
Mild anemia
DM not well controlled
Hyperlipidemia
Obesity
Smoking history
Risk for prostatism/obstruction
NSAID use for episodic gout
Let’s customize an action plan for our patient ~

BP control not optimal ~ Add ACEI or ARB, titrate
Stage 3 CKD by eGFR ~ implement CKD plan***
Nephrotic proteinuria ~ ACEI/ARB may help ↓
Modest hyponatremia ~ HCTZ? ↑glucose? CHF?
Modest hyperkalemia ~ Type IV RTA (hyporenin-hypoaldosteronism)
Modest acidosis ~ ditto; check for diarrhea
Mild anemia ~ blood loss? Iron deficiency? Low Epo?
DM not well controlled ~ D/C metformin; Insulin?
Hyperlipidemia ~ diet/exercise counseling; statin?
Obesity ~ diet/exercise counseling
Smoking ~ smoking cessation counseling
Risk for prostatism/obstruction ~ renal U/S
NSAID use for episodic gout ~ allopurinol, colchicine, prednisone
Stage 3 CKD Management Plan:
Evaluate and treat complications

In addition to usual supportive management, 2 critical complications to watch for ~

Anemia

Mineral/Bone Metabolism
Anemia in CKD

- Decreased kidney production of erythropoeitin
- Shortened RBC survival in the uremic state
- Contributes to the development of LVH, CHF and increased mortality in CKD
- Contributes to decreased functional status
The Prevalence of Anemia in CKD

Patients with Hgb < 12 g/dL (%)

GFR (mL/min/1.73m²)

>90 Stage 1 60-90 Stage 2 30-60 Stage 3 15-30 Stage 4 < 15 Stage 5

13 33 42 54 76

The downside of anemia in CKD

Relative risk of death in:
- CKD: 2x
- CKD + anemia: 3.7x
- CKD + CHF + anemia: 6x

Risk of LVH 30% higher for every .5g/dL decrease in Hgb
LVH is an independent determinant of mortality in ESRD
Treatment of anemia in CKD has shown at least partial regression of LVH

Pereira et al  KI 68:1432-1438, 2005
Levin et al  AJKD 32:125-134, 1999
Disorders of Bone and Mineral Metabolism in CKD

Classic renal osteodystrophy is characterized by:

- Increased production and secretion of PTH
- Parathyroid hyperplasia
- Hyperphosphatemia
- Hypocalcemia
- 1,25 (OH)2 vitamin D3 deficiency
Secondary HPT Develops as Kidney Function Declines

AJKD 1997
Figure 1. Unadjusted, case-mix-adjusted, and multivariable-adjusted relative risks (RR; of death) and 95% confidence intervals (CI) for eight categories of serum phosphorus (referent range, 4.0 to 5.0 mg/dl). For all analyses, case mix adjustment refers to adjustment for age, gender, race or ethnicity, diabetes, and vintage. Multivariable adjustment refers to case mix plus body weight, URR, serum albumin, creatinine, predialysis BUN, bicarbonate, cholesterol, hemoglobin, ferritin, and aluminum. Phosphorus models simultaneously adjusted for calcium + parathyroid hormone (PTH), calcium models simultaneously adjusted for phosphorus + PTH, PTH models simultaneously adjusted for phosphorus + calcium. *Inclusion of linear and quadratic terms. Categories of vintage: <2 yr (referent), 2 to 5 yr, ≥5 yr, and missing. Categories of cholesterol: <120, 120 to 160, 160 to 200 (referent), 200 to 240, ≥240 mg/dl, and missing. Companion models substituting body surface area, Quetelet’s index, or calculated total body water for body weight, and Kt/V or Kt for URR did not change parameter estimates for phosphorus, calcium, or PTH.
<table>
<thead>
<tr>
<th>CKD stage</th>
<th>GFR range (mL/min/1.73m²)</th>
<th>Measurement of Calcium/Phosphorus</th>
<th>Measurement of intact PTH</th>
<th>Target intact PTH</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>30-59</td>
<td>Every 12 months</td>
<td>Every 12 months</td>
<td>35-70 (OPINION)</td>
</tr>
<tr>
<td>4</td>
<td>15-29</td>
<td>Every 3 months</td>
<td>Every 3 months</td>
<td>70-110 (OPINION)</td>
</tr>
<tr>
<td>5</td>
<td>&lt;15 or dialysis</td>
<td>Every month</td>
<td>Every 3 months</td>
<td>150-300 (EVIDENCE)</td>
</tr>
</tbody>
</table>

Laboratory screening and recommended PTH targets for CKD
Management of secondary hyperparathyroidism

If PTH elevated, check 25(OH)vit D level
  – Replace if low with ergocalciferol
### Table 26. Recommended Supplementation for Vitamin D Deficiency/Insufficiency in Patients with CKD Stages 3 and 4

<table>
<thead>
<tr>
<th>Serum 25(OH)D (ng/mL) [nmol/L]</th>
<th>Definition</th>
<th>Ergocalciferol Dose (Vitamin D$_2$)</th>
<th>Duration (months)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5 [12]</td>
<td>Severe vitamin D deficiency</td>
<td>50,000 IU/wk orally x 12 wks; then monthly</td>
<td>6 months</td>
<td>Measure 25(OH)D levels after 6 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>500,000 IU as single I.M. dose</td>
<td></td>
<td>Assure patient adherence; measure 25(OH)D at 6 months</td>
</tr>
<tr>
<td>5-15 [12-37]</td>
<td>Mild vitamin D deficiency</td>
<td>50,000 IU/wk x 4 weeks, then 50,000 IU/month orally</td>
<td>6 months</td>
<td>Measure 25(OH)D levels after 6 months</td>
</tr>
<tr>
<td>16-30 [40-75]</td>
<td>Vitamin D insufficiency</td>
<td>50,000 IU/month orally</td>
<td>6 months</td>
<td></td>
</tr>
</tbody>
</table>
Management of secondary hyperparathyroidism

If PTH elevated, check 25(OH)vit D level
- Replace if low with ergocalciferol
- If 25(OH)vit D level is above 30ng/mL, and PTH is above 200 pg/dl, start a vitamin D analog such as calcitriol, paracalcitrol or doxercalciferol.
- Monitor Ca / Phos / intact PTH levels closely (q 3-4 months)
- Educate pts about dietary phosphate restriction
HIGH PHOSPHORUS FOODS

These are foods you may need to limit or avoid. Check with your Dietitian.
Phosphorus Binders

Calcium acetate ~ Tums, PhosLo, PhosLyra
Sevelamer ~ Renagel, Renvela
Lanthanum carbonate ~ Fosrenol
Sucroferric oxyhydroxide ~ Velphoro
Aluminum hydroxide ~ Amphogel, Dialume, Alternagel
Treatments to Slow the Progression of Chronic Kidney Disease in Adults

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Diabetic Kidney Disease</th>
<th>Nondiabetic Kidney Disease</th>
<th>Kidney Disease in the Transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strict glycemic control</td>
<td>Yes&lt;sup&gt;a&lt;/sup&gt;</td>
<td>NA</td>
<td>Not tested</td>
</tr>
<tr>
<td>ACE-inhibitors or angiotensin-receptor blockers</td>
<td>Yes</td>
<td>Yes (greater effect in patients with proteinuria)</td>
<td>Not tested</td>
</tr>
<tr>
<td>Strict blood pressure control</td>
<td>Yes</td>
<td>Yes</td>
<td>Not tested</td>
</tr>
<tr>
<td>Dietary protein restriction</td>
<td>Uncertain</td>
<td>Uncertain</td>
<td>Not tested</td>
</tr>
<tr>
<td>Lipid-lowering therapy</td>
<td>Probable LDL&lt;100 mg/d</td>
<td>Probable LDL&lt;100 mg/d</td>
<td>Not tested</td>
</tr>
</tbody>
</table>

<sup>a</sup> Prevents or delays the onset of diabetic kidney disease. Inconclusive with regard to progression of established disease.
How can a PCP possibly do all of this?

First, realize you are ALREADY doing most of it:

– Diagnosing and treating hypertension
– Diagnosing and treating diabetes
– Diagnosing and treating dyslipidemia

The rest of it should be simple
How can I possibly do all of this?

~For those at risk:
  1. BP check
  2. Serum creatinine (with calculated eGFR)
  3. Urinalysis and measurement of proteinuria

~If eGFR is < 60 cc/min, check a Hgb and intact PTH, calcium and phosphorus once a year

~ACE-I &/or ARB therapy for diabetics and pts with proteinuric CKD (proteinuria > 200mg/day)

~Refer to a nephrologist if eGFR < 30 ml/min, cause of CKD unclear or you need help with any component of management
And now, a few Pearls ~

* Remember, insulin is excreted by the kidney
* Metformin should be stopped at eGFR <40 ml/min
* NSAIDs/combination analgesics are detrimental to kidney function, especially with chronic use
* In pts who are intolerant of ACEI, ARB or DRI therapy, non-dihydropyridine calcium channel blockers are next line for proteinuria reduction
* The #1 cause of death in the ESRD population is cardiovascular disease and conversely, proteinuria is a bad prognostic marker in pts with CAD
Questions?

Protect your kidneys, Save your heart.
Thank you!