

# 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

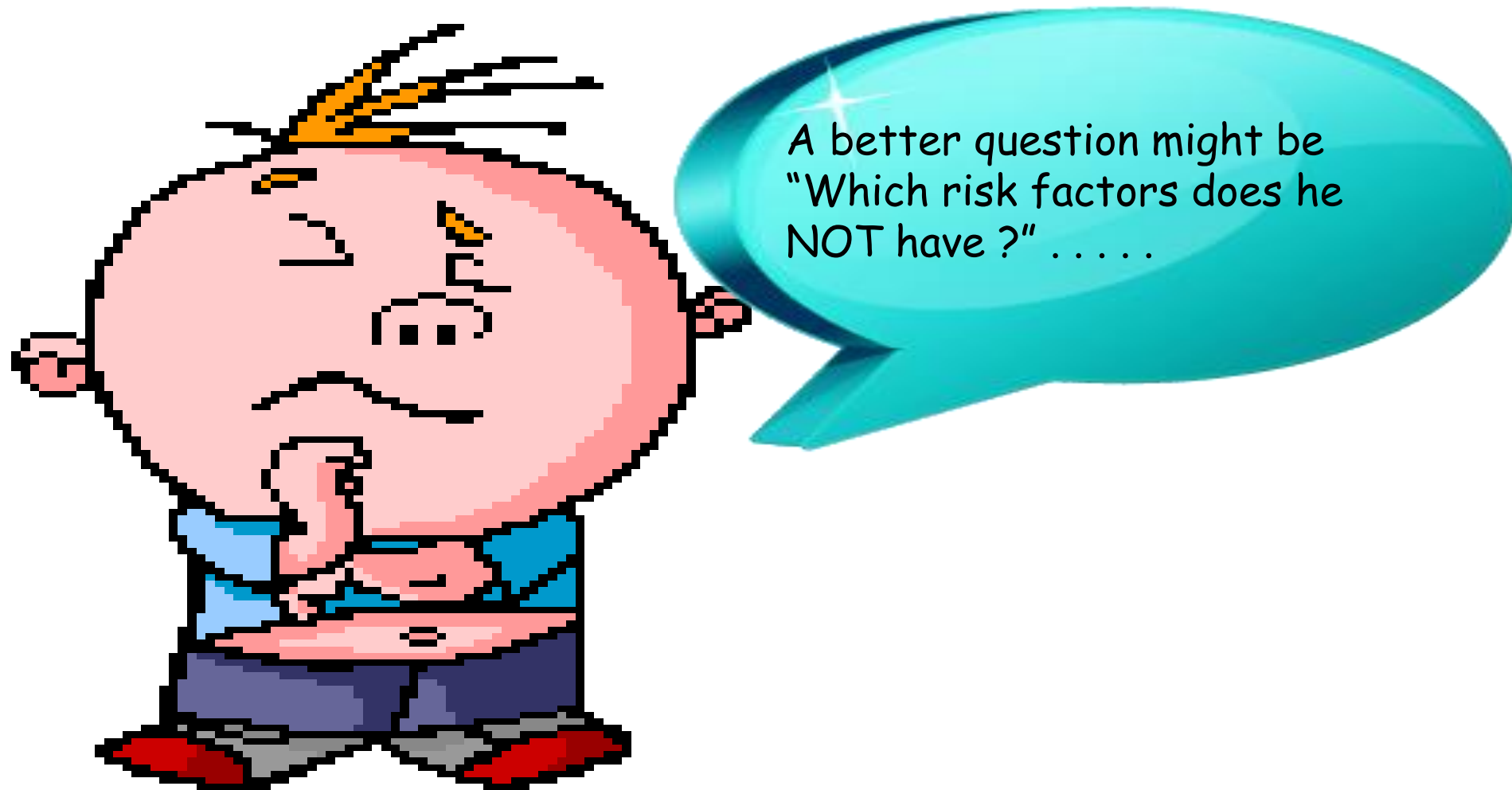
# Our Case

- **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 ?



# 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 (eg, PCKD)

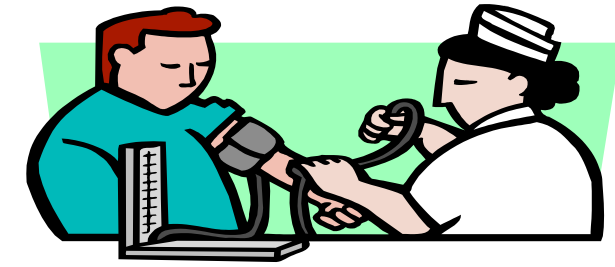


mr. filter  
kidney

# 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 m<sup>2</sup>



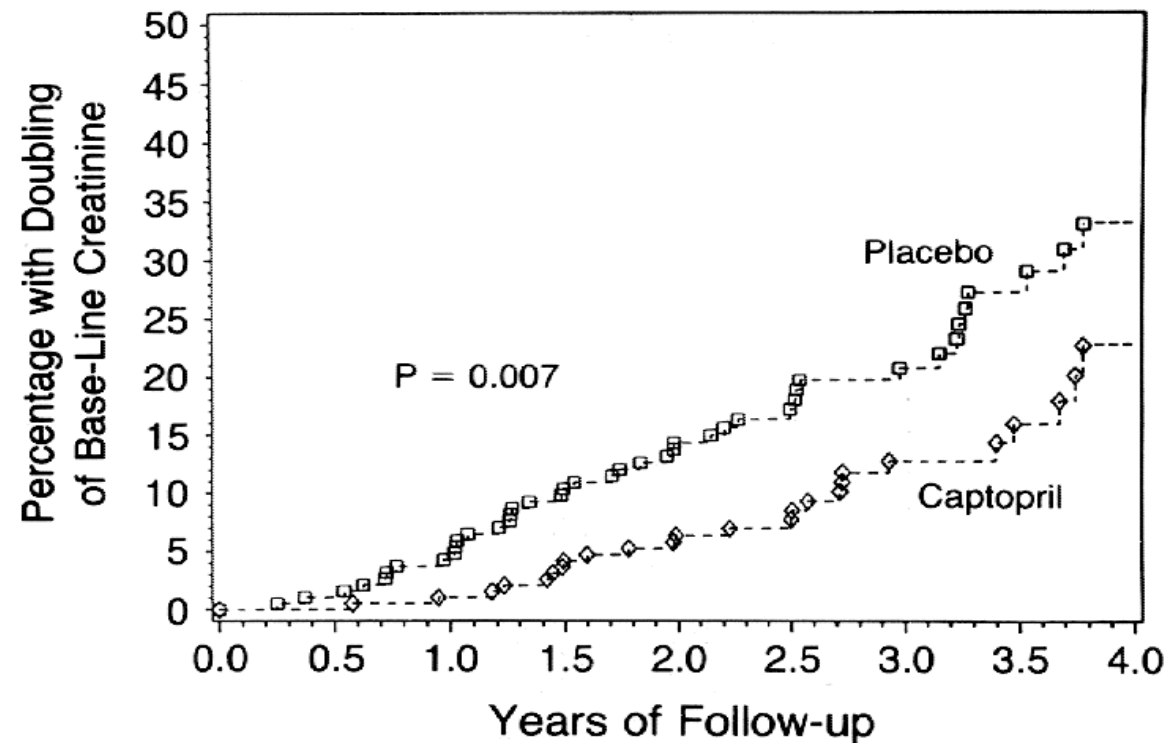
# Treatment of Hypertension in CKD: Goals of Therapy

- 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

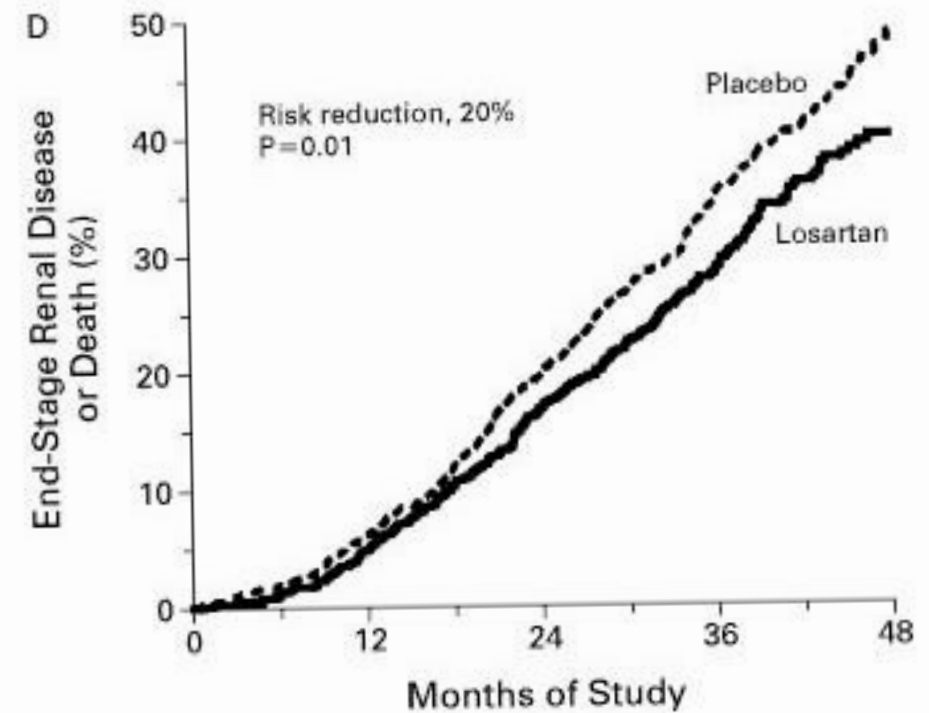
## ACE inhibitors



Placebo	202	184	173	161	142	99	75	45	22
Captopril	207	199	190	180	167	120	82	50	24

N Engl J Med 1993; 329:1456-1462

## ARBs



762	715	610	347	42
751	714	625	375	69

N Engl J Med 345:861-869, 2001



# Estimating GFR: MDRD and Cockcroft-Gault

- **Abbreviated MDRD Equation**

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

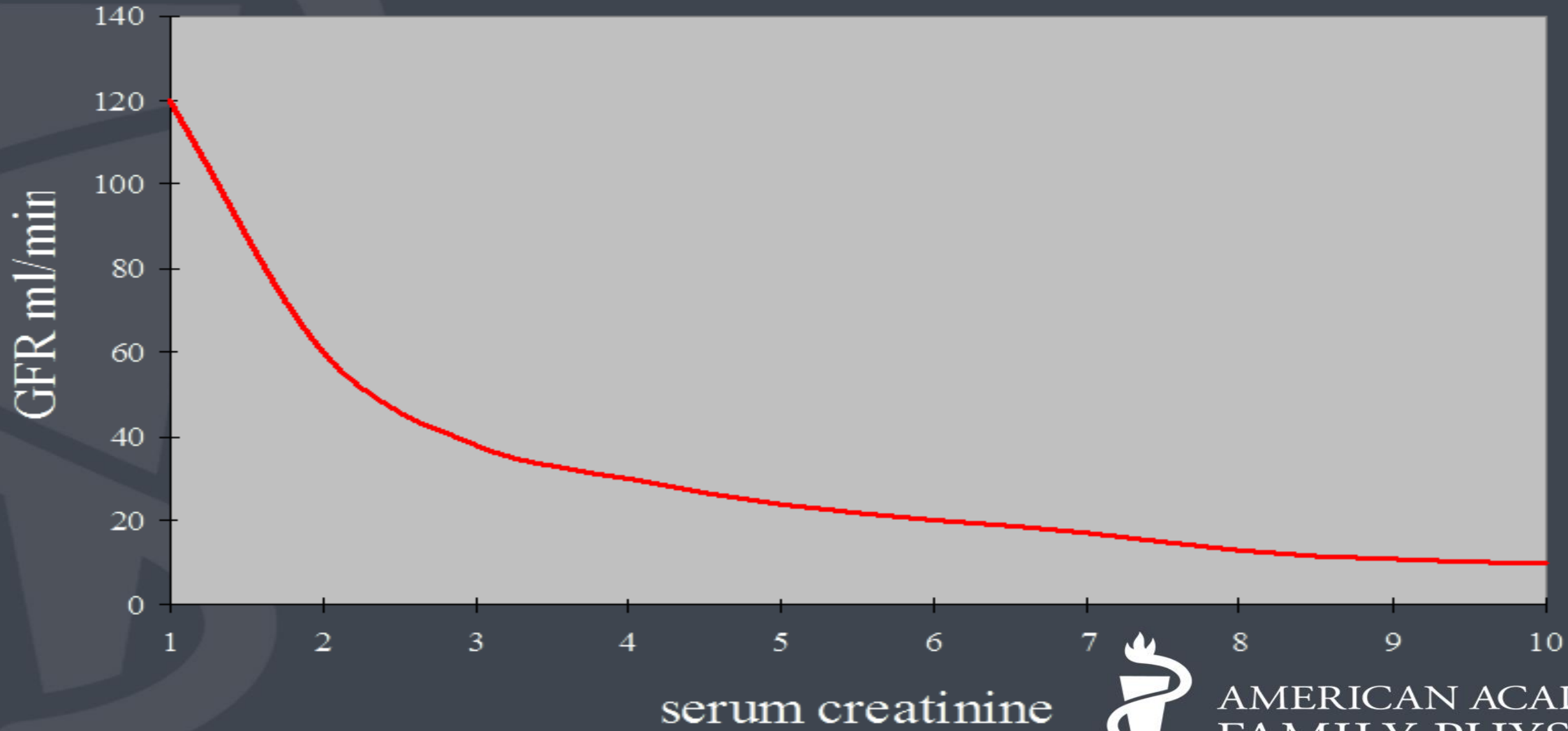
- **Cockcroft-Gault Equation**

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

$C_{\text{Cr}}$  = creatinine clearance; MDRD = Modification of Diet in Renal Disease.

Levey AS, et al. *Ann Intern Med*. 2003;139:137-147.

# Progression of CKD

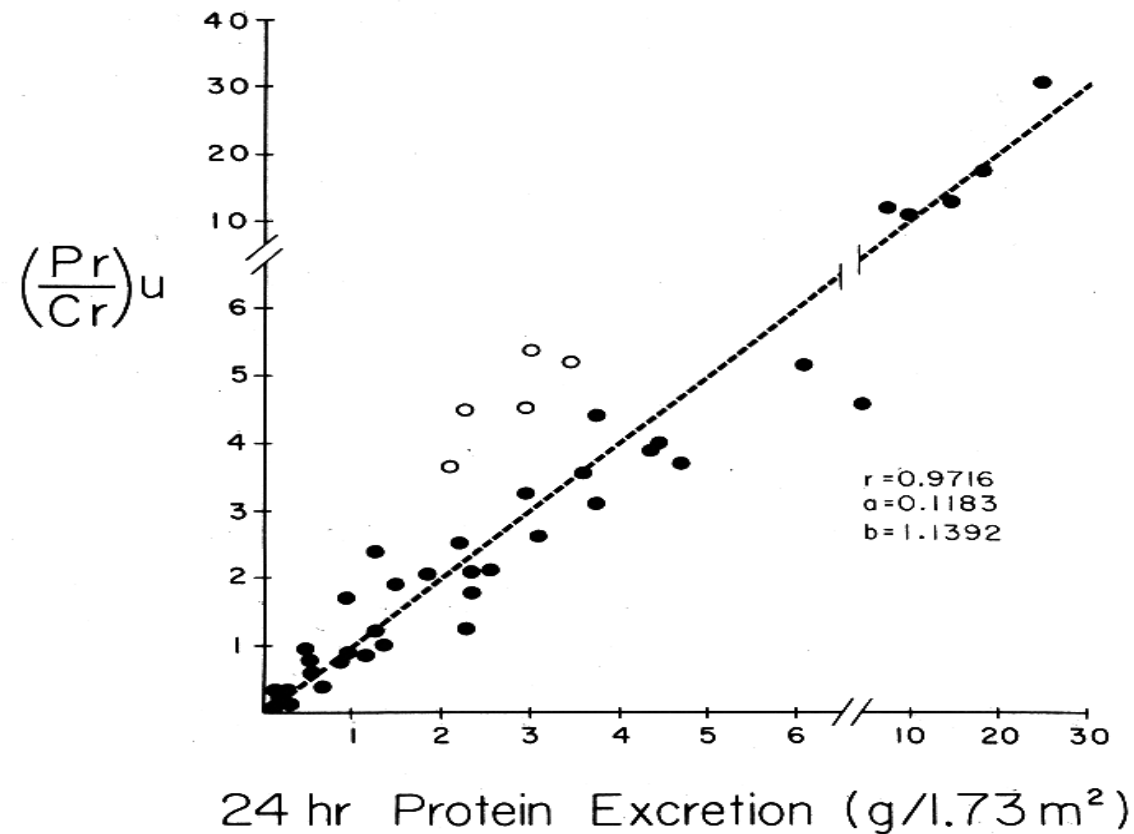


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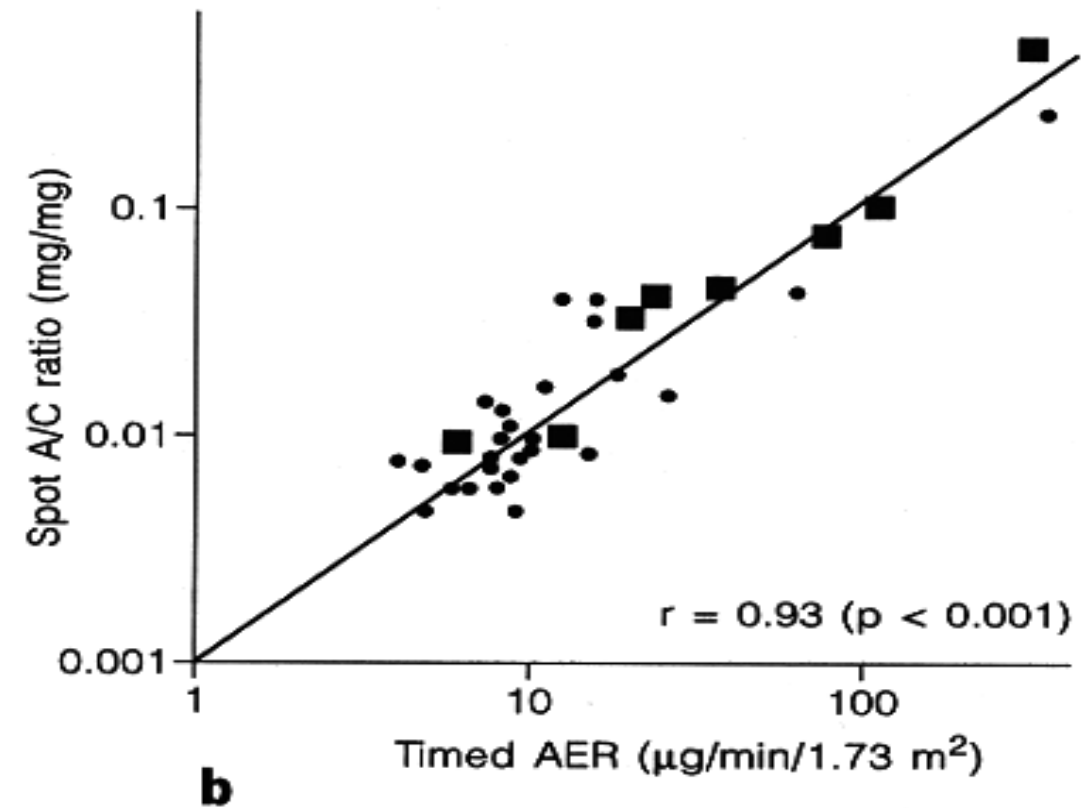
# Measurement of Proteinuria

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

Spot Urine creatinine = 50mg/dL



Cottiero. Nephron 1995;69:140-6



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<sup>+</sup>] 131 meq/l, [K<sup>+</sup>] 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 51. Stages of CKD: A Clinical Action Plan**

Stage	Description	GFR (mL/min/1.73 m <sup>2</sup> )	Action*
1	Kidney damage with normal or ↑ GFR	≥90	Diagnosis and treatment, Treatment of comorbid conditions, Slowing progression, CVD risk reduction
2	Kidney damage with mild ↓ GFR	60–89	Estimating progression
3	Moderate ↓ GFR	30–59	Evaluating and treating complications
4	Severe ↓ GFR	15–29	Preparation for kidney replacement therapy
5	Kidney failure	<15 (or dialysis)	Replacement (if uremia present)

CKD is defined as either kidney damage or GFR <60 mL/min/1.73 m<sup>2</sup> 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

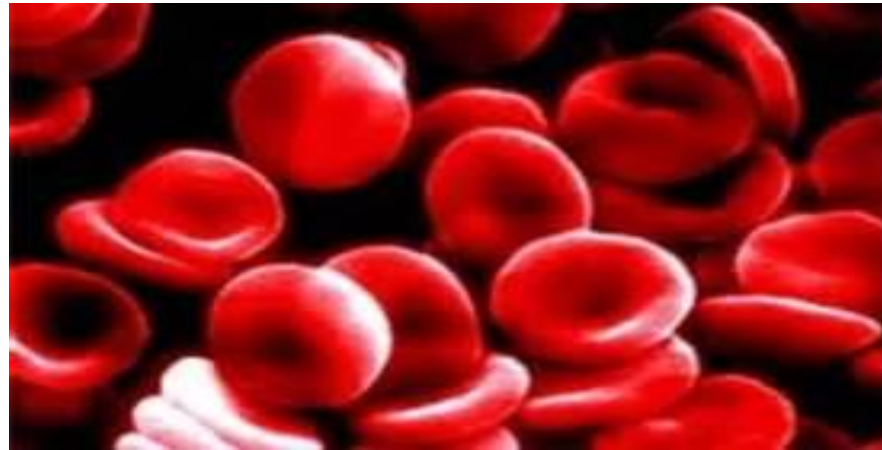
# Let's customize an action plan for our patient ~

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 ~

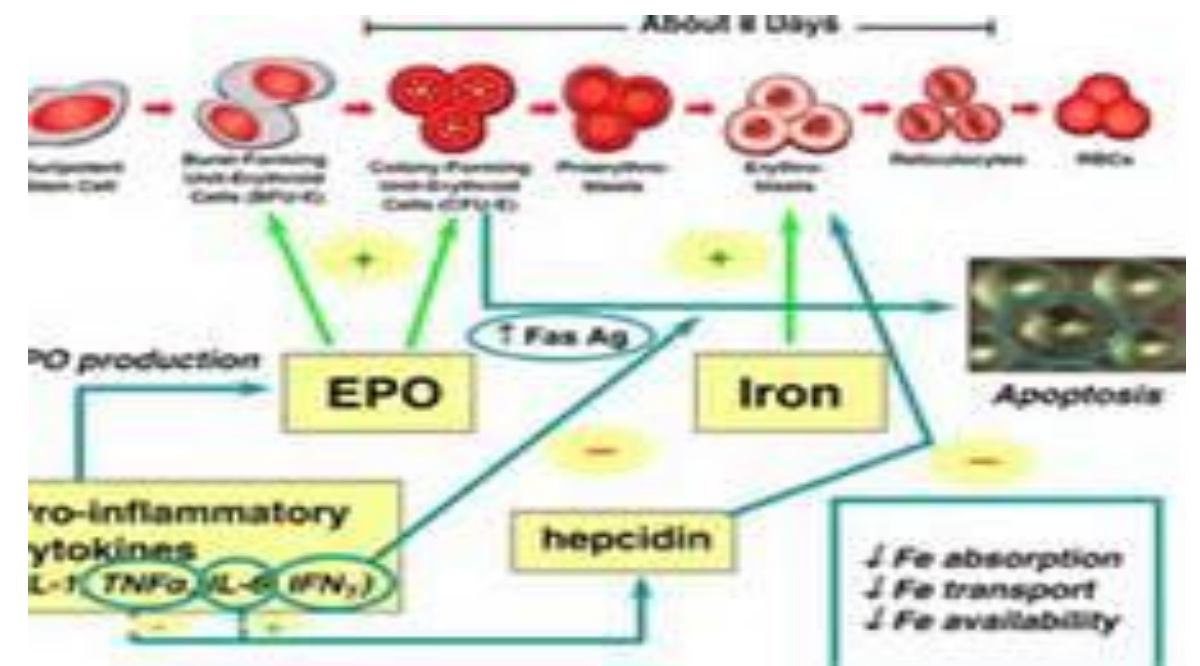
**Anemia**



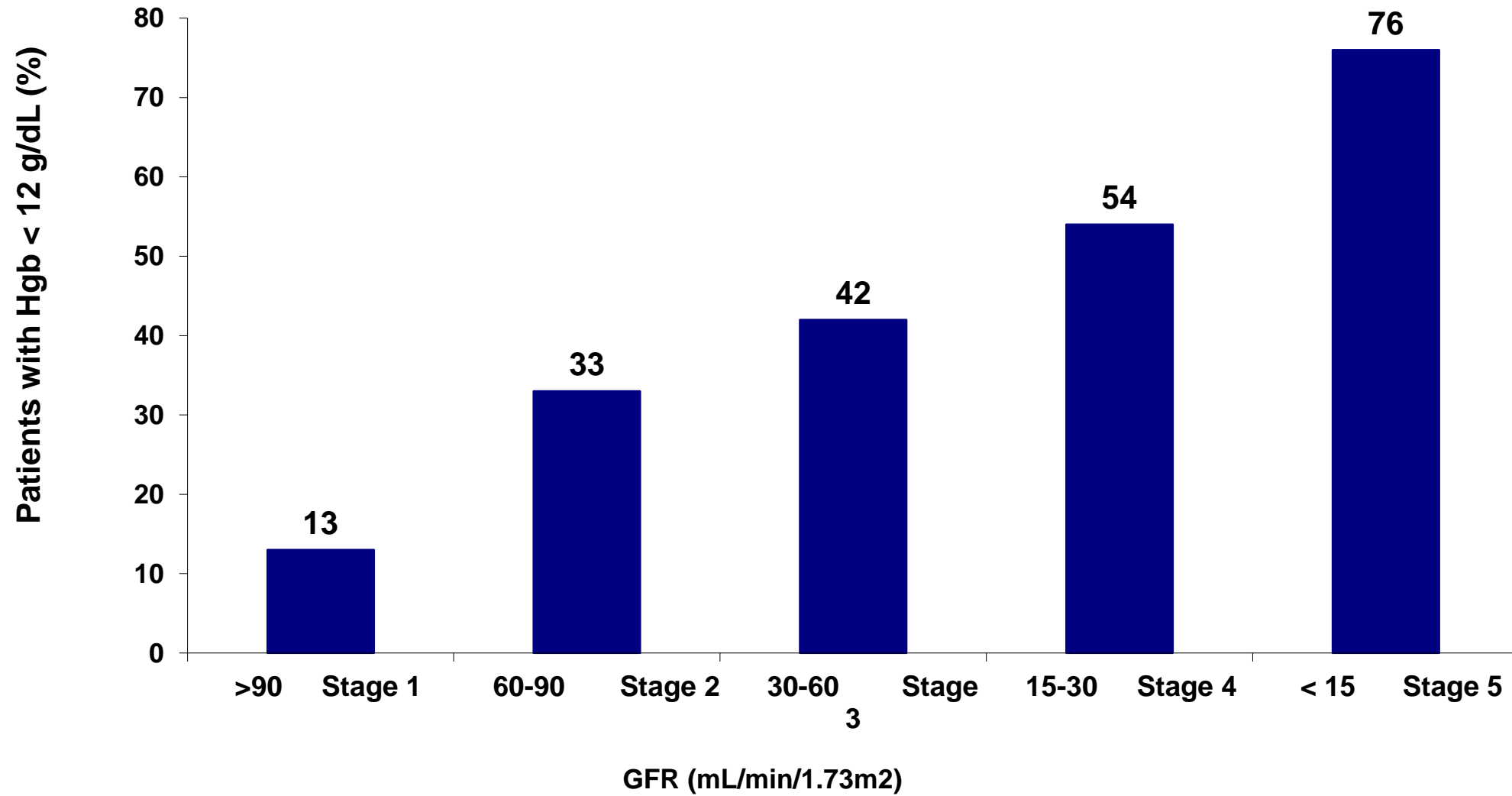
**Mineral/Bone Metabolism**

# Anemia in CKD

- Decreased kidney production of erythropoietin
- 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



*Curr Med Res Opin.*  
2004;20:1501-1510.

# 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

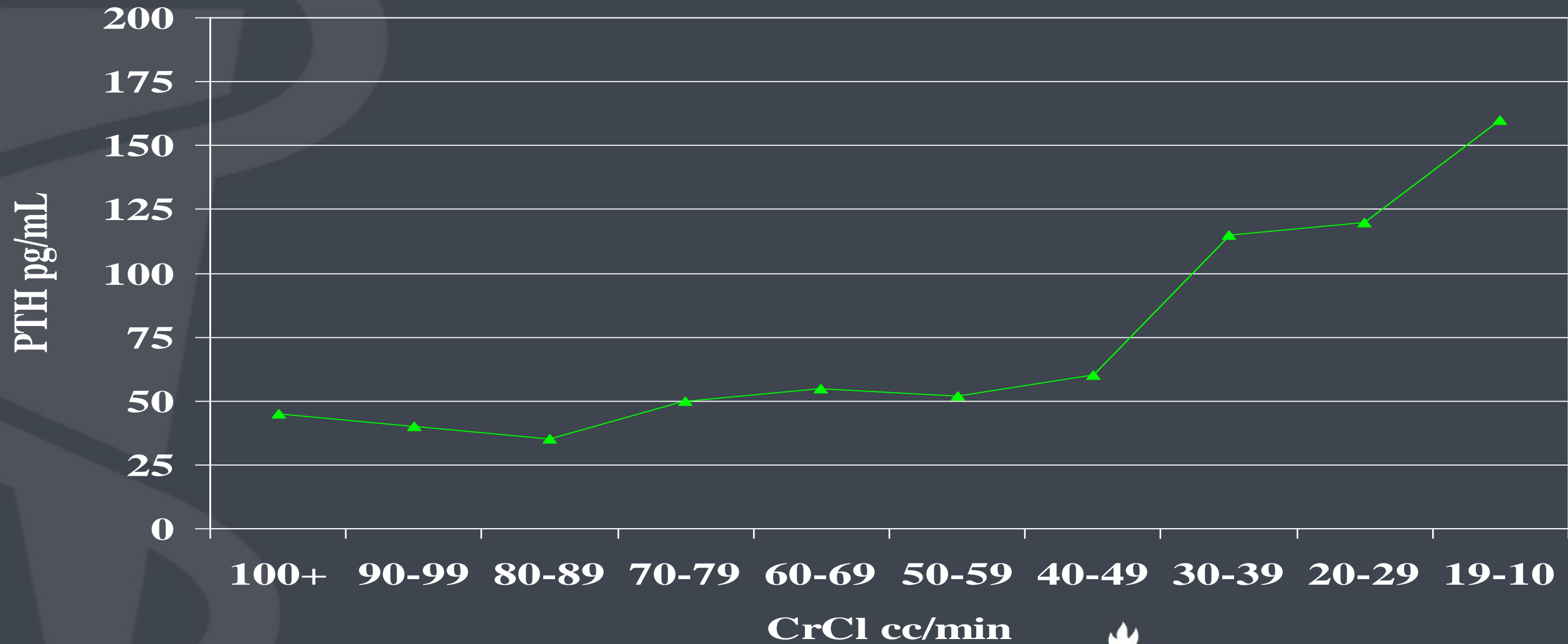
Parathyroid hyperplasia

Hyperphosphatemia

Hypocalcemia

1,25 (OH)<sub>2</sub> vitamin D<sub>3</sub> deficiency

# Secondary HPT Develops as Kidney Function Declines



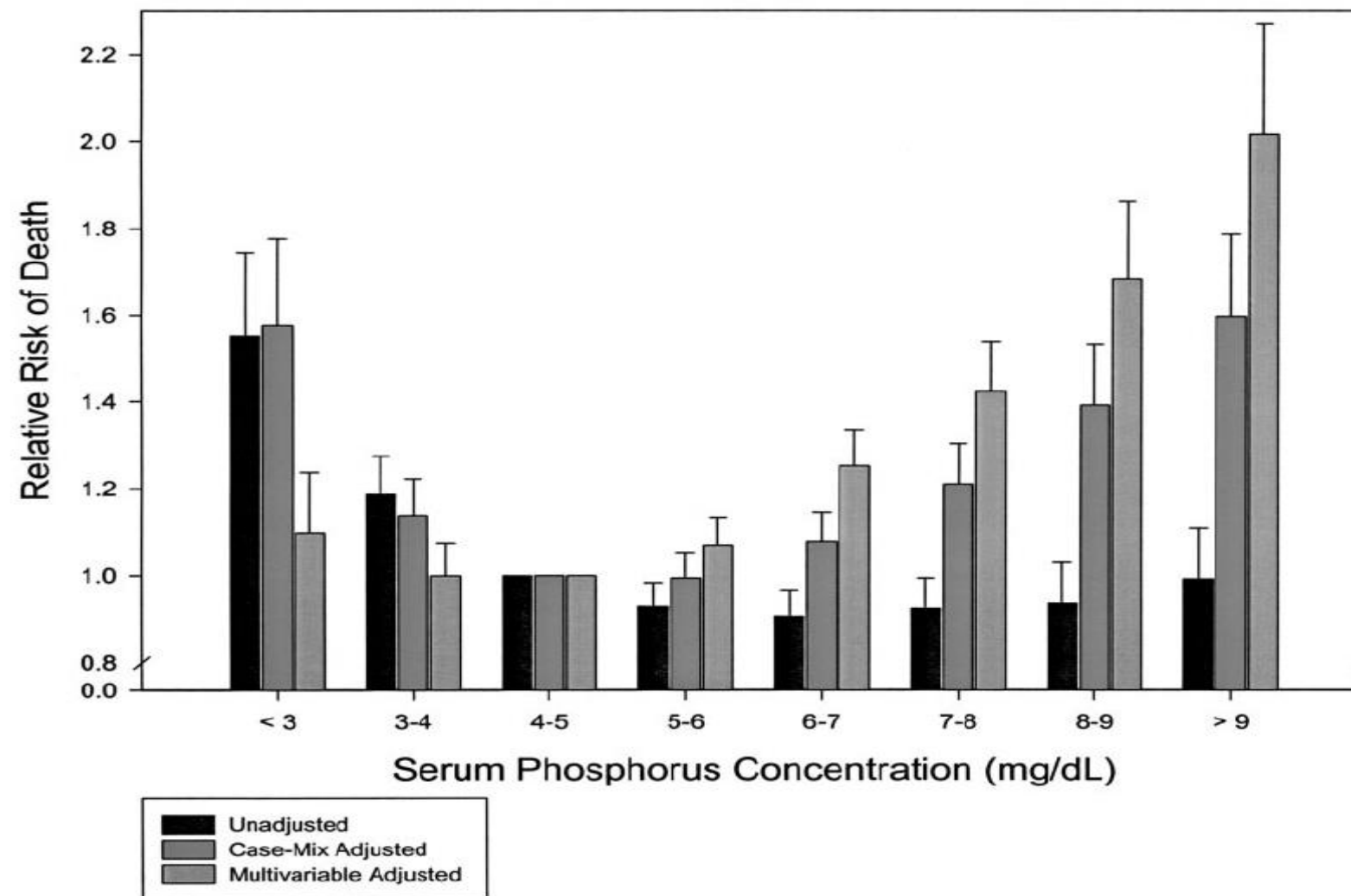
AJKD 1997



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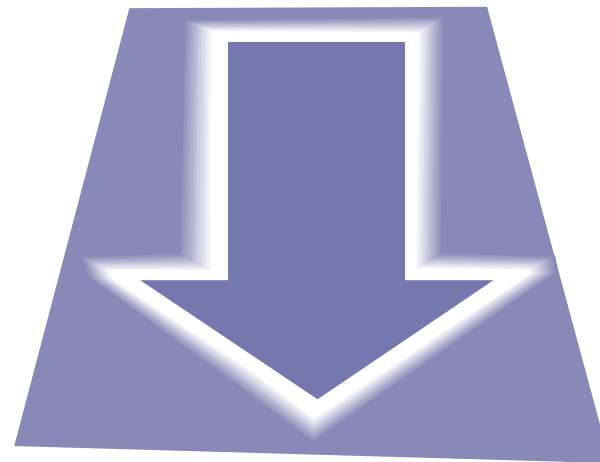
*Figure 1.* Unadjusted, case mix-adjusted, and multivariable-adjusted relative risks (RR; of death) and 95% confidence intervals (CI) for eight categories of serum phosphorus (referent range, 4.0 to 5.0 mg/dl). For all analyses, case mix adjustment refers to adjustment for age, gender, race or ethnicity, 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.

# Laboratory screening and recommended PTH targets for CKD

CKD stage	GFR range (mL/min/1.73m <sup>2</sup> )	Measurement of Calcium/Phosphorus	Measurement of intact PTH	Target intact PTH
3	30-59	Every 12 months	Every 12 months	35-70 (OPINION)
4	15-29	Every 3 months	Every 3 months	70-110 (OPINION)
5	<15 or dialysis	Every month	Every 3 months	150-300 (EVIDENCE)

# Management of secondary hyperparathyroidism

If PTH elevated, check 25(OH)vit D level  
– Replace if low with ergocalciferol



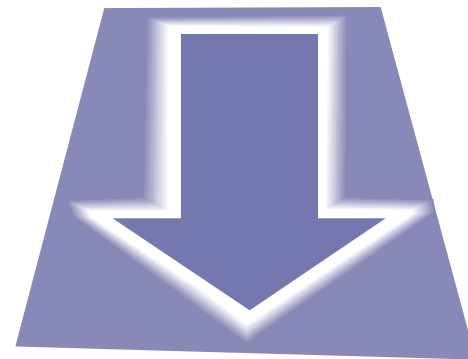
**Table 26. Recommended Supplementation for Vitamin D Deficiency/Insufficiency in Patients with CKD Stages 3 and 4**

Serum 25(OH)D (ng/mL) [nmol/L]	Definition	Ergocalciferol Dose (Vitamin D <sub>2</sub> )	Duration (months)	Comment
<5 [12]	Severe vitamin D deficiency	50,000 IU/wk orally x 12 wks; then monthly	6 months	Measure 25(OH)D levels after 6 months
		500,000 IU as single I.M. dose		Assure patient adherence; measure 25(OH)D at 6 months
5-15 [12-37]	Mild vitamin D deficiency	50,000 IU/wk x 4 weeks, then 50,000 IU/month orally	6 months	Measure 25(OH)D levels after 6 months
16-30 [40-75]	Vitamin D insufficiency	50,000 IU/month orally	6 months	

# 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, paracalcitol or doxercalciferol.
- Monitor Ca / Phos / intact PTH levels closely (q 3-4 months)
- Educate pts about dietary phosphate restriction



Biscuits  
(mix)



Nuts



Macaroni &  
Cheese



Cola



Pizza



Hotdogs &  
Sausage

Cheese



Peanut  
Butter



# HIGH PHOSPHORUS FOODS

Cream  
Soup



Ice  
Cream



Chocolate

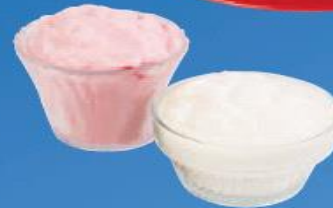
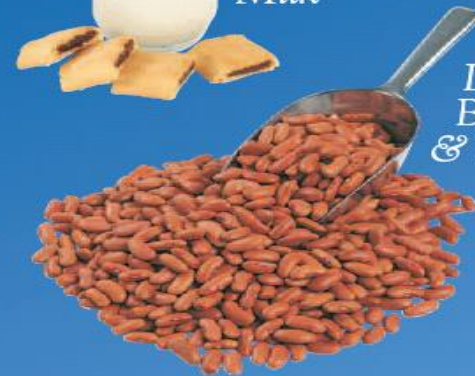


Liver &  
Organ Meats



Milk

Dried  
Beans  
& Peas



Yogurt &  
Pudding

Pancakes  
(mix)



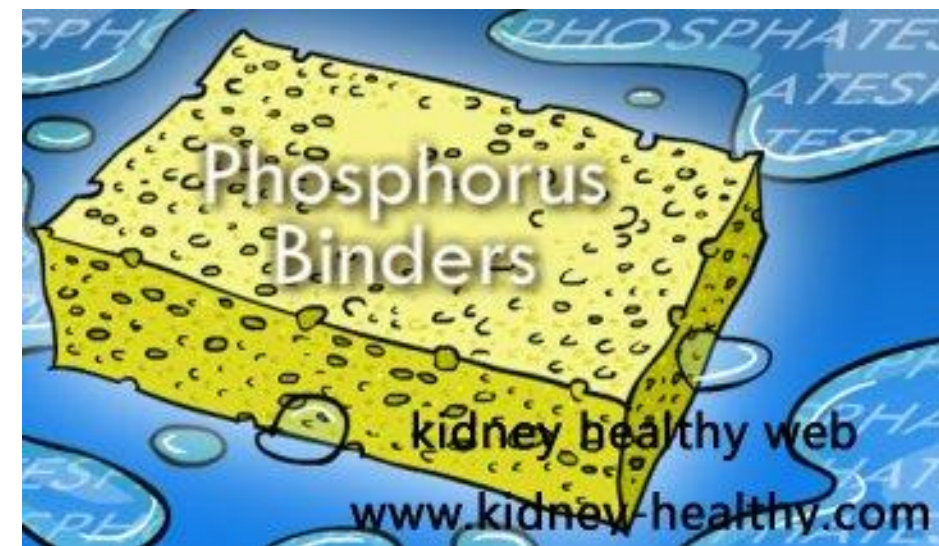
Pork  
& Beans



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

Reference: Pennington JAT, Bowers ADP, Church HN: *Boxes and Charts: Food Values of Portions Commonly Used*. 17th ed. New York: Harper & Row; 1997.

# 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

	<b>Diabetic Kidney Disease</b>	<b>Nondiabetic Kidney Disease</b>	<b>Kidney Disease in the Transplant</b>
<b>Strict glycemic control</b>	Yes <sup>a</sup>	NA	Not tested
<b>ACE-inhibitors or angiotensin-receptor blockers</b>	Yes	Yes (greater effect in patients with proteinuria)	Not tested
<b>Strict blood pressure control</b>	Yes <130/80 mm Hg	Yes <130/80 mm Hg	Not tested
<b>Dietary protein restriction</b>	Uncertain 0.6-0.8 g/kg/d	Uncertain 0.6-0.8 g/kg/d	Not tested
<b>Lipid-lowering therapy</b>	Probable LDL<100 mg/dl	Probable LDL<100 mg/dl	Not tested

<sup>a</sup> Prevents or delays the onset of diabetic kidney disease. Inconclusive with regard to progression of established disease.

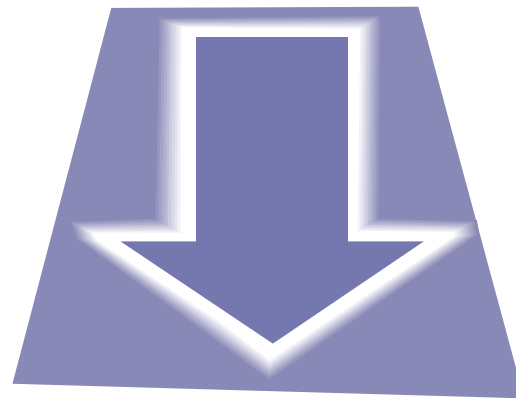


# How can a PCP possibly do all of this?

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  $> 200$ mg/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 fxn, 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!