

Chronic Kidney Disease

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Q/A Screening (MKSAP 16)

A 32 yo woman is evaluated during a new patient visit. She is healthy, exercises regularly without symptoms, and takes no medications. Medical history is unremarkable. Family history is notable for her father and paternal aunt who both have hypertension and chronic kidney disease. There is no family history of polycystic kidney disease. Her father began dialysis when he was 50 years old and now has a kidney transplant.

Physical examination and vital signs are normal.

Which of the following should be done to screen for chronic kidney disease?

- A. 24- hr urine collection for creatinine clearance
- B. Kidney ultrasonography
- C. Radionuclide kidney clearance scanning
- ✓ D. Serum creatinine, estimated GFR, and urinalysis

Definitions

Chronic kidney disease affects 10-13% of the adult US population with increased risk for ESRD, cardiovascular disease and death.

Main focus of renal protection is long-term stabilization of glomerular filtration rate to an age related decrease in GFR of 0.5-1 ml/min/year.

Screening methods used are serum creatinine and proteinuria. Proteinuria is used as a *surrogate* for “kidney damage”.

Serum creatinine is a by-product of muscle breakdown. Its production is balanced by its excretion thus maintaining a steady state balance in the blood.

Rather than routinely collect a 24 hr urine sample to measure creatinine excretion, we estimate kidney function based on formulas.

Protein excretion or albumin excretion is measured as a ratio of creatinine excretion and reported as “protein to creatinine ratio (PCR)” or “albumin to creatinine ratio (ACR)”.

Chronic kidney disease – GFR vs serum creatinine

- Serum creatinine is not sufficiently accurate on which to base decisions
- Estimation of GFR is the best overall index of the level of kidney function
- A decrease in GFR precedes kidney failure in all forms of progressive kidney disease
- Estimation of GFR in clinical practice allows proper dosing of drugs excreted by glomerular filtration

Prediction equations

1. Cockcroft and Gault equation

$$\frac{(140 - \text{Age}) \times \text{Body Weight (Kg)}}{72} \times \text{Serum Creatinine} \times (0.85 \text{ females})$$

Measures creatinine clearance which overestimates true GFR

2. Modification of Diet in Renal Disease – MDRD equation

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

Measures GFR

Underestimates true GFR

Less dependable in ages <18 and >70

Not accurate in amputees or strict vegetarians

Diagnosis of CKD should include

- **Kidney damage for >3 months**
- **Diagnosis (type of kidney disease)**
- **Severity (level of GFR)**

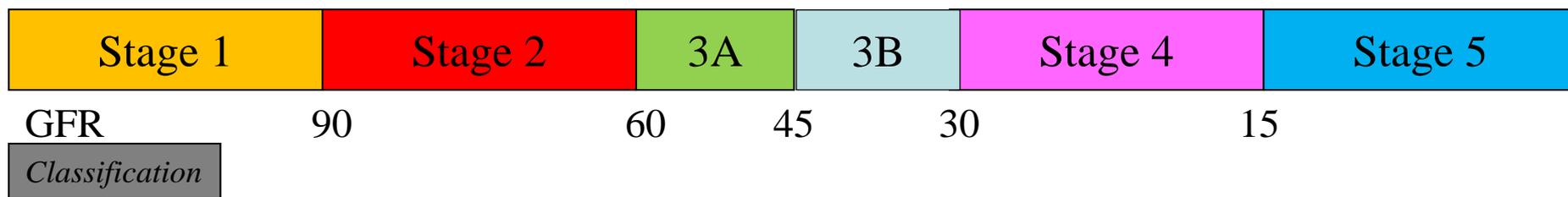


Markers of kidney damage

- **Persistent proteinuria**
- **Abnormal urinary sediment – especially if urine dipstick is positive for WBC or RBC**
- **Abnormal findings on imaging studies**
- **Abnormalities in blood or urine chemistry measurements that identify renal tubular syndromes**

Expanded Classification System for CKD

Stage	Description	GFR mL/min/1.73 m ²
1	Kidney damage with normal or ↑ GFR	≥90
2	Kidney damage with mild ↓ GFR	60-89
3	Moderate ↓ GFR	30-59
	3A	40-59
	3B	30-44
4	Severe ↓ GFR	15-29
5	Kidney failure	<15 (or dialysis)



Evaluation of chronic kidney disease = Screening

- *All individuals* should be assessed at routine health encounters to determine if they are at *increased risk* for developing kidney disease
- Kidney disease is more prevalent in (**increased risk group**) :
 - Age older than 50
 - Diabetes
 - Hypertension
 - Cardiovascular disease

Screening should include

- Blood pressure measurement
- Serum creatinine
- Urine PCR or ACR
- Urinalysis and sediment

PCR = Protein to Creatinine Ratio
ACR = Albumin to Creatinine Ratio

Q/A Screening

A 69 yo man is evaluated during a new patient visit. Medical history includes a 23 year history of HTN as well as several kidney stones 15 years ago. Family history includes his mother who began dialysis at age 72 years for unknown reasons and died of “kidney disease” 5 years later. Medications are lisinopril, furosemide, and aspirin.

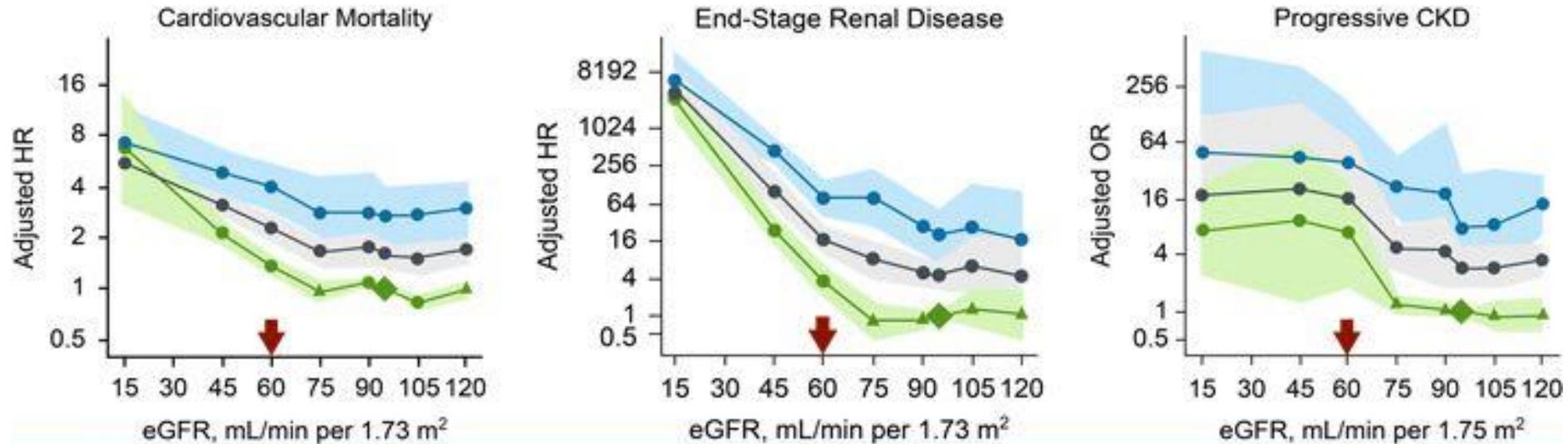
On examination temp is 36.9°C, BP is 134/72 mmHg, pulse rate is 72/min and resp rate is 14/min. BMI is 29. The rest of the exam is normal.

Labs: Creatinine 1.9 mg/dl (1year ago 1.8 mg/dl; 6 years ago 1.4 mg/dl) eGFR 37 ml/min
Hgb 12 g/dl; Urinalysis 2+ protein; 0-2 RBC/hpf; 2-4 WBC/hpf; Urine culture no growth

Which of the following is the most appropriate diagnostic test to perform next?

- A. Abdominal CT with contrast
- B. Kidney biopsy
- ✓ C. Kidney ultrasonography
- D. Radionuclide kidney clearance scanning

Proteinuria as a surrogate of kidney damage



Medscape

- ACR > 300 mg/g
- ACR 30 – 300 mg/g
- ACR < 30 mg/g

At an eGFR of 60 ml/min, a patient with ACR of >300 mg/g has an eightfold increased chance of having progressive kidney disease and ESRD than one with < 30 mg/g

New proposed staging for CKD

Composite ranking for relative risks by GFR and albuminuria (KDIGO 2009)

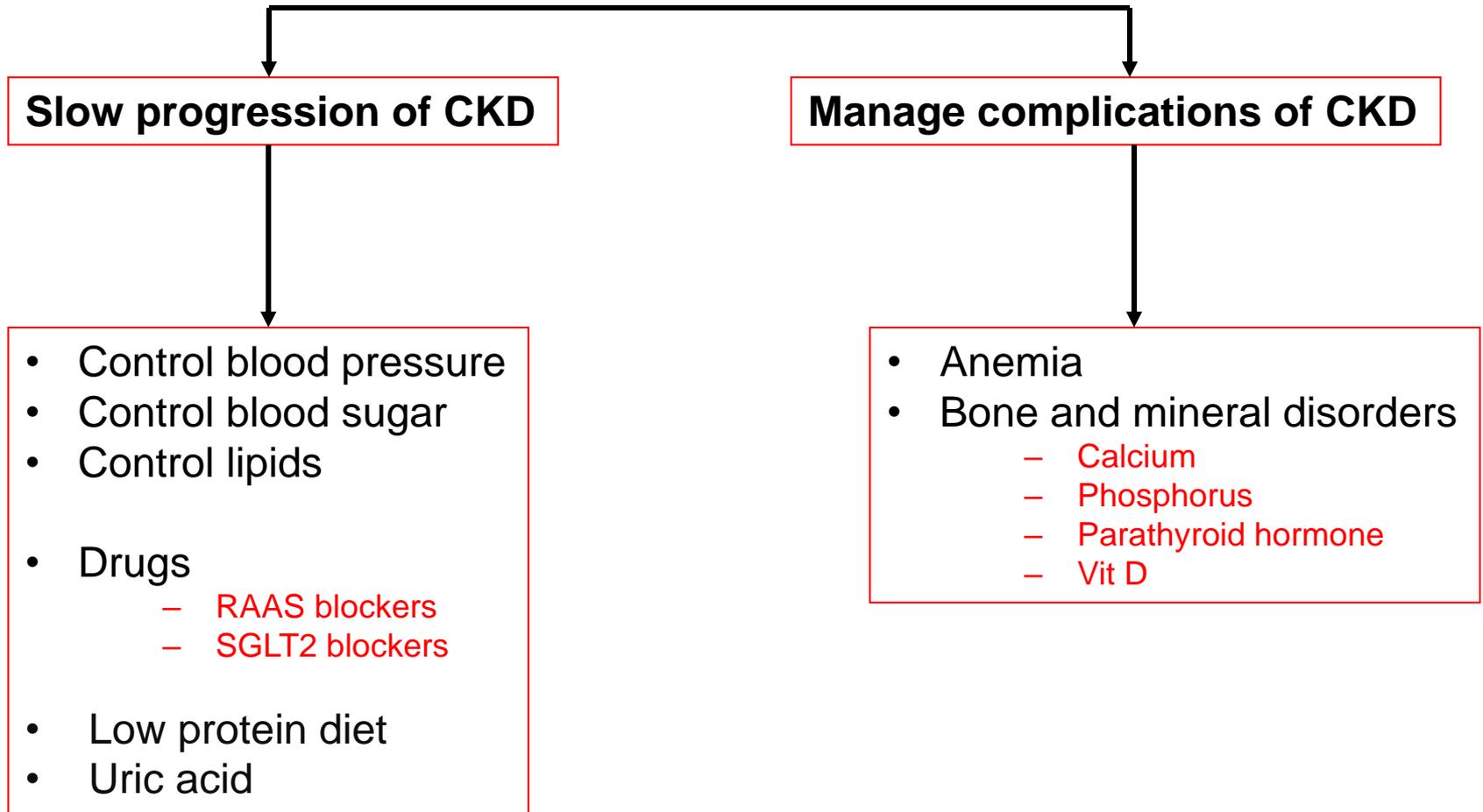
Composite ranking for relative risks by GFR and albuminuria (KDIGO 2009)				Albuminuria stages, description, and range (mg/g)				
				A1		A2	A3	
				Optimal and high-normal		High	Very high and nephrotic	
				< 10	10-29	30-299	300-1999	≥ 2000
GFR stages, description, and range (mL/min per 1.73 m ²)	G1	High and optimal	> 105					
			90-104					
	G2	Mild	75-89					
			60-74					
	G3a	Mild-moderate	45-59					
	G3b	Moderate-severe	30-44					
	G4	Severe	15-29					
G5	Kidney failure	< 15						

Q/A Screening

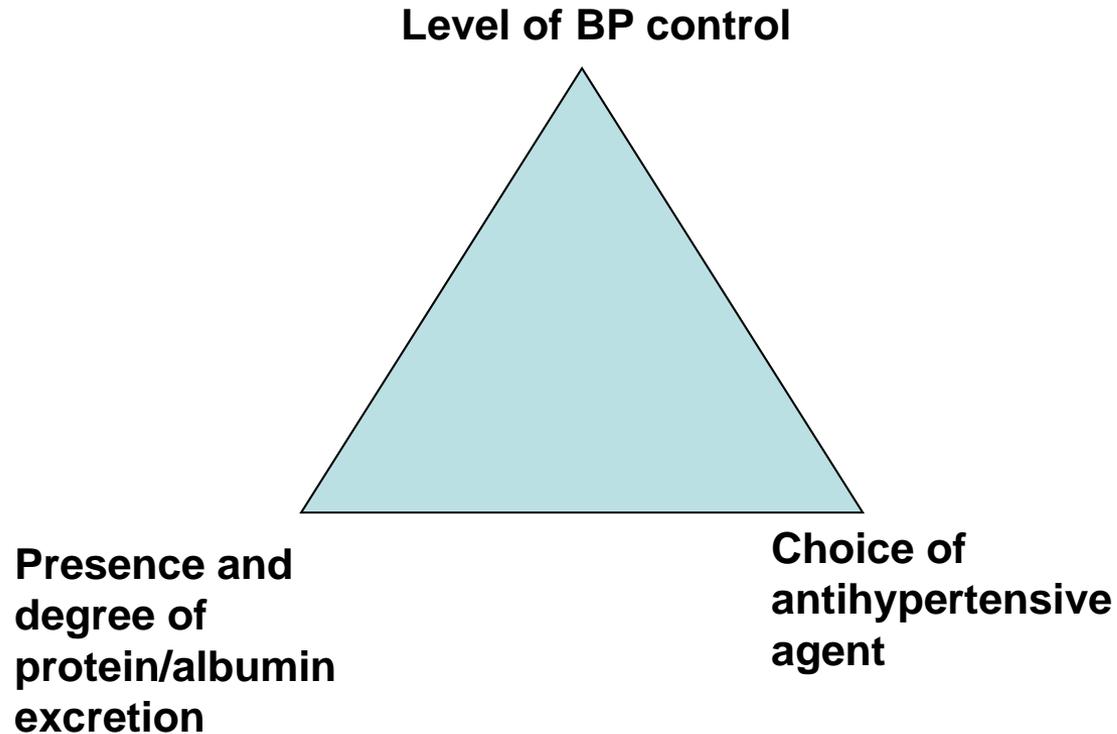
Which ONE of the following individuals is more likely to have progression of his or her CKD to the point of requiring renal replacement therapy rather than dying prior to the initiation of renal replacement therapy?

- A. A 45 yo Caucasian female with hypertensive kidney disease, eGFR 65 ml/min and a urine albumin to creatinine ratio (ACR) of 200 mg/g.
- B. A 58 yo Caucasian male with diabetic nephropathy, eGFR 65 ml/min and ACR of 30 mg/g.
- C. A 75 yo African American male with diabetic nephropathy, eGFR 55 ml/min and ACR of 30 mg/g.
- ✓ D. A 50 yo African American male with hypertensive kidney disease, eGFR 55 ml/min and ACR 1500 mg/g.

Goals of treatment in CKD



Considerations for BP control in CKD



Currently a target BP of $< 130/80$ mmHg in patients with CKD is better for renoprotection than a higher level in the presence of proteinuria

Q/A HTN – 1

A 47 yo man is evaluated during a follow-up visit for stage 3 CKD attributed to type 2 Diabetes and HTN. He feels well and has no complaints. Medications are lisinopril, amlodipine, and glipizide.

On exam, seated BP is 148/82 mmHg, and pulse is 80/min. BMI is 25. There is no JVD. Cardiac and pulmonary exams are normal. There is no edema.

Labs	139	101	BUN 45 eGFR 41 Creat 1.7	Calcium: 9.0 mg/dl; Phosphorus: 4.3 mg/dl; PTH: 69 pg/ml; Urine PCR: 0.17 mg/mg
	4.3	22		

Which of the following changes to this patient's therapeutic regimen should be made next?

- A. Add sodium bicarbonate
- B. Begin activated vitamin D therapy
- ✓ C. Increase antihypertensive therapy
- D. No change

Q/A HTN – 2

A 57 yo man is for a 20-yr history of hypertension. He reports a 4.5 Kg weight gain during the past 6 months. The patient is black. He does not smoke cigarettes. His only medication is low-dose chlorthalidone.

On exam, seated BP is 146-150/90 mmHg, and pulse is 78/min. BMI is 29. The remainder of the exam is unremarkable.

Labs: Creatinine:1.7 mg/dl; eGFR 51 ml/min; Urine PCR 0.45 mg/mg.

Which of the following is the most appropriate next step in managing this patient's hypertension?

- A. Add amlodipine
- B. Add metoprolol
- ✓ C. Add lisinopril/losartan
- D. Increase the chlorthalidone dose

RAAS blockers

- Treat high BP
- Decrease proteinuria
- Slow progression of CKD

Role of Renin Angiotensin System Blockade in Preventing Progression of CKD

4 major RAS blocking drug groups:

- Angiotensin converting enzyme inhibitors (ACEi)
- Angiotensin receptor blockers (ARB)
- Direct renin inhibitors (DRI)
- Aldosterone antagonists (AA)

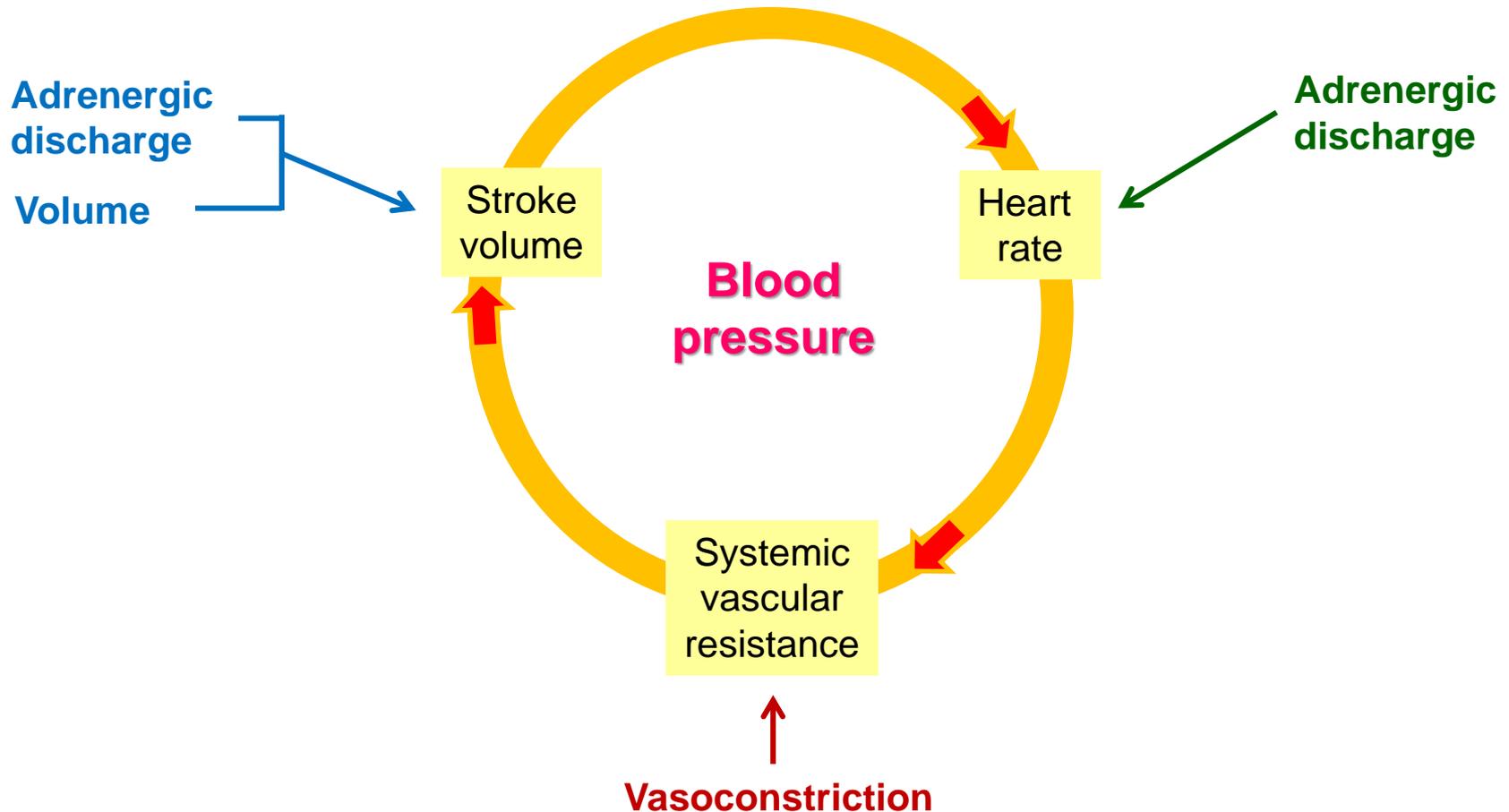
Questions to be answered:

- Is the benefit of RAS blockers related to the decrease in BP and what is the BP level for delaying progression of renal disease?
- Is one type of RAS blockade better than another?
- What is the optimal dose?
- Is using more than one class of RAS blockers together more effective in retarding CKD progression than using one alone?
- Do other medications added to a RAS blocker, help or hinder the impact of these drugs?

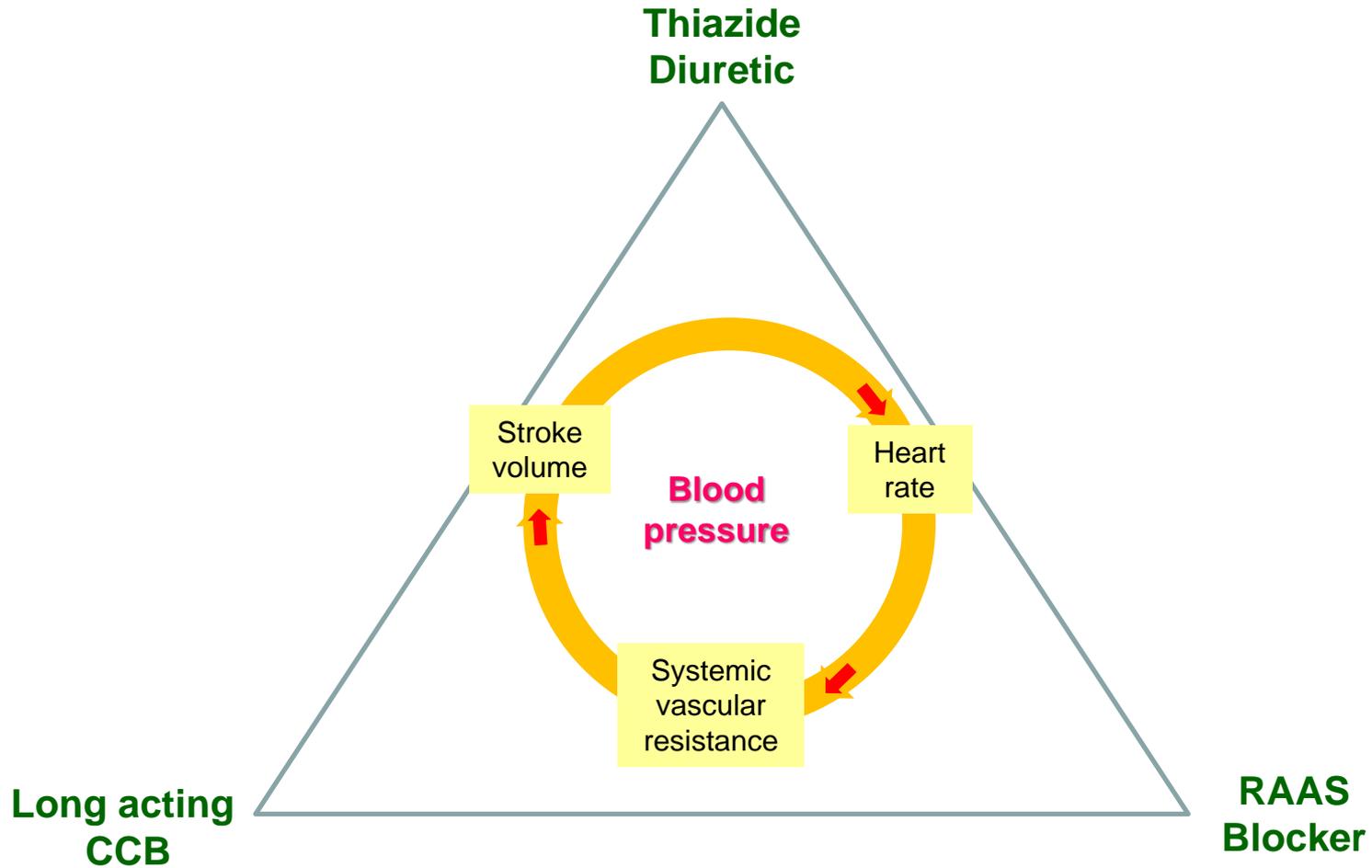
Determinants of blood pressure

BP = cardiac output X vascular resistance

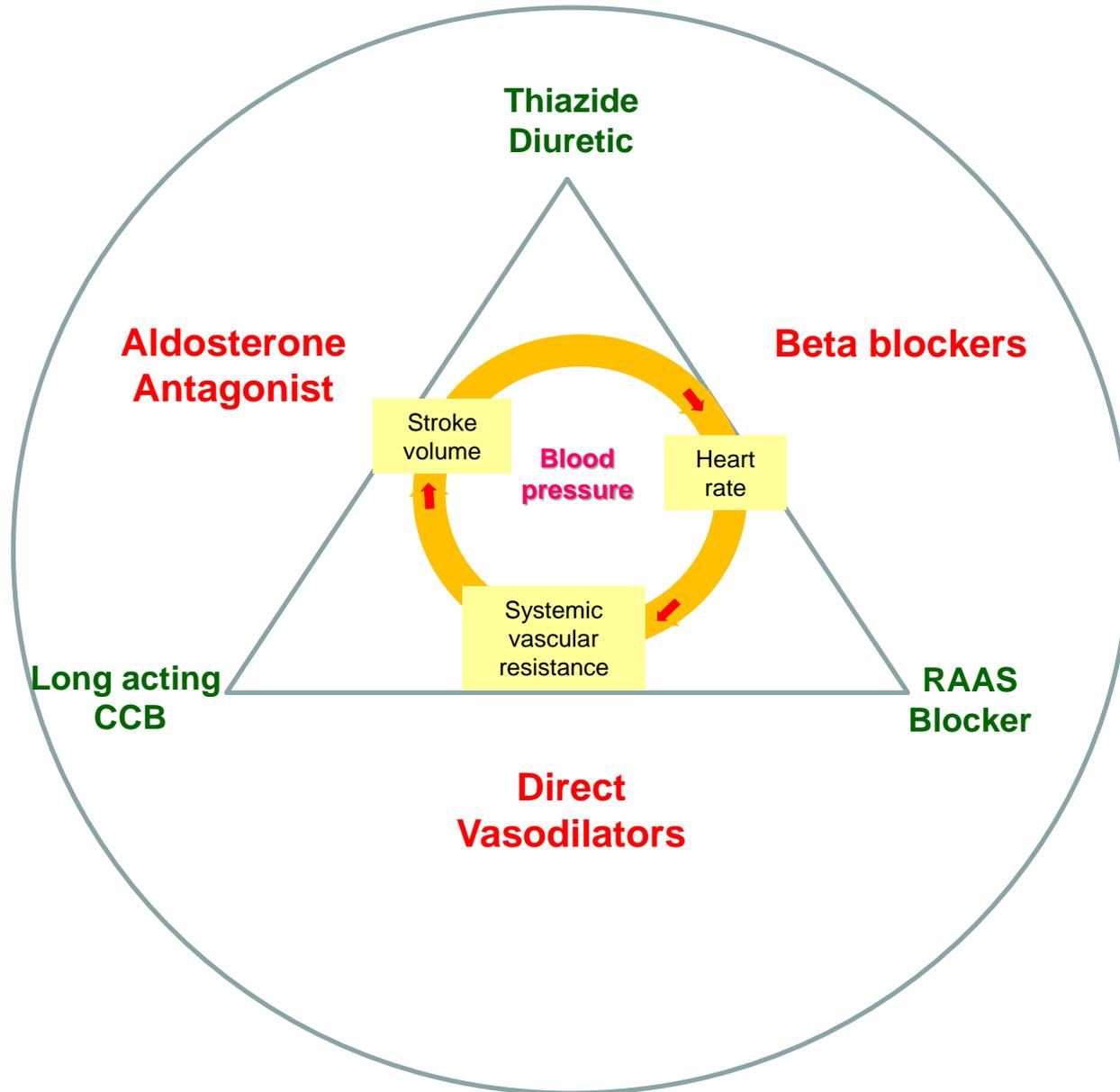
Cardiac output = heart rate X stroke volume



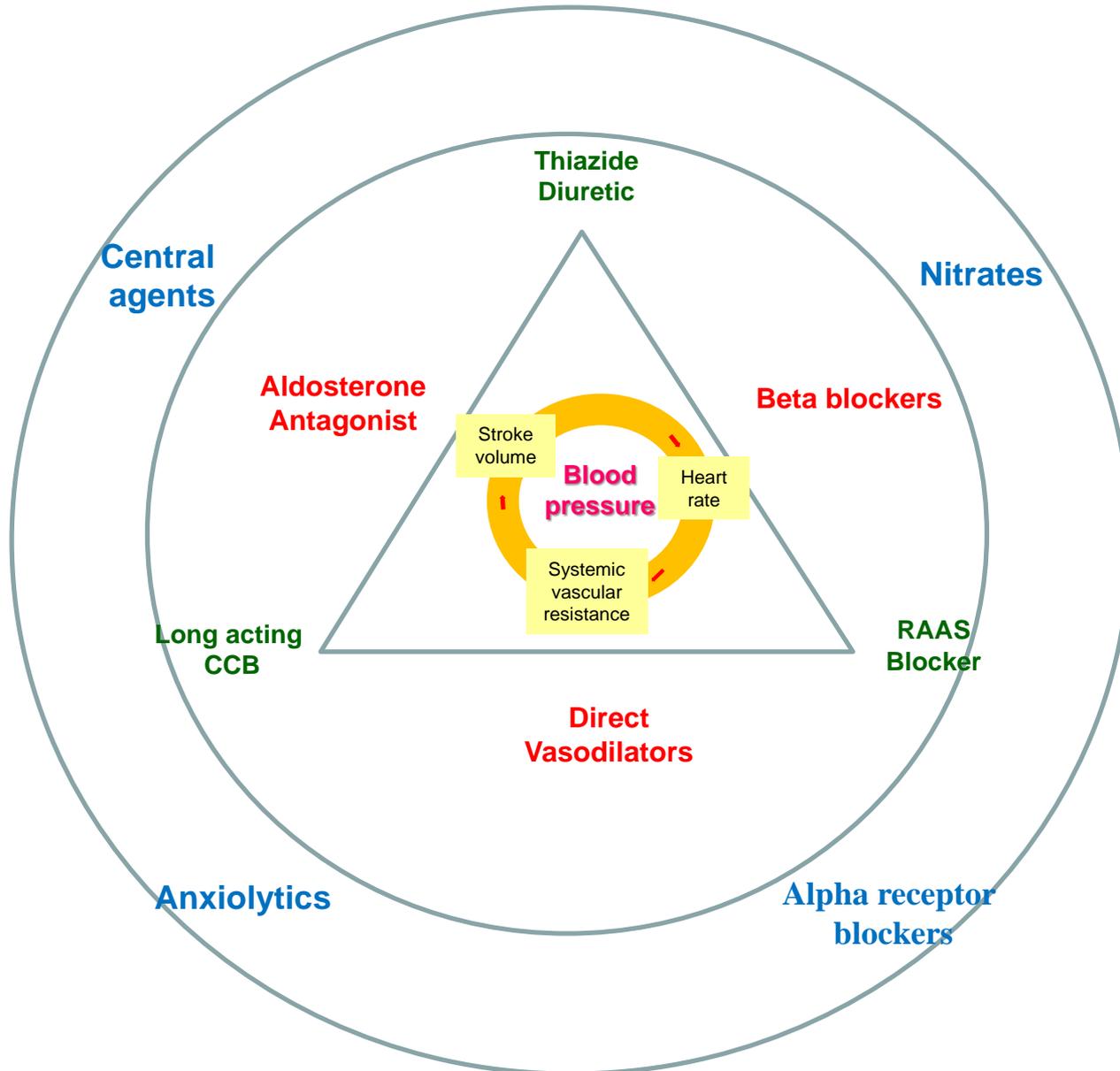
Initial Drug Therapy



Additions to Initial Drug Therapy



More Choices



Q/A HTN – 3 (MKSAP 16)

A 72 yo man is evaluated during a follow-up visit for difficult to control HTN. He has diabetes mellitus and stage 4 CKD. A review of his laboratory studies shows his serum creatinine level has gradually increased over the past 3 years, consistent with his CKD. He has been on the same antihypertensive regimen for years and takes HCTZ 25 mg daily, lisinopril 40 mg daily, amlodipine 10 mg daily, and metoprolol succinate 100 mg daily. He adheres to his medication regimen and reports no side effects. He is not taking any over the counter medications. He eats a low salt diet and exercises 20-30 min daily.

On exam the patient is afebrile. BP is 162/74 mmHg, and HR 62/min without orthostatic changes. There is no elevation in JVP. Cardiac exam is normal with no murmurs; lungs are clear. There is a trace of edema of the lower extremities.

Labs: Creatinine: 3.2 mg/dl; Potassium 4.7 mEq/L; eGFR 24 ml/min; Urine ACR 650 mg/g

Which of the following is the most appropriate adjustment to this patient's hypertensive medications regimen?

- A. Add clonidine
- B. Add hydralazine
- C. Add valsartan
- ✓D. Change HCTZ to furosemide

How does one improve RAS blockade?

- ACEi + ARB – ONTARGET study
 - Facilitates anti-proteinuric response
 - Higher incidence of AKI and hyperkalemia

- ACEi / ARB +DRI – ALTITUDE study
 - Improved BP control and anti-proteinuric effect
 - 6% higher incidence of CVA in diabetics - Black box warning

- **Improved BP control** seen when ACEi/ARB combined with
 - Mineralocorticoid antagonist
 - Diuretics
 - Calcium channel blocker

- **Improved anti-proteinuric effect** seen when ACEi/ARB combined with
 - Diuretic
 - Mineralocorticoid antagonist

Slow progression of CKD

- Control blood pressure
- Control blood sugar
- Control lipids

Goal <130/80 or lower with a RAAS blocker

Goal HgA1C < 7%

Goal LDL < 100 and further < 70 with CAD

- Drugs

- RAAS blockers
- SGLT2 blockers

- Maximally dose tolerated
- Never in combination of ACE + ARB
- Never in pregnancy or allergies

- New indication especially with proteinuric CKD
- Do not start in CKD 4 or greater
- Be careful in obese individuals and those prone to frequent UTI

- Low protein diet

0.6 G/Kg/day – restriction of meat protein especially helpful

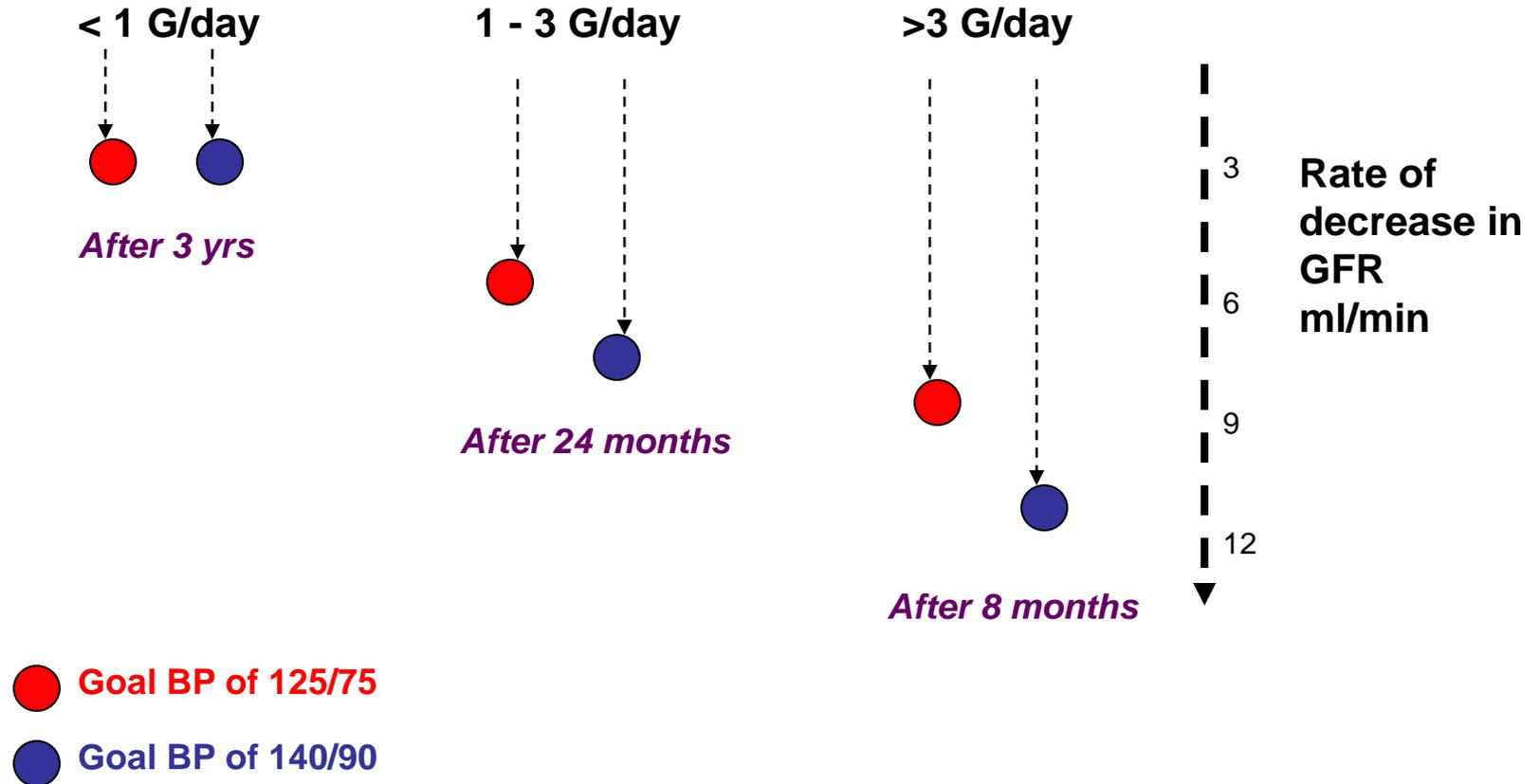
- Uric acid control

- Controversial whether it is helpful
- Weigh risk of drug side effect and benefit

MDRD trial – 840 patients randomized to lower BP and lower protein intake

Modification of Diet in Renal Disease

In Stage 3 and 4 non diabetic kidney disease and 24 hr protein excretion



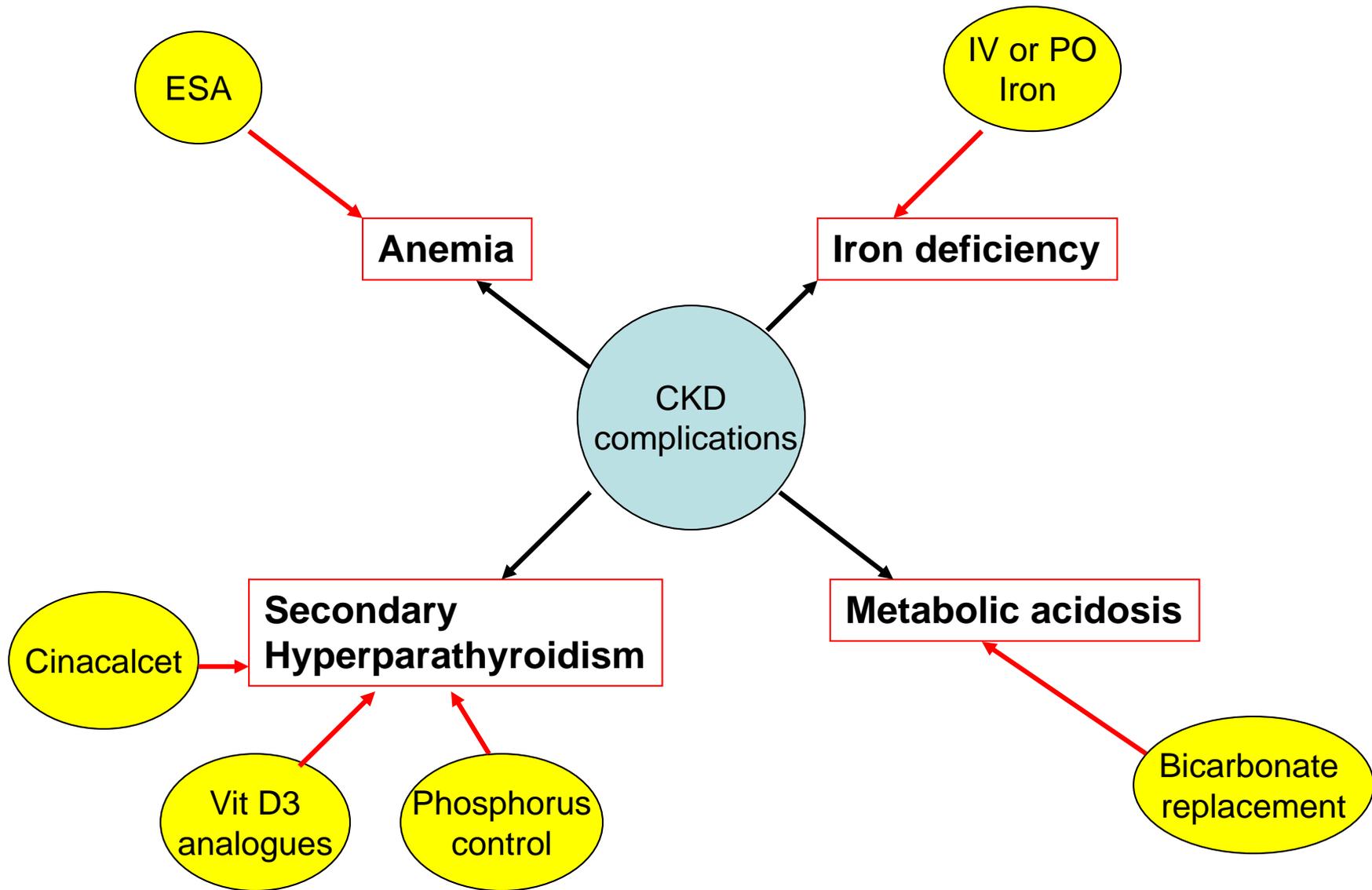
Question P-2 (V)

A 37 yo AA man presents with edema. BP is 150/100 mmHg. He is found to have a serum creatinine of 2.8 mg/dl and a urinary protein excretion of 6 g/24 h. A renal biopsy shows FSGS. He is started on the ACEi Lisinopril 20 mg/d and a loop diuretic Furosemide 40 mg/d. One week later, his BP is 125/75 mmHg, his protein excretion has decreased to 3 g/24 h, but his serum creatinine has increased to 3.2 mg/dl.

Which ONE of the following should be recommended?

- A. Stop the ACEi, switch to a beta blocker, and evaluate for renal artery stenosis.
- B. Stop the loop diuretic.
- ✓ C. Continue the current antihypertensives, and recheck serum creatinine in 1 week.
- D. Stop the ACEi and switch to an angiotensin receptor blocker.
- E. Start steroids and cyclophosphamide to treat his glomerular disease.

Managing complications of CKD



Q/A – A 1 (MKSAP 16)

A 65 yo woman is evaluated during a follow-up visit for long-standing diabetic nephropathy and HTN. She feels well but reports mild dyspnea with exertion. Medications are lisinopril, metoprolol, HCTZ, NPH insulin and regular insulin.

On exam , BP is 138/78 mmHg, pulse is 65/min Cardiac exam is normal. Lungs are clear. The remainder of the exam is unremarkable.

Labs: Hct 29%; WBC count and differential is normal; MCV 88; Retic count 0.5%; Creatinine 2.3 mg/dl; eGFR 21 ml/min: Peripheral smear – normocytic anemia

Which of the following is the most appropriate next step in the management of this patient's anemia?

- A. Discontinue lisinopril
- B. Initiate erythropoiesis-stimulating agents
- C. Measure serum erythropoetin level
- ✓D. Measure serum iron stores

Iron goals

- Transferring saturation >20%
- Ferritin > 100

Q/A – A 2 (MKSAP 16)

A 55 yo Asian woman is evaluated during a routine visit. She was diagnosed with CKD 3 years ago. For the past year, she has had increasing fatigue. She reports no shortness of breath or chest pain. Medications are lisinopril, furosemide, calcium acetate, ferrous sulfate, and a multivitamin.

On exam, temperature is normal, BP is 100/70 mmHg, pulse is 76/min and resp rate is 14/min. BMI is 30. Abdominal exam is normal. A stool specimen is negative for blood.

Labs: Hgb 8.9 (1 year ago 11); MCV 91; MCHC 33; Retic count 1%; Creatinine 2 mg/dl; Ferritin 250 ng.ml; Transferrin saturation 33%; Folate and B12 normal

Which of the following is the most appropriate intervention for this patient's management?

- A. Add Ascorbic acid.
- ✓ B. Add an erythropoiesis-stimulating agent
- C. Perform a blood transfusion.
- D. Switch from oral to intravenous iron therapy.

1. Hgb < 10 g/dl
2. CKD Stage 3,4,5
3. Iron studies
 - Ferritin >100
 - Transferrin sat > 20
4. Blood work prior to each dose
5. EPO should be held when Hgb reaches >11 g/dl
6. No active cancer
7. Controlled BP

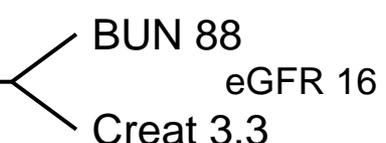
Question – AB 1

A 47 yo woman is evaluated during a follow-up visit for diabetic nephropathy. She also has CKD, HTN, retinopathy and mild neuropathy. She has been well and is maintaining a healthy lifestyle. Medications are glyburide, amlodipine, and gabapentin.

On exam, BP is 124/80 mmHg; Cardiac exam is normal without a rub. Lungs are clear. Abdomen benign and trace edema is present .

Labs:

134	100
4.8	17

 BUN 88
eGFR 16
Creat 3.3 Phosphorus 4.5; Uric acid 8.0

Based on the laboratory studies, which of the following is the most appropriate addition to this patient's CKD therapeutic regimen?

- A. Allopurinol
- B. Non calcium containing phosphate binder
- ✓ C. Sodium bicarbonate therapy
- D. Sodium polystyrene

Bicarbonate goal
– Bring to a level of 22-26

Q/A Bone Mineral

A 38 yo woman is evaluated during a follow-up visit for stage 3 CKD. Her only medication is lisinopril. Her daily dietary calcium intake is restricted to 1000 mg.

Exam: BP is 124/80 mmHG; Cardiopulmonary exam is normal. Abdominal exam is notable for bilateral palpable kidneys. Remainder exam is normal.

Labs: Calcium: 8.2 mg/dl; Creatinine 1.7 mg/dl; Phosphorus 4.3 mg/dl; PTH 163 pg/ml; 25 Vit D3 12 ng/ml; eGFR 34 ml/min

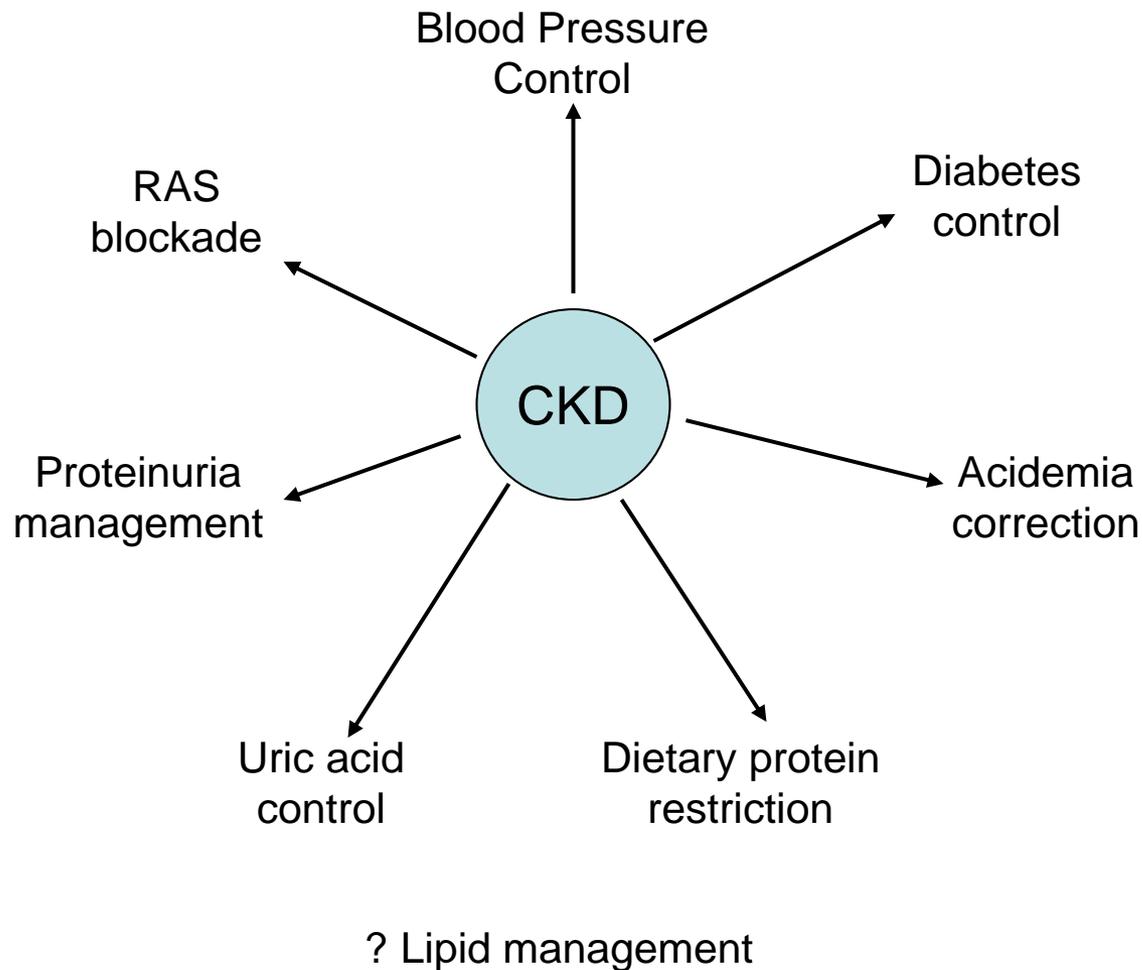
Which of the following is the most appropriate next step in management?

- A. Begin calcitriol (1,25 – Di hydroxy Vit D3)
- B. Begin calcium carbonate
- ✓ C. Begin cholecalciferol (Vit D3)
- D. Begin sevelamer
- E. Continue current regimen

Hyperparathyroidism of renal disease

- Low calcium – correct
- Low vit D – replace
- High phosphorus – give binders
- High PTH – Specialized therapy

Slowing progression of CKD - Summary



So

- Identify patients with chronic kidney disease
- Determine cause and correct if possible
- Manage complications
- Slow progression of kidney disease
- Prepare for dialysis and/or transplantation
- Refer to nephrologist

Questions