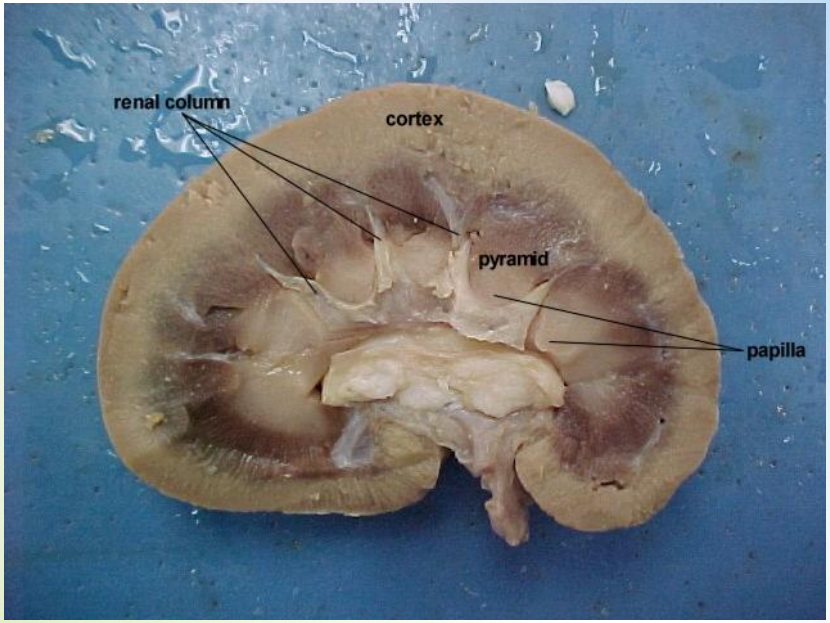
Nurse Practitioner
Residency Training Program

Chronic Kidney Disease:
(basically all things kidney)



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4/16/23

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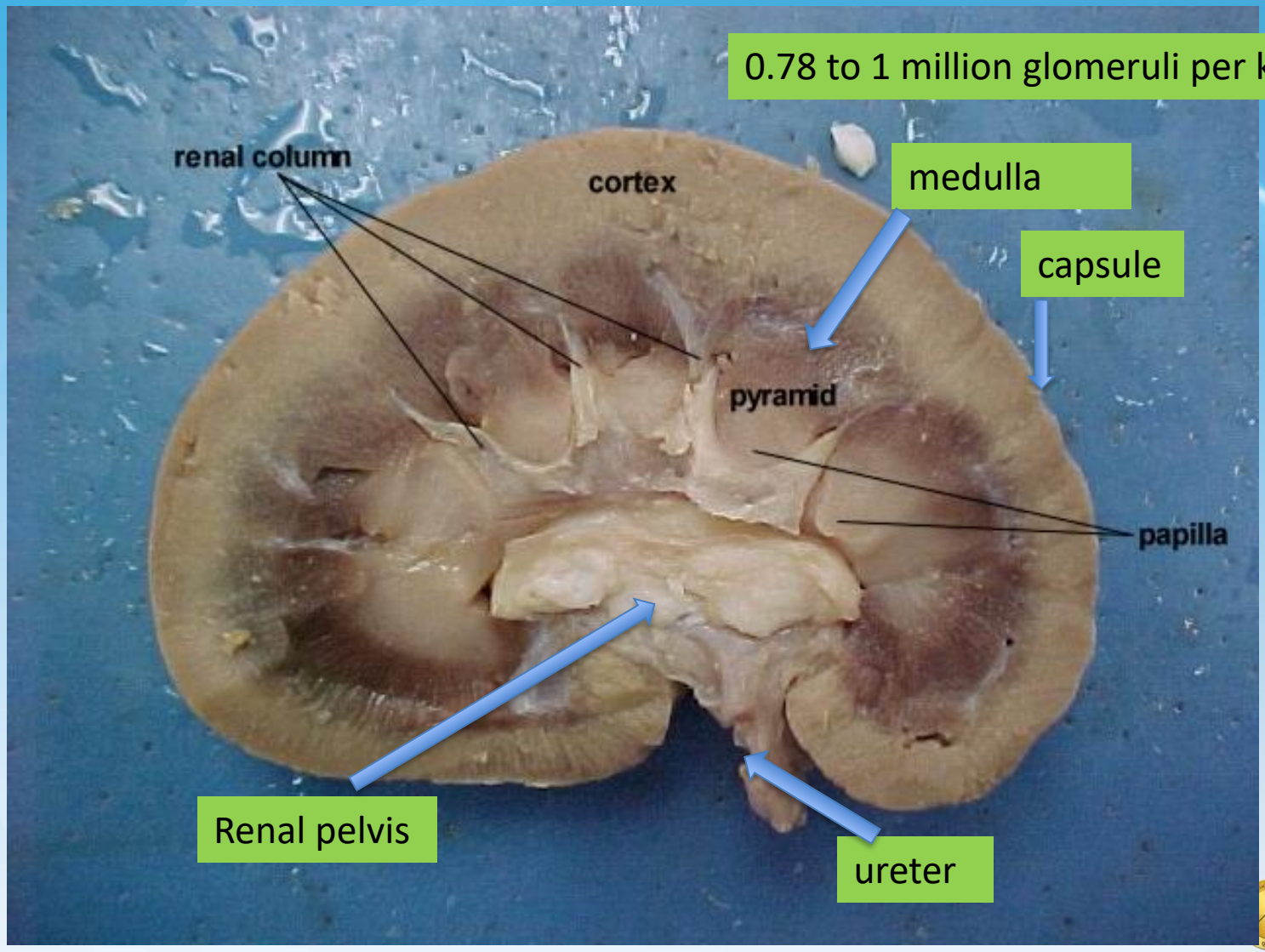
Learning Objectives

By the end of this didactic, the NP Resident will:

- Have a better understanding of how to take care of patients with CKD.
  - Assessment
  - Prevention
  - Treatment
  - Referral indicators

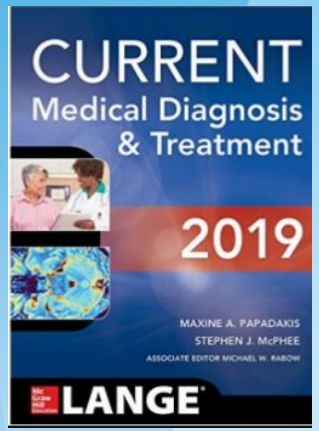
- Have a better understanding of renal physiology, pathology, and general health ramifications.
- Recognize that NSAIDs are poison.

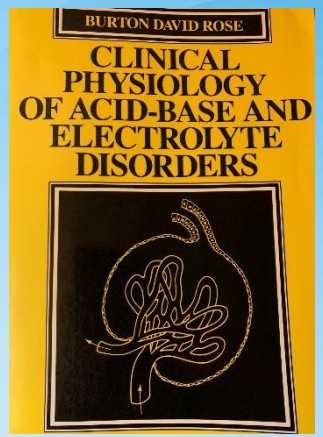

0.78 to 1 million glomeruli per kidney
renal column
cortex
medulla
capsule
pyramid
papilla
Renal pelvis
ureter

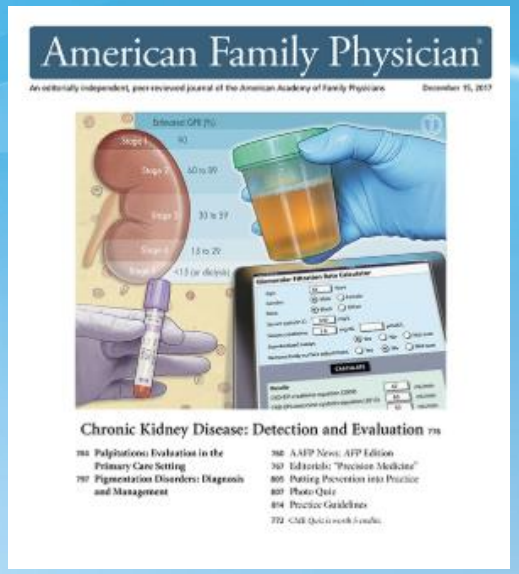
With any subject, start with questions:

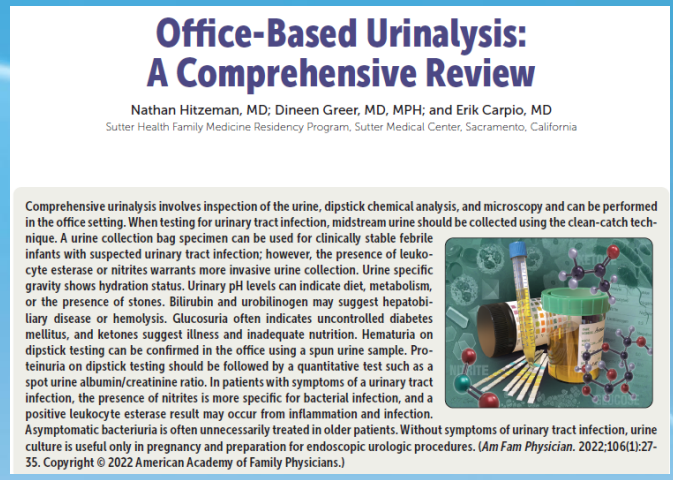
- What do the kidneys do?
- What does it mean to be chronic?
- What does the kidney even look like?
- What is a horseshoe kidney and do we care?
- Can you have 3 kidneys?
- How common is kidney disease?
- What do we do with people who want to donate a kidney?
- How does aging impact renal function?
- How do we assess renal function?
- What do we do with transplants?
- If I want to learn about kidney disease (say to be a better clinician, or to give a talk on the subject) how might I go about it?
- Is there an easier way to think about renal dosing of medications?
- Why do we care about kidney disease?
- What is dialysis like?
- What is up with these Yanomamo wrestlers?

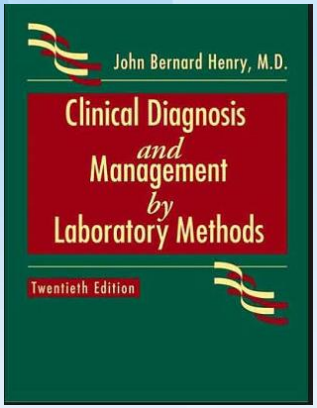
Ways to learn:

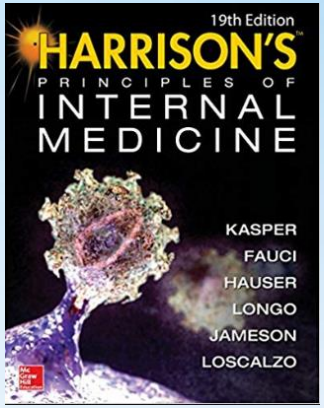


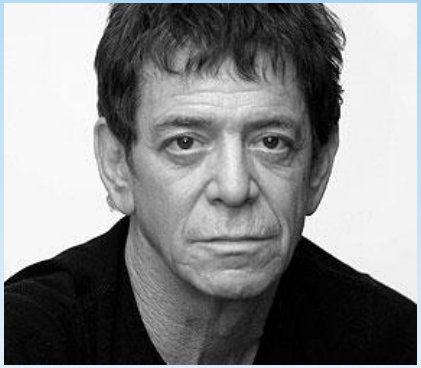


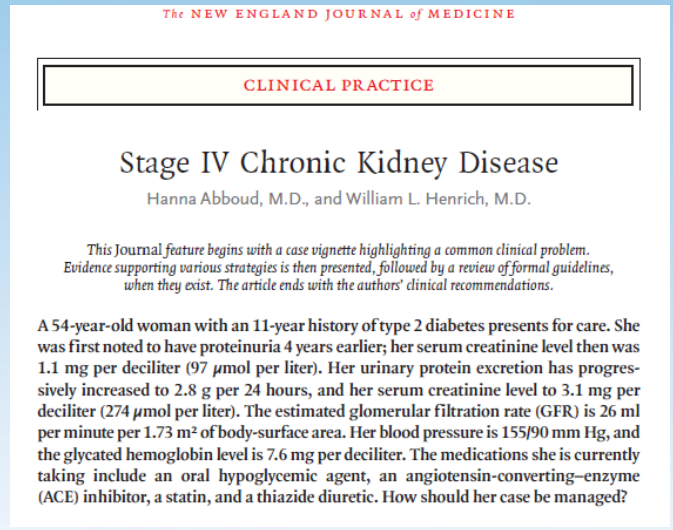












What does the kidney do?

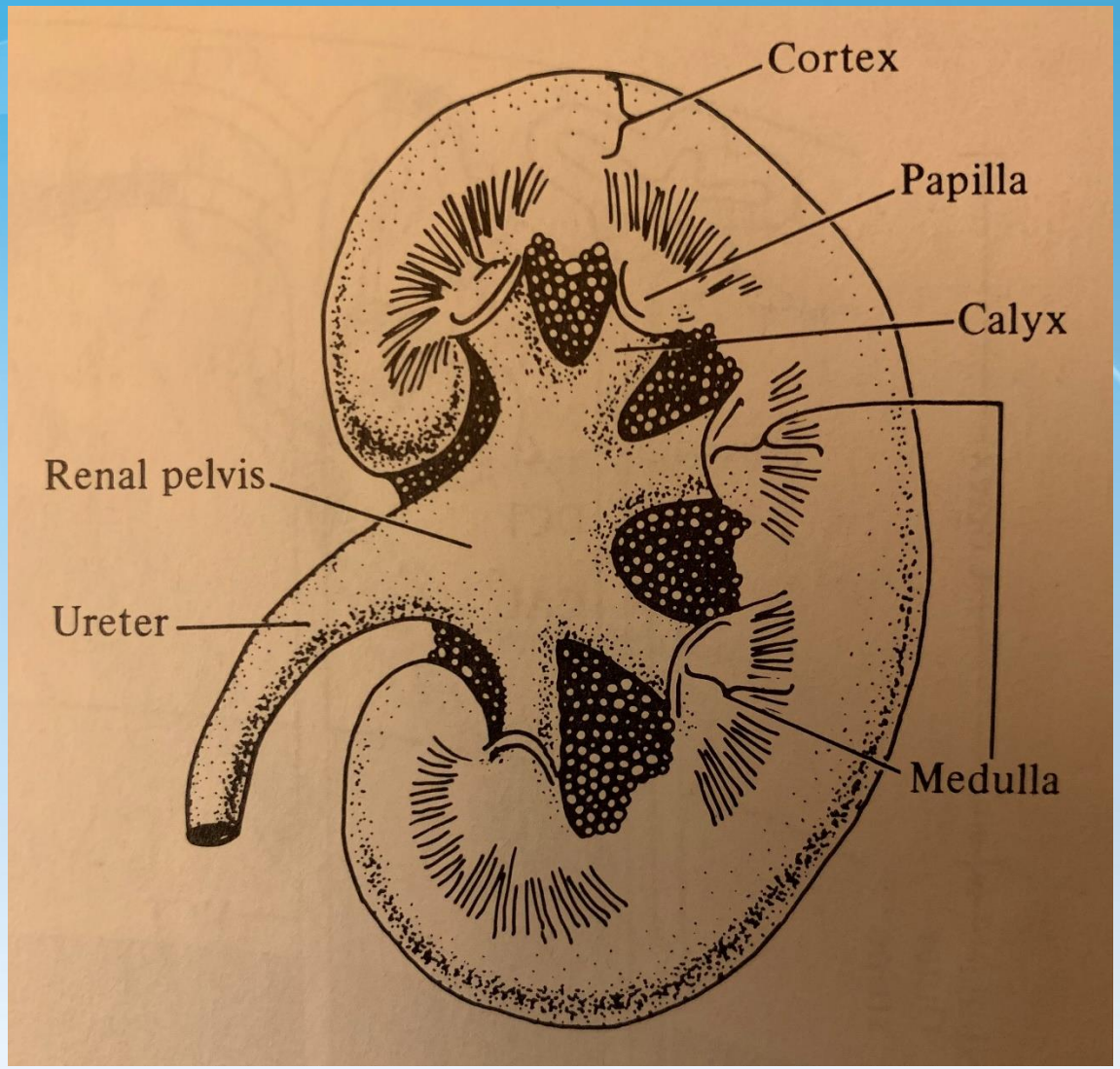
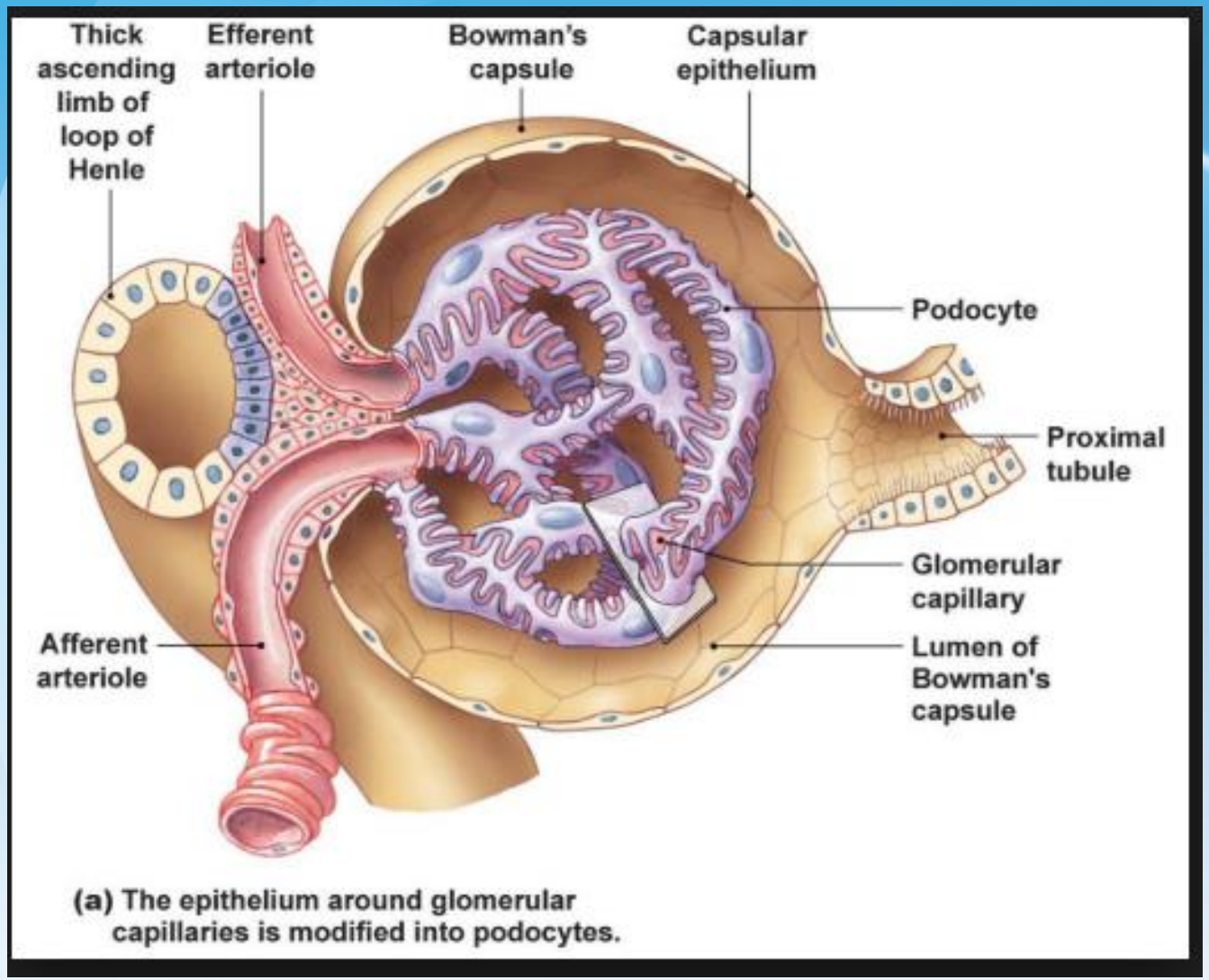


Table 1-1 Summary of the net daily reabsorptive work performed by the kidney[a]

Substance	Filtered	Excreted	Percent net reabsorption
Water	180 liters	0.5–3 liters	98–99
Na^+	26,000 meq	100–250 meq	>99
Cl^-	21,000 meq	100–250 meq	>99
HCO_3^-	4,800 meq	0	~100
K^+	800 meq	40–120 meq	85–95[b]
Urea	54 g	27–32 g	40–50



(a) The epithelium around glomerular capillaries is modified into podocytes.

Basic Functions of the Kidney: i.e. what does the kidney do?

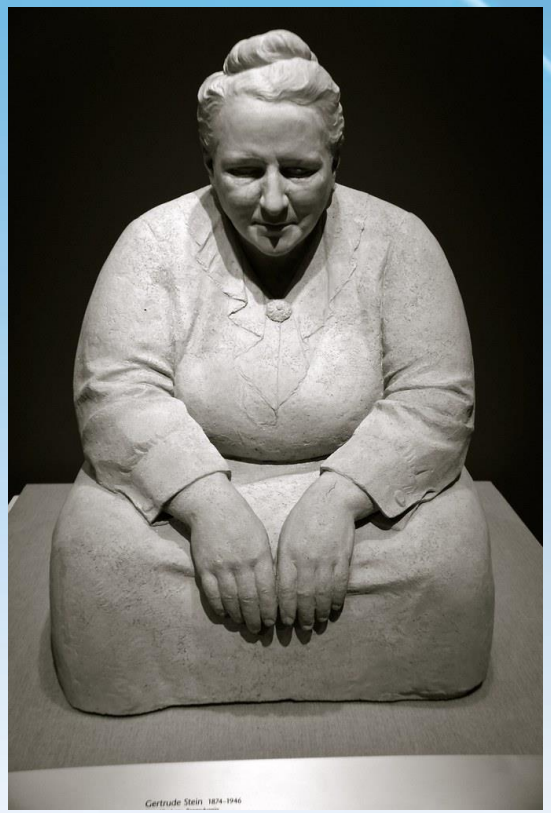
- Regulatory
  - Fluid balance
  - Electrolyte balance
  - Acid-base balance
- Excretory
  - Metabolic end-products (urea, creatinine)
  - Drugs and toxins
- Endocrine
  - Renin (blood pressure regulation)
  - Erythropoietin (RBC production)
  - 1,25 dihydroxyvitamin D3 (bone metabolism)

66 year old woman with a creatinine value:

Tell me about her based on her medications.

Taking

- Alirocumab 75 MG/ML Solution Auto-injector 75 mg Subcutaneous every 2 weeks, Notes: Praluent: PCSK9 inhibitor
- amLODIPine Besy-Benazepril HCl 5-40 MG Capsule 1 cap(s) orally once a day
- B-12 1000 MCG Tablet 1 tab(s) orally once a day
- DULoxetine HCl 20 MG Capsule Delayed Release Particles 1 cap(s) orally 2 times a day
- Hydrocortisone 2.5 % Cream 1 application Externally Once a day as needed
- LORazepam 2 MG Tablet 1 tab(s) orally 3 times a day
- Ondansetron HCl 8 MG Tablet 1 tab(s) orally 2 times a day as needed
- oxyCODONE-Acetaminophen 7.5-325 MG Tablet 2 tablets orally three times per day
- OxyCONTIN 30 MG Tablet ER 12 Hour Abuse-Deterrent 1 tab(s) orally every 12 hours
- tiZANidine HCl 4 MG Tablet 2 cap(s) orally 4 times a day



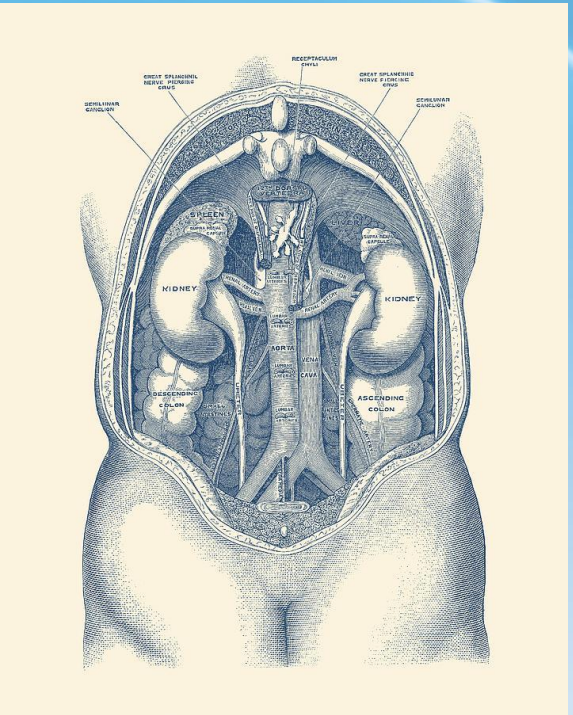
Past Medical History

Multiple sclerosis, dx'd 1997 (9/21, seeing neurology).
h/o ovarian cancer dx at age 18 years, s/p TAH and bilateral oophorectomy.
Fibromyalgia (intolerant of gabapentin; tried duloxetine (and noted it helped a bit but interfered w/ her sleep).
Disc disease, cervical spine and lumbar spine (inoperable per pt.).
H/o bowel obstruction s/p surgery (2019) per pt.
anxiety, in past seen by therapist, and on SSRI; long term benzodiazepine use.
Hypertension.
osteoporosis, was on Prolia, began roughly 2016 (per pt. memory, no DEXA available).
pulmonary nodule, 12/21 (seen by pulmonology, biopsy pending); 1/21 (biopsy negative: pulmonary plan to repeat CT at 3, 6 and 12 months), CT of the chest on 3/31/2022 findings unchanged from prior exam compared with the penultimate imaging; order was placed for a repeat in 3/23).
HCM: A1c, 9/21 (6.2).
HCM: colon CA screen, 9/21 (states had colonoscopy, but prior GI retired; has appt. pending), 10/22 (postponed due to positive COVID test; rescheduled for 1/23), 1/23 (had colonoscopy, 11 polyps; repeat 2 years).
HCM: lipids, 9/21 (273/50/158; ASCVD 9.7%).
HCM: GFR, 9/21 (40), 4/22 (50), 3/23 (42).
22HCM: mammogram, 1/22 (states will be ordered by GYN), 3/22 (BI-RADS 1).
HCM: DEXA, (LS-spine 0, total left hip -0.8).
HCM: microalbumin/creatinine, 11/21 (9).
chronic pain: dx, MS, back and neck pain.
Chronic pain: consults, neurology.
chronic pain: PMP screen, 8/21, 11/21 (went to ED for bridge of benzodiazepine), 4/22, 6/22, 7/22.
chronic pain: imaging, per pt. 2021 (imaging, at Yale).

Vital Signs

MA/Nurse: 000059, Temp: **97.5 F**, Temp Site: T, Ht: 65.5 in, Wt: 239 lbs, BMI: **39.16**, BP: 143/92 mm Hg, BP Site/Pos: ra, HR: **92**, RR: **18**, Smoking: never, Pain Scale: 8, O2 Sat: **95**, Repeat pulse: 89, Repeat BP: 142/86 arm and leg pain.

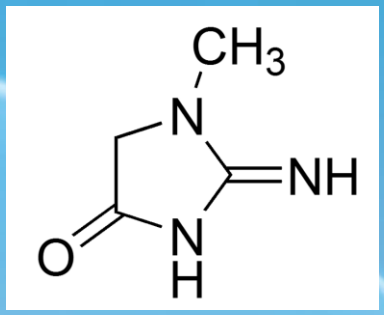
What do you glean from this?



eGFR	**42 L**	**> OR = 60 - mL/min/1.73m2**
Glucose	**100 H**	**65-99 - mg/dL**
Urea Nitrogen	**29 H**	**7-25 - mg/dL**
Creatinine	**1.39 H**	**0.50-1.05 - mg/dL**
BUN/Creatinine Ratio	21	6-22 - (calc)
Sodium	142	135-146 - mmol/L
Potassium	4.6	3.5-5.3 - mmol/L
Chloride	107	98-110 - mmol/L
Carbon Dioxide	23	20-32 - mmol/L
Calcium	9.7	8.6-10.4 - mg/dL

- https://www.kidney.org/professionals/kdoqi/gfr_calculator

Creatinine



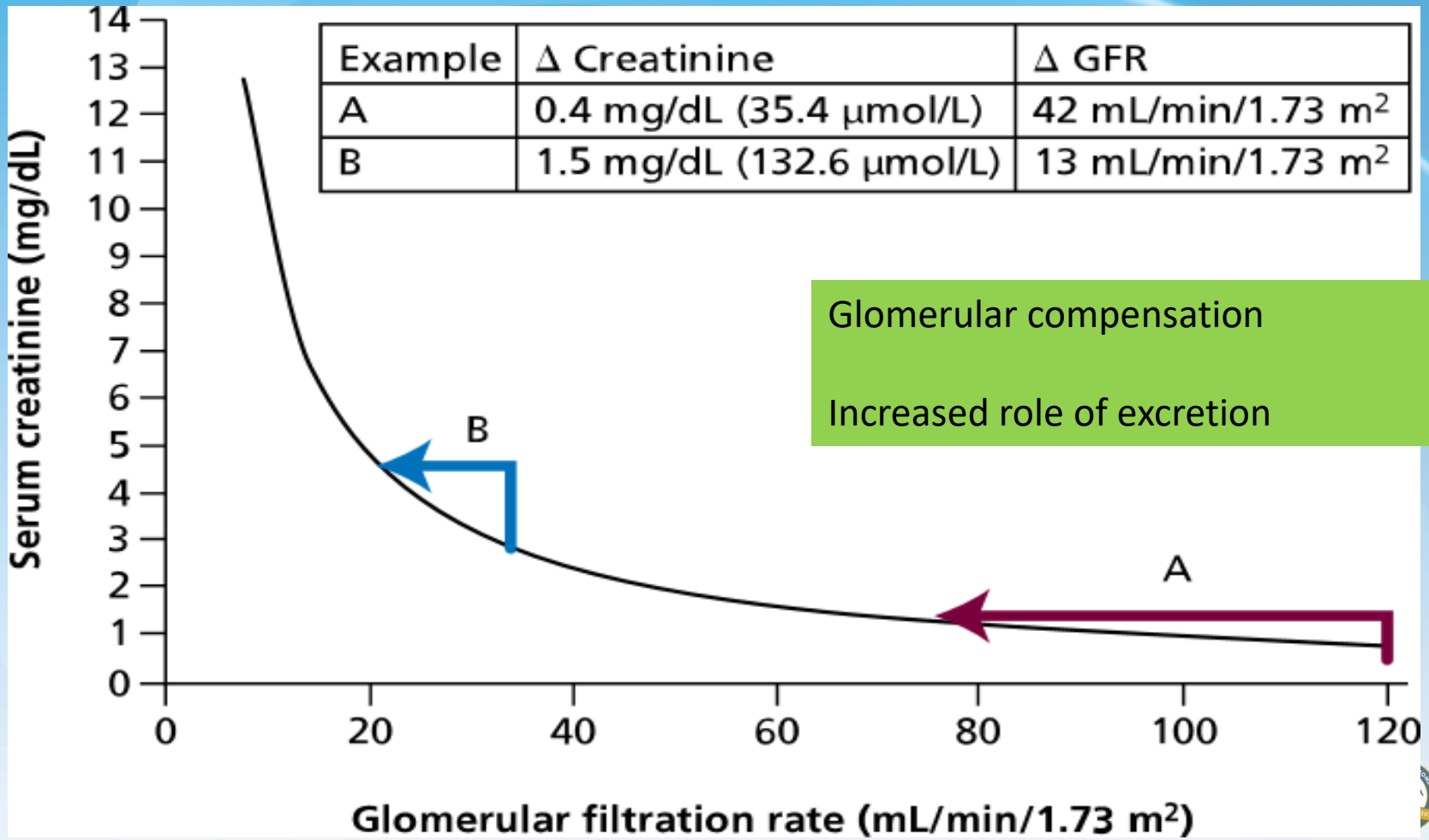
- Generated from the metabolism of creatine in muscle and from dietary meat. (where is creatine made?)
- Filtered by the glomerulus without metabolism or reabsorption by renal tubules.
- (Basically, but it's more complex than that…)

Creatinine

- May over-estimate GFR
  - Muscle wasting (less creatine, less creatinine)
  - Malnutrition
  - Amputations
  - Elderly
  - Women
  - Liver disease : this is where creatine is made (w/ precursor from kidney)
- May under-estimate GFR
  - Black Persons
  - High muscle mass
  - Men
  - Drugs – TMP, cimetidine, DTG, COBI
  - Protein supplementation; meat diet
  - Trauma, sepsis, major surgery

Creatinine increase is non-linear

Example	Δ Creatinine	Δ GFR
A	0.4 mg/dL (35.4 µmol/L)	42 mL/min/1.73 m^2
B	1.5 mg/dL (132.6 µmol/L)	13 mL/min/1.73 m^2



Glomerular compensation

Increased role of excretion

BUN (Blood Urea Nitrogen)

- Derived from protein metabolism
- Poor marker of kidney function because
  - not produced at a constant rate
  - reabsorbed along renal tubules
- May be elevated with:
  - Hypovolemia (pre-renal azotemia): decreased effective circulatory volume
  - GI Bleeding
  - Steroids
  - Tetracycline
  - High protein diet

BUN (Blood Urea Nitrogen)

- May be decreased with:
  - Liver disease
  - Malnutrition
  - Sickle cell disease
  - SIADH

Assessment of Kidney Function

- Glomerular Filtration Rate (GFR) :
  - Cumulative sum of filtration rate of nephrons
  - Provides a filtration rate of fluid passing through the kidneys per minute

Estimation of GFR

Method	Considerations	Application
Creatinine Clearance		
U_{Cr} (mg/dL) × 24-hour urine volume (mL/24 h)/S_{Cr} (mg/dL) × 1440 (min/24 h)	Overestimates GFR 10%-20% Incomplete or excessive 24-hour urine collections limit accuracy	Useful in pregnancy, extremes of age and weight, amputees, and patients with cirrhosis

Estimation of GFR

Method	Considerations	Application
Cockcroft-Gault Equation (CGE)		
$CrCl = (140 - age) \times (weight\ in\ kg) \times (0.85\ if\ female)/(72 \times S_{Cr})$	Most accurate when eGFR is 15-60 mL/min/1.73 m^2 Underestimates GFR in obesity Overestimates GFR when BMI <25 Takes into account lean body weight, age, and gender	Improved accuracy when age is <65 years - Older and less accurate - Used as basis for drug dosing guidelines.

Estimation of GFR

Method	Considerations	Application
****Modification of Diet in Renal Disease (MDRD) Study Equation[a]**		
GFR = 175 × $(S_{Cr})^{-1.154}$ × $(age)^{-0.203}$ × 0.742 (if female) or × 1.212 (if black)	Most accurate when eGFR is 15-60 mL/min/1.73 m^2 Underestimates GFR when GFR >60 mL/min/1.73 m^2 Less accurate in populations with normal or near normal eGFR, extremes of age and weight, amputees, in pregnancy, and in patients with cirrhosis	Chronic kidney disease when eGFR is 15-60 mL/min/1.73 m^2

MDRD Study Equation

- Most clinical laboratories employ the MDRD study equation to estimate GFR, with higher levels of GFR reported as “>60 mL/min/1.73 m^2
- Clinicians may ignore other signs or symptoms of CKD (such as proteinuria) after erroneously assuming that a level reported as normal means an absence of structural kidney disease

- 67-year-old man from Liberia.

amLODIPine Besylate 10 MG Tablet 1 tab(s) orally once a day.
Aspirin Adult Low Dose 81 MG Tablet Delayed Release 1 tablet Orally Once a day.
Atorvastatin Calcium 20 MG Tablet 1 tab(s) orally once a day.
Clotrimazole 1 % Cream APPLY TOPICALLY TWICE DAILY AS NEEDED FOR 7 DAYS.
Fluconazole 100 MG Tablet 1 tab(s) orally now and then in a week.
Jardiance 10 MG Tablet 1 tablet Orally Once a day.
HYDROcodone-Acetaminophen 5-325 MG Tablet 1 tablet as needed Orally three times a day as needed.
Lantus 100 UNIT/ML Solution 5 units subcutaneously twice a day.
Ozempic (0.25 or 0.5 MG/DOSE) 2 MG/3ML Solution Pen-injector 0.5 mg Subcutaneous once a week.
Tamsulosin HCl 0.4 MG Capsule 1 cap(s) orally once a day.

- What can you tell about him from his medications?

- 67-year-old man from Liberia.

- ischemic stroke, 2/07, with right arm and leg paresis
- diabetes, type 2
- dyslipidemia
- obesity
- chronic pain: dx, back pain, since stroke
- 4/19, acute renal failure (severe), related to excessive ibuprofen; GFR 8/19 (31), 10/19 (32), 12/19 (36), 9/21 (creatinine 2.01), 9/22 (eGFR 32)
- glaucoma
- HCM: A1c, 4/07, 2/08, 6/08 (9.0), 10/08 (7.7), 6/09 (8.8), 12/10 (7.6), 8/11 (7.4), 11/11 (7.1), 8/12 (6.4), 2/13 (6.7), 8/13 (7.3), 4/14 (6.8), 4/15 (7.2), 2/16 (7.2), 9/16 (6.8), 1/17 (7.0), 6/17 (7.1), 1/18 (6.5), 6/18 (6.8), 11/18 (6.0), 6/19 (7.3), 10/19 (7.2), 12/19 (6.8), 10/20 (7.8), 4/21 (8.3), 6/21 (8.2), 9/21 (6.7), 1/22 (7.9), 3/22 (8.2), 6/22 (7.4), 9/22 (6.9), 4/23 (6.4)
- HCM: foot check, 10/07, 6/09, 12/10, 4/12, 4/14 (dry, hammertoes, callus), 1/16 (same), 1/17, 1/18, 12/18, 4/21 (same), 6/22 (normal)
- HCM: lipid panel, 4/07, 2/08, 10/08, 12/10, 1/13 (143/54/79), 4/15 (114/36/62), 1/17 (123/43/68), 1/18 (121/37/66), 9/21 (109/34/59), 9/22 (106/40/54)
- HCM: microalbumin, 3/07 (nml), 3/08 (nml), 6/09 (< 30), 12/10 (30-300), 4/12 (< 30), 4/15 (< 30), 5/16 (< 30), 6/17 (34), 11/18 (83), 12/19 (53), 4/21 (121), 7/22 (30-300)
- HCM: ophthal., 12/07, 12/10 (declines), 1/13 (needs), 5/14 (repeat one year), 3/17, 6/17, 1/18, 12/21
- HCM: FOBT, 2/08 (negative), 7/09 (not detected), 6/11 (not detected), 8/12 (not detected), 1/13, 4/14 (not detected), 4/15 (not detected), 6/16 (not detected), 9/17 (cards given), 10/17 (not detected), 11/18 (not detected), 1/20 (not detected), 2/21 (negative (no date on sample)), 6/22 (not detected)
- HCM: dental, 5/10, 1/13 (owes dental money...), 7/15, 6/22 (recommended)
- HCM: HCV screen, 4/15 (negative)
- HCM: HBV screen, 4/15 (cAb pos., sAb pos.: immune)
- HCM: HAV screen, 4/15 (immune)
- HCM: PMP screen, 6/17 ***
- HCM: vitamin B12 screen, 11/18 (normal)
- HCM: PSA 4/19 (4.5), 10/19 (20.5), 12/19 (6.8), 10/5/20 (4.0), 6/22 (4.50)
- HCM: FHx screen, 1/16

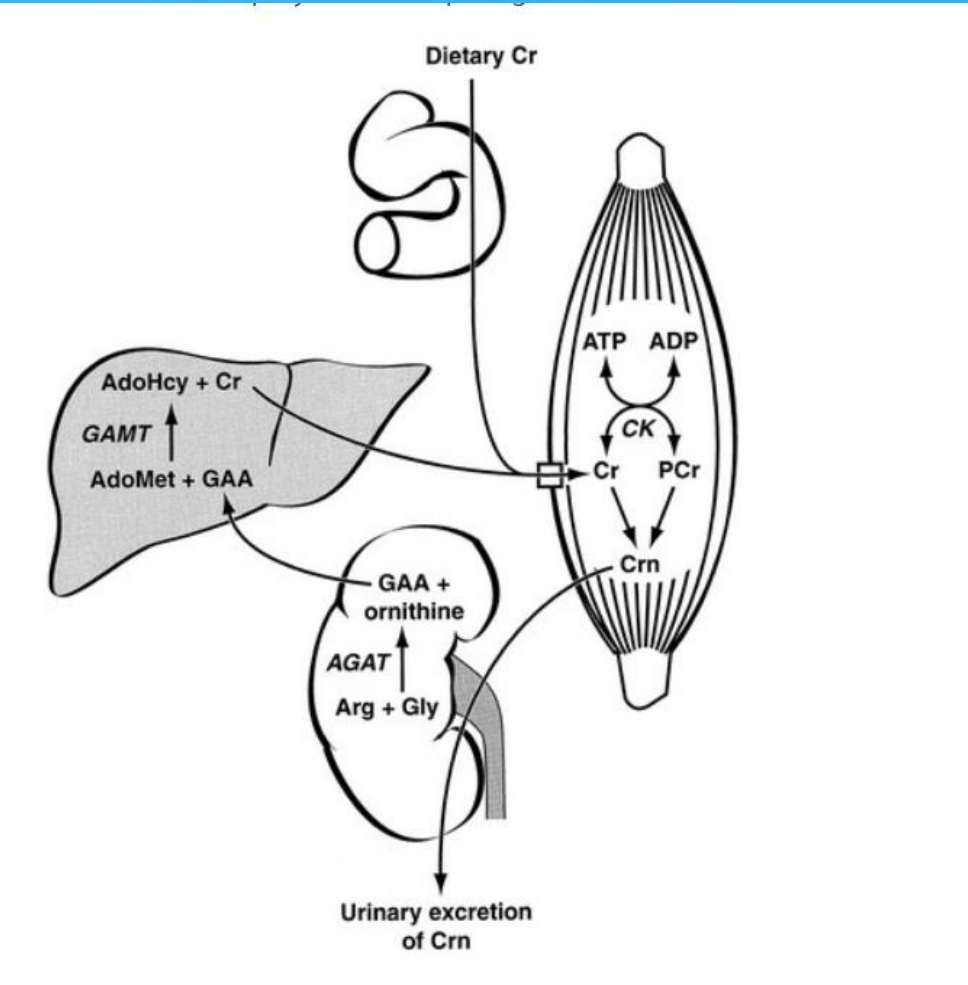
67-year-old man from Liberia.

- 11/18 creatinine 1.21, BUN 19, EGFR between 60 and 70
- 4/19 creatinine 5.17, BUN 47, EGFR between 11 and 13.
- Most recent labs

Color	Yellow	
UA Appearance	Clear	
Specific Gravity	1.020	
pH	6.0	
Protein	30	!
Glucose	>=1000	!
Ketones	Negative	
Bilirubin	Negative	
Blood	Negative	
Nitrite	Negative	
UA Urobilinogen	0.2	
Leukocyte Esterase	Negative	
UA RBC	0-2	
UA WBC	None Seen	
Bacteria	None Seen	
Yeast	None Seen	
UA EPI CELL	1-4	
Cast	Rare	
Small Round Cells	None Seen	
Path Cast	None Seen	

SODIUM	145	
POTASSIUM	4.0	
CHLORIDE	110	
CARBON DIOXIDE	26.9	
Anion Gap	8	
Glucose	122	▲
BUN	21	
Creatinine	2.1	▲
BUN/Creatinine Ratio	10.0	
Glomerular Filtrat...	34 *	!-
CALCIUM	9.7	
Protein, Total	6.7	
Albumin	4.0	
A/G Ratio	1.5	
Total Bilirubin	0.5	
ALT	20	
AST	23	
ALKALINE PHOSPHATASE	83	
Phosphorus	3.2	

Creatine and creatinine



https://journals.physiology.org/doi/full/10.1152/physrev.2000.80.3.1107

31-year-old man with history of obesity, BMI of 54, presented to the emergency room with nausea, vomiting, abdominal pain and diarrhea.

Found to have a creatinine of 5.8 and a BUN of 43.

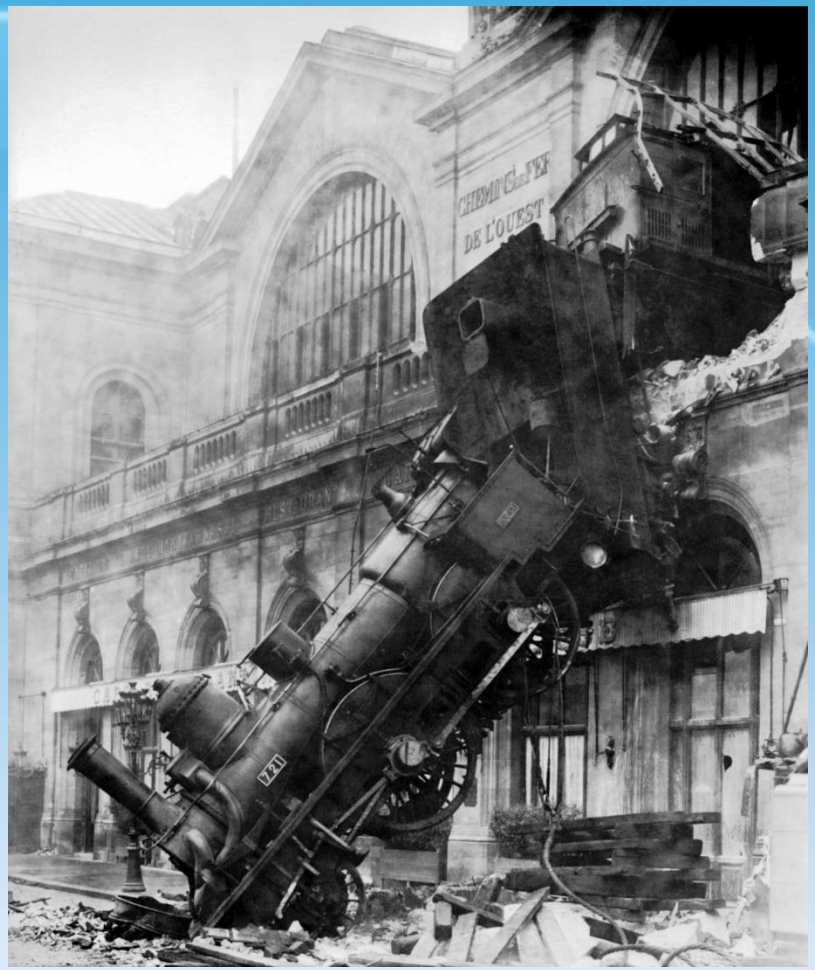
Potassium 5.0, calcium 8.6, total protein 6.2.

Random urine protein 743. A1c 5.7.

Blood pressure 136/89.

CT of the abdomen notes that kidneys are unremarkable. No hydronephrosis.

Hepatitis B negative, hepatitis C negative

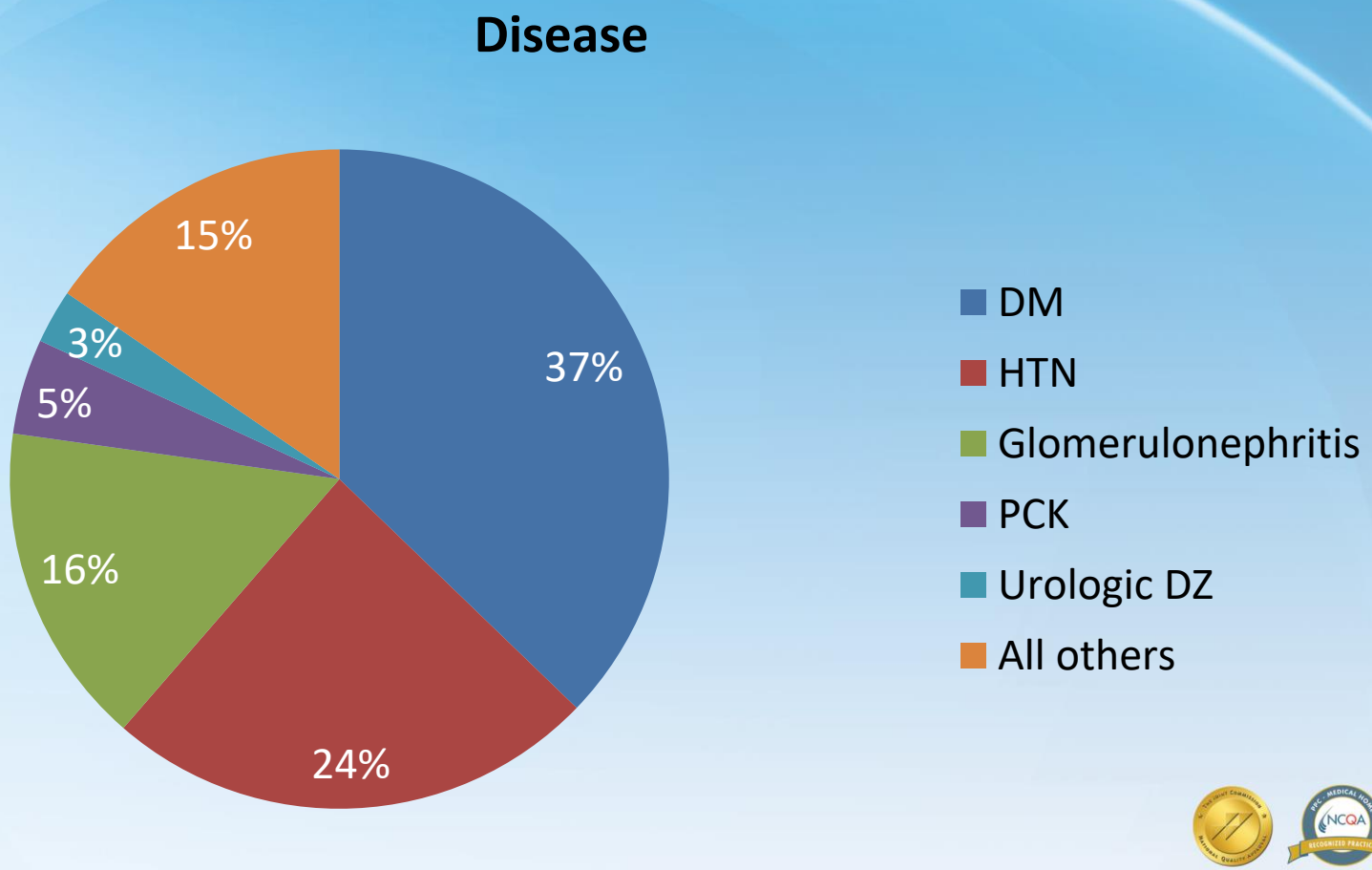


Epidemiology of kidney disease

- 7% of U.S. adults over the age of 20 years have an eGFR <60
  - increases to 12.3% when those with albuminuria are included.

- The most common causes in U.S.
  - diabetic nephropathy (45%)
  - hypertension (29%),
  - glomerulonephritis (5.5%).

Epidemiology



Risk Factors

- Diabetes
  - Type 1: 30-40% over 20 years
  - Type 2: 15-20%... (contested…)
- Hypertension
- Autoimmune
- Systemic Infections
- UTI
- LUT obstruction
- Neoplasia
- Family history of CKD
- Recovery from ARF/AKI
- Drugs
- Low birth weight

Sociodemographic factors

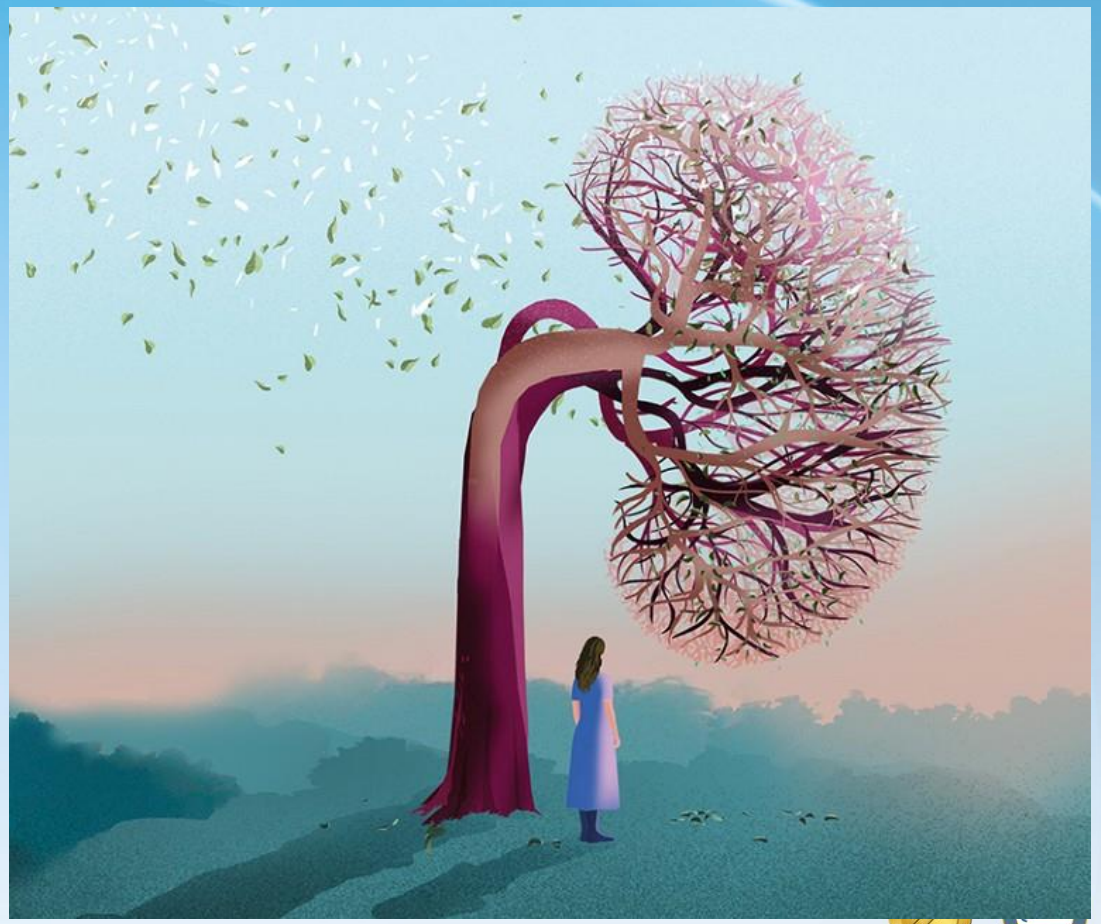
- Older Age
- African American
- Male
- Low income
- Low education
- Environmental exposure
- Occupational exposure

Progressive Factors

- Higher level of proteinuria
- Higher blood pressure
- Poor glycemic control in DM
- Smoking
- Acidemia

How can we tell if the kidney is doing what it should be?

- Urinalysis
- Blood labs
- Imaging



Let's start with urine…

47-year-old comes in because when she went to urinate yesterday she found the toilet full of blood, although when she wiped herself front and back she noted no blood on the tissue paper.

What is this?

What do you want to do?

Lab: Urinalysis IH	
Exp. Date	08/31/2019
Lot No.	802079
Leuko	Trace
Nitrite	neg
Urobilinogen	0.2
Protein	neg
pH	7.0
Blood	neg
Sp. Gr.	1.020
Ketone	neg
Biliruben	neg
Glucose	neg

What can we know from the urine?

Color

Clarity

Odor

Taste

TABLE 1

Causes of Abnormal Urine Appearance

Appearance	Physiologic/pathologic	Food/drug/herb related
Brownish-black	Bile pigments, copper poisoning, melanin, methemoglobin, myoglobin, porphyria, stool from fistula	Aloe, cascara sagrada or senna (bitterbark), fava beans, levodopa, methocarbamol (Robaxin), methyldopa, metronidazole (Flagyl), nitrofurantoin, some antimalarial agents, sorbitol
Cloudy or white	Chyle, infection, lipids, oxalates, phosphates	Propofol (Diprivan), purine-rich foods (hyperuricosuria)
Foamy	Dehydration, frank proteinuria	—
Green or blue	Biliverdin, pseudomonas	Amitriptyline, cimetidine (Tagamet), indigo carmine (diagnostic agent), indomethacin, methylene blue (ProvayBlue; methemoglobin treatment), prochlorperazine, propofol, triamterene (Dyrenium)
Orange	Bile pigments, uric acid in newborns	Carrots, phenazopyridine, rifampin, sulfasalazine (Azulfidine)
Purple	Bacterial overgrowth from indwelling catheter	—
Red	Hematuria, hemoglobinuria, myoglobinuria	Beets, blackberries, phenothiazines, phenytoin (Dilantin), rhubarb, senna

Urine Dipstick Analysis

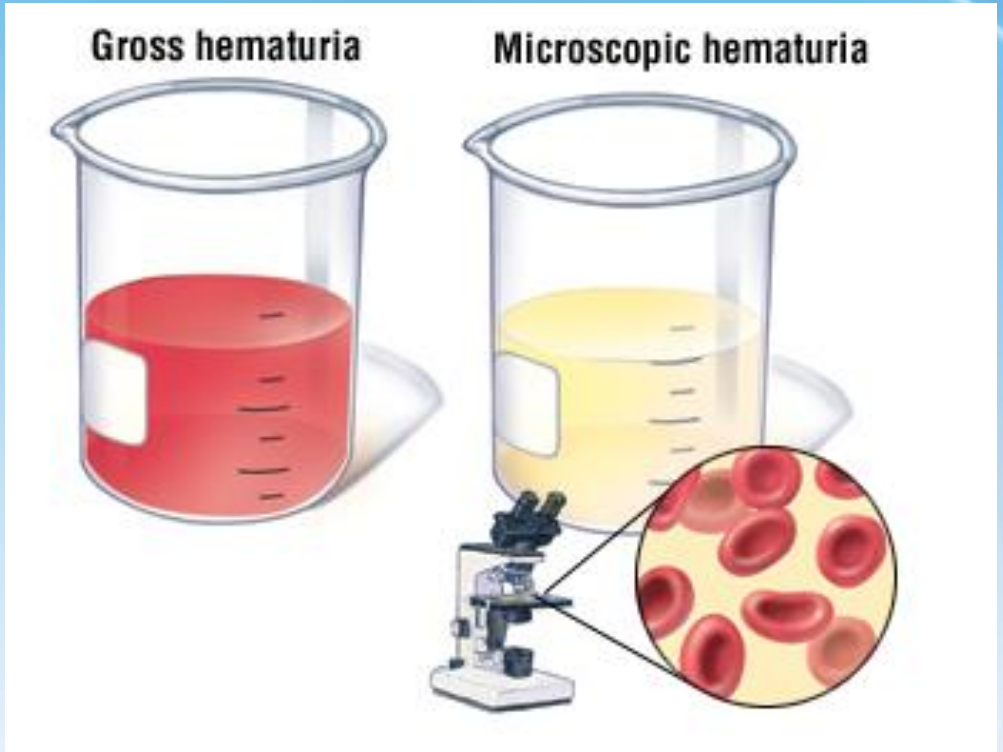
Specific gravity	1.016-1.022 (normal); minimum of 1.003. Low with dilute urine; high with concentrated urine or hypertonic product excretion such as with glycosuria and contrast dye. Usually SG from urea (20%), NaCl (25%) and sulfates and phosphate. What is isothenuria? 1.010, and fixed = bad kidney damage
pH	4.6-8.0: Elevated with low acid ingestion, alkaline tide postprandial, inability to excrete acid load (renal tubular acidosis), urease-splitting organisms, or lots of citrus. Acid urine w/ eating meat and cranberries.

Urine Dipstick Analysis

Blood

What causes a positive?
(and do you trust the strip?)

Give a differential.



Urine Dipstick Analysis

Blood

What causes a positive?

Blood (hemoglobin, hemosiderin, myoglobin)

Give a differential.

cancer, trauma, bleeding disorder, anticoagulants, traumatic exercise (marathon running, marching, karate);
malaria, UTI, burns, brown recluse spider bite, mothball exposure, prosth. cardiac valves, HUS, TTP etc.
kidney stones, glomerulonephritis…

Causes of Hematuria

Glomerular causes

Familial
- Fabry disease
- Hereditary nephritis (Alport syndrome)
- Nail-patella syndrome
- Thin basement membrane nephropathy

Primary glomerulonephritis
- Focal segmental glomerulonephritis
- Goodpasture syndrome
- Henoch-Schönlein purpura
- Immunoglobulin A nephropathy (Berger disease)
- Mesangial proliferative glomerulonephritis
- Postinfectious glomerulonephritis
- Rapidly progressive glomerulonephritis

Secondary glomerulonephritis
- Hemolytic uremic syndrome
- Systemic lupus nephritis
- Thrombotic thrombocytopenic purpura
- Vasculitis

Renal causes

Arteriovenous malformation
Hypercalciuria
Hyperuricosuria
Loin pain–hematuria syndrome
Malignant hypertension
Medullary sponge kidney
Metabolic causes
Polycystic kidney disease
Renal artery embolism
Renal papillary necrosis
Renal vein thrombosis
Sickle cell disease or trait
Tubulointerstitial cause
Vascular cause

Urologic causes

Benign prostatic hyperplasia
Cancer (bladder, kidney, prostate, ureteral, or urethral)
Cystitis/pyelonephritis
Nephrolithiasis
Prostatitis
Schistosoma haematobium infection
Tuberculosis

Other causes

Drugs (e.g., cyclophosphamide, heparin, nonsteroidal anti-inflammatory drugs, warfarin)
Trauma (e.g., contact sports, running, Foley catheter)

Urine Dipstick Analysis

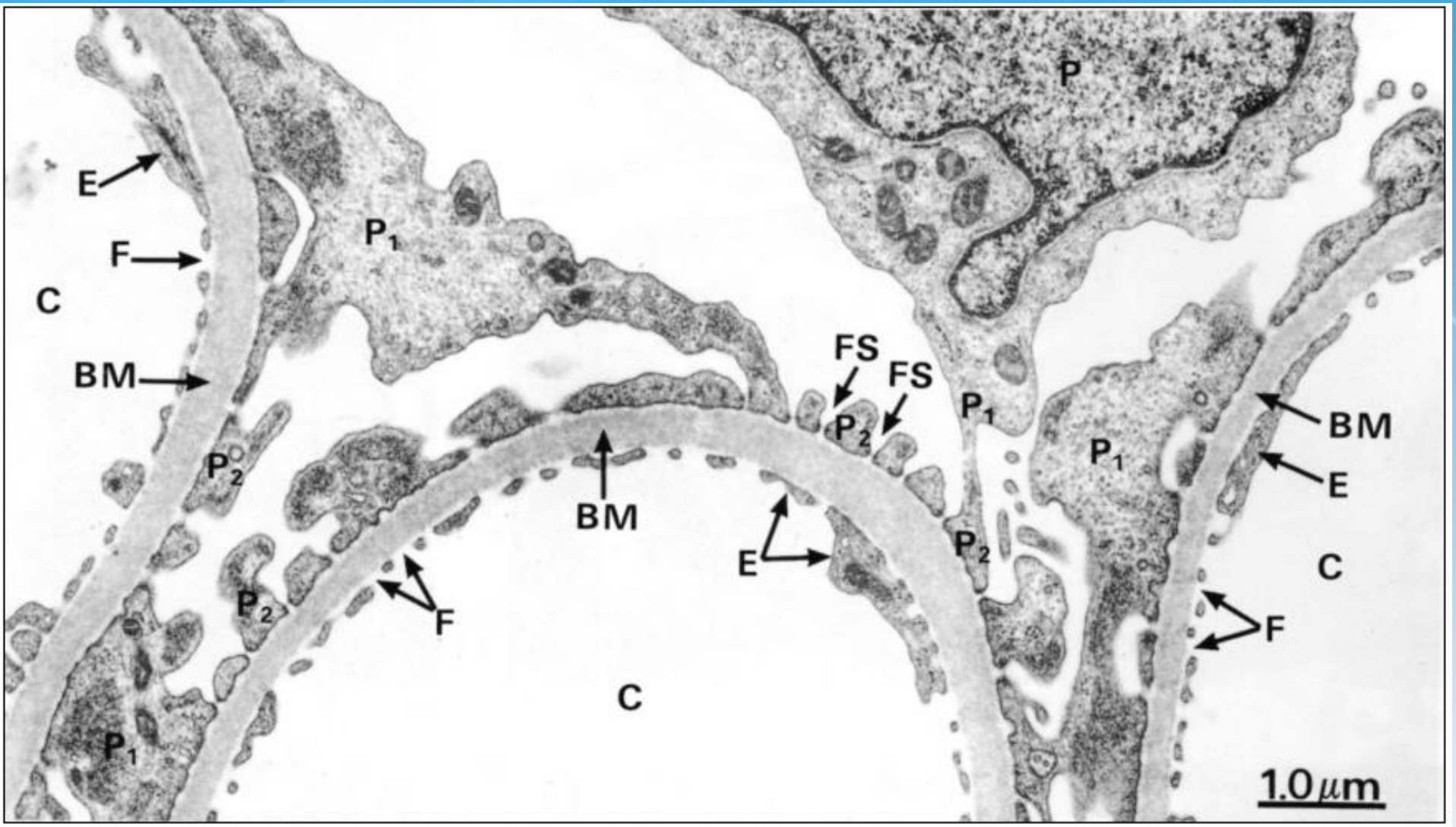
Albumin

Most dipsticks detect primarily albumin; trace positive can be normal in a concentrated specimen; specialized dipsticks designed to detect small amounts of albumin for detection of moderately increased albuminuria are available.

Which starts to get complicated…

How is protein filtered in the kidney?
What is the glomerular basement membrane?
Why are we paying attention to this?

How do we confirm this?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Urine Dipstick Analysis

Albumin

So, albumin has a molecular weight of 69k. Plasma particles with MW of <50-60k pass freely through the GBM. (i.e. usually not albumin). The GBM has a negative charge, which repels albumin (and other proteins). When the GBM is damaged, then more protein is leaked, w/ a fairly low maximal rate of resorption…

Albuminuria can be an early indicator of kidney disease.

In itself proteinuria is also independently linked with increased mortality (4-6x's the risk of CV mortality)

Urine Dipstick Analysis

Glucose	Positive when plasma glucose level exceeds 180 mg/dL (10.0 mmol/L) with lower threshold in pregnancy or Fanconi syndrome
Ketones	Positive for acetoacetic acid, not acetone or β-hydroxybutyrate
Nitrites	Detects nitrite converted from dietary nitrate by bacteria; normally, no nitrites are present in urine (urine needs to be in bladder for >4 hours; some bacteria don't reduce nitrates…)
Leukocyte esterase	Detects the presence of leukocytes in the urine; positive test requires at least 3 leukocytes/hpf

Urine Microscopy

Erythrocytes	Urine microscopy should be performed to evaluate erythrocyte morphology
Leukocytes	The presence of any leukocytes may be abnormal depending on clinical circumstances
Casts	Hyaline casts are indicative of poor kidney perfusion but can be benign or reversible; other casts are indicative of intrinsic injury
Crystals	Most common include calcium oxalate, calcium phosphate, uric acid, and struvite; occur when urine is supersaturated with a specific substance

Pathologies From Urine Dipstick Results and Sources of False Results

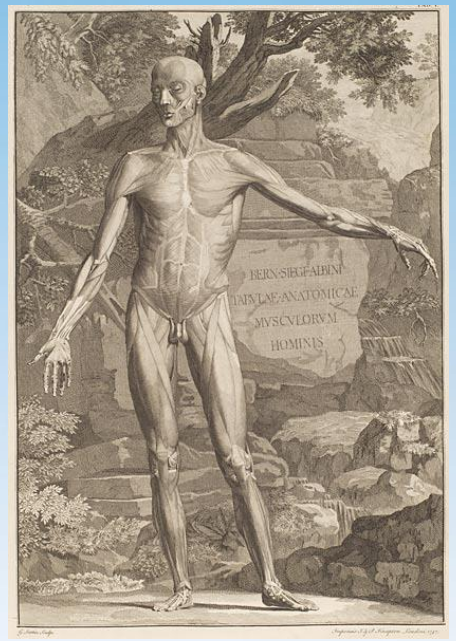
Dipstick test result	Suggested diagnoses	False-positive results	False-negative results
Bilirubin	Biliary obstruction, hepatic disease	Chlorpromazine, phenazopyridine	Prolonged light exposure, selenium, vitamin C
Blood	Glomerular disorders, hypercalciuria, hyperuricosuria, kidney stones, trauma, tubular disorders, tumor, UTI	Exercise, hemoglobinuria, menses, myoglobinuria	High urine specific gravity, vitamin C
Glucose	Diabetes mellitus, Fanconi syndrome, pregnancy, sodium-glucose cotransporter-2 inhibitor use	Levodopa, strong oxidizing agents	High pH, high urine specific gravity, uric acid, vitamin C
Ketones	Diabetes, ketogenic diet, pregnancy, starvation	High urine specific gravity, low pH, some drug metabolites	Delay in examination of urine; certain ketones not detectable depending on brand of test
Leukocyte esterase	Inflammatory process, sexually transmitted infection, UTI	Contamination	Antibiotics; high glucose, protein, or urine specific gravity; vitamin C
Nitrites	UTI	Contamination, dipstick exposure to air, phenazopyridine	High urine specific gravity, bacteria that do not reduce nitrates, short bladder incubation time, vitamin C
pH	High: alkalemia, carbonic anhydrase inhibitors, heavy antacid use, potassium/sodium citrate, type 1 renal tubular acidosis, UTI Low: acidemia, methenamine	—	Presence of formaldehyde
Protein	Fever, glomerular disorders, tubular disorders, UTI	Phenazopyridine, concentrated or alkaline urine, quaternary ammonium compounds	Nonalbumin proteinuria, acidic or diluted urine
Urine specific gravity	High: dehydration, glucosuria, syndrome of inappropriate antidiuretic hormone Low: adrenal insufficiency, aldosteronism, diabetes insipidus, impaired renal function, water intoxication	Dextran solutions, intravenous radiopaque dyes, phenazopyridine, proteinuria	Alkaline urine
Urobilinogen	Intravascular hemolysis, hepatic disease, sometimes a normal finding	Phenazopyridine, sulfonamides	Improper storage of the urine sample, preservatives

62-year-old man currently on the following medications:

allopurinol 400 mg daily
ranitidine 150 mg twice a day
lisinopril 5 mg daily
metoprolol 50 mg 2 times a day
diltiazem CD 120 mg daily
rivaroxaban 20 mg daily
pravastatin 10 mg daily
nortriptyline 10 mg daily
darunavir/cobicistat 800/150 daily
lamivudine, 150 daily
dolutegravir 50 mg daily
furosemide 40 mg twice a day

What can you tell me about him?

What can you say about when this case was written?



Case: creatinine

62-year-old man:

Creatinine 2.1

BUN 34

vitamin D 17.2

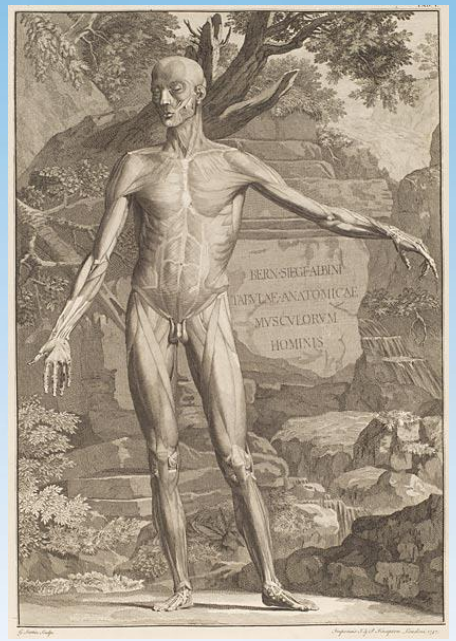
microalb./creatinine: 289

PTH 82.7

What is this? What questions do you have?

Do we care?

Does anything need to be done?



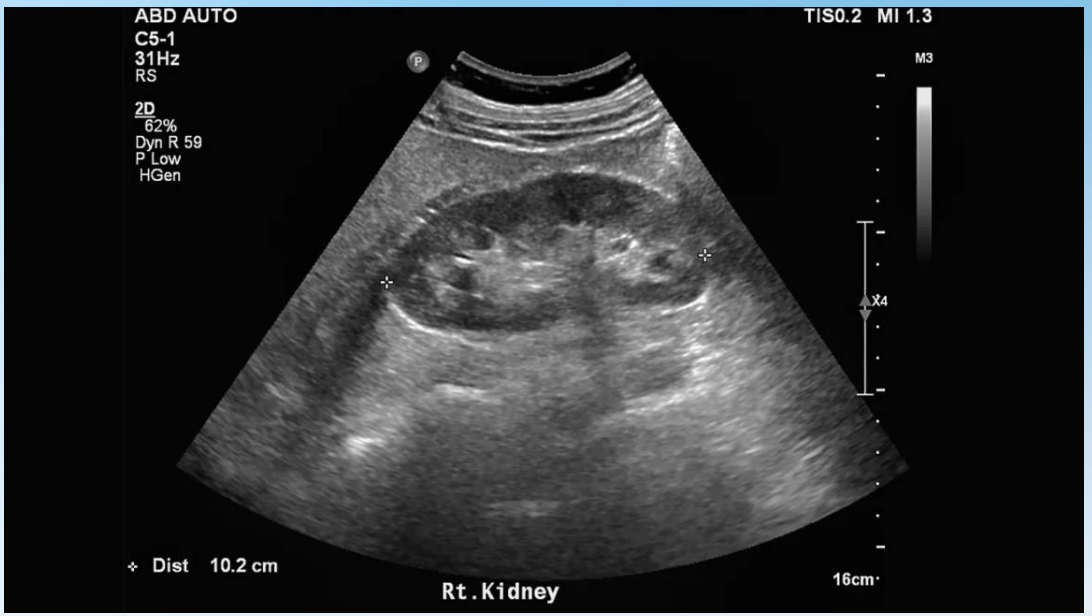
- How to approach a patient in your office…

Review of systems	Recent infections	Poststreptococcal glomerulonephritis
	Risk factors for sexually transmitted infection or injection drug use	Hepatitis B or C, HIV infection
	Skin rash or arthritis	Autoimmune disease (e.g., cryoglobulinemia, systemic lupus erythematosus)
	Symptoms during urination	Urinary tract infection, obstruction, or stone
Medical history	Diabetes mellitus	Moderately increased albuminuria with or without retinopathy and elevated blood pressure
	Hypertension	Severely elevated blood pressure, often with target organ damage
Family history of kidney disease	Men and women are affected equally in every generation	Autosomal dominant polycystic kidney disease
	Men in every generation are affected	Sex-linked recessive disease (e.g., Alport syndrome)
	Less frequent than every generation	Autosomal recessive polycystic kidney disease

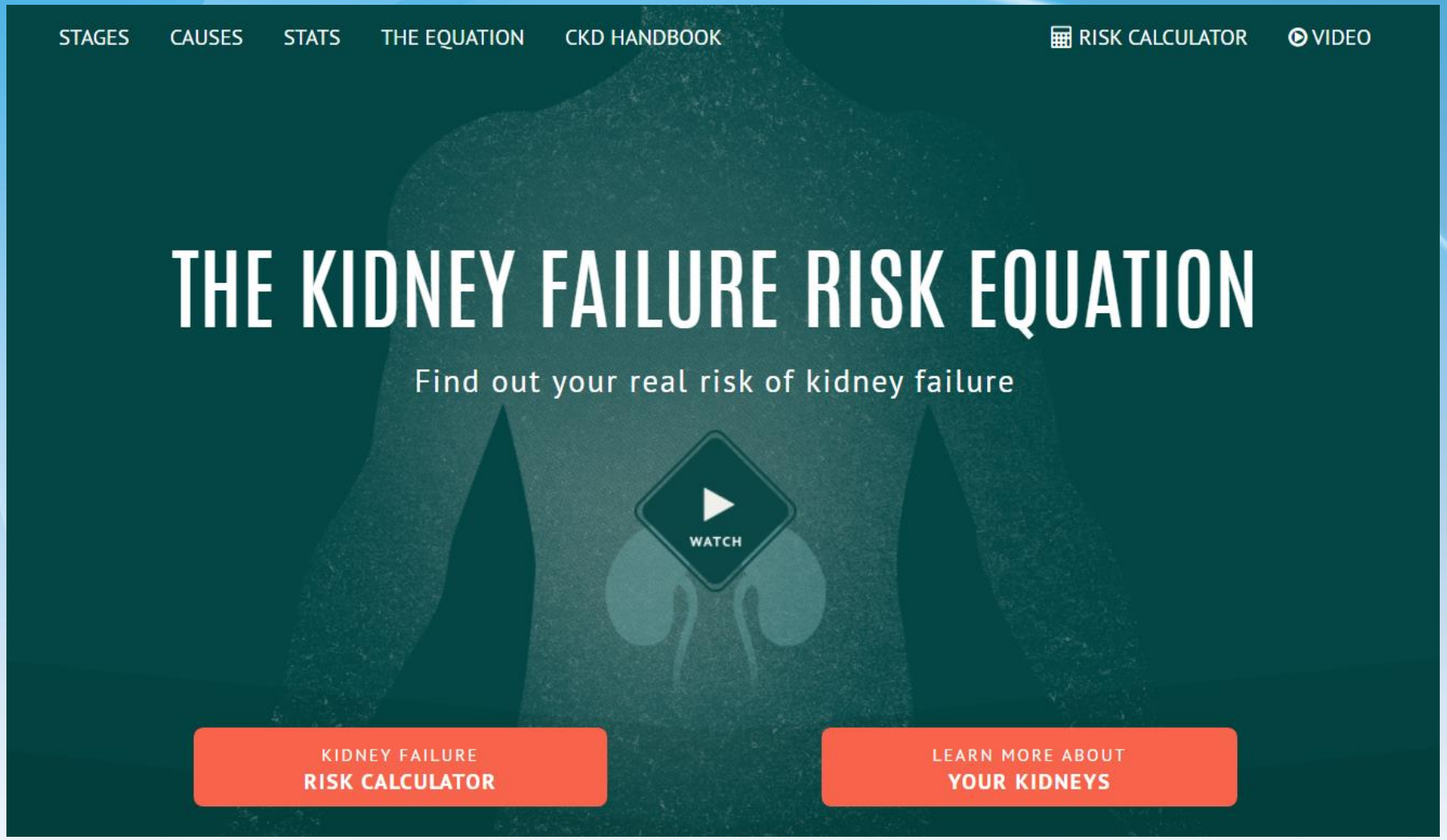
Physical examination	Abdominal findings	Bruit (atherosclerotic renal artery stenosis, fibromuscular dysplasia), distended bladder, flank pain
	Cardiovascular findings	Heart failure, ventricular hypertrophy
	Carotid bruit	Carotid artery disease
	Decreased peripheral pulses	Peripheral vascular disease
	General findings	Cushingoid appearance, edema
	Increased blood pressure and weight	Hypertension, obesity
	Musculoskeletal findings	Arthritis, synovitis
	Ophthalmoscopic findings	Hypertensive or diabetic retinal disease
	Skin changes	Rash and skin changes in autoimmune disease or neurofibromatosis

Laboratory tests	Abnormal serum and urine protein electrophoresis	Amyloidosis, light chain deposition disease, multiple myeloma
	Decreased serum complement levels C3 and C4	Cryoglobulinemia, lupus nephritis, membranoproliferative glomerulonephritis, poststreptococcal glomerulonephritis
	Dysmorphic urinary red blood cells or red blood cell casts	Immunoglobulin A nephropathy, rapidly progressive glomerulonephritis
	Eosinophiluria	Atheroembolic disease, tubulointerstitial disease
	Positive antiglomerular basement membrane antibody test	Antiglomerular basement membrane–associated rapidly progressive glomerulonephritis, Goodpasture syndrome
	Positive antineutrophil cytoplasmic antibody test	Granulomatosis with polyangiitis, microscopic polyangiitis, pauci-immune rapidly progressive glomerulonephritis
	Positive antinuclear antibody test	Lupus nephritis
	Positive cryoglobulin test	Cryoglobulinemia
	Positive hepatitis B serology*	Membranoproliferative nephritis, membranous nephropathy
	Positive hepatitis C serology*	Mixed cryoglobulinemia, membranoproliferative glomerulonephritis, membranous nephropathy
	Positive HIV serology*	Focal and segmental glomerulosclerosis

Ultrasonography	Doppler ultrasonography	May be useful in investigation of venous thrombosis, less so in arterial stenosis
	General findings	May show nephrocalcinosis, discrete stones, hydronephrosis, cysts,† or masses
	Increased echogenicity	May indicate cystic disease or medical renal disease
	Large kidneys	Generally indicate tumors, infiltrating diseases, or diseases causing nephrotic syndrome, including diabetic nephropathy
	Size disparities and scarring	Suggest vascular, urologic, or tubulointerstitial diseases due to stones or infection
	Small hyperechoic kidneys	Generally indicate long-standing CKD



https://kidneyfailurerisk.com/



More on proteinuria…

- Proteinuria is most commonly **Albumin**
- Also
  - Immunoglobulins
  - Myoglobin
  - Hemoglobin
  - Low Molecular weight proteins secreted by nephron

Quantification of Proteinuria: Urine Dip-stick

- 1+ corresponds to 30 mg of protein/dL
- 2+ corresponds to 100 mg/dL,
- 3+ corresponds to 300 mg/dL,
- 4+ corresponds to 1,000 mg/dL

But this isn't necessarily reliable: A dilute urine will underestimate the degree of albuminuria.

Evaluating Proteinuria

- 24-hour urine collection
  - challenges in feasibility, accuracy, and patient adherence
    - How do you actually collect this?
- Spot urine protein-creatinine
  - measures all proteins present in the urine
  - may be elevated in systemic or intrinsic renal diseases
- Spot urine albumin-creatinine ratio
  - measures only albumin in the urine
  - helpful in evaluating for diabetic kidney disease
    - Mid stream, early morning, no menses/infection/strenuous exercise…

Urine albumin-creatinine ratio

- Albuminuria is one of the earliest indicators of diabetic kidney disease
- ADA Recommends annual assessment
- type 1 diabetes mellitus of 5 years' duration
- type 2 diabetes starting at the time of diagnosis
  - Why is there a difference in the recommendations between type 1 and type 2?

Urine Albumin

Urine Collection Method	Normal	Moderately Increased Albuminuria (Microalbuminuria)	Severely Increased Albuminuria (Macroalbuminuria)
24-Hour Excretion	<30 mg/24 h	30-300 mg/24 h	>300 mg/24 h
Spot Urine Albumin-Creatinine Ratio[a]	<30 mg/g ≈ <30 mg/24 h	30-300 mg/g ≈ 30-300 mg/24 h	>300 mg/g ≈ >300 mg/24 h

Urine albumin-creatinine ratio

- The diagnosis of moderately increased albuminuria (microalbuminuria) in patients with diabetes is made when
- 2-3 random (morning, mid-stream) samples over 6 months

- ACE-I or ARB's in these patients has been shown to delay progression of CKD

- ACP recommends against further screening for albuminuria because it will not significantly influence management decisions

What is postural proteinuria?

- 3-5% of apparently healthy young adults (<30 years old).
- How do you figure this out?

What else can cause protein in the urine?

- Strenuous exercise
- CHF
- Cold exposure
- Fever
- Menses
- UTI

Proteinuria more broadly…

1. Functional proteinuria
    1. Acute illness
    2. Exercise
    3. Orthostatic proteinuria
2. Overload proteinuria
    1. Monoclonal gammopathy
    2. Plasma cell myeloma
    3. rhabdomyolysis
3. Glomerular proteinuria
    1. Damage to epithelial foot processes… (ex. DM nephropathy)
4. Tubular proteinuria
    1. Faulty resorption of protein (ATN, lead, Wilson disease, fanconi…)

Causes of Proteinuria

Transient

Dehydration

Exercise

Fever

Malignant hypertension

Orthostatic proteinuria

Preeclampsia

Seizure

Stress

Primary glomerular

Focal segmental glomerulosclerosis

Immunoglobulin A or IgM nephropathy

Membranoproliferative glomerulonephritis

Membranous nephropathy

Minimal change disease

Secondary glomerular

Allergic (e.g., antitoxins, poison ivy or oak, stings, venomous bites)

Collagen vascular diseases (e.g., IgA vasculitis, Sjögren syndrome, systemic lupus nephritis)

Drugs (e.g., contrast media, heroin, lithium, NSAIDs)

Genetic (e.g., Alport syndrome, Fabry disease, sickle cell disease)

Infection (e.g., hepatitis B and C, HIV, malaria, poststreptococcal, syphilis)

Metabolic (e.g., amyloidosis, diabetes mellitus, thyroid disease)

Neoplastic (e.g., carcinomas, leukemia/lymphoma, multiple myeloma)

Tubular (typically nonalbumin dominant, < 2 g per day)

Acute tubular necrosis

Drugs (e.g., lithium, NSAIDs)

Fanconi syndrome

Heavy metals (e.g., copper, lead, mercury)

Renal transplant rejection

Tubulointerstitial nephritis

Overflow disorders

Hemoglobinuria

Multiple myeloma

Myoglobinuria

So to review thus far…

- If you're thinking about the kidneys…
  - How long has what's been going on been going on?
  - What are possible diagnoses?
    - What conditions do they have?
      - DM, HTN, HIV, HCV, SLE, sarcoid, amyloidosis etc.
    - What does the person look like?
      - Arthralgia? Obesity? Rashes? Stigmata?
  - Check the urine.
  - Check the GFR (BMP)

Diabetic Kidney Disease: Diagnosis, Treatment, and Prevention

Kathryn McGrath, MD, Sidney Kimmel Medical College at Thomas Jefferson University Hospital, Philadelphia, Pennsylvania
Rina Edi, MD, University of California, San Diego, California

Globally, approximately 20% of the 400 million individuals with diabetes mellitus have diabetic kidney disease (DKD). DKD is associated with higher cardiovascular and all-cause morbidity and mortality, so timely diagnosis and treatment are critical. Screening for early DKD is best done with annual spot urine albumin/creatinine ratio testing, and diagnosis is confirmed by repeated elevation in urinary albumin excretion. Treatment includes management of hyperglycemia, hypertension, hyperlipidemia, and cessation of tobacco use. Multiple antihyperglycemic medications, including sodium-glucose cotransporter-2 inhibitors, glucagon-like peptide-1 receptor agonists, and dipeptidyl-peptidase-4 inhibitors, may help prevent DKD by lowering blood glucose levels and through intrinsic renal protection. Blood pressure should be monitored at every clinical visit and maintained at less than 140/90 mm Hg to prevent microvascular changes. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers prevent progression of DKD and may decrease albuminuria. Statin therapy should be considered for all patients with DKD, and tobacco cessation reduces the risk of DKD. Given the complexity of the disease and the risk of poor outcomes, patients who progress to stage 3 DKD or beyond may benefit from referral to nephrology subspecialists. (*Am Fam Physician*. 2019;99(12):751-759. Copyright © 2019 American Academy of Family Physicians.)

of kidney damage, consideration should be given to the possibility of other causes of an elevated urine albumin/creatinine ratio *(Table 3)*.[9,11] Because of this variability in urinary albumin excretion, two of three urine albumin/creatinine ratio specimens collected over a three- to six-month period must be abnormal (30 mg albumin per g creatinine to 300 mg albumin per g creatinine) before diagnosis of microalbuminuria can be made.[9] Macroalbuminuria (more than 300 mg per g) on a single sample can confirm diagnosis in the absence of complicating factors[11]

Chief Complaint(s):

HPI:

Renal insufficency

Pt. w/ history of microalbuminuria:.

Current Medication:

Medical History:

Allergies/Intolerance:

ROS:

Objective:

Vitals:

Past Results:

Examination:

Assessment:

Assessment:

- Microalbuminuria - R80.9 (Primary)

Plan:

Treatment:

Microalbuminuria

Notes: Repeat after avoiding heavy exercise, high protein meal, menses (if applicable), and UTI. If still w/ albuminuria then check first-void spot urine twice within 3-6 months. If of 3 tests positive consider start of ACE-I or ARB, and if >300 then referral to nephrology.

CKD Definition (KDIGO)

- Markers of Kidney Damage
  - Abnormal proteinuria
  - Abnormal urine sediment (e.g. hematuria)
  - Electrolyte abnormalities from tubular dysfunction
  - Structural abnormality
  - Histological abnormality
  - Transplant
- +/- Reduced GFR <60 mL/min/1.73 m^2
- Greater than 3 months

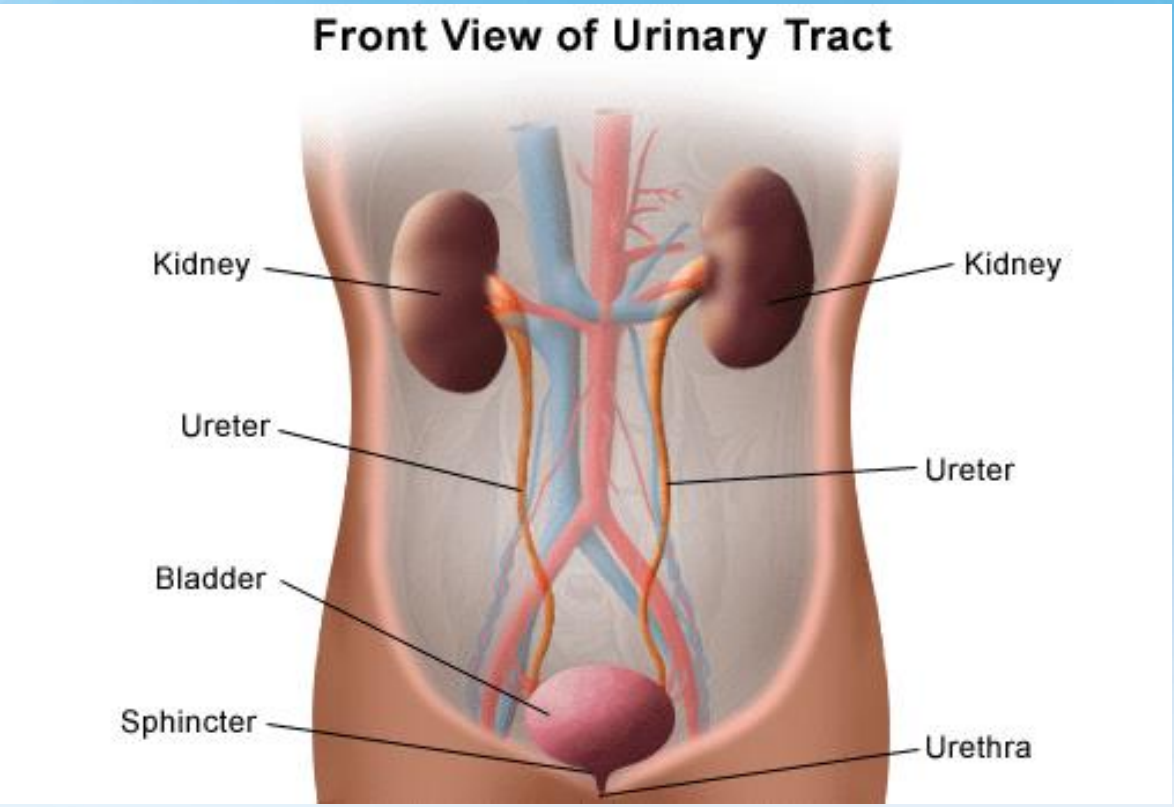
Stages of CKD

Stage	<60 mL/min/1.73 m^{2}Description	GFR (ml/min/1.73m^2)
1	Kidney damage with normal or ↑ GFR	≥90
2	Kidney damage with mild ↓ in GFR	60-89
3	Moderate ↓ GFR	30-59
4	Severe ↓ GFR	15-29
5	Kidney Failure	<15 or dialysis

GFR categories (mL/min/1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g	30-300 mg/g	>300 mg/g
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red: very high risk.

What are the bad things that can happen to the kidney?



- Pre-renal:
  - Decreased intravascular volume
    - Dehydration
    - Burns
    - Diarrhea and vomiting; sweating
    - CHF, sepsis, anaphylaxis
    - Renal artery occlusion
- Renal:
  - Everything under the sun…
- Post-renal:
  - Blockage:
    - Urethral block
    - Stones
    - Cancer
    - Clots, sloughed tissue

Diagnosis of CKD cause

Acute kidney injury (unresponsive to initial management)*

Anemia of CKD

Family history of kidney disease

Presence of red blood cell casts in the urine

Progression of CKD†

Management of CKD complications

Anemia of chronic kidney disease when hemoglobin < 10 g per dL (100 g per L)

CKD and refractory hypertension

Mineral and bone disorder of CKD

Persistent abnormalities in serum potassium

Persistent elevated albuminuria (albumin/creatinine ratio > 300 mg per g [> 30 mg per mmol]) or refractory proteinuria (urinary protein/creatinine ratio > 500 to 1,000 mg per g [> 50 to 100 mg per mmol])

Recurrent nephrolithiasis or concern for nephrocalcinosis

Preparation for renal replacement therapy

GFR < 30 mL per minute per 1.73 m^2 (KDIGO GFR categories G4 and G5)

Case…

- 35-year-old man seen 3/7/19, history of HIV, hypertension, and alcohol abuse; presents feeling as though he had the flu, lightheaded.
- Medications: TAF/FTC, dolutegravir, hydrochlorothiazide-lisinopril 12.5/10, rosuvastatin 40 (h/o TG>1000).
- Blood pressure 89/57, heart rate 117, no acute distress.
- What would you do?

Case…

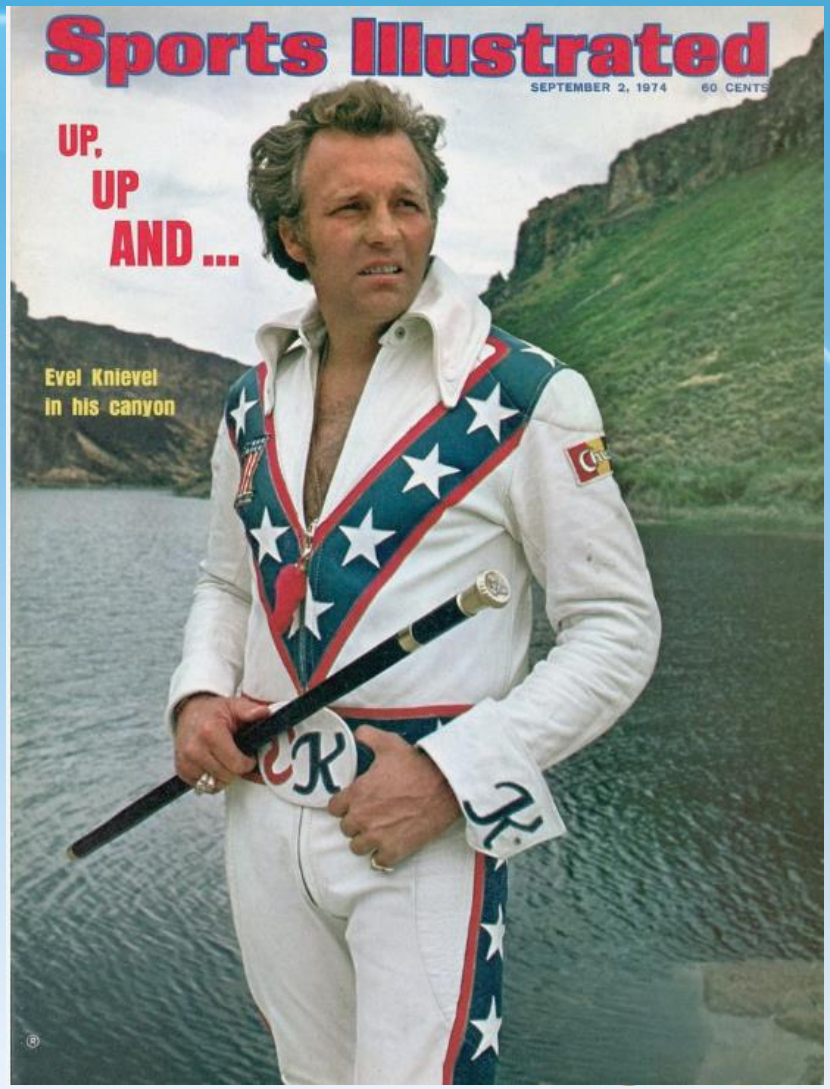
- 35-year-old man…
- 3 days later admitted to the hospital.
- Creatinine 16.4
- BUN 85
- GFR 3
- potassium 3.7
- ALT 143, AST 300
- alkaline phosphatase 505
- CK 1590
- hemoglobin 11.6
- phosphorus 6.6

So what was he feeling?

Clinical Manifestations

- Often asymptomatic until eGFR is <30 and/or when nephrotic-range proteinuria (>3500 mg/g)
- eGFR <30 = Fatigue, signs of volume overload, hypertension, and/or pruritus
- eGFR <10 to 15 (stage G5) overt symptoms of uremia, including fatigue, anorexia, nausea, vomiting, confusion, uremic pericarditis, malaise, asterexis, confusion, seizures, irritability, insomnia, restless legs, decreased libido, menstrual irregularity, metallic taste in the mouth…

- 35-year-old daredevil with a fondness for red bull and motorcycle racing.
- Do screen him for kidney disease?



Screening

- The American College of Physicians (ACP): recommend against screening for CKD in asymptomatic adults
- USPSTF: concludes that there is insufficient evidence for screening for CKD in asymptomatic adults without risk factors for CKD
- The American Society of Nephrology: screening all adults for CKD, including, but not limited to, those with a family history of kidney disease and adults with diabetes, hypertension, or cardiovascular disease

Screening: KDOQI (Kidney Disease Outcomes Quality Initiative)

Individuals at increased risk for CKD should be tested at the time of a health evaluations to determine if they have chronic kidney disease. Including

- Diabetes (type 2)
- Hypertension
- Autoimmune diseases
- Systemic infections
- Exposure to drugs or procedures associated with acute decline in kidney function
- Recovery from acute kidney failure
- Age > 60 years
- Family history of kidney disease
- Reduced kidney mass (includes kidney donors and transplant recipients)

Comorbid conditions associated with increased risk of CKD

- Diabetes mellitus
- Hypertension
- Cardiovascular disease
- Infection with HIV or hepatitis C
- Obesity

Monitoring

- **The ratio of protein or albumin to creatinine in spot urine samples should be monitored in all patients with chronic kidney disease
- Estimated GFR should be monitored yearly in patients with chronic kidney disease, and more frequently in patients with:
- GFR <60 mL/min/1.73 m^2
- Fast GFR decline in the past (≥ 4 mL/min/1.73 m^2)
- Risk factors for faster progression
- Ongoing treatment to slow progression
- Exposure to risk factors for acute GFR decline

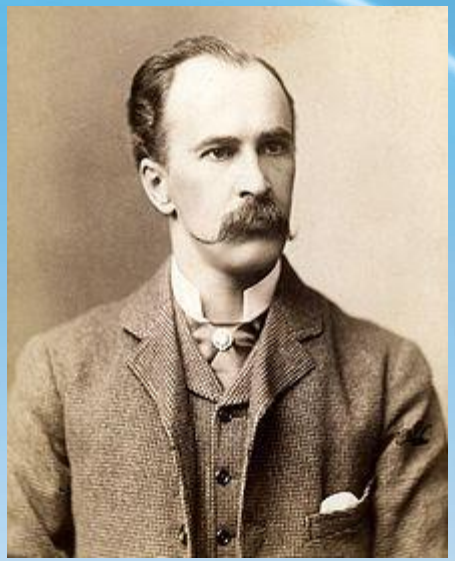
Monitoring (KDOI)

- Patients with GFR <60 mL/min/1.73 m^2 should be evaluated and treated for complications of decreased GFR. This includes measurement of:
  - Anemia (hemoglobin);
  - Nutritional status (dietary energy and protein intake, weight, serum albumin, serum total cholesterol);
  - Bone disease (parathyroid hormone, calcium, phosphorus);
  - Functioning and well-being (questionnaires).

Case: chess piece

45 year old man, h/o DM, HTN, orthostatic hypotension, peripheral and autonomic neuropathy, homelessness and Stage G5 A3 CKD, not on dialysis.

What do you want to know?



Creatinine 6.4, BUN 64, GFR 9

K 3.8, calcium 7.9, phos. 5.5, vit. D 13

Ferritin 41, hgb 9.5

PTH 2,183

Started on calcitriol 0.5 mcg twice a week, ergocalciferol 50,000 units weekly

Cardiovascular Disease

- The most common cause of death in patients with CKD :
  - 80% of pts w/ CKD die before dialysis, most due to CVD
  - Of pts on HD, 45% die of CVD
    - Why is that???

- Increasingly recognized that CKD is one of the strongest risk factors for cardiovascular morbidity and mortality

- They should be considered in the "highest risk group" for evaluation and management according to established guidelines.
  - Regardless of levels of "traditional" risk factors

Blood Pressure Management

- Blood pressure should be monitored in all patients with CKD.
- JNC 8 recommends a blood pressure target goal of <140/90 mm Hg ; others recommend <130/80
- The JNC 8 recommends ACE inhibitors or ARBs as first-line therapy for hypertension in most patients with CKD
  - black patients without proteinuria, treatment options include a diuretic, calcium channel blocker, ACE inhibitor, or ARB
  - What about HCTZ? What about furosemide and spironolactone?

–This Clinical Resource gives subscribers additional insight related to the Recommendations published in–

trc pharmacist's letter ™ trc prescriber's letter ™ trc pharmacy technician's letter ™ trc nurse's letter ™

August 2018 ~ Resource #340806

Chronic Kidney Disease Checklist

Control Blood Pressure and Manage Cardiovascular (CV) Disease

- ☐ Slow progression of chronic kidney disease (CKD) by controlling blood pressure.[2]
  - A goal of **<140/90 mmHg** is appropriate for many patients with CKD.[2,3,10]
  - Some experts recommend a goal of **<130/80 mmHg** for CKD patients with albuminuria (all patients with diabetes [Canada]).[1,10]
  - An ACEI or ARB is preferred for CKD patients with high blood pressure AND albuminuria.[4,10]
- ☐ Manage cholesterol with a statin and use daily aspirin 81 mg, especially in patients with CV disease, unless otherwise contraindicated.[2]

Reduce Albuminuria

- ☐ Reduce albuminuria (defined as ≥300 mg/g creatinine [Canada: albumin-to-creatinine ratio ≥2 mg/mmol]), especially in patients with diabetes.[2,4,17]
- ☐ Use an angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB).[3,4,10]
  - Avoid combining an ACEI with an ARB in the same patient.[3,10]
  - Monitor patients taking an ACEI or ARB for hyperkalemia (potassium [K^+] >5 mEq [mmol]/L).[8]
  - Limit dietary potassium intake and consider diuretics or potassium binders to keep K^+ <5 mEq (mmol)/L.[2,8,9]
- ☐ Discuss weight loss goals with patients, as weight loss may slightly reduce albuminuria.[2,6]
  - Provide our patient handout, *Tips for Getting to a Healthy Weight*.

Blood Pressure Management

- All things ACE and ARB…

- 45 year old man, CKD G3a A2, on amlodipine 5, furosemide 20, spironolactone 25.
- In the past on lisinopril 10 but stopped due to potassium of 7.3.

Dyslipidemia

- Current KDIGO (Kidney Disease Improving Global Outcomes) guidelines recommend treatment with statins for patients over age 50 years with an eGFR <60 mL/min/1.73 m^2 and/or albuminuria.

- Recently published guidelines from the American College of Cardiology/AHA recommend that all patients with stages 1 through 5 CKD not on dialysis be treated with statin therapy independent of their cholesterol levels (contested)

CKD Mineral and Bone Disorder

- As kidney function declines, the normal homeostasis of calcium and phosphorus levels by the kidney becomes compromised resulting in alterations in bone mineralization
  - Renal osteodystrophy
    - Osteitis fibrosa cystica
    - Adynamic bone disease
    - osteomalacia

- Calcium and phosphorus homeostasis is regulated primarily by three hormones:
  - parathyroid hormone (PTH)
  - vitamin D
  - fibroblast growth factor 23 (FGF-23) – <u>from osteoclasts</u>

Chronic Kidney Disease-Mineral and Bone Disorder

- Increased FGF-23 and decreased nephron mass reduce the conversion of 25-hydroxy vitamin D to 1,25-dihydroxy vitamin D by renal tubular cells

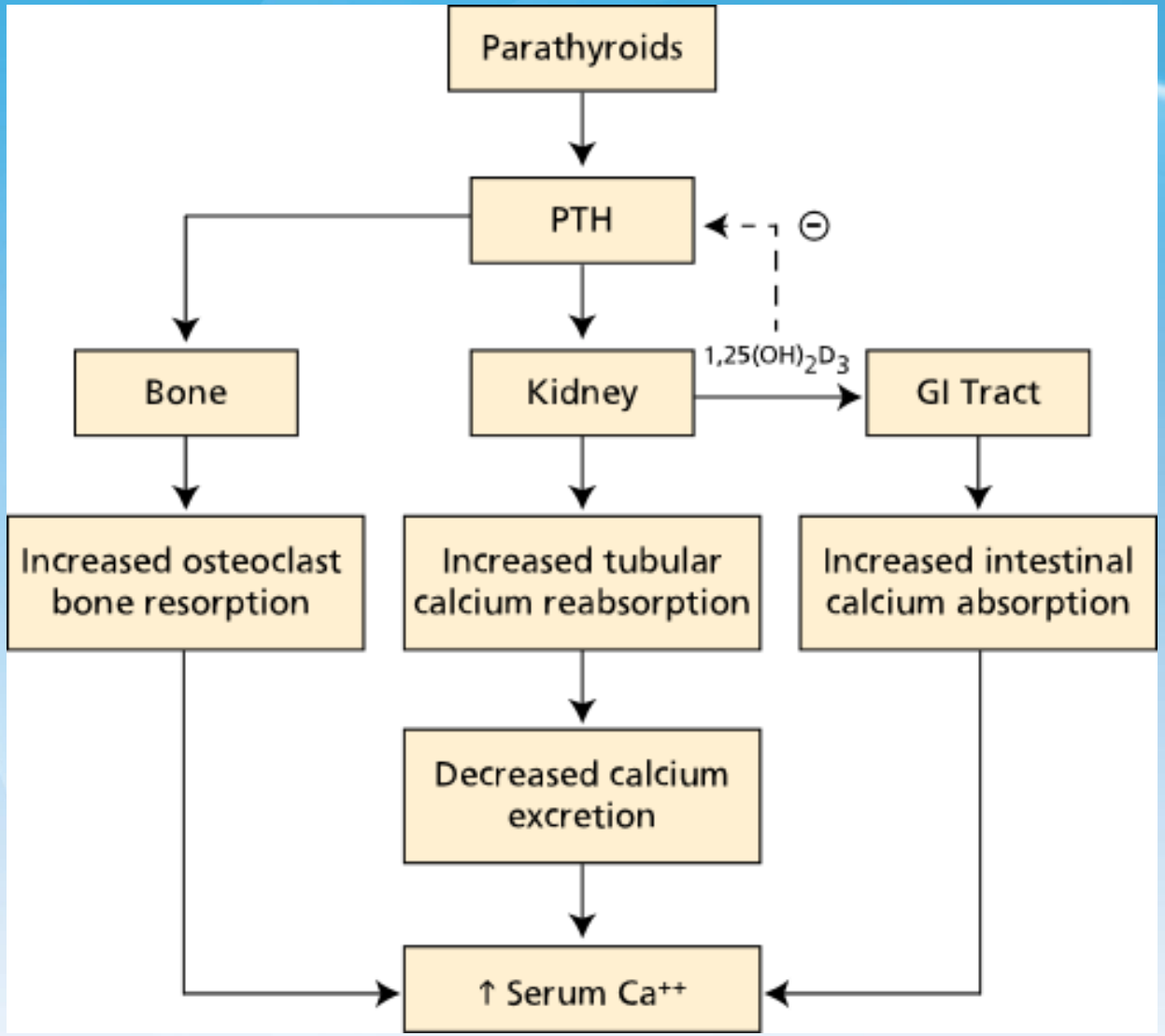
- Reduction in 1,25-dihydroxy vitamin D levels results in lower intestinal absorption of calcium and phosphorus and increased PTH production by the parathyroid glands.

- Increased PTH from CKD is referred to as *secondary hyperparathyroidism*

- Increased PTH levels cause:
  - reduced calcium excretion
  - increased phosphorus excretion

- This activate osteoclasts, resulting in bone resorption

- as CKD progresses, the kidney is unable to compensate for the increased release of phosphorus from bone, and phosphorus levels rise. This results in a vicious cycle as phosphorus stimulates PTH


Parathyroids
PTH
⊖
Bone
Kidney
1,25(OH)2D3
GI Tract
Increased osteoclast bone resorption
Increased tubular calcium reabsorption
Increased intestinal calcium absorption
Decreased calcium excretion
↑ Serum Ca++

CKD-MBD Assessment

- Serum Ca+ and Phos+ levels typically remain in the normal range until the eGFR drops below 20-30 mL/min/1.73 m^2
  - Hyperphosphatemia occurs
  - Metastatic calcification
  - Hypocalcemia due to poor Vitamin D conversion

- KDIGO guidelines recommend monitoring calcium, phosphorus, intact PTH, and vitamin D levels in patients with an eGFR <60 mL/min/1.73 m^2 (stages G3-G5).

CKD-MBD Management

- In patients with an eGFR <60 mL/min/1.73 m^2 not on dialysis, KDIGO guidelines suggest attempting to normalize PTH
  - correct 25-hydroxy vitamin D deficiency and normalize the serum calcium and phosphorus
    - this eliminates the stimulus for PTH secretion

- If PTH levels remain elevated (goal is 2-5 x's ULN in ESRD) after correction of 25-hydroxyvitamin D deficiency, calcitriol or calcitriol analogues may be used
  - Calcitriol = 1,25 Vit D analogue

CKD-MBD Management

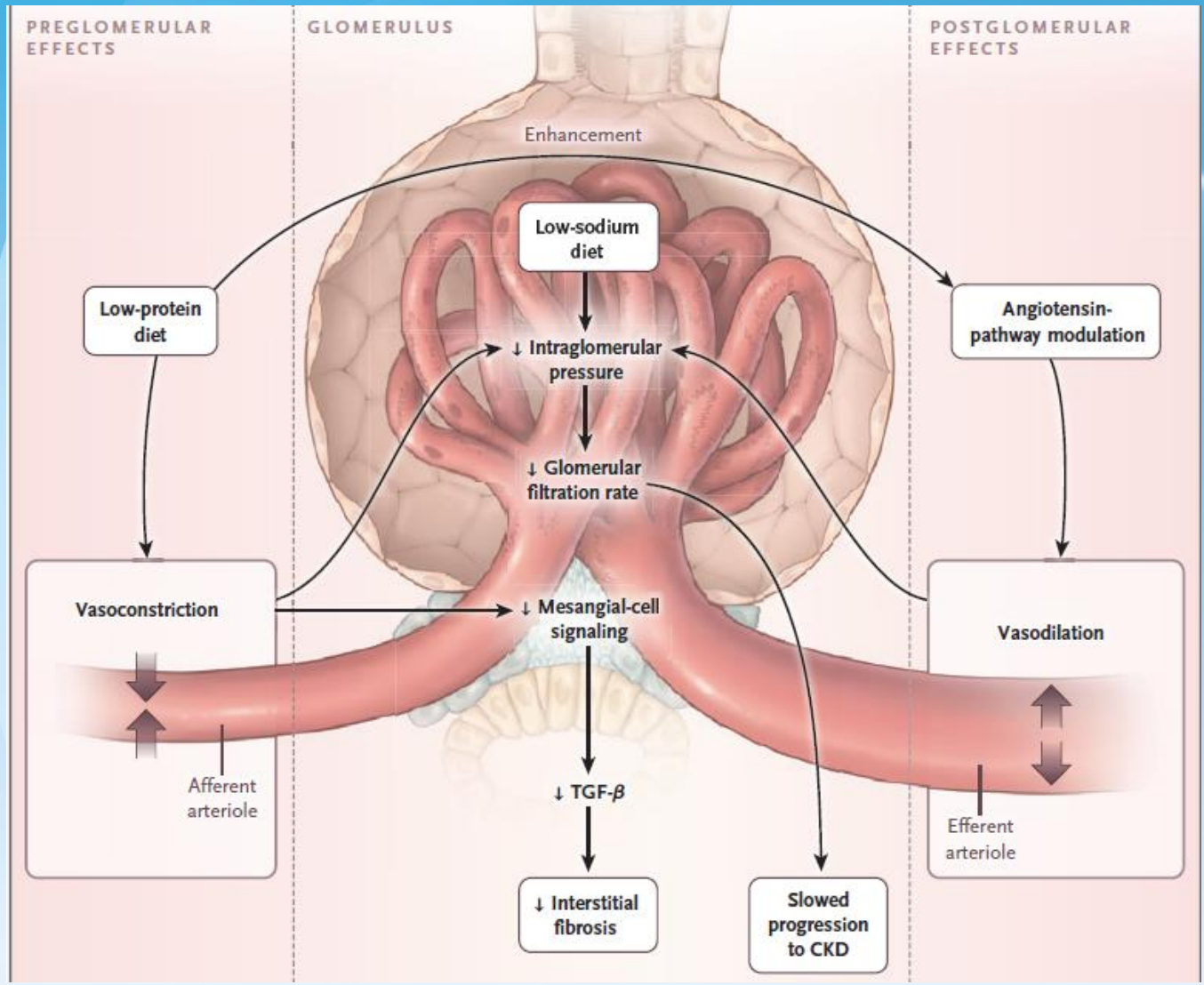
- Hyperphosphatemia is an important complication in patients with an eGFR <30 mL/min/1.73 m^2,
  - severity is directly associated with mortality
- Patients with CKD and hyperphosphatemia should be counseled regarding a low phosphate diet, and most patients require phosphate binders.
- So… what is a low phosphate diet?

CKD-MBD Management

- So… what is a low phosphate diet?
  - Avoid processed foods and colas
  - Limit eggs, dairy, nuts, beans and meat (which is a catch-22 as you also need to support protein intake)
    - Likely decrease animal sources most, as more bioavailable

<2 g/d sodium, sometimes fluid restriction

Nutritional therapy



CKD-MBD Management

- And what are possible phosphate binders?
- Choose…

A. Aluminum hydroxide
B. Calcium carbonate
C. Calcium acetate
D. Sevelamer carbonate
E. Sevelamer hydrochloride
F. Lanthanum carbonate

CKD-MBD Management

- Tertiary hyperparathyroidism results from prolonged (PTH) stimulation
  - results in increased calcium levels and severe hyperparathyroid hyperplasia and elevated PTH levels
  - does not respond to phosphate binders and calcitriol therapy
  - often require **parathyroidectomy**

Anemia in CKD

- The prevalence of anemia increases as CKD progresses due to several factors:
  - impaired erythropoietin production
  - erythropoietin resistance
  - reduced erythrocyte life span

Anemia in CKD

- CKD-related anemia is normocytic
- There is no specific test to establish the diagnosis.
  - KDIGO recommendations suggest maintaining transferrin saturation levels of >30% and serum ferritin levels of >500 ng/mL (at least >200, no higher than 800)
- Although erythropoietin levels are often decreased in patients with CKD, there is little evidence to support the utility of measuring erythropoietin levels in patients with CKD.

Anemia in CKD

- As the eGFR declines below 30 mL/min/1.73 m^2 (stages G4-G5), anemia can become symptomatic. Erythropoiesis-stimulating agents (ESAs) are highly effective in raising hemoglobin concentrations and alleviating symptoms
  - Expensive, associated with thromboembolic events and tumor progression in patients with malignancy

Avoidance of Nephrotoxins

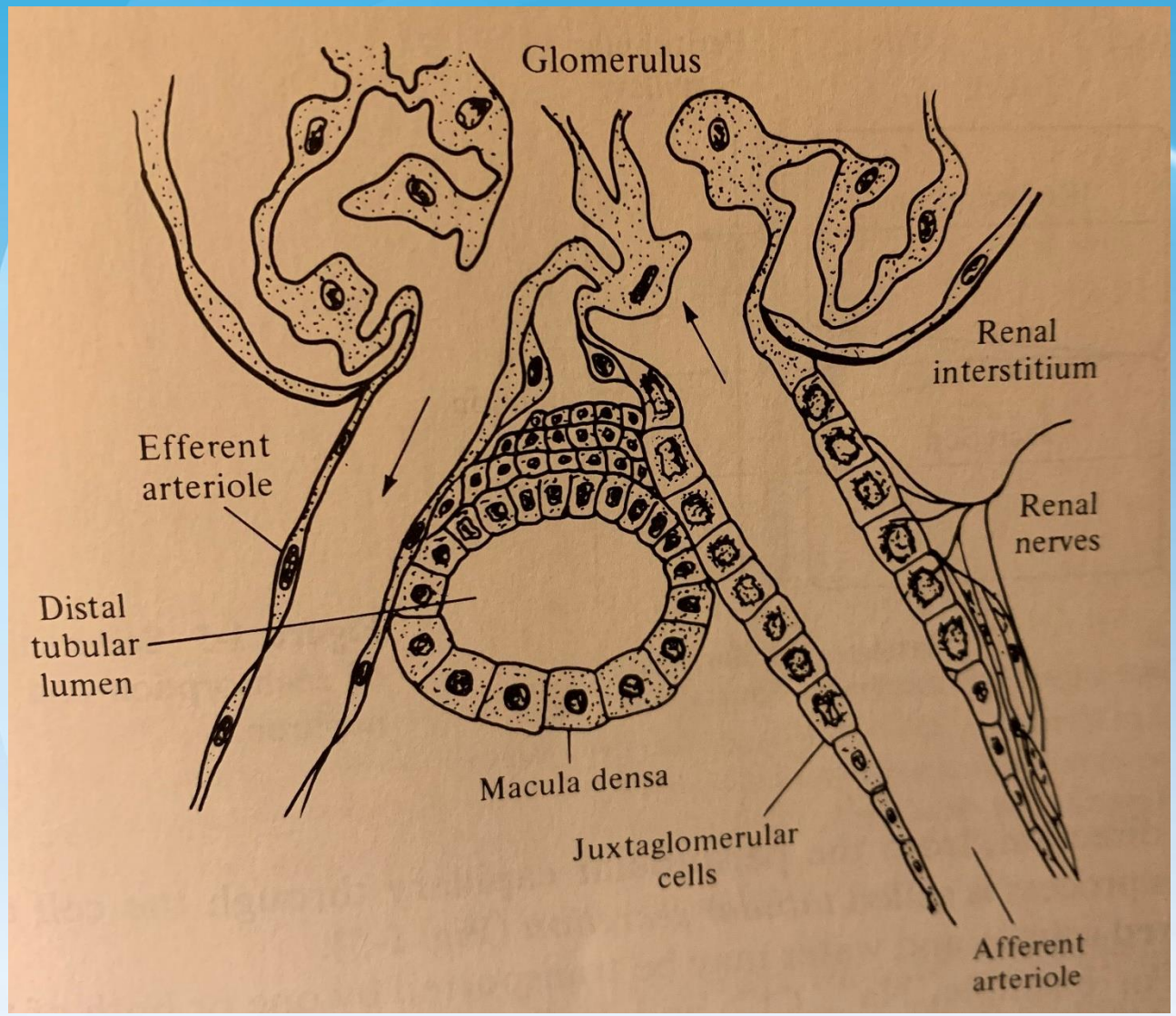
- Alteration in kidney blood flow
  - NSAIDS
  - ACEI
  - Cyclosporine
  - Radiocontrast agents
- Direct tubular injury
  - Aminoglycosides
  - Radiocontrast
  - Amphotericin B
- Allergic interstitial nephritis
  - NSAIDS
  - PCNs
  - Cephalosporins
  - Sulfonamides
- Intratubular obstruction
  - Acyclovir
  - Sulfonamides

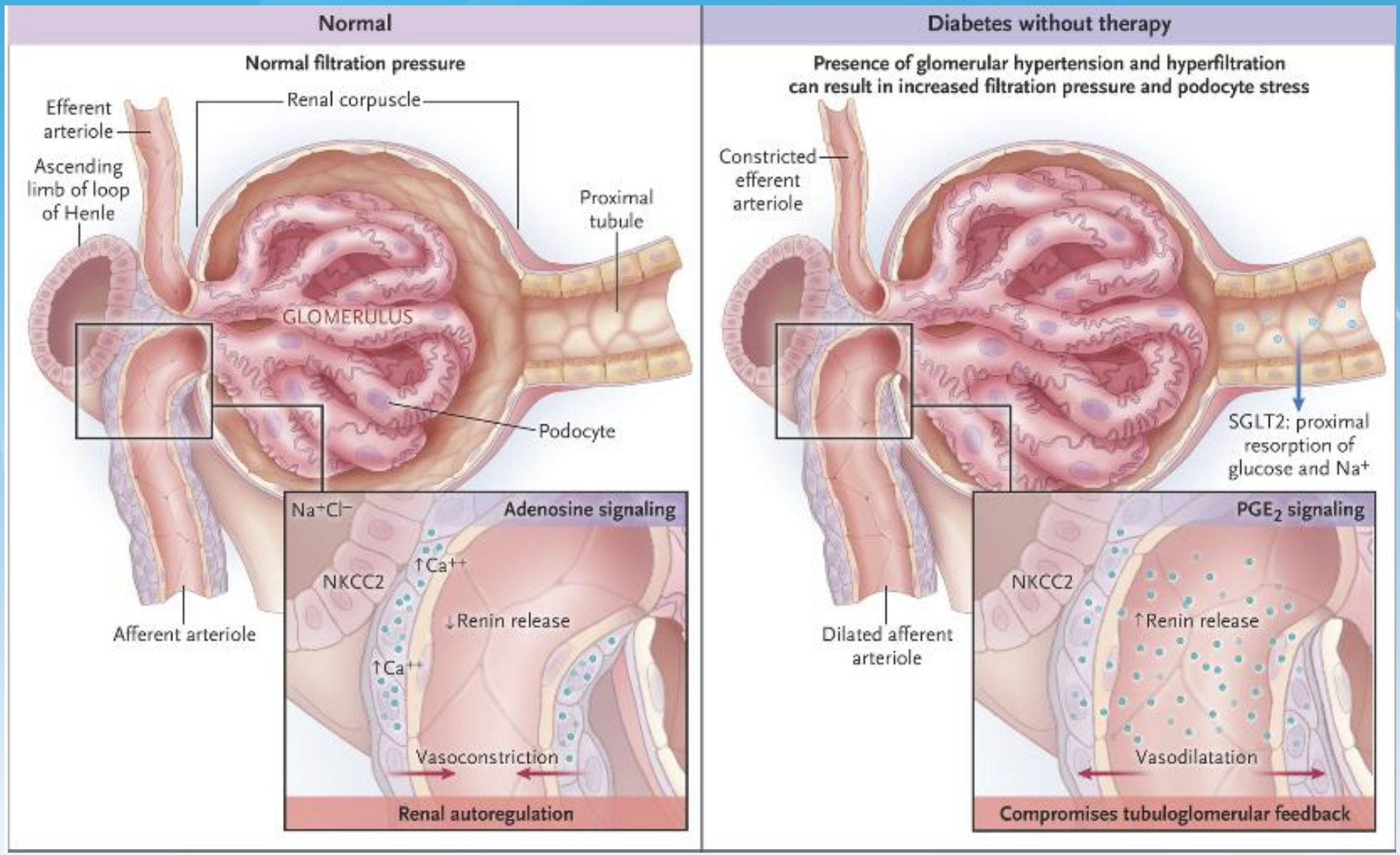
Analgesics	NSAIDs (including COX-2 inhibitors)	AKI; hyperkalemia; increased blood pressure
Vasoconstricting decongestants	Pseudoephedrine; ephedrine; phenylephrine; oxymetazoline	Increased blood pressure
Laxatives	Magnesium hydroxide	Hypermagnesemia
	Sodium phosphate (oral or enema)	Hyperphosphatemia
Antacids	Aluminum hydroxide	Aluminum toxicity; osteomalacia
	Magnesium hydroxide	Hypermagnesemia
	Sucralfate	Aluminum toxicity
Nutritional supplements	Creatine	Fluid overload; factitious increase in creatinine; AKI (rarely)
	Germanium	AKI
	Salt substitutes	Hyperkalemia
Herbal remedies	Aristolochia/aristolochic acid	AKI; chronic tubulointerstitial fibrosis
	Ephedra (ma huang)	Increased blood pressure; myocardial infarction; stroke; AKI

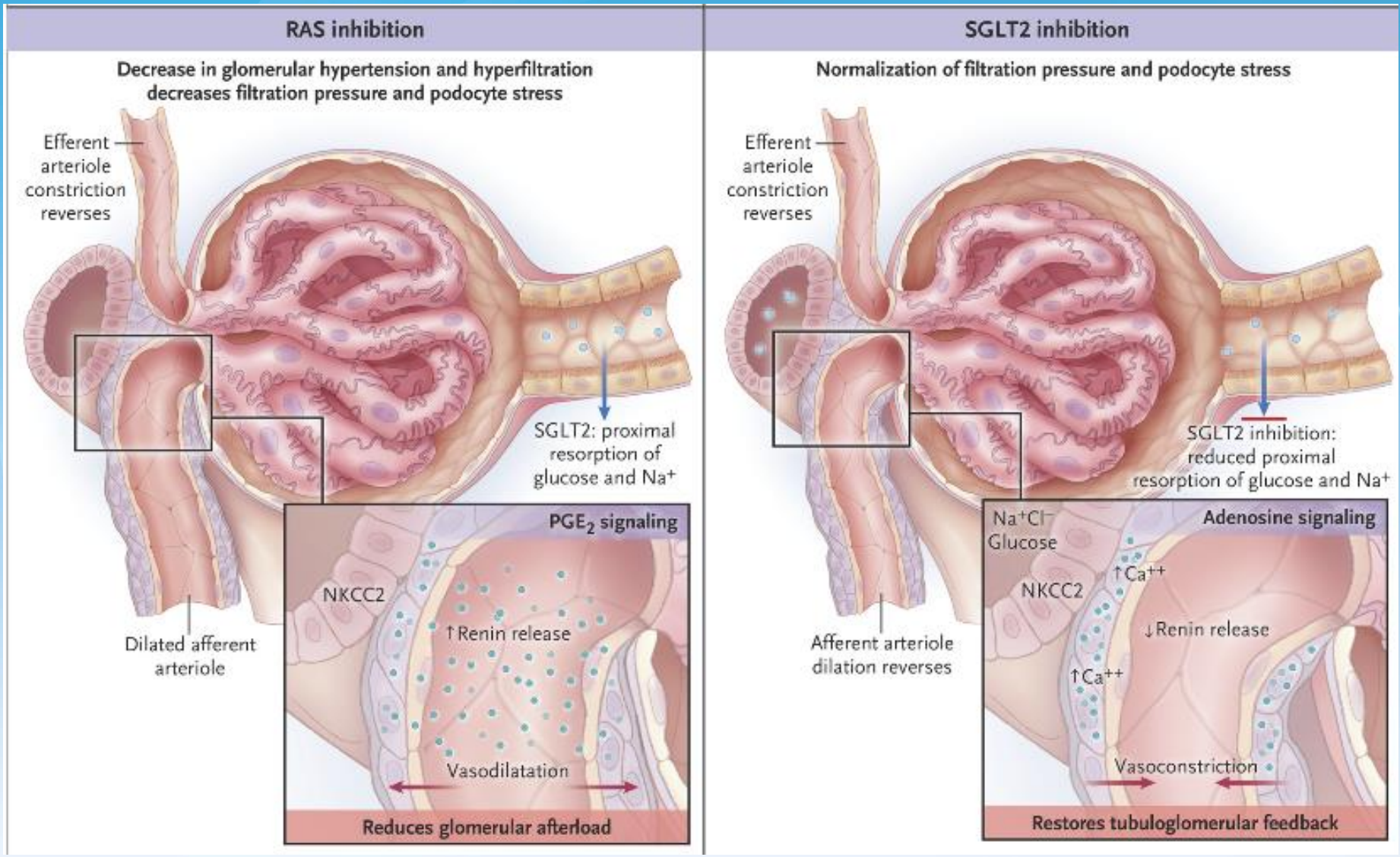
Proteinuria

- The severity of proteinuria is strongly associated with adverse clinical outcomes, including progression of CKD to ESRD, cardiovascular morbidity, and mortality

- ACE inhibitors or ARBs decrease proteinuria and slow the progression of proteinuric kidney diseases
  - associated with increased risk of hypotension and hyperkalemia if not used cautiously


Glomerulus
Renal interstitium
Efferent arteriole
Renal nerves
Distal tubular lumen
Macula densa
Juxtaglomerular cells
Afferent arteriole


Normal
Normal filtration pressure
Efferent arteriole
Renal corpuscle
Ascending limb of loop of Henle
Proximal tubule
GLOMERULUS
Podocyte
Afferent arteriole
Na+Cl−
Adenosine signaling
NKCC2
↑Ca++
↓Renin release
↑Ca++
Vasoconstriction
Renal autoregulation
Diabetes without therapy
Presence of glomerular hypertension and hyperfiltration can result in increased filtration pressure and podocyte stress
Constricted efferent arteriole
SGLT2: proximal resorption of glucose and Na+
Dilated afferent arteriole
PGE2 signaling
NKCC2
↑Renin release
Vasodilatation
Compromises tubuloglomerular feedback


RAS inhibition
Decrease in glomerular hypertension and hyperfiltration decreases filtration pressure and podocyte stress
Efferent arteriole constriction reverses
SGLT2: proximal resorption of glucose and Na+
Dilated afferent arteriole
PGE2 signaling
NKCC2
↑Renin release
Vasodilatation
Reduces glomerular afterload
SGLT2 inhibition
Normalization of filtration pressure and podocyte stress
Efferent arteriole constriction reverses
SGLT2 inhibition: reduced proximal resorption of glucose and Na+
Afferent arteriole dilation reverses
Na+Cl−
Glucose
Adenosine signaling
↑Ca++
NKCC2
↓Renin release
↑Ca++
Vasoconstriction
Restores tubuloglomerular feedback

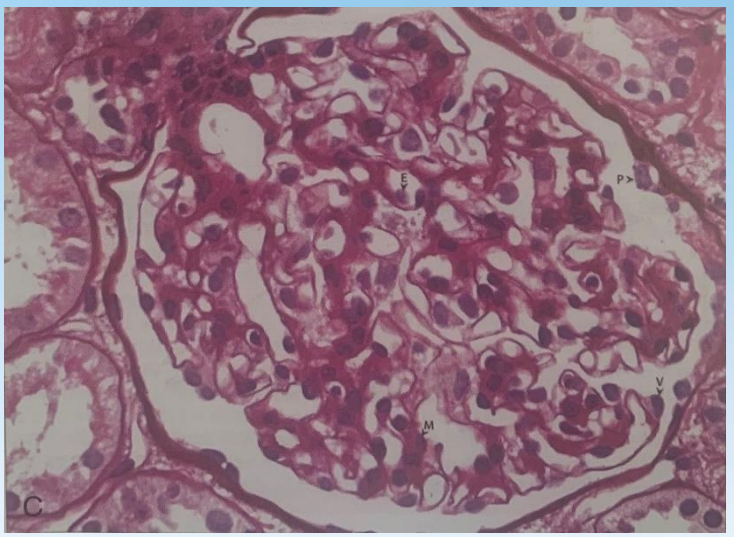
Vaccination

- CDC guidelines:
  - All susceptible patients with CKD should be vaccinated against hepatitis B virus.
  - Patients with CKD should also receive the 23- and 13-valent pneumococcal vaccines, with revaccination with the 23-valent vaccine after a minimum of 5 years. Or, now, the PCV 20 (one and done).
  - The influenza vaccine should be administered annually to patients with CKD

    - should only receive the inactivated influenza vaccine due to the risks associated with the live vaccine in immunocompromised patients.

Glomerular Disease

- Glomerular disease should be suspected when:
  - proteinuria and/or hematuria are seen on urinalysis.
  - nephrotic-range proteinuria
  - dysmorphic erythrocytes and erythrocyte casts in the urine sediment



Glomerular Disease

- may be limited primarily to the kidney but frequently occurs secondary to other systemic conditions including infectious and auto-immune Causes:
  - Diabetic Nephropathy
  - Hypertensive nephrosclerosis
  - poststreptococcal GN
  - HIV-associated glomerulopathy
  - hepatitis C–associated cryoglobulinemic GN
  - Systemic lupus erythematosus
  - IgA vasculitis and pauci-immune small-vessel vasculitis

Nephrotic Syndrome

- characterized by a urine protein excretion of >3500 mg/24h or a urine protein-creatinine ratio of >3500 mg/g that may be accompanied by hypoalbuminemia, edema, and hyperlipidemia.

- Diabetes mellitus is the most common cause of the nephrotic syndrome in adults

Nephritic Syndrome

- Associated with glomerular inflammation with evidence of hematuria, variable proteinuria, and sometimes leukocytes in the urine sediment; it may be associated with edema, hypertension, and kidney failure.

When to Refer

- Preparation for kidney replacement therapy (dialysis and transplantation), as well as vascular access care, should be initiated when the estimated GFR declines to <30 mL/min/1.73 m^2.

- Because AVF placement can be technically challenging and may require several months for full maturation, referral to an experienced surgeon many months before dialysis is initiated

When to Refer

- Assistance with management of Hyperparathyroidism and CKD-BMD
- Refractory Hypertension
- Severe Anemia unresponsive or unable to tolerate oral supplements
  - To consider ESA or IV iron
- Suspicion for Glomerulonephritis and need for kidney biopsy

Dialysis

- **Hemodialysis**
  - three times a week during 3.5- to 4-hour in-center sessions and what does that feel like?
- **Peritoneal Dialysis**
  - dialysate is intermittently instilled into the peritoneal cavity via an indwelling catheter
  - excess water and solutes are removed by osmosis and diffusion across the peritoneal membrane
  - Peritonitis is one of the most important complications
  - Provides more patient autonomy but requires training and ability to manage at home

Quick Case

- 56 year old woman on hemodialysis, not a transplant candidate, requests a mammogram.
- What do you do?

Renal biopsy

Indications:

- AKI and CKD questions
- Unexplained protein or heme
- Previously identified and tx'd lesions, to guide therapy
- Check on renal involvement in SLE, GBM disease etc…
- Transplant rejection

Contraindications

- Uncorrected bleeding disorder
- Uncontrolled HTN
- Renal infection
- Neoplasm
- Hydronephrosis

And maybe…

- Horseshoe kidney
- ESRD
- Multiple cysts
- Solitary kidney

Renal biopsy

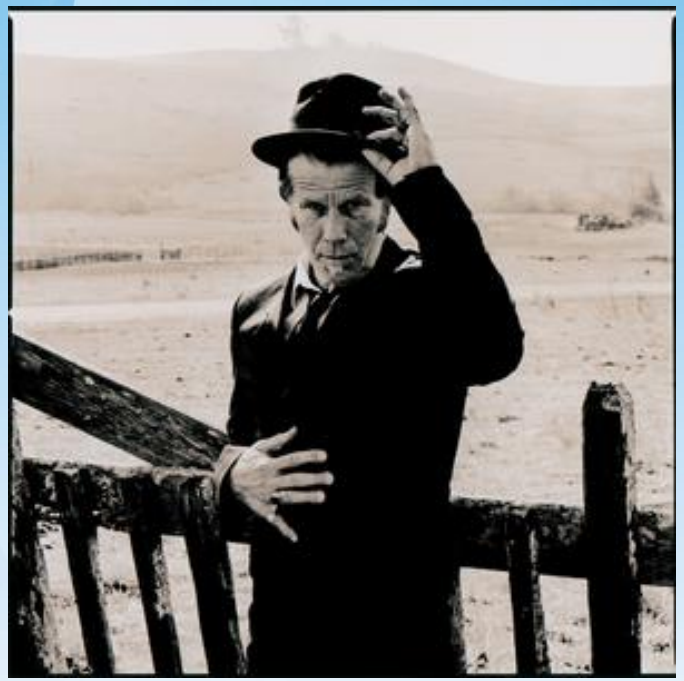
- Hold anticoagulation for 5-7 days after
- Most w/ hematuria, 1 in 10 w/ macroscopic hematuria
- 1% need a transfusion
- 0.06-0.08% die

Renal transplant

- Average wait for transplant is 2-6 years
- Survival rates: 1 and 5 years
  - Living donor: 95% and 80%
  - Cadaveric donor: 89% and 66%
- v. HD (5 year survival rate of 40%)

Not Quick Case

- 70 year old man with history of hypertension and CKD.



Past Medical History

Heart murmur.

Smoking, since 16 years old, 6/19 (maybe 2 cigarettes a month) - quit as of 12/19.

Hypertension.

Gout, 12/13.

Alcohol history.

Anemia.

chronic kidney disease, stage G3b A3 (9/16), G4 (11/18: GFR 29), 2/19 (39), 12/19 (< 30; w/ potassium of 6.5), 10/20 (22), 4/21 (23), 11/21 (11), 1/22 (26), 6/22 (21).

BPH s/p TURP; thickened bladder wall, seen by urology 6/19 (declined cystoscopy) and recommendation to see them again in 1 year, 4/21 (denies hematuria).

Remote facial injury w/ titanium reconstruction of right zygomatic arch (hit w/ a hatchet).

Myelitis w/ left leg weakness, 7/15.

HCM: HCV screen, 1996 (negative), 5/16 (negative).

HCM: HIV screen, 3/14 (negative).

HCM: PSA, 3/14 (1.2).

HCM: GFR, 3/14 (26), 10/15 (38), 5/16 (37), 5/17 (39), 7/17 (39), 3/18 (45), 11/18 (29), 2/19 (39), 10/20 (22), 4/21 (23), 2/23 (19).

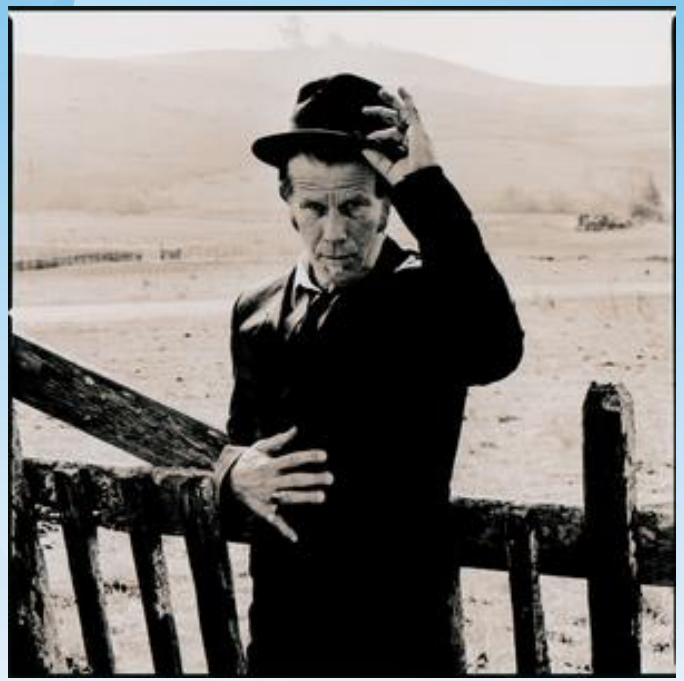
HCM: lipids, 10/15 (178/41/98), 2/17 (190/40/124), 3/18 (167/41/100; ASCVD 26%)).

HCM: microalbumin/cr, 5/16 (1406: seen by nephrology), 5/17 (>300), 3/19 (993), 12/19 (706), 4/21 (455).

HCM: FOBT, 6/17 (cards given twice; pt. declines further), 10/17 (declines), 5/18 (cards given), 6/18 (states sent in; no results; declines any further efforts), 9/18 (same), 12/19 (negative), 4/21 (cards given).

Not Quick Case

- 70 year old man with history of hypertension and CKD.



WBC	4.2 3.8-10.8 Thousand/uL
RBC	3.02 L 4.20-5.80 Million/uL
Hemoglobin	8.9 L 13.2-17.1 g/dL
Hematocrit	27.1 L 38.5-50.0 %

eGFR	19 L > OR = 60 mL/min/1.73m2
Glucose	132 65-139 mg/dL
Urea Nitrogen	38 H 7-25 mg/dL
Creatinine	3.30 H 0.70-1.28 mg/dL
BUN/Creatinine Ratio	12 6-22 (calc)
Sodium	135 135-146 mmol/L
Potassium	5.5 H 3.5-5.3 mmol/L
Chloride	106 98-110 mmol/L
Carbon Dioxide	20 20-32 mmol/L

Ferritin	132 24-380 ng/mL

Phosp. 4.0
PTH 58
Vit. D 50

u/s: hyperechoic small kidneys c/w medical renal disease

Question 1

- A 77-year-old woman is evaluated 4 months following a left middle cerebral artery ischemic stroke. The severity of her stroke required prolonged initial hospitalization and a 3-month stay in a rehabilitation center before returning home. Residual deficits include dense right-sided hemiparesis and dysphagia requiring oral feeding with thickened liquids. Medical history is otherwise significant for hypertension and diabetes mellitus. Current medications are aspirin, chlorthalidone, lisinopril, tolterodine, and insulin.
- On physical examination, temperature is 37.2 °C (99.0 °F), blood pressure is 136/86 mm Hg, and pulse rate is 86/min. BMI is 18. The general medical examination is unremarkable. Neurologic examination reveals dysarthria, left-sided facial droop, 1/5 strength in the right arm and leg, and bilateral distal sensory neuropathy

Hemoglobin A_{1c}	7.2%
Albumin	2.4 g/dL
Blood urea nitrogen	12 mg/dL (4 months ago: 28 mg/dL)
Creatinine	0.8 mg/dL (4 months ago: 1.4 mg/dL)
Urinalysis	Normal

Question 1

Which of the following is the most likely cause of this patient's decreased serum creatinine level?

1. Decreased Muscle Mass
2. Improvement in Diabetic Kidney Disease
3. Inititiation of Chlorthalidone
4. Initiation of Lisinopril

Question 2

- A 65-year-old man is evaluated during a follow-up visit for stage G3b/A3 chronic kidney disease due to diabetic nephropathy. He reports doing well with good baseline exercise tolerance and no shortness of breath. Medical history is also significant for type 2 diabetes mellitus and hypertension. Medications are basal bolus insulin and lisinopril, 20 mg/d.
- On physical examination, temperature is normal, blood pressure is 145/75 mm Hg, pulse rate is 82/min, and respiration rate is 16/min. BMI is 28. There is no jugular venous distention. The lungs are clear
- Kidney ultrasound shows mildly echogenic kidneys that are of normal size with no obstruction

Question 2

Bicarbonate	Normal
Creatinine	1.9 mg/dL
Potassium	4.0 mEq/L (4.0 mmol/L)
Estimated glomerular filtration rate	42 mL/min/1.73 m^2
Urine protein-creatinine ratio	3900 mg/g

Question 2

Which is the most appropriate Management?

1. Add an ARB
2. Increase Lisinopril Dose
3. Replace Lisinopril with Amlodipine
4. No Change to Medications

Question 3

- A 45-year-old man is evaluated during an annual routine health maintenance visit. History is notable for type 2 diabetes mellitus (diet controlled) diagnosed 3 months ago. Family history is significant for his father who developed end-stage kidney disease due to diabetes at age 68 years. He reports no symptoms and takes no medications.
- On physical examination, temperature is 37.0 °C (98.6 °F), blood pressure is 135/78 mm Hg, pulse rate is 70/min, and respiration rate is 12/min. BMI is 31. Cardiac examination reveals no murmur or gallop. The lungs are clear. There is 1+ peripheral edema.
- Laboratory studies show a serum creatinine level of 1.0 mg/dL (88.4 µmol/L).

Question 3

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

1. Measure urine albumin excretion
2. Order kidney ultrasonography
3. Perform dipstick urinalysis
4. Start an angiotensin receptor blocker

Question 4

- A 54-year-old woman is evaluated during a follow-up visit for stage G4/A3 chronic kidney disease due to diabetic nephropathy. She is asymptomatic except for mild fatigue and peripheral edema and reports a good appetite. Medications are ramipril, furosemide, and calcium acetate.
- On physical examination, temperature is 37.0 °C (98.6 °F), blood pressure is 128/73 mm Hg, pulse rate is 80/min, and respiration rate is 14/min. BMI is 29. Pallor and pale mucous membranes are noted. There is no jugular venous distention. There is no pericardial friction rub. The lungs are clear. There is no asterixis. Neurologic examination is normal.
- Laboratory studies are significant for a serum creatinine level of 2.6 mg/dL (229.8 µmol/L) and an estimated glomerular filtration rate of 19 mL/min/1.73 m^2 (1 year ago: 30 mL/min/1.73 m^2).
- After discussing the goals of care, the patient wishes to explore renal replacement options and kidney transplantation.

Question 4

- **Which of the following is the most appropriate management?**

1. Nephrologist referral now
2. Nephrologist referral in 6 months
3. Repeat creatinine measurement in 2 weeks
4. Continue current management

Question 5

- A 61-year-old woman is evaluated during a routine health maintenance visit. She has no symptoms or concerns at this time. She has stage G4/A1 chronic kidney disease due to autosomal dominant polycystic kidney disease and a 22-year history of hypertension. Medications are fosinopril, furosemide, and sodium bicarbonate.
- On physical examination, temperature is 37.0 °C (98.6 °F), blood pressure is 129/72 mm Hg, pulse rate is 84/min, and respiration rate is 14/min. BMI is 28. Bilateral flank fullness is noted. The lungs are clear. There is no peripheral edema

Calcium	9.0 mg/dL High
Creatinine	2.8 mg/dL
Phosphorus	3.5 mg/dL Normal
Intact parathyroid hormone	450 pg/mL Very High
25-Hydroxy vitamin D	42 ng/mL High

Question 5

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

1. Bisphosphonate therapy
2. Dual-energy x-ray absorptiometry scan
3. Oral calcitriol
4. Parathyroidectomy

Question 6

- A 60-year-old man is evaluated during a routine visit. He has stage G4/A3 chronic kidney disease due to membranous glomerulopathy. He received treatment with cyclosporine and prednisone and received rituximab 2 years ago. Current medications are lisinopril, atorvastatin, furosemide, and calcium carbonate/vitamin D. He received the complete hepatitis B immunization series, pneumococcal polysaccharide, tetanus and diphtheria combined with acellular pertussis, and influenza immunizations 6 months ago.
- On physical examination, vital signs are normal. BMI is 27. The remainder of the examination is noncontributory.

Question 6

Which of the following is an appropriate approach to pneumococcal vaccination in this patient?

1. Administer the pneumococcal conjugate vaccine now
2. Administer the pneumococcal conjugate vaccine in 6 months
3. Administer the pneumococcal polysaccharide and pneumococcal conjugate vaccines in 6 months
4. Repeat the pneumococcal polysaccharide vaccine now