Drug Safety in Chronic Kidney Disease

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Disclosure

Advisory Board: AstraZeneca; CSL Vifor; Vera

Consultant: Bayer; Corcept; Mineralys; Novo Nordisk

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Learning Objectives

- Recognize risk factors for drug-related adverse events in patients with CKD
- Identify ways how drugs could lead to adverse events in patients with CKD
- Recognize commonly used drugs that require dose adjustment or use with caution in patients with CKD

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New Analysis Suggests Adverse Drug Events Are the 3rd Leading Cause of Death in USA

- American Society of Pharmacovigilance
- Prescribing errors, prescription drug overdoses, prescription drug misuse, drug-drug interactions, allergic reactions and adverse drug reactions
- 250,000 deaths/year

National Adverse Drug-Event Awareness Day: March 24, 2025

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Medication Errors

- Wrong Dose or Drug: Administering the incorrect amount of a drug or the wrong medication entirely.
- Wrong Route: Giving a drug via an inappropriate method, such as intravenously when it should be oral.
- Wrong Patient: Administering medications to the incorrect individual.
- Incorrect Prescription: Errors from hard-to-read physician prescriptions or those miscommunicated by staff.
- Omitted or Missed Dose: Failing to administer a prescribed medication.

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Adverse Drug Reactions (ADRs)

- Allergic Reactions: Ranging from mild hives (urticaria) to severe, life-threatening anaphylaxis
- Gastrointestinal Effects: Nausea, vomiting, and diarrhea are commonly reported ADRs
- Fatigue and Drowsiness: General feelings of tiredness and sleepiness
- Skin Reactions: Besides hives, other skin issues like hair loss(alopecia) are common in certain cancer treatments
- Drug-Drug Interactions: When two or more drugs interact, increasing the risk of harm or reducing effectiveness
- Drug Overdoses and Misuse: Inadvertent or Intentional misuse of prescription drugs
- Withdrawal: Occurs when a drug is discontinued, leading to symptoms like opioid withdrawal.

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Factors Influencing Events

- Patients age and health: Very young or old age, as well as compromised kidney or liver function, can increase susceptibility to adverse effects
- Hereditary Factors: Genetic variations can make some people more susceptible to a drugs toxic effects

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DRUG-RELATED ADVERSE SAFETY EVENTS IN CKD

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How Often? And Who's at Risk?

- Occurs in ~50% of patients with estimated GFR (eGFR) <60 ml/min
- Risk factors
  - Non-white
  - Older age
  - ACEi/ ARB use
  - Diabetes
  - More advanced CKD

Ginsberg JS, et al. *J Am Soc Nephrol* 2014.

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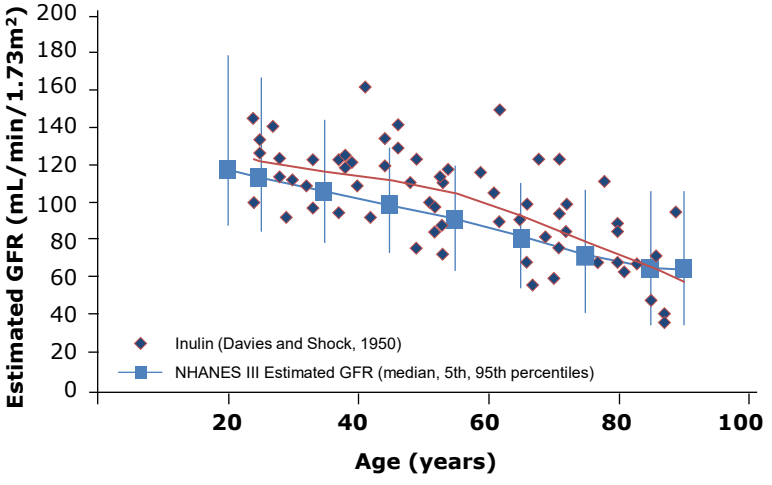
Estimated Glomerular Filtration and Normal Aging



Uremia, Ca-PO_4 imbalance, volume overload, oxidative stress, inflammation, anemia → incident CVD, CVD death

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Serum Creatinine Is Not a Good Measure of Estimated GFR!

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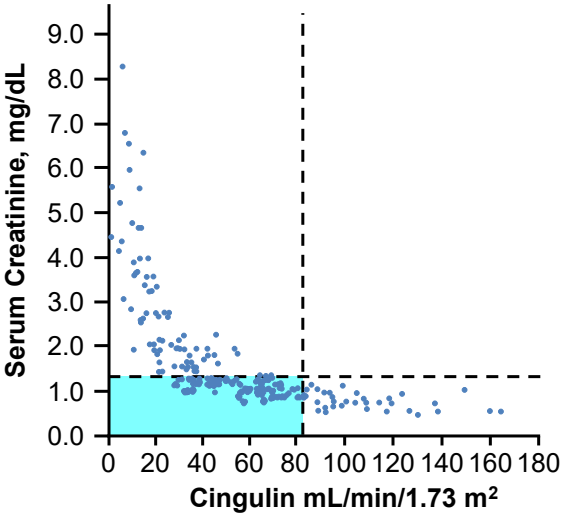
Serum Creatinine Is a Misleading Guide to GFR



N=117

Shemesh et al. *Kidney Int.* 1985;28:830-838.

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Rate of Adverse Drug Events in Ambulatory Patients with CKD

N=267	Rate (per 100 patients)*
PATIENT REPORTED	
Hypoglycemia	57.6
Falling/ severe dizziness	23.1
Nausea, vomiting ± diarrhea	21.1
Hyperkalemia	18.1
Confusion	16.9
DETECTED AT STUDY VISIT	
Hypoglycemia	8.3
Hyperkalemia	8.3
Bradycardia	6.4
*Adjusted for sociodemographics, comorbid conditions, GFR, and number of medications	

Adapted from Ginsberg JS, et al. *J Am Soc Nephrol* 2014.

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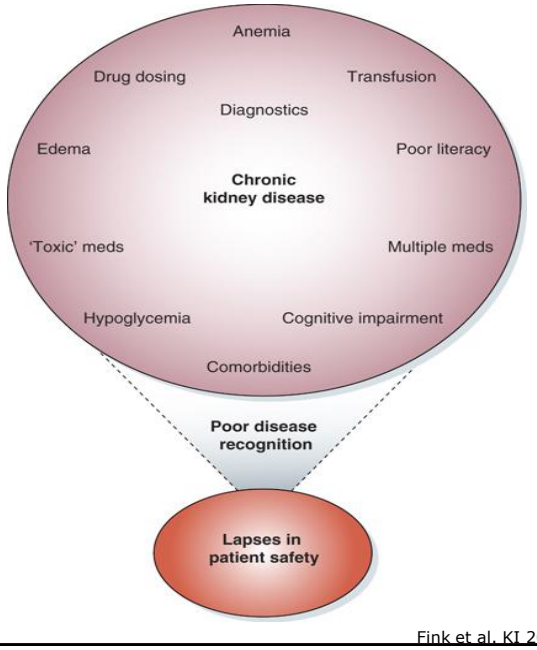
CKD and Medication Safety



Fink et al. KI 2009;76:1123–1125

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Medication Errors

- IOM Report in 1999: "To err is human: building a safer health system"
- Medical errors annually:
  - 1 million injuries
  - 98,000 deaths
- More than MVA, breast cancer, or AIDS causes / year
- 13% of hospitalized Medicare beneficiaries in 2008 experienced a medical care-related safety event.

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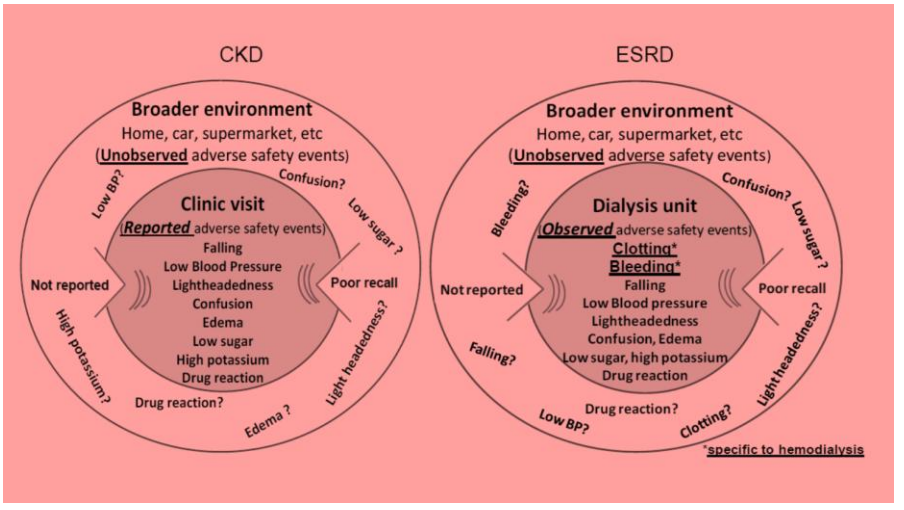
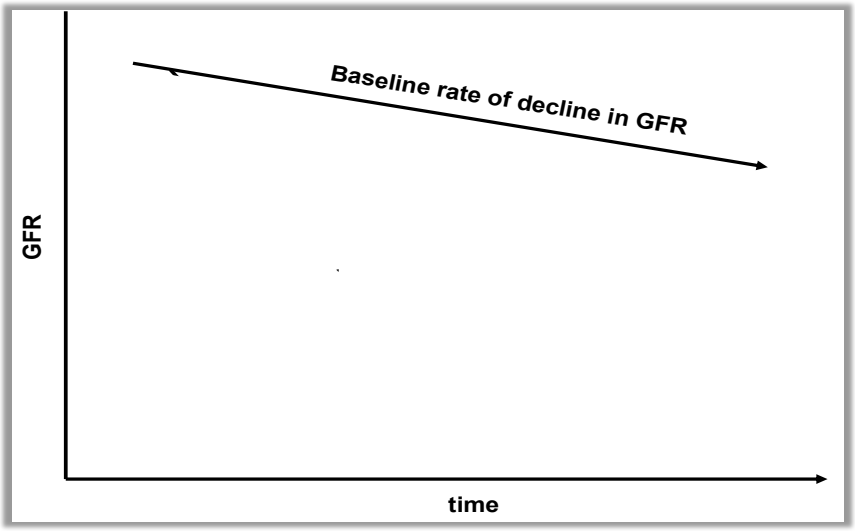
Does a Tree Falling in the Forest Make a Sound?



Weir M and Fink J. Curr Opin Nephrol Hypertens. 2014 May;23(3):306-13.

16

CKD Progression: Biology Versus "Latrogenesis"?



Fink, et al, AJKD, 2009

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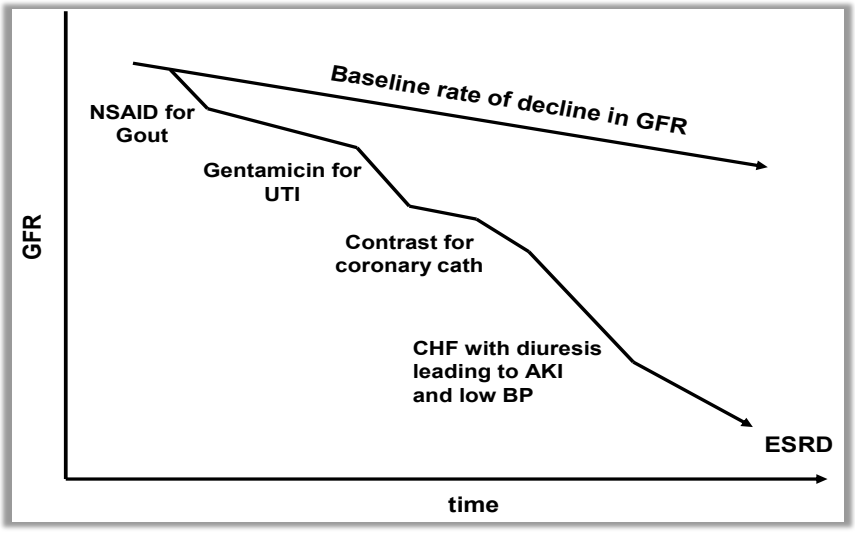
CKD Progression: Biology Versus "Latrogenesis"?



Fink, et al, AJKD, 2009

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Modes of Drug-Related Adverse Events in CKD

- Direct kidney injury
- Dosing error
- Drug-drug interaction

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Drug Elimination in CKD

- Adjustments usually needed when >25-30% of active drug/metabolite eliminated renally:
  - Azithromycin 5-12%
  - Moxifloxacin 15-21%
  - Pioglitazone (Actos) 15-30%
  - Ciprofloxacin 30-57%
  - Amoxicillin 50-70%
  - Digoxin 57-80%

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DRUGS TO AVOID IN CKD PATIENTS

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74 yo W Woman with Right Hip Pain. 2 Wks Earlier Scr was 1.3 mg/dl, eGFR of 43ml/min/1.73m2. Meds: Tramadol 50 mg qd, HCTZ 25 mg qd, Irbesartan 300 mg qd. Added Gabapentin 300 mg qd. Pain Continued and She Took OTC Ibuprofen 200 mg qid. Poor Po Intake. Fell and Was Admitted. BP 110/60 mmHg, HR 100. Scr ↑1.6 mg/dl Given IVF and Discontinued HCTZ .

Which Other Medication(s) Would You Stop For The AKI?

A. Irbesartan
B. Ibuprofen
C. Both irbesartan and ibuprofen
D. Tramadol

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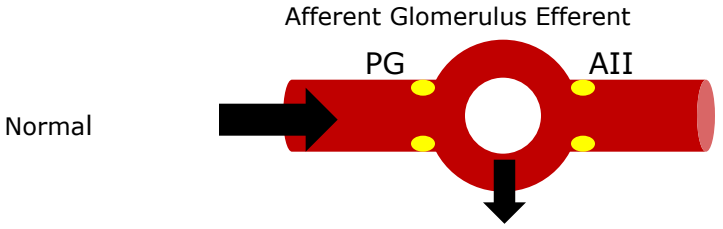

Baker M and Pezarella MA. Am J Kid Dis 2020;76:546-559

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NSAIDs

- Injure kidneys directly
  - Induce acute kidney injury (AKI) from “pre-renal” or ATN
  - Interstitial nephritis
  - Nephrotic syndrome
- Decrease kidney potassium excretion ⟶ hyperkalemia
- Decrease sodium excretion ⟶ HTN, edema

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NSAIDs

- Avoid in patients with:
  - CKD
  - Conditions that could lead to "pre-renal physiology" or dehydration
    - CHF
    - Cirrhosis
    - Renal artery stenosis
    - RAAS-blockade

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70 yo W Woman with HTN, DM, CKD. 3 Mo Ago - Scr 1.2 mg/dl, eGFR 42 ml/min/1.73m2, CO2 23 mEq/l, Urine Albumin to Creatinine Ratio (ACR) 320 mg/g. She Is Fatigued. Severely Constipated with ↓Oral Intake, But Now with Loose Stools After OTC Laxatives, But Not Dizzy. Meds: Losartan/HCTZ, Metformin. BP 136/70 mmHg (~ Baseline 140/80). Scr 4.0 mg/dl, CO2 21 mEq/l. You Call Her to Tell Her to Go to the ER and Ask About OTC NSAIDs.

What Do You Think Happened?

A. Progression of CKD
B. Too much RAAS blockade with too low target blood pressure
C. Metformin induced AKI
D. Phosphate containing laxatives

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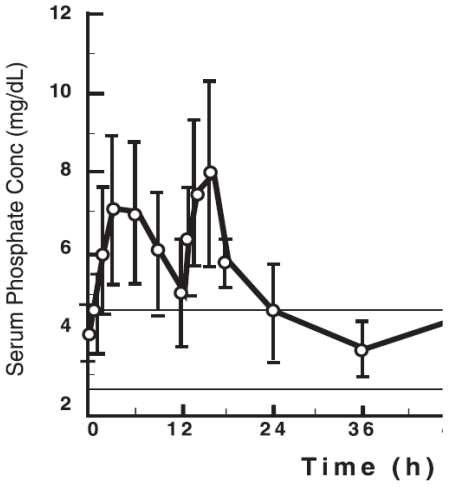
Oral Sodium Phosphate – Phosphate Content

	Phosphate content (mmol)
Osmoprep (32 tablets)	**345.6 mmol**
Visicol (40 tablets)	**432 mmol**
Fleets enema (133 ml)	**90 mmol**
Mean phosphate intake USA (men/women)	**48 / 33 mmol**



OSMOPREP **Package Insert**, 2007

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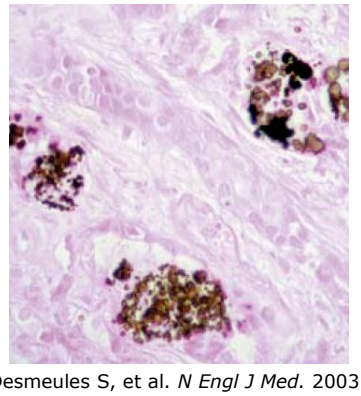
Oral Sodium Phosphate Preparations

- Hyperphosphatemia + volume depletion
- Acute Phosphate Nephropathy
  - Ca-phosphate deposits in tubules & interstitial
  - Leads to AKI/ CKD within days to months

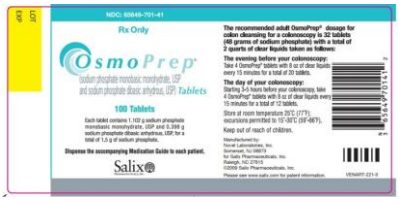


Desmeules S, et al. *N Engl J Med.* 2003

28

Sodium Phosphate Bowel Preparations

- 1/14/14 - FDA Blackbox warning for OTC oral sodium phosphate tablets: do not to take more than one dose/24 hours
- Risk Factors
  - Older age,
  - Impaired kidney function
  - Pre-renal state/ physiology
  - Decreased GI motility
  - ACEi, ARB or NSAID use



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Iodinated Contrast

- Leads to AKI
- Risk factors
  - CKD (esp. eGFR <30 ml/min/1.73m^2)
  - Diabetes, CHF, gout
  - Dehydration
  - Concurrent use of NSAIDs or RAAS-antagonists
  - High osmolality agents, large or repeated doses
  - Intra-arterial injection

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Iodinated Contrast

- Minimize risk of AKI
  - Use low or iso-osmolar agents at lowest doses possible
  - Consider d/c NSAIDS, diuretics or RAAS-antagonists prior and shortly after procedure
  - Optimize volume status
  - Check Scr 48-96 hrs post-procedure
  - Avoid repeated contrast load within days
- Prophylactic hemofiltration/hemodialysis of *no* benefit

KDIGO Guidelines on CKD Diagnosis and Management. *Kidney Int*. 2013.

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Does Fluid Type Matter in Preventing Contrast Nephropathy?

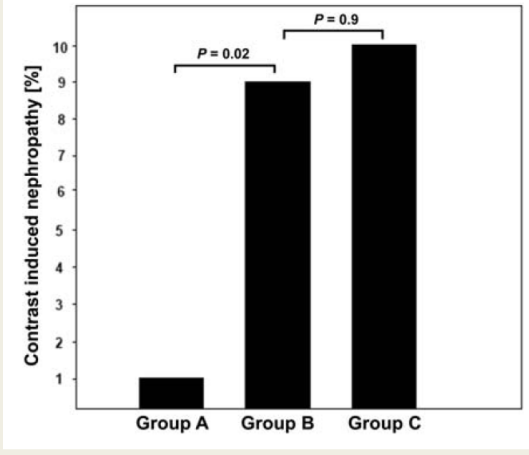

Figure 3 Incidence of contrast induced nephropathy defined as an increase of ≥25% in the baseline serum creatinine concentration within 48 h in the three groups.

Group A: NS 1 ml/kg/h starting @ 8 h pre- and continued ≥12h post-procedure

Group B: $NaHCO_3$ (166 mEq/L) 3 ml/kg/h 1h pre- and 1ml/kg/h for 6h post-procedure

Group C: $NaHCO_3$ 3ml/kg bolus 20 mins pre + 1,500 mg tab/10kg + 100-200 ml mineral water orally and 500 ml of mineral water post-procedure

Klima T, et al. *Euro Heart J*, 2012.

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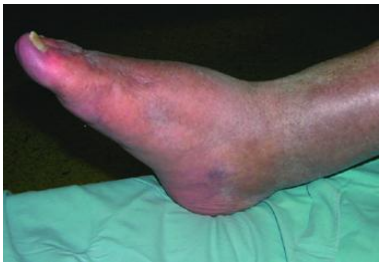
Gadolinium

- Linked to nephrogenic systemic fibrosis (NSF)
  - Rare, but painful debilitating fibrosing disease
  - Primarily in extremities but may involve lung and heart
- Increased risk w/ decreased kidney function (AKI, CKD, post-transplant)
- Avoid gadolinium in patients w/ eGFR <30 ml/min



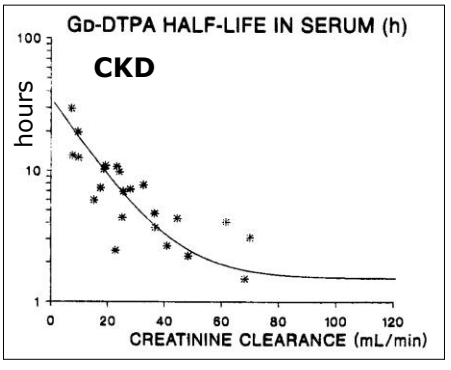
Grobner T and Prischl FC. Kidney Int 2007

- Contraindication in PD
- HD patients require immediate HD post-exposure x 3 d
- No effective treatment available

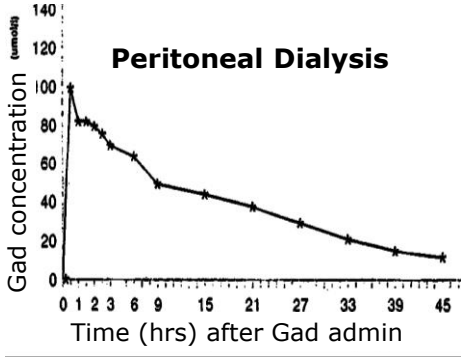
Swaminathan S and Shah S. *J Am Soc Nephrol.*2007.

33

Gad Clearance – ↓↓ in CKD and Peritoneal Dialysis



Magnevist 0.1 mmol/kg x1 (N=24)
CrCl 7.2-70 ml/min
92.1% recovered in urine



Magnevist 0.1 mmol/kg
CAPD 2L exchanges 4x/day
½ life 9 hrs

Swan, S Invest Radiol 34:443,1999; Swan, S J Mag Res Imag 9:317,1999 Dorsam, J. NDT10:1228,1995

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DRUGS THAT REQUIRE CAUTION IN CKD PATIENTS

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Antihypertensives: RAAS Antagonists

- Expect rise in SCr ≤30%
- Can lead to AKI, hyperkalemia
- Risk management
  - Avoid in patients with renal artery stenosis
  - Assess eGFR and serum K^+ 1 wk after initiation or ↑dose
  - Prior to contrast, major surgery, procedures /conditions that predispose to dehydration - consider temporarily d/c
  - D/C or reduce if SCr increase > 30% or serum K+ > 5.5 mEq/L

KDIGO Guidelines on CKD Diagnosis and Management. *Kidney Int*. 2013.

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What Proportion of (Highly-selected) Patients in Pivotal Trials of RAASi Therapies Experienced Hyperkalemia (K+ >5.5 mEq/L) During Follow-up?

A. <1%
B. <10%
C. 10-30%
D. 30-50%
E. >50%

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Consequences of Hyperkalemia

Trial	Population	Outcome	Hyperkalemia Rates
RENAAL	CKD, DM (Diabetic Nephropathy)	**22% risk reduction**	**38% @ >5.0mEq/L; 23% @ >5.5 mEq/l**
IDNT	CKD, DM (Diabetic Nephropathy)	**20% risk reduction**	**18.6% @ >6.0mEq/L**
RALES	Moderate-Severe HF	**30% risk reduction**	**2% in RALES; 13% >5.5 mEq/L (25mg in RALES pilot)**
EPHESUS	HF post MI	**15% risk reduction**	**16% @ >5.5mEq/L 5% @ >6.0mEq/L**
EMPHASIS-HF	Mild HF	**37% risk reduction**	**12% @ >5.5mEq/L**

Courtesy of Dr. Matthew Weir

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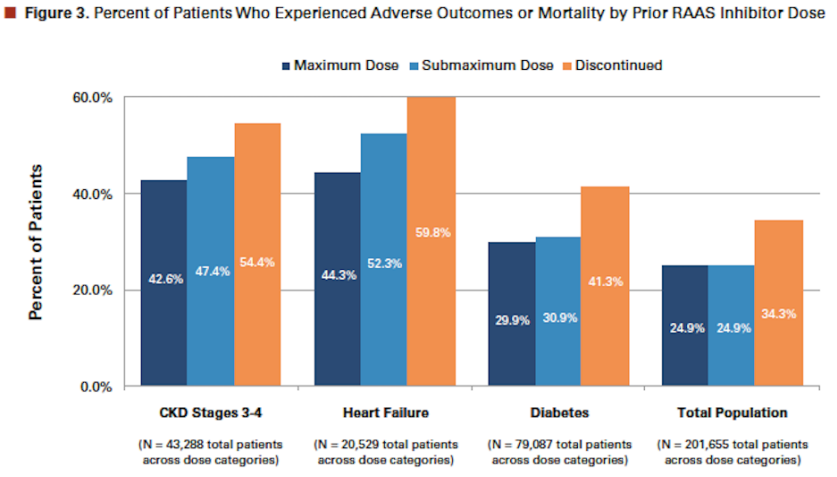
Consequences of Hyperkalemia – Downstream…



Epstein M, et al. *Am J Manag Care* 2015;21:S212

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Consequences of Hyperkalemia

- Hyperkalemia is the #1 reason why recommended RAASi treatments are discontinued
- As a result patients may not reap the full potential of these therapies on clinical outcomes important to them
- Strategies are needed to better manage hyperkalemia in these patients and maintain RAASi therapy longer
- Whether an intervention that allows prolonged RAASi treatment actually improves patient outcomes is currently theoretical and must be established through rigorous trials

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74 yo Woman with Right Hip Pain. 2 Wks Earlier Scr 1.3 mg/dl. Fell and Was Admitted. Scr 1.6 mg/dl. Given IVF and Discontinued HCTZ, Ibuprofen and Irbesartan. Urinalysis Shows ATN. More Hip Pain. Tramadol 50 mg qd. ↑Gapabentin 300 tid. 5 Days After Admission: Na 132 mEq/l, BUN 50 mg/dl, Scr 2 mg/dl. She Has ↑Drowsiness + Asterixis.

What Is Contributing Most to Her Sxs and Signs and What Should We Do?

A. Dialysis for uremia
B. D/c tramadol, give naloxone
C. D/c gabapentin
D. Treat hyponatremia

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Gabapentin Toxicity in Patients with Chronic Kidney Disease: A Preventable Cause of Morbidity

Ladan Zand, MD, Kevin P. McKian, MD, Qi Qian, MD
Department of Medicine, Division of Nephrology and Hypertension, Mayo Clinic College of Medicine, Rochester, Minn.

THE AMERICAN JOURNAL of MEDICINE®

- Mayo Clinic – 33/594 with GFR < 90 Ml/Min Developed Side Effects
- 7/9 ESRD Patients Had Side Effects

Table 5 Symptoms of Gabapentin Intoxication, Corresponding Serum Gabapentin Concentration, and Hospital Admission

	Group II	Group III
No. of Symptomatic Patients	33	7
Symptoms[a,b,c]	Reduced consciousness (13,[a] 21.9 ± 1.29,[b] 4[c]) Unsteady gait or ataxia (9,[a] 31.7 ± 4,[b] 0[c]) Dizziness and weakness (8,[a] 29.5 ± 3.84,[b] 1[c]) Myoclonus (8,[a] 29.9 ± 5.71,[b] 0[c]) Confusion (5,[a] 23.0 ± 0.49,[b] 2[c]) Tremulousness and asterixis (5,[a] 42.6 ± 3.84,[b] 1[c])	Reduced consciousness (6,[a] 59.6,[b] 6[c]) Unsteady gait or ataxia (1,[a] 25.0,[b] 1[c])

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Gabapentin Toxicity in Patients with Chronic Kidney Disease: A Preventable Cause of Morbidity

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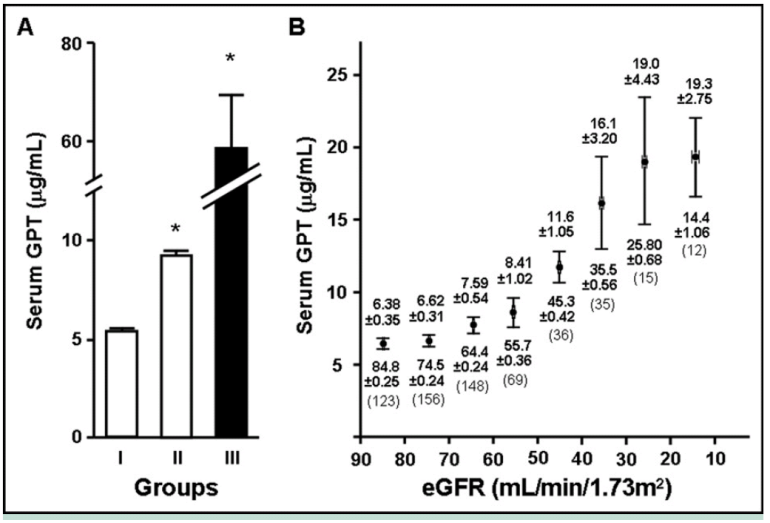

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Gabapentin

CrCl (mL/min)	Total daily dose (mg)	Dosage regimen
> 60	1,200	400 mg TID
31 – 60	600	300 mg BID
15 – 30	300	300 mg QD
< 15	150	300 mg QOD
Hemodialysis	—	200 – 300 mg post-HD

Loading dose: 300 – 400 mg
Maintenance dose: 200 – 300 mg after each 4-h HD session

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74 yo W Woman Scr of 1.9 mg/dl, eGFR 34 ml/min/min/1.73m2 Has Dysuria, Urgency. Urinalysis Reveals 3+ Leukocyte Esterase.

Which Antibiotic Will Be the Best for Efficacy, But Will Also Need to Be Dose Adjusted for CKD?

A. Cephalexin
B. Ciprofloxacin
C. Nitrofurantoin
D. All of the above

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Treatment Considerations in CKD Patients with UTI

Ampicillin*	• Achieve good urine concentration
Cephalosporins*	• Generally low urine concentrations • Exceptions: cefazolin and ceftriaxone, but not FDA approved for UTI treatment
Carbapenems	• <50% of active drug present in urine • Unknown efficacy for UTI in CKD patients
Quinolones*	• Ciprofloxacin and levofloxacin achieve good urine concentrations
Nitrofurantoin	• Low renal excretion, avoid if eGFR <50 ml/min
Trimethoprim*	• Achieve good urine concentration
Aminoglycosides*	• Achieve high urine concentrations • Nephrotoxic

***Requires dose adjustment in CKD**

Adapted from Gilbert DN, *J Am Soc Nephrol*. 2006

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Antimicrobials with CKD

- Most require renal dose adjustments
  - Common exceptions: Ceftriaxone, moxifloxacin, macrolides, doxycycline, clindamycin, linezolid
- Careful monitoring of drug levels needed for:
  - Vancomycin. Aminoglycosides
- **Trimethoprim/ sulfamethoxazole**
  - May ↑SCr slightly due to ↓renal tubular creatinine excretion– no change in GFR.
  - Distinguish from AKI due to drug allergic interstitial nephritis
  - Hyperkalemia
- **Imipenem/ cilastatin**
  - High seizure risk in CKD patients, use carbapenem in CKD

KDIGO Guidelines on CKD Diagnosis and Management. *Kidney Int*. 2013.
Munar MY and Singh H. *Am Fam Physician,* 2007.

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45 yo AA Man with Diabetes and HTN. He Is on Metformin with a HgbA1C 6.9 and Has Lost 15 lbs. Scr 1.5 mg/d Last Year, ↑1.6 mg/dl with eGFR of 59 ml/min/1.73m2, ACR 200 mg/g, Serum K+ 5 mEq/l. He Is on Losartan 100 mg/d with BP 130/80 mmHg. He Has No Complaints.

What Should We Do for His Diabetes?

A. D/c metformin, add glyburide
B. D/c metformin, add glipizide
C. Add lisinopril
D. No medication changes

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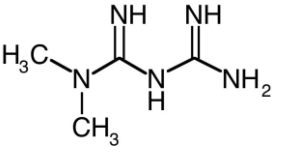
Metformin



- Ideal agent
  - Does not raise insulin levels
  - No hypoglycemia
- Lactic acidosis
  - 1/20th of phenformin
  - ~3 cases per 100,00 pt-yr
- Original cutpoints based on metabolizing 3 g in 24–48 h
  - Females, SCr 1.4 mg/dL
  - Males, SCr 1.5 mg/dL

Lipska KJ, et al. Diabetes care. 2011;34:931. 49

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Proposed Metformin Use in CKD

- eGFR 45 to 60 mL/min/1.73m^2
  - Continue metformin use and ↑ monitoring of eGFR to every 3 - 6 months
- eGFR 30 to 45 mL/min/1.73m^2
  - Use metformin with caution with lower dose (50% maximal)
- eGFR < 30 mL/min/1.73m^2
  - Stop metformin

Lipska KJ, et al. Use of Metformin in the Setting of Mild-to-Moderate Renal Insufficiency. Diabetes Care 2011;34:1431-37.

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Proposed Metformin Use in CKD

- Avoid or hold if Acute Kidney Injury or high risk AKI
  - Iodinated contrast exposure
- Monitor Serum Bicarbonate in addition to eGFR
  - Stop metformin for any new acidosis

Lipska KJ, et al. Use of Metformin in the Setting of Mild-to-Moderate Renal Insufficiency. Diabetes Care 2011;34:1431-37.

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Hypoglycemics

- **Sulfonylureas**
  - Dose adjustment needed for renally excreted drugs: **chlorpropamide, glyburide**
  - Avoid above two if eGFR < 50 ml/min
- **Insulin**
  - Partially renally excreted and dose adjustment may be needed for eGFR <30 ml/min

KDIGO Guidelines on CKD Diagnosis and Management. *Kidney Int*. 2013.
Munar MY and Singh H. *Am Fam Physician,* 2007.

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Antidiabetic Drugs & CKD

Generic Name	↓A_{1c}	Hypoglycemia	↑Wt	Initial Dose	Max Dose	CKD
Sulfonylureas	1.0–1.5	Yes	Yes			
glyburide				2.5–5 mg/d	10 mg BID	**avoid**
glipizide				5 mg/d or XL 5 mg/d	20 mg BID or XL 20 mg/d	**use this one**

http://www.corbisimages.com/stock-photo/rights-managed/SF9381/stephen-hales-measuring-horses-blood-pressure

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Case Presentation

64 yo AA woman with weakness. PMH of HTN, hypercholesterolemia

CKD with Scr of 1.4 mg/dl, eGFR of 45 ml/min/1.73m^2, ACR 30 mg/g,

Meds: Diltiazem, Simvastatin, ASA

EGD with H. pylori. Rx: Clarithromycin, Metronidazole, Bismuth + PPI

7 d after starting regimen c/o severe weakness

Exam: 110/70 mmHg, tachycardia, ↓ lower extremity strength.

Na 138 K 6.4 Cl 98 HCO3 14 BUN 89 Cr 5.8. CK 80,000 IU/L

Why did this happen?

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Lipid-Lowering Drugs

- **Statins**
  - No renal dose adjustment needed for atorvastatin
  - Dose adjustments needed when eGFR <30 ml/min for **fluvastatin, lovastatin, pravastatin, rosuvastatin and simvastatin**
- **Fibrates**
  - Associated with AKI esp. in CKD patients
  - May transiently raise SCr by increased creatinine production rather than decreased GFR

KDIGO Guidelines on CKD Diagnosis and Management. *Kidney Int*. 2013.
Munar MY and Singh H. *Am Fam Physician,* 2007.

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Warfarin

- Warfarin, primarily metabolized by the liver, can still be affected by CKD
- Patients with moderate to severe CKD may need adjustments to their initial and ongoing dosage, and those with ESRD may experience more INR fluctuations, requiring frequent monitoring
- Warfarin is associated with a higher bleeding risk in CKD patients

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DOAC Kidney Clearance

- As all DOACs used for treatment of atherothrombosis rely on the kidneys for elimination to varying degrees. Agents that hinder this organ's ability to clear DOAC may place the patient at increased risk for bleeding complications.
- Common agents to monitor are NSAIDs, diuretics, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, and immunosuppressants
- No DOAC-specific dose adjustments are required but warrant more frequent monitoring of renal function and possibly holding therapy or consideration for transition to an agent with less renal involvement if renal function is compromised (especially if GFR<30 mL/min)

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H2 Blockers

- When prescribing H2 blockers for patients with chronic kidney disease (CKD), a dose reduction is necessary because these medications are eliminated by the kidneys
- Failure to adjust the dose can lead to drug accumulation and increase the risk of central nervous system side effects, such as confusion and delirium
- Reduce dose 25% for GFR of 10-50 ml/min
- It is important to note that ranitidine has been withdrawn from the market due to nitrosamine impurities

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Proton Pump Inhibitors

- There are concerns that PPI may cause acute interstitial nephritis.
- Similar to other causes of drug-induced acute interstitial nephritis, the use of PPI does not appear to be dose dependent, and recurrence of exacerbation can occur with additional exposure.
- PPI have also been associated with an increased risk for CKD, CKD progression, and end-stage kidney disease.
- However, there is insufficient evidence to show or conclude that PPIs cause CKD, CKD progression, or ESRD.
- No plausible biological process has been demonstrated that would explain the development of CKD following PPI use.

Geevasinga N, et al. Clin Gastroenterol Hepatol. 2006;4(5): 597-604.
Praga M, et al. Kidney Int. 2010;77(11): 956-961.
Gooch K, et al. Am J Med. 2007;120(3): 280.e281-287.
Lazarus B, et al. JAMA Intern Med. 2016;176(2): 238-246.
Muriithi AK et al. Am J Kidney Dis. 2014;64(4): 558-566.
Xie Y, et al. J Am Soc Nephrol. 2016;27(10): 3153-3163.
Kuo HW, et al. Pharmacoepidemiol Drug Saf. 2010;19(7): 745-751.

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PPIs Are Important, Safe, and Effective Therapeutic Considerations in CKD Patients

Medical Comorbidities in CKD Patients

Osteoarthritis, different forms of **bone disease**
↓
Pain & Use of NSAIDs
↓
GI intolerance
↓
PPIs required

CKD patients often require **anticoagulation**
↓
Risk of GI Bleeding
↓
Require utilization of PPI

CKD patients often have **GERD**
↓
PPIs required

There is **abundant observational data that associate NSAID use with interstitial nephritis**

11/20/2025 60

Weir MR. Proton Pump Inhibitors and Kidney Disease: Fact or Fiction? *Am J Nephrol.* 2024;55(4):499-508.

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Published Data Fails to Demonstrate an Association Between Use of PPI and Development or Progression of CKD

Observational Studies Indicates No Validity to the Observations Linking PPI Use to CKD

Use of PPI in a CKD Population Was Not Associated with Progression to ESRD or Death

PPI Discontinuation After Prolonged Continuous Use in CKD Patients Not Associated with a Significant Change in Kidney Function After 1 Year of Observation

No change in kidney function has been seen in **kidney transplant recipients** maintained on a PPI

Lack of consistency of the observations from observational studies indicates NO VALIDITY of the data

Weir MR. Proton Pump Inhibitors and Kidney Disease: Fact or Fiction? *Am J Nephrol.* 2024;55(4):499-508.

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Given the lack of evidence of direct nephrotoxicity or a mechanistic cause of renal injury and the dearth of adequate epidemiologic data linking PPI to incident CKD or CKD progression, there is no need to limit the use of PPI in patients with CKD. There are no data suggesting that the PPI dose needs to be adjusted in patients with reduced kidney function. They should be considered as important, safe, and effective therapeutic considerations in patients with CKD who have gastric acid-associated clinical symptoms and disease. The dose and duration need to be carefully considered on an individual basis considering their known risks and benefits.

There is no consistent relationship between PPI use and development or progression of CKD

Weir MR. Proton Pump Inhibitors and Kidney Disease: Fact or Fiction? *Am J Nephrol.* 2024;55(4):499-508.

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Antacids

- Antacids are another type of medicine that can be used for heartburn (GERD) or upset stomach
- Antacids are also widely available over the counter (OTC) and usually contain one or more of the following ingredients: calcium, magnesium, bismuth, and aluminum. All of these can build up in the body if the patient has reduced GFR

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Lithium

- Lithium is a very effective medicine used to treat mania in people with bipolar disorder
- It can harm the kidneys when used at higher doses or over very long periods of time (multiple years/decades)
- The most common problem is nephrogenic diabetes insipidus
- Lithium may also increase the risk of chronic kidney disease with very long-term use (also known as lithium nephropathy)

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AWARENESS OF DRUG SIMA INTERACTIONS IN PATIENTS

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Rhabdomyolysis with Statins: Cytochrome P450 3A4 Interactions

Lova >/= Simva > Atorva – not Rosuva or Prava

- Azoles (ketoconazole the worst)
- Diltiazem and Verapamil
- Clarithro and Erythro >>> Azithro
- Ritonavir in HIV patients
- Cyclosporine and FK506 (Tacrolimus)

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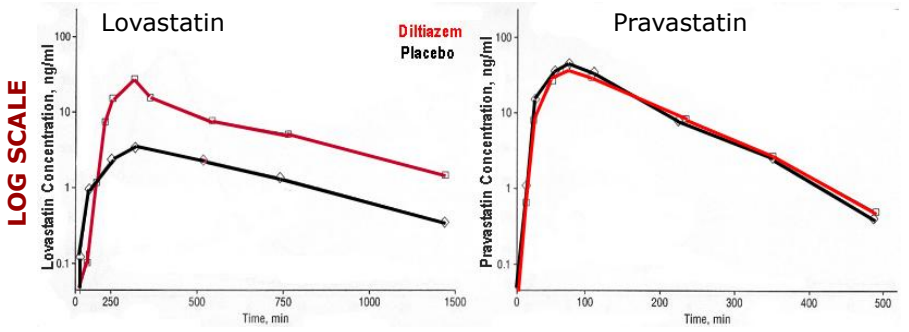
CYP450 3A4 Interactions
Diltiazem with Lovastatin and Pravastatin



Azie NE,et al. Clin Pharmacol Ther 1998; 64:369

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74 yo old AA Woman with eGFR of 20 ml/min/1.73 m2
DEXA Scan Shows Osteopenia/Osteoporosis.
25 OH Vitamin D Level with Supplementation 65, Intact PTH 25, Calcium 10.8 mg/dl, Phosphate Is 5.1 mg/dl.

What Would You Do for the DEXA Scan Findings?

A. Add bisphosphonate
B. Increase vitamin D
C. Repeat DEXA next year as repeat testing ↑accuracy of test
D. None of the above.

CONTINUING EDUCATION COMPANY

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Bisphosphonates

- Bisphosphonates for eGFR > 30 mL/min/ 1.73 m^2 with normal Ca, phos, intact PTH with DEXA scans showing osteoporosis .
- Efficacy?
  - BMD weakly related to fracture risk with stages 4 and 5 CKD*
- Patients with Chronic Kidney Disease -Mineral Bone Disorder have a spectrum of bone diseases
  - secondary hyperparathyroidism with ↑bone turnover **BUT** adynamic bone disease with ↓bone turnover as well.

Ott SM. Nat Rev Nephology 2013;9:681-692.

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Bisphosphonates

- Safe?
  - Long term treatment with bisphosphonates may cause or exacerbate adynamic bone disease.
- Refer to a bone specialist with osteoporosis with eGFR< 30 min per 1.73 m^2ml/min
- Rare kidney toxicity
  - IV zoledronic acid associated with AKI due to ATN.
  - IV pamidronate, zoledronic acid, oral alendronate reported with collapsing FSGS.

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AVOIDING DRUG TOXICITY IN CKD PATIENTS

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Minimizing Risk of Adverse Drug Events

- Minimize pill burden as possible
  - 10 – 12 MEDICATIONS PER CKD PATIEN
    17 FOR TRANSPLANTED INDIVIDUALS
- Review medications carefully for
  - Dosing
  - Potential interactions
- Educate patient on:
  - OTC meds to avoid (mainly NSAIDs)
  - Signs/symptoms of potential drug adverse effects

St. Peter WL, Adv Chronic Kidney Dis. 2010;17:413-9
Yee J. Adv Chronic Kidney Dis. 2010;17:379-380

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Dosing Adjustments

- Don't rely on SCr alone – calculate eGFR or Cr clearance
  - SCr misleading in: extremes of body weight, poor nutrition
- Cannot rely on eGFR in AKI
  - If SCr rapidly rising, assume eGFR <10 ml/min
- When in doubt, look up dosing adjustment/ potential interactions or call pharmacy

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Key Points

- CKD patients at high risk for drug-related adverse events
- Several classes of drugs renally eliminated
- Consider kidney function and current eGFR (not just SCr) when prescribing meds
- Minimize pill burden as much as possible
- Remind CKD patients to avoid NSAIDs

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K^+ Quiz

75

Dairy Products

Ice cream

Yoghurt

Cheddar

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Advising Your Patient About K^+ Intake

1. None of these are high in potassium
2. Yoghurt > Ice cream > Cheddar
3. Ice cream > Yoghurt > Cheddar
4. Cheddar > Ice cream > Yoghurt
5. Ice cream > Cheddar > Yoghurt

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Dairy Products


Food	Per Serving	mEqs
Cheddar cheese	1.5 oz.	1.1
Cottage cheese	1/2 cup	2.4
Ice cream, hard	1/2 cup	3.2
Milk, low fat 2%	1 cup	10.6
Yoghurt, plain, low fat	1 cup	13.6

78

Advising Your Patient About K^+ Intake

1. None of these are high in potassium
2. Yoghurt > Ice cream > Cheddar
3. Ice cream > Yoghurt > Cheddar
4. Cheddar > Ice cream > Yoghurt
5. Ice cream > Cheddar > Yoghurt

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Fresh Fruits

Blueberry

Watermelon

Cantaloupe

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Advising Your Patient About K^+ Intake

1. All of these are high in potassium
2. Blueberries > Cantaloupe > Watermelon
3. Cantaloupe > Watermelon > Blueberries
4. Watermelon > Cantaloupe > Blueberries
5. Cantaloupe > Blueberries > Watermelon

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Fresh Fruits

FRUIT	Serving	K(mEq)
Blueberries, raw	1/2 cup	1.7
Grapes	10	2.4
Pineapple, raw	1/2 cup	2.9
Plum	1	2.9
Strawberries	1/2 cup	3.2
Cherries, sweet, raw	10	3.9
Apple	1 medium	4.1
Peach	1	4.4
Peaches, canned	1/2 cup	4.1
Pear	1	5.3
Orange	1	6.1
Banana	1 medium	11.6
Raisins	1/4 cup	14.2
Watermelon	1/8	14.4
Avocado	1/2	15.4
Grapefruit	1/2	21.2
Cantaloupe	1/2	21.2

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Advising Your Patient About K^+ Intake

1. All of these are high in potassium
2. Blueberries > Cantaloupe > Watermelon
3. ⇒ Cantaloupe > Watermelon > Blueberries
4. Watermelon > Cantaloupe > Blueberries
5. Cantaloupe > Blueberries > Watermelon

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Vegetables



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Advising Your Patient About K^+ Intake

1. All of these are unacceptably high in potassium
2. Butternut squash > Brussels sprouts > Spinach
3. Brussels sprouts > Butternut squash > Spinach
4. Spinach > Brussels sprouts > Butternut squash
5. They all taste dreadful

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Advising Your Patient About K^+ Intake

⇨ 1. All of these are unacceptably high in potassium
2. Butternut squash > Brussels sprouts > Spinach
3. Brussels sprouts > Butternut squash > Spinach
4. Spinach > Brussels sprouts > Butternut squash
5. They all taste dreadful

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