The Good, The Bad and The Iatrogenic

Kim Zuber, PAC

American Academy of Nephrology PAs

St Petersburg, FL

Disclosures: none

Disclosure

I have no relevant relationships with ineligible companies to disclose within the past 24 months

I am presently running for AAPA Secretary/Treasurer

Put a nephrology math geek in charge of AAPA's finances

While all these stories are true and used with permission, the photos and names are intermixed

Learning Objectives

1) Using patient examples, highlight medication errors that occur in the office, in the emergency room and in the hospital
2) Using patient examples, review both dosing and medication selection errors including the pathophysiological rationale for medication selection
3) Using patient examples highlight errors in OTC meds and cannabis

Nephrology Axiom

- First blame the drug

Fun with Kidneys

Caveats

- All of the stories are true
- Names and faces have been changed *'to protect the innocent'*
- This lecture is not to blame but to educate
- These stories highlight the most common dosing errors seen across the US
  - We want to encourage use of FDA dosing guidelines
- A pharmacist and a good list serve is everyone's best friends!
- A **HUGE** thank you to the PAs and NPs of the National Kidney Foundation for sharing their stories

Stages of CKD 2013

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

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

KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of CKD, *Kidney International*, Jan 2013, Vol 3, Issue 1

Sam

45 y/o male

PMH: HTN, IDDM, CKD (eGFR 22), PVD, smoker, diabetic retinopathy, hyperkalemia, edema, SHPT, R BKA, foot ulcer L, obesity, W/C dependent

Labs: BUN 50, SCr 4.16, Na 140, K 4.5, bicarb 16, Hgb 11.3, UACR 8380, A1C 8.9%

Pt calls with c/o BP 190-180s w/pain posterior skull, referred to ED
Seen by neph in ED and Bystolic (nebivolol) increased with f/u 3days
ED labs: WBC 12.03 (nl for pt 11.6-13.7), K 4.3, bicarb 13, eGFR 15.4

____

Neph office calls house 24 hours after ED visit.
Pt refusing to let wife take BP but feels poorly, told to return to ED
Pt presents to a Retail Clinic

Sam

45 y/o male

PMH: HTN, IDDM, CKD (eGFR 22), PVD, smoker, diabetic retinopathy, hyperkalemia, edema, SHPT, R BKA, foot ulcer L, obesity, W/C dependent

Labs: BUN 50, SCr 4.16, Na 140, K 4.5, bicarb 16, Hgb 11.3, UACR 8380, A1C 8.9%

Pt diagnosed with pneumonia

RX: Levaquin (Levofloxacin) 750mg daily X 5D

____

Neph office calls pt on Monday after no f/u in ED and he feels worse

Encouraged to go to ED

States he will wait for wife to come home to drive

Wife comes home 2 hours later and he is found dead and 'cold'

What Killed Him?

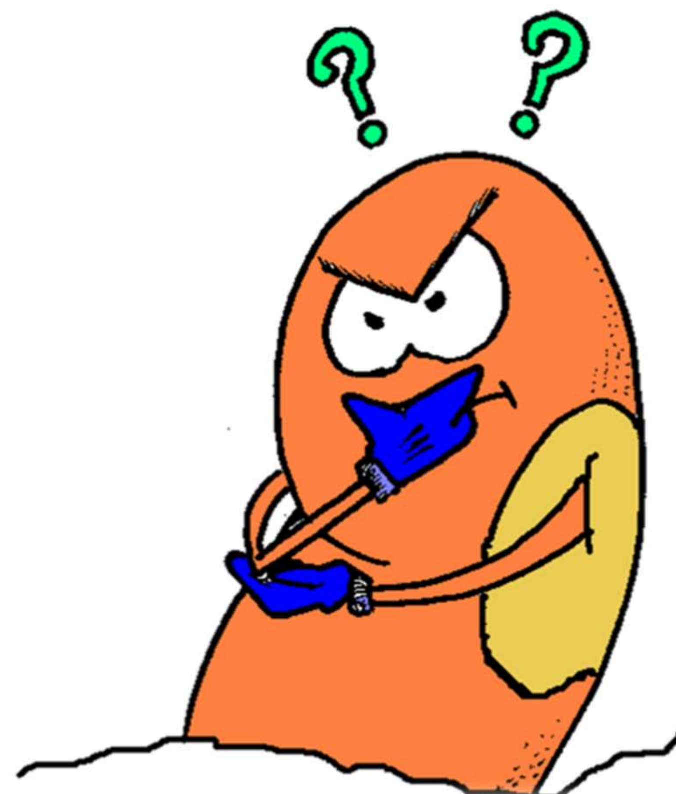
ker,
SHPT,

D'OH!

His Heart Stopped

Fun with Kidneys

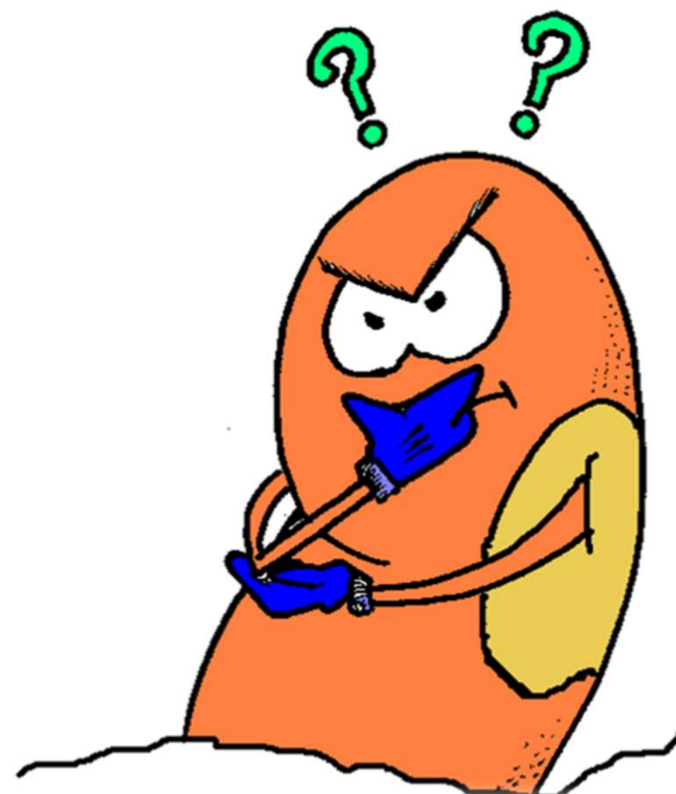
Sam



A) Fast eGFR drop with antibiotics in CKD
B) QT interval increased with Levaquin (Levofloxacin)
C) Sudden death in a poorly controlled IDDM
D) Infectious death from pneumonia

Fun with Kidneys

Sam



A) Fast eGFR drop with antibiotics in CKD

B) QT interval increased with Levaquin (Levofloxacin)

C) Sudden death in a poorly controlled IDDM

D) Infectious death from pneumonia

Fun with Kidneys

Sam

45 y/o male

PMH: HTN, IDDM, CKD (eGFR 22), PVD, smoker, diabetic retinopathy, hyperkalemia, edema, SHPT, R BKA, foot ulcer L, obesity, W/C dependent

Labs: BUN 50, SCr 4.16, Na 140, K 4.5, bicarb 16, Hgb 11.3, UACR 8380, A1C 8.9%

Pt diagnosed with pneumonia

RX: Levaquin (Levofloxacin) 750mg daily X 5D

____

All Fluroquinolones increase QT intervals

IE: Cipro (Ciprofloxacin) /Levaquin(Levofloxacin)

Black Box Warning…Renal Dosing is ½ to ¼ 'normal dose'

Loading Doses are OK

Medication Errors

Each year, in the US alone, 7,000-9,000 people die as a result of a medication error

69% given an incorrect medication in the hospital

In 2020: The total cost of medication-associated errors exceeds $40 billion

Drugs and aging report: Adverse Drug Events in Patients with CKD Associated with Multiple Drug Interactions and Polypharmacy

66% with hyperkalemia, 10% with hypercoag, 33% with QT prolongation

Joan

Forty something ER PA brings her 45 y/o husband to ER due to poor appetite, N&V, weight loss and crackles on his lung field exam (of course she examined him first!)

PMH: kidney transplant at Hopkins 24 years ago, had been slowly failing, HTN

Meds: metoprolol, oral Fe, atorvastatin

Labs: BUN 50, SCr 4.16 (eGFR 16ml/min), Na 140, K 4.5, bicarb 20, Hgb 11.3, UACR 60mg/g, CXR-'fluffy' diffuse white out with lobar consolidation in LLL

DX: Pneumonia

RX: Levofloxacin 750mg qd X 10d, 1st dose in the ED (antibiogram for this hospital includes MRSA)

Joan texts me from the ED

Table 3: Levofloxacin Dosage Adjustment in Adult Patients with Renal Impairment (Creatinine Clearance less than 50 mL/minute)			
Creatinine Clearance greater than or equal to 50 mL/minute	**Creatinine Clearance 20 to 49 mL/minute**	**Creatinine Clearance 10 to 19 mL/minute**	**Dialysis: HD or PD**
750 mg every 24 hours	750 mg every 48 hours	750 mg initial dose, then 500 mg every 48 hours	750 mg initial dose, then 500 mg every 48 hours
500 mg every 24 hours	500 mg initial dose, then 250 mg every 24 hours	500 mg initial dose, then 250 mg every 48 hours	500 mg initial dose, then 250 mg every 48 hours
250 mg every 24 hours	No dosage adjustment required	250 mg every 48 hours. If treating uncomplicated UTI, no dosage adjustment required	No information on dosing adjustment is available

1) His SCr is 4.16 (eGFR 16ml/min)
2) It is NOT STABLE, losing function!

Joan

Forty something ER PA brings her 45 y/o husband to ER due to poor appetite, N&V, weight loss and crackles on his lung field exam (of course she examined him first!)

PMH: kidney transplant at Hopkins 24 years ago, had been slowly failing, HTN

Meds: metoprolol, oral Fe, atorvastatin

Labs: BUN 50, SCr 4.16 (eGFR 16ml/min), Na 140, K 4.5, bicarb 20, Hgb 11.3, UACR 60mg/g, CXR-'fluffy' diffuse white out with lobar

DX: Pneumonia

RX: Levofloxacin 750mg qd X 10d, 1st dose in the ED

When Joan asks about the dose, Doc states 750mg was just a loading dose and the 'real' RX was 250mg qd

He states that the nurse (?!) made a mistake and takes away the written RX

Bina

64 y/o Pakistani female visiting her grandkids
Presents to ED feeling poorly, not eaten x 2 days
PMH: DM, HTN, N&V
Meds: Glucophage (Metformin), lisinopril, Maxide (triamterene + HCTZ), Aleve (naproxen)
Labs: pH 7.17, lactic Acid 9, SCr 8.1mg/dL

What caused Bina's severe lactic acidosis?

A) Metformin
B) Lisinopril
C) Aleve
D) Maxide (triamterene + HCTZ)

Bina

64 y/o Pakistani female visiting her grandkids
Presents to ED feeling poorly, not eaten x 2 days
PMH: DM, HTN, N&V
Meds: Glucophage (Metformin), lisinopril, Maxide (triamterene + HCTZ), Aleve (naproxen)
Labs: pH 7.17, lactic Acid 9, SCr 8.1mg/dL

What caused Bina's severe lactic acidosis?

A) Metformin

B) Lisinopril

C) Aleve

D) Maxide (triamterene + HCTZ)

Bina

64 y/o Pakistani female visiting her grandkids
Presents to ED feeling poorly, not eaten x 2 days
PMH: DM, HTN, N&V
Meds: Glucophage (Metformin), lisinopril, Maxide (triamterene + HCTZ), Aleve (naproxen)
Labs: pH 7.17, lactic Acid 9, SCr 8.1mg/dL

More common with patients who continue meds while 'sick'

Europe and Canada have **'sick day rules'** to decrease iatrogenic AKI

Conservative treatment to start

Hold medications, start IV NS with bicarb

It ended up taking 5 days of hemodialysis to stabilize Bina

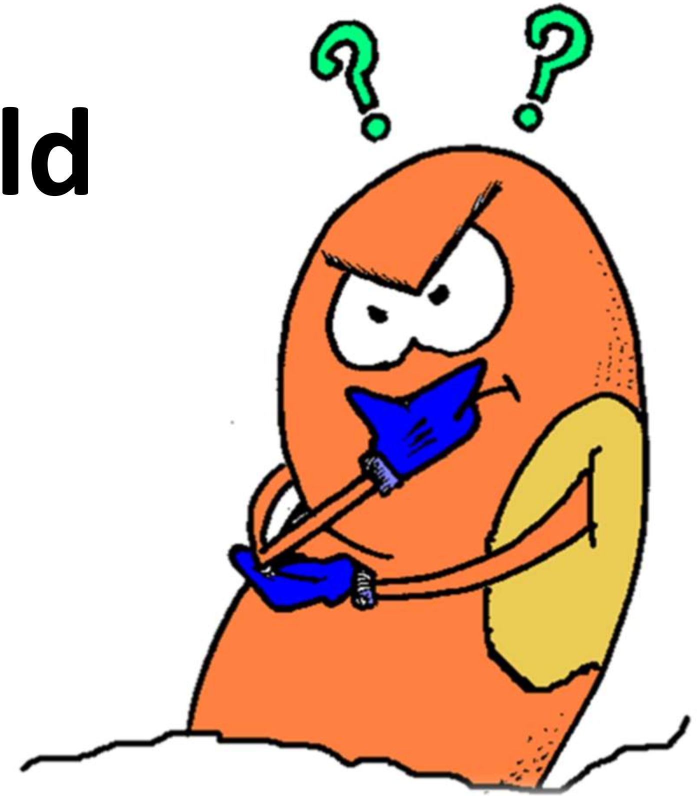
Ronald

65 y/o male
PMH: HTN, CP, chronic leg edema
Meds: lisinopril, furosemide, metolazone

Patient had been living at home with caretaker sister
Sister frustrated that PCP office not handicapped accessed
No follow-up for a year due to inability to get into office
Presents to ED for blood work

BUN 219/SCr 10.5

Ronald

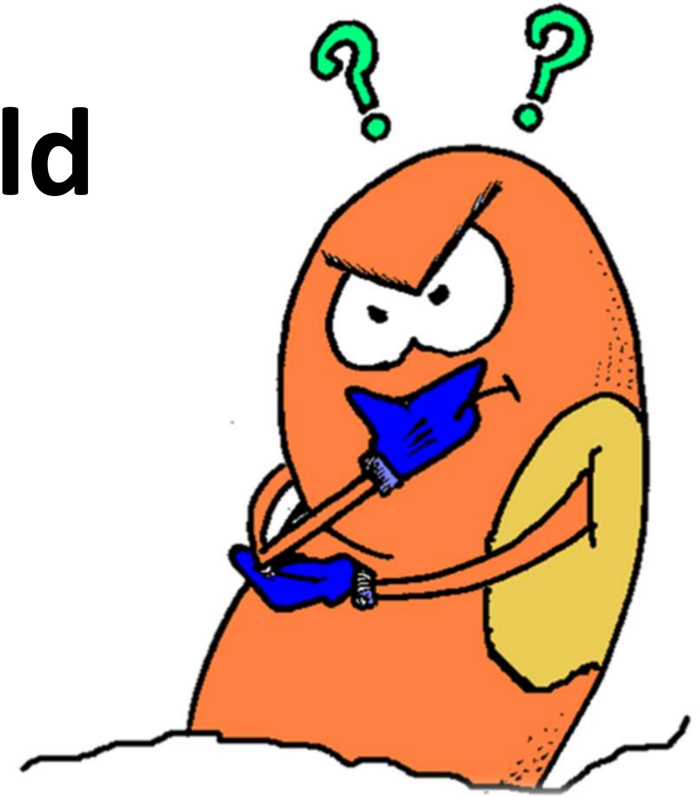


What is the treatment?

A) OMG! Get him to dialysis
B) Foley- must be post renal
C) IV fluids
D) None

Fun with Kidneys

Ronald

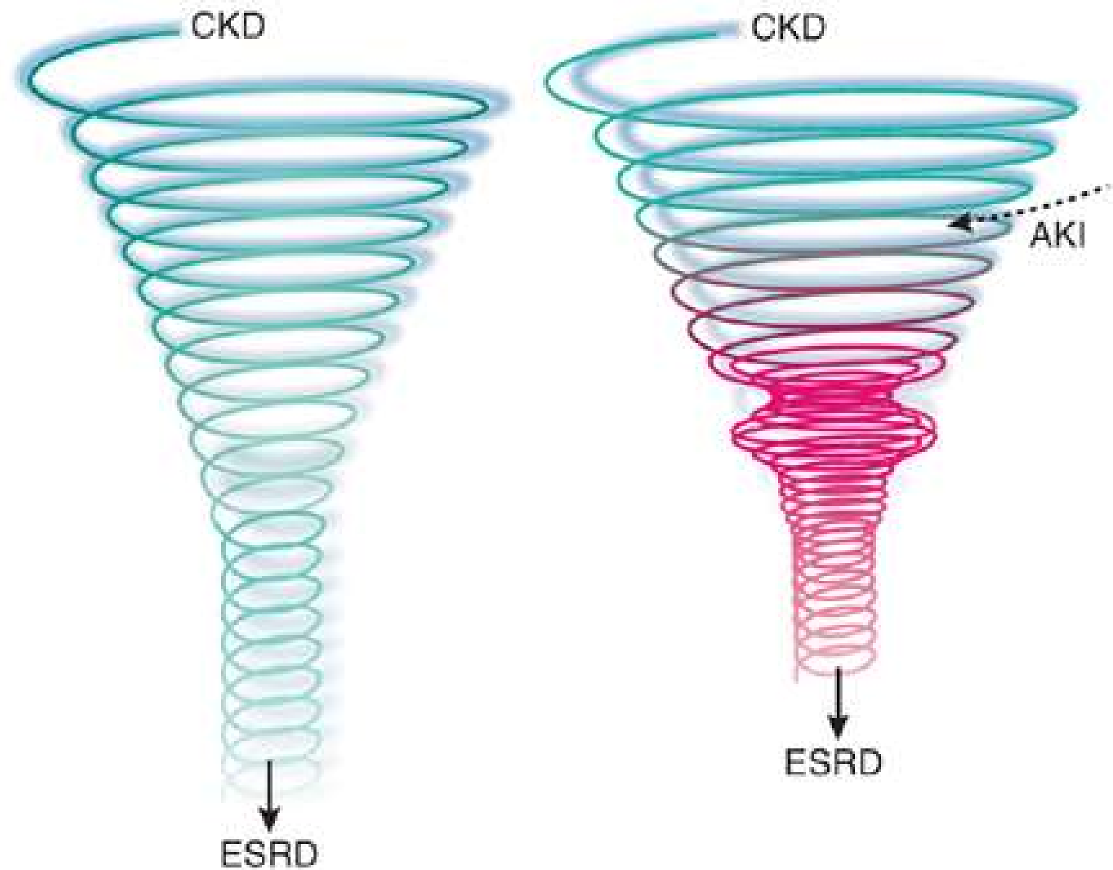


What is the treatment?

A) OMG! Get him to dialysis
B) Foley- must be post renal
C) IV fluids
D) None

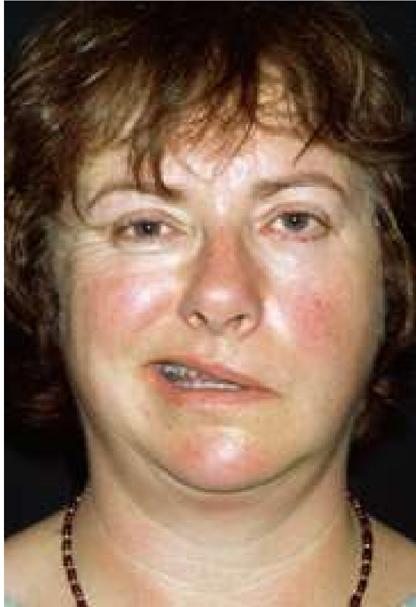
Fun with Kidneys

AKI on CKD



His BUN/SCr corrects to 3/1.4 with IV fluids

However, he will be at continued risk of ESRD due to his AKI



Yvette

48 y/ female

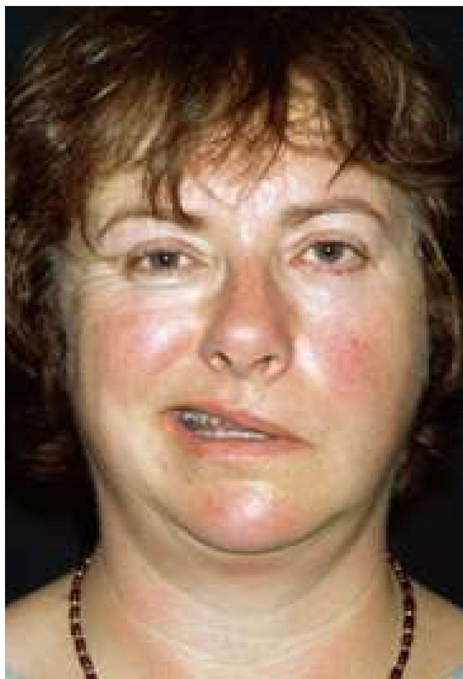
PMH: HTN, CAD, CKD (eGFR 25), obesity

Meds: Diovan (valsartan), ASA, furosemide, Prozac (fluoxetine), Calan (verapamil)

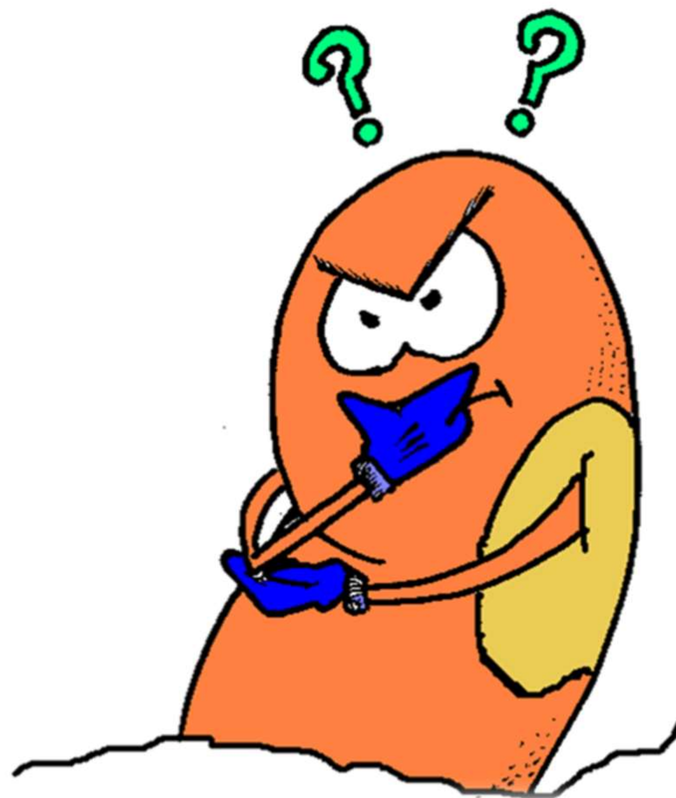
HPI: Patient presents to the urgent care section of the ED with new onset partial paralysis of the L side of her face, pt knows she's at risk of stroke

A STAT CT scan rules out a stroke
Her facial paralysis follows CN VII
Since she fits the 'classic' symptoms of Bell's palsy, you reassure her
She is discharged on prednisone (20mg/day) and Zovirax (acyclovir) 400mg tid)
72 hours later she returns to the urgent care with mental status changes

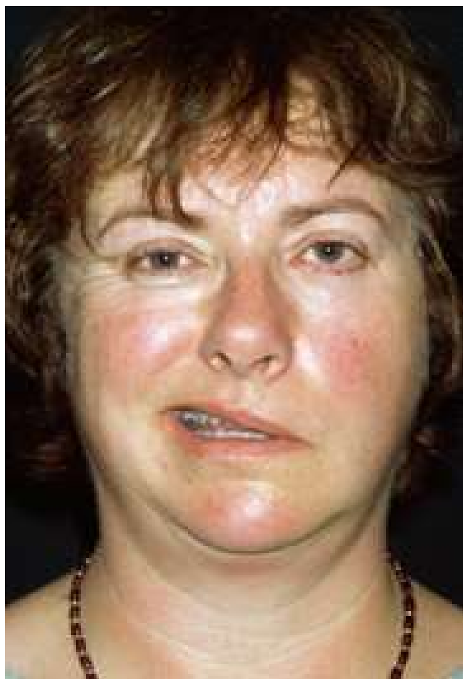
What happened?



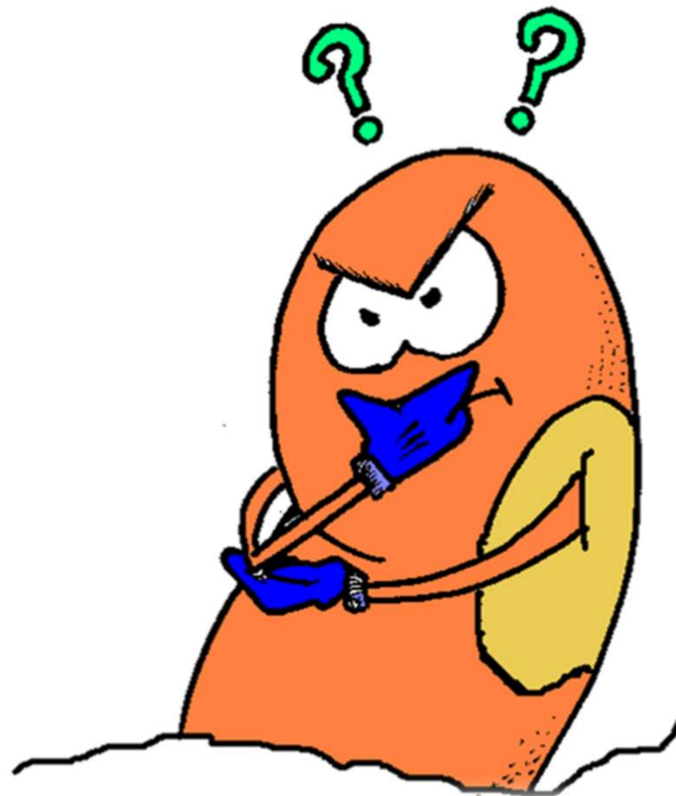
Yvette



A) We gave too high a dose
B) We picked the wrong drug
D) Hard to say-I am just randomly guessing at this point
D) She is having an evolving stroke



Yvette



A) We gave too high a dose

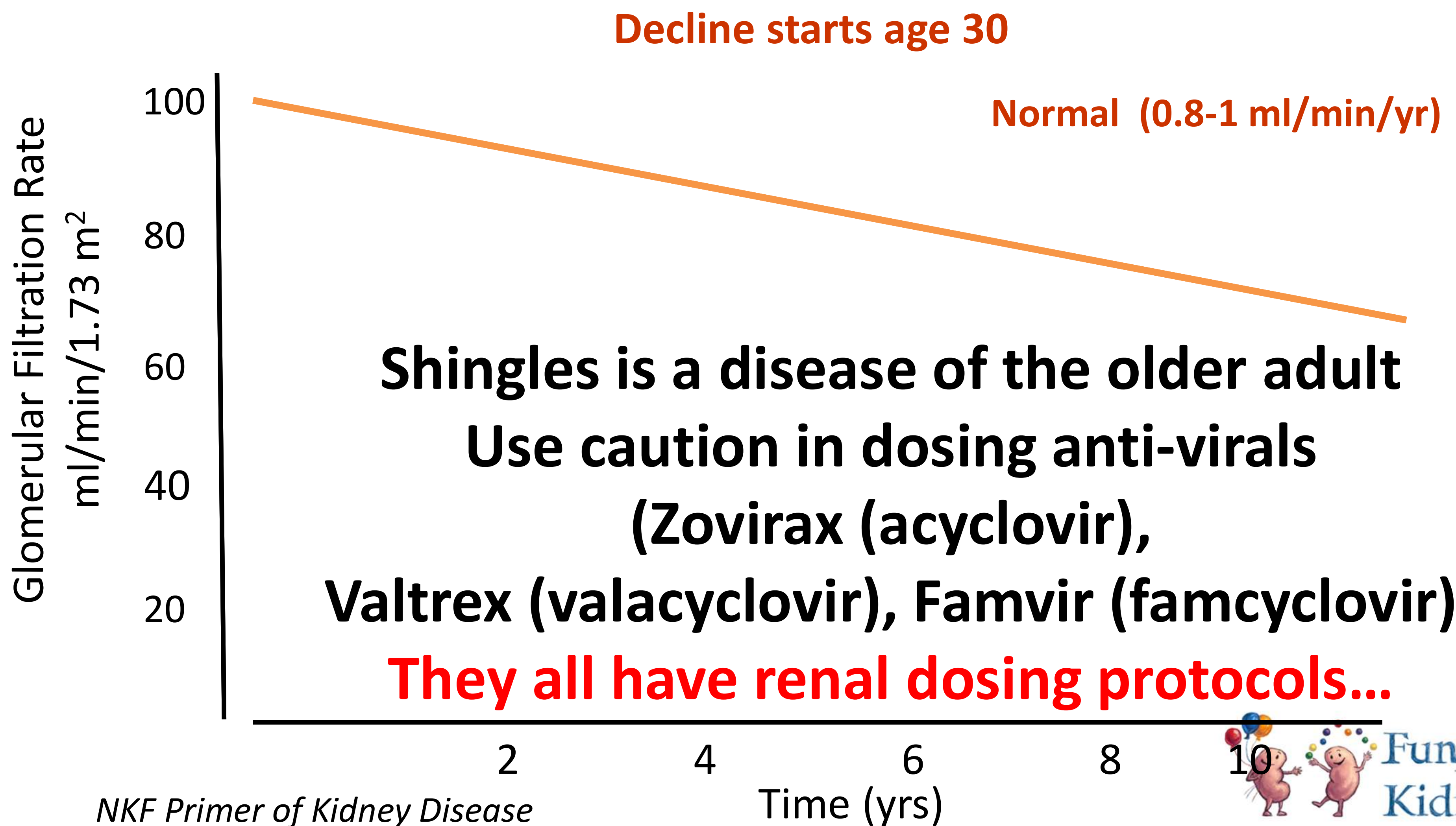
B) We picked the wrong drug

D) Hard to say-I am just randomly guessing at this point

D) She is having an evolving stroke

Fun with Kidneys

Normal Age Related Kidney Function Loss



NKF Primer of Kidney Disease 5th edition

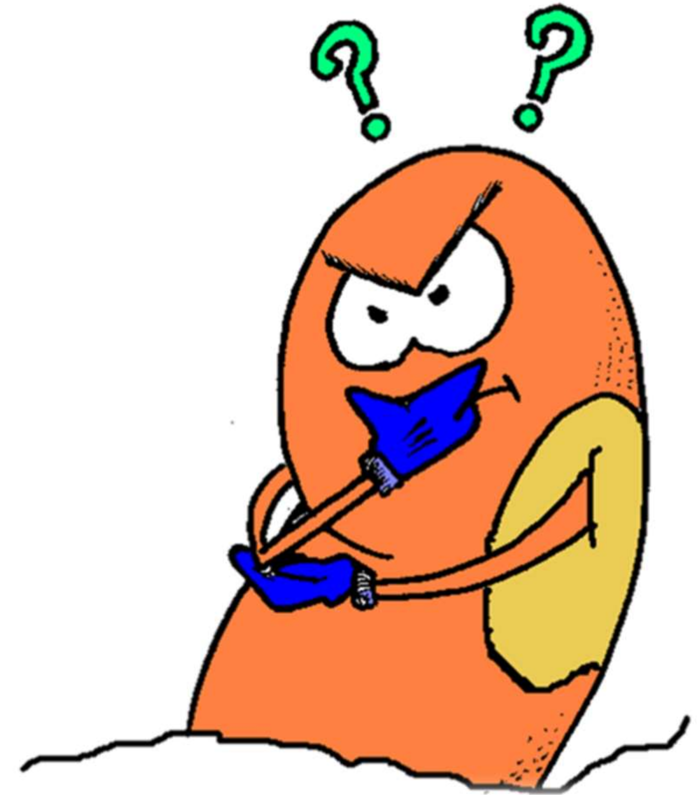
Ted

64 y/o male
PMH: smoker (previous), CKD (eGFR 45), CAD (1 stent), BPH, BMI 29
Meds: ASA, Plavix (clopidogrel), lisinopril, atorvastatin

Works as the head PA in the OR
Was seen by cardiology recently who doubled his lisinopril
Is having palpations during surgery and steps away from the OR table
Collapses in the midst of surgery
Anesthesia calls a code and he is rolled the 200 ft to the ED

What abnormality is seen on his EKG?

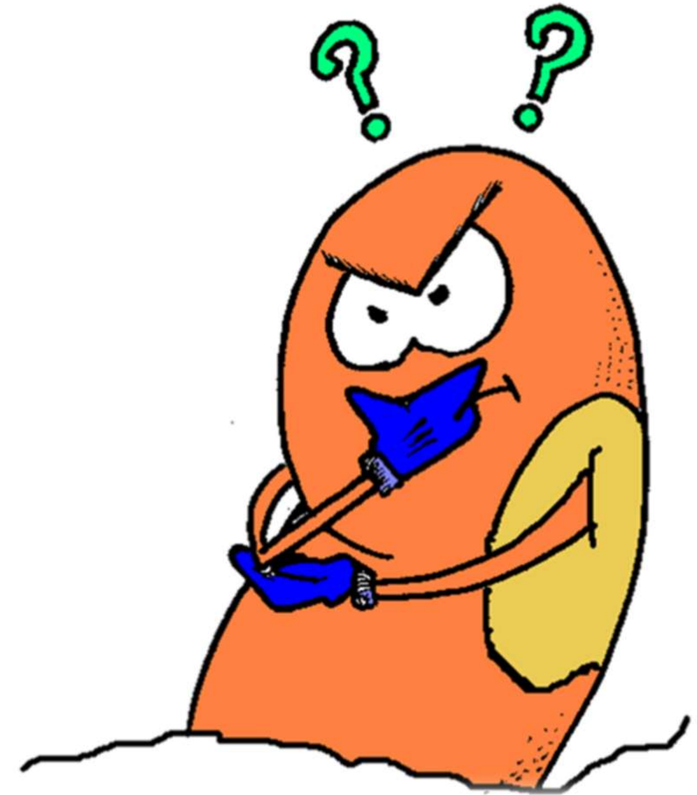
Ted



A) Prolongation of the QT interval
B) 2nd degree heart block
C) Atrial fibrillation
D) Peaked T waves

Fun with Kidneys

Ted



A) Prolongation of the QT interval

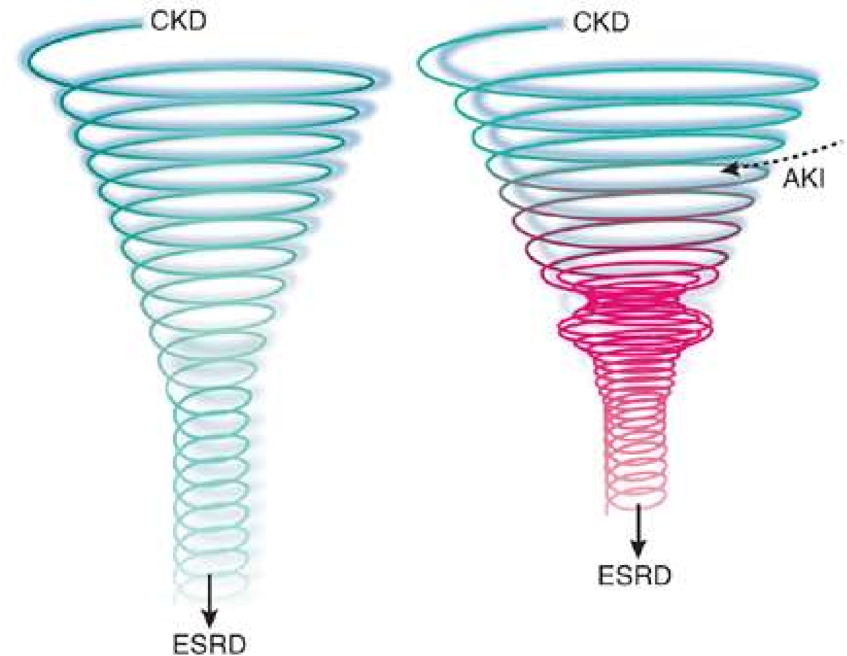
B) 2nd degree heart block

C) Atrial fibrillation

D) Peaked T waves

Fun with Kidneys

Ted



His K is **6.8 meq/dL** and corrects to 4.5meq/dL with IV fluids/foley
His GFR drops to 12 and rebounds to 15
He undergoes a TURP
He starts the work-up for a kidney transplant
At 5 months post AKI, his eGFR rises to 24!
However, he will be at continued risk of ESRD due to his AKI

Remember: All males above 50 have some BPH

(no matter what they tell you)

s

‘Ralph’

38 y/o male presents to ED with hyperemesis X 2weeks, ‘peeing blood’ for last 2 days, states only hot showers dec N&V

PMH: Medical marijuana

PE: poor skin turgidity, ‘ill-looking’, N&V, tachycardia, 90/54

Labs: K 6.2, mixed metabolic acidosis, SCr 8.1mg/dL, UA 4+blood on dip, no RBCs on micro

What is the diagnosis?

A) Acute marijuana poisoning
B) Compensated respiratory alkalosis
C) Rhabdomyolysis
D) Nephrolithiasis

‘Ralph’

38 y/o male presents to ED with hyperemesis X 2weeks, ‘peeing blood’ for last 2 days, states only hot showers dec N&V

PMH: Medical marijuana

PE: poor skin turgidity, ‘ill-looking’, N&V, tachycardia, 90/54

Labs: K 6.2, mixed metabolic acidosis, SCr 8.1mg/dL, UA 4+blood on dip, no RBCs on micro

What is the diagnosis?

A) Acute marijuana poisoning
B) Compensated respiratory alkalosis
C) Rhabdomyolysis
D) Nephrolithiasis

‘Ralph’

38 y/o male presents to ED with hyperemesis X 2weeks, ‘peeing blood’ for last 2 days,

How did that happen?

Think dehydration due to N&V with hot showers

Reports from NC and CA state that the N&V from chronic marijuana use is

NOT uncommon

They don’t report seeing **AKI**

BUT they also admit they really didn’t know to ask….

Or look for it!

Kidneys

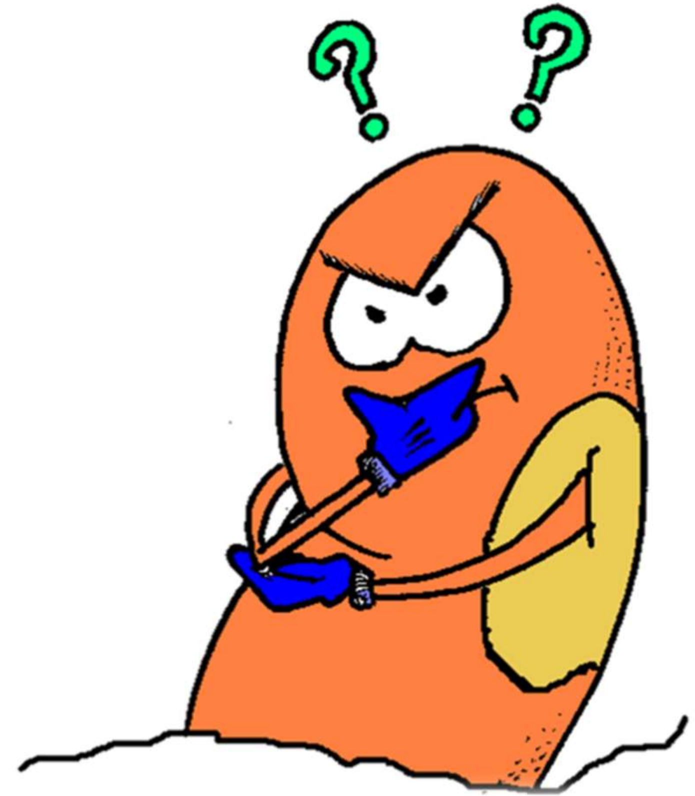
Edith

64 y/o female
PMH: DM, PVD, morbid obesity, CKD (eGFR 32) CAD, CHF, HTN
Meds: Lantus (glargine), Humalog (insulin lispro), lisinopril, furosemide, gabapentin, atorvastatin, ASA, Plavix (clopidogrel), Procardia (nifedipine), metoprolol

Presents to the ED at a teaching hospital on July 1st with an open wound on her L foot
Resident treats for presumed infection in known diabetic
Labs: WBC 11, K 4.5, SCr 2 (eGFR 27ml/min), BG 289
RX: Bactrim DS (sulfamethoxazole/trimethoprim) 2 BID
(MRSA is part of the antibiogram in this area)

What can be the complication?

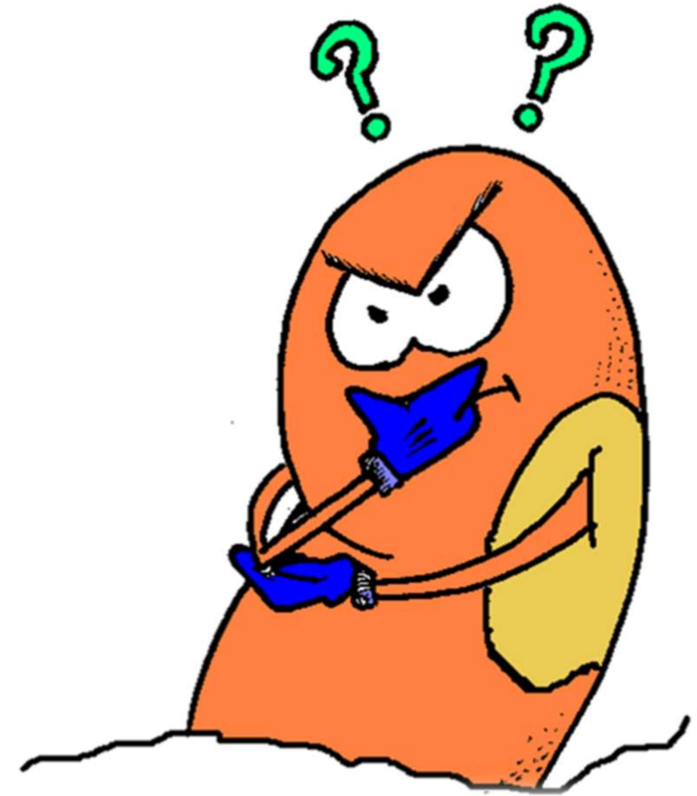
Edith



A) Metabolic acidosis
B) Nausea with the antibiotic
C) Hyperkalemia
D) Prolonged QT interval

Fun with Kidneys

Edith



A) Metabolic acidosis
B) Nausea with the antibiotic
C) Hyperkalemia
D) Prolonged QT interval

Fun with Kidneys

Edith

64 y/o female

PMH: DM, PVD, morbid obesity, CKD (eGFR 32) CAD, CHF, HTN

Meds: Lantus (glargine), Humalog (insulin lispro), lisinopril, furosemide, gabapentin, atorvastatin, ASA, Plavix (clopidogrel), Procardia (nifedipine), metoprolol

Bactrim (sulfamethoxazole/trimethoprim) works as a K+ competitor in the loop of Henle

K+ is retained with Bactrim (sulfamethoxazole/trimethoprim)

CKD causes an increase in the half-lives of the drug and its metabolite

It can be used with caution and renal dosing

BUT NOT AT 2X STANDARD DOSING!!

Art

78 y/o male

PMH: DM, CAD, PVD, CKD (eGFR 26), CABG CHF, edema, HLD, gout, obesity

Meds: Ramipril, furosemide, clopidogrel, ASA, colchicine, verapamil, metoprolol, atorvastatin

Presents to his primary care office with complaints of leg/foot pain

Follows stocking glove distribution

Decreased sensitivity with severe pain

Described as ‘pins and needles’ since he had just seen the commercial on TV!

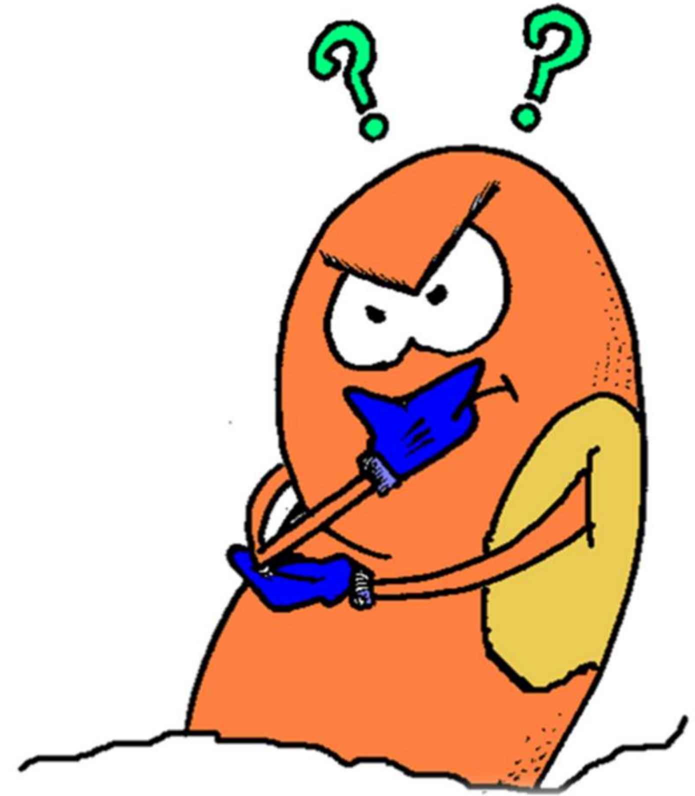
You agree to start him on gabapentin and give him 300mg tid

You tell him to take it for 1 week before increasing the dose

You get a call from his son 5 days later telling you Dad is not making sense

Which medication caused Art’s MS changes?

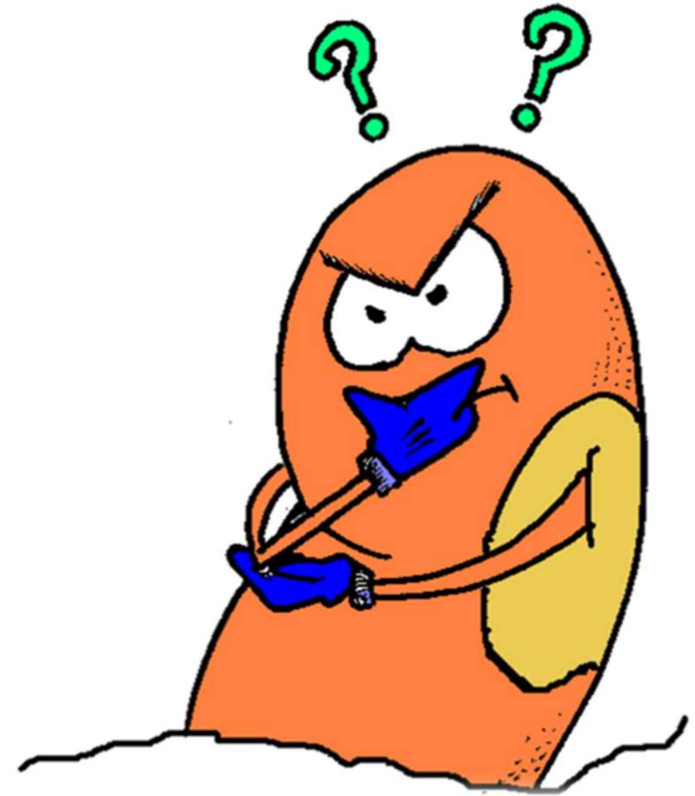
Art



A) The combo of all the HTN meds
B) Colchicine
C) Gabapentin
D) Polypharmacy

Fun with Kidneys

Art



A) The combo of all the HTN meds
B) Colchicine
C) Gabapentin
D) Polypharmacy

Fun with Kidneys

Art

78 y/o male

PMH: DM, CAD, PVD, CKD (eGFR 26), CABG CHF, edema, HLD, gout, obesity

Meds: Ramipril, furosemide, clopidogrel, ASA, colchicine, verapamil, metoprolol, atorvastatin

FDA insert:

Usual Dosing (Adults): 300mg q8h.

Usual maintenance dose: 300-600mg q8h. Maximum dosage/day: 3600 mg

Renal Dosing

eGFR >60ml//min: Give usual dosage

eGFR 30-59ml/min: Dosage range: 400-1400mg/day in divided doses - Usually bid

eGFR 15-29ml/min: Dosage range: 200-700mg/day

eGFR<15ml/min: Dosage 100-300 mg/day. Use lower end of this range for CRCL <7.5 ml/min.

Hemodialysis: 100-300 mg/day. Give supplemental dose of 125-350mg after each dialysis

Art

78 y/o male

PMH: D… (eGFR 26), CABG

C…

…grel, ASA,

…vastatin

FDA insert:

Usual Dosin…

Usual main… mg

Renal Dosi…

eGFR >60m…

eGFR 30-59… Usually bid

eGFR 15-29ml/…

eGFR<15ml/min. … …nge for CRCL <7.5 ml/min.

Hemodialysis: 100-300 …

125-350mg after each dialysis…

This is the most common 'overdose' we see nationwide

All FDA inserts after 1998 MUST include renal dosing

George

78 y/o male
PMH: HDL, HTN, neuropathy, CKD (eGFR 48) BPH, hypothyroidism
Meds: HCTZ, levothyroxine, Cymbalta (duloxetine), atorvastatin, Fosamax (alendronate), lisinopril, omega 3, amlodipine, MVI, CoQ10, oxycodone

Retired military who still works full time @ golf shop
Presents to ED with unsteadiness, sleepiness, sluggish
Confusion and difficulty concentrating
Recently started on Percocet (oxycodone) & Cymbalta (duloxetine) for neuropathy
Serum Na is ***108***

What is causing the hyponatremia?

George

A) HCTZ
B) Oxycodone
C) Atorvastatin
D) Duloxetine

Fun with Kidneys

George

A) HCTZ
B) Oxycodone
C) Atorvastatin
D) Duloxetine

Fun with Kidneys

George

78 y/o male

PMH: HDL, HTN, neuropathy, CKD (eGFR 48) BPH, hypothyroidism

Meds: HCTZ, levothyroxine, Cymbalta (duloxetine), atorvastatin, Fosamax (alendronate), lisinopril, omega 3, amlodipine, MVI, CoQ10, oxycodone

SSRIs and SRNIs can cause hyponatremia
More common in the elderly
While considered rare per the literature* (9%) we see 4-5/year
Mechanism of action felt to be SIADH or polydipsia

*Characteristics, prevalence, risk factors, and underlying mechanism of hyponatremia in elderly patients treated with antidepressants: a cross-sectional study. Maturitas. 2013 Dec;76(4):357-63

Maggie

66 y/o female

PMH: HTN, DM, HLD, PVD, COPD, obesity
CKD (eGFR 21)

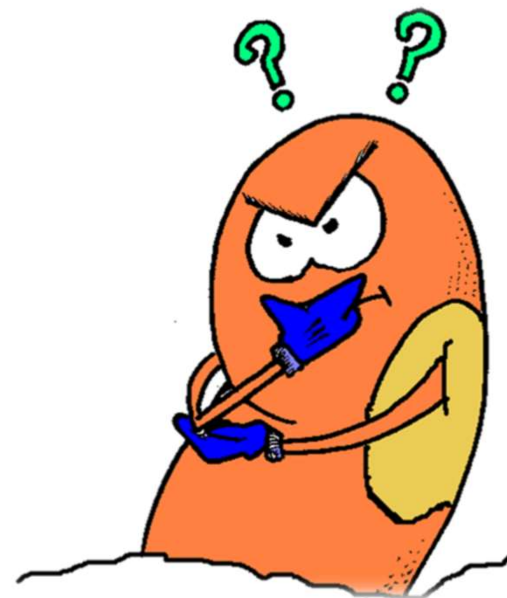
Meds: Maxide (triamterene/HCTZ), carvedilol, amlodipine, Nasonex (mometasome furoate), Allegra (fexofenadine), metformin, atorvastatin, ASA, clopidogrel

Presents to the ED with sudden-onset CP, SOB, nausea, diaphoresis
EKG shows junctional bradycardia with hypotension

K 7.8 meq/dL

Maxide is a combination of triamterene and HCTZ

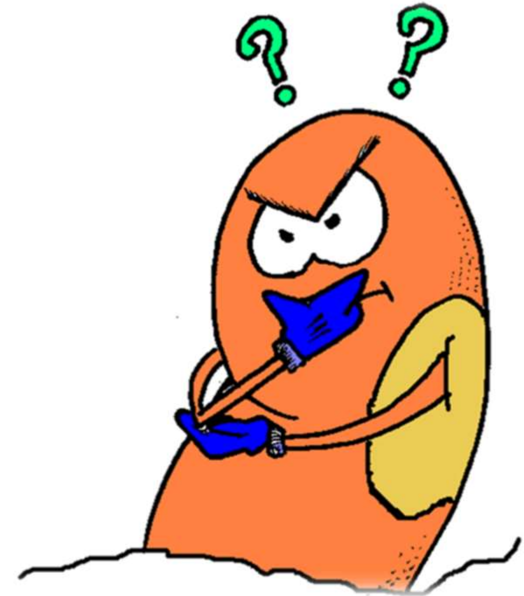
Maggie



Why is there an issue with Maxide (triamterene/HCTZ)?

A) The triamterene is less effective at lower eGFRs
B) The HCTZ is less effective at lower eGFRs
C) Mixing allergy medications with Maxide is dangerous
D) I seriously have no bloody idea

Maggie



Why is there an issue with Maxide (triamterene/HCTZ)?

A) The triamterene is less effective at lower eGFRs
B) The HCTZ is less effective at lower eGFRs
C) Mixing allergy medications with Maxide is dangerous
D) I seriously have no bloody idea

Maggie

It is recommended that you move to a Loop diuretic at an eGFR < 30ml/min
If losing kidney function fast,
Consider moving to a loop earlier

B) **The HCTZ is less effective at lower eGFRs**
C) Mixing allergy medications with Maxide is dangerous
D) I seriously have no bloody idea

Fun with Kidneys

Laurie

52 y/o female

PMH: Diabetes, HDL , neuropathy, obesity

Meds: metformin, gabapentin, simvastatin, ASA

Presents to ED with inability to swallow

PE: painful oral herpetic lesions with drooling, healing lesions on face with crusts/pus

Diagnosis: oral herpes zoster

Labs: WBC 11K, SCr 1.2mg/dL (GFR 57), K 3.2meq/L, FENA <1%

Admitted for IV Acyclovir (Zovirax), IV antibiotics

Laurie

52 y/o female

PMH: Diabetes, HDL , neuropathy, obesity

Meds: metformin, gabapentin, simvastatin, ASA

Labs: WBC 11K, SCr 1.2mg/dL (GFR 57), K 3.2meq/L, FENA <1%

What kidney dosing protocol should be used?

A) Dose off the GFR (57ml/min)
B) Dose off the SCr (1.2mg/dL)
C) Dose off both and average
D) Neither one is useful

Laurie

52 y/o female

PMH: Diabetes, HDL , neuropathy, obesity

Meds: metformin, gabapentin, simvastatin, ASA

Labs: WBC 11K, SCr 1.2mg/dL (GFR 57), K 3.2meq/L, FENA <1%

What kidney dosing protocol should be used?

A) Dose off the GFR (57ml/min)
B) Dose off the SCr (1.2mg/dL)
C) Dose off both and average
D) Neither one is useful

Laurie

52 y/o female

PMH: Diabetes, HDL , neuropathy, obesity

Meds: metformin, gabapentin, simvastatin, ASA

Patient has been NPO due to painful lesions

Lesions are healing and thus, this is multi-day process

GFR is only useful in stable situations

FYI: FENA<1% shows that kidneys are functioning

This is pre-renal (dehydration) AKI

AKI dosing is best left to the pharmacists

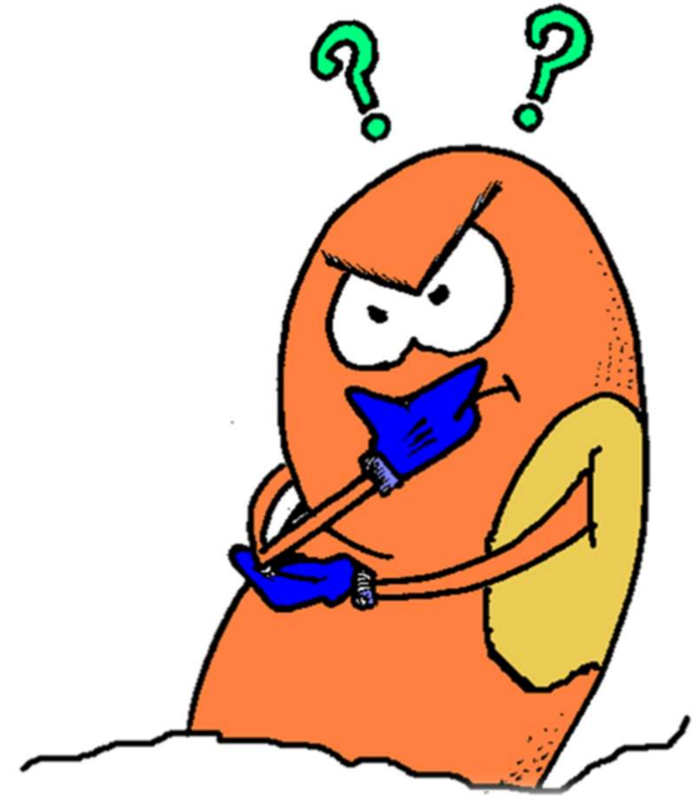
Caleb

35 y/o male
PMH: ETOH use
Meds: none

Presents to ED with 5 days of crampy lower abdominal pain, N&V, tenesmus
Admits heavy ETOH use
Scr 2.2mg/dL (baseline 0.6mg/dL)
CT of abdomen shows 1.1cm non-obstructing stone on the L
You medicate with IV Ketorolac (30mg)

Why did the nurse look at you funny?

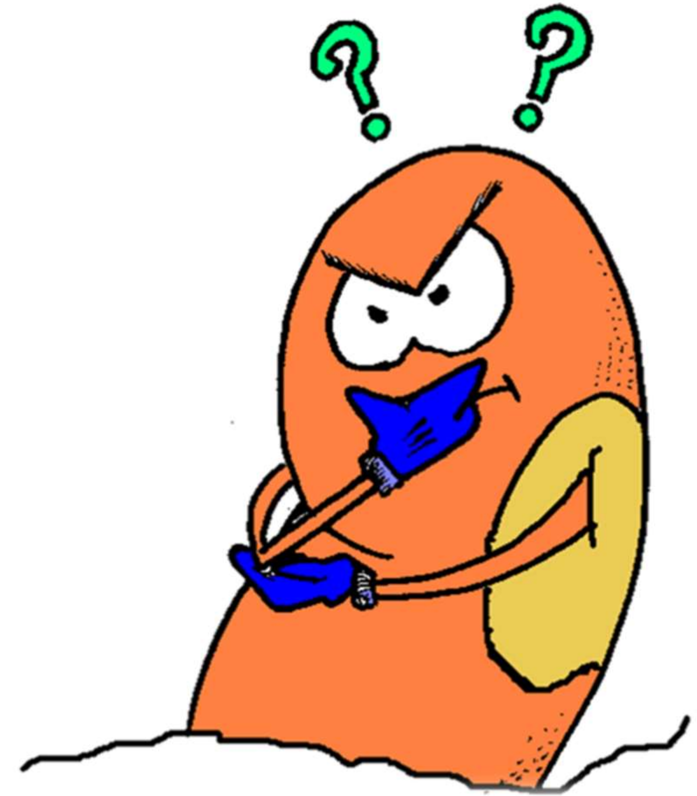
Caleb



A) Wrong medication
B) Wrong dose
C) Didn't cover for thiamine (banana bag!!)
D) She has an issue with vomiting....

Fun with Kidneys

Caleb



A) Wrong medication

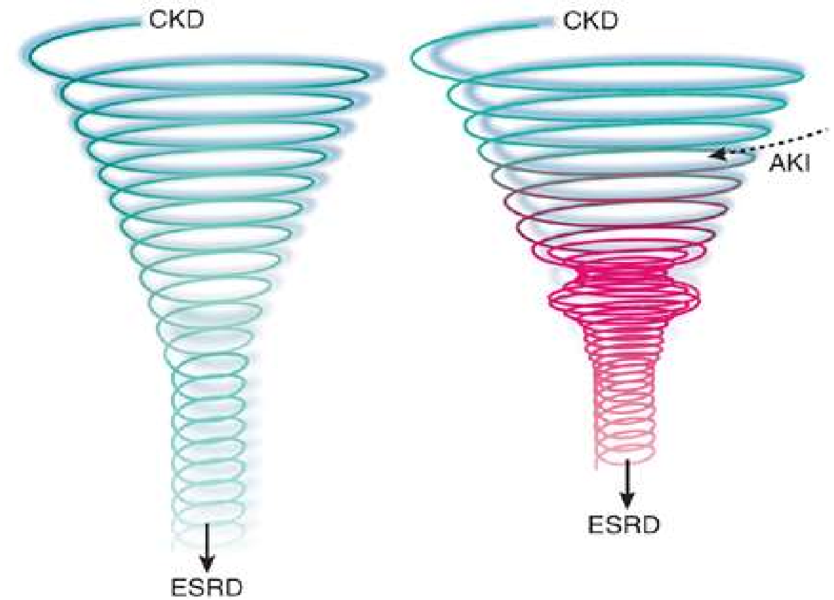
B) Wrong dose

C) Didn’t cover for thiamine (banana bag!!)

D) She has an issue with vomiting….

Fun with Kidneys

Caleb



You realize your error before anyone else sees it
You hang 2L NS
The SCr drops from 2.2mg/dL to 1.8mg/dL
Even though you corrected your error ASAP,
Caleb will be at continued risk of ESRD due to his AKI
AND…the stones were **incidentalomas**
NON-obstructing

Conclusions

- Medication dosing errors are common in CKD
- A pharmacist can be your best friend
- When in doubt, look it up! (***I do!!***)
- CKD = go low, go slow and recheck labs often
- All FDA inserts have renal dosing protocols
  - When using **Epocrates Rx**, you need to go to 'adults' and then to renal dosing!