## What's a kidney?

Rory Silverberg September 13, 2019





# **Conflict of Interest Declaration: Nothing to Disclose**

Presenter: Rory Silverberg, MD, Nephrology

Title of Presentation: What's a kidney?

I have no financial or personal relationship related to this presentation to disclose.

### Disclosures

Speaker: Rory Silverberg, MD, Nephrology

Relationships with commercial interests:

Grants/Research Support: None

Speakers Bureau/Honoraria: Janssen Pharmaceutical, Sanofi

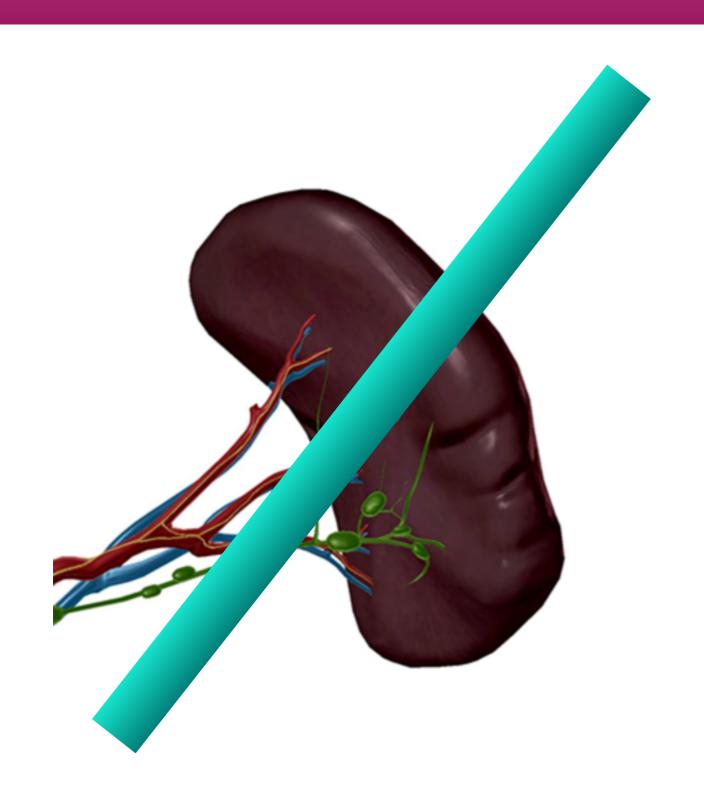
Consulting Fees: None

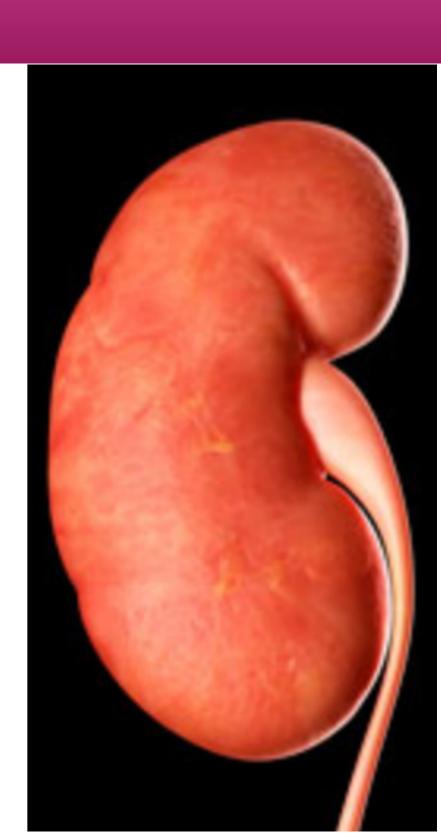
Other: None

#### The Plan

- What's a Kidney?
- The question I ask friends, medical students, residents and 4 year olds and the answers they give me...
- Azotemia vs AKI
- The Lazy River The circle of blood flow
- Renal Anatomy 101, 201, and 301
- Approach to AKI [or maybe just azotemia :]
- Estimating renal function [eGFR, CrCl, and proteinuria]
- Basic management of CKD related issues
- Drug prescribing in CKD/ESRD including pain meds
- A brief discussion about some common issues in nephrology: Contrast, IVFs...
- Other important things that should be covered in this talk but time won't allow for...

## What's a kidney?





## The Big Question

How does water get from your mouth to the toilet?

# This presentation is supposed to have 25% participation from the learners...

How does water get from your mouth to the toilet? Please choose from the following answer choices:

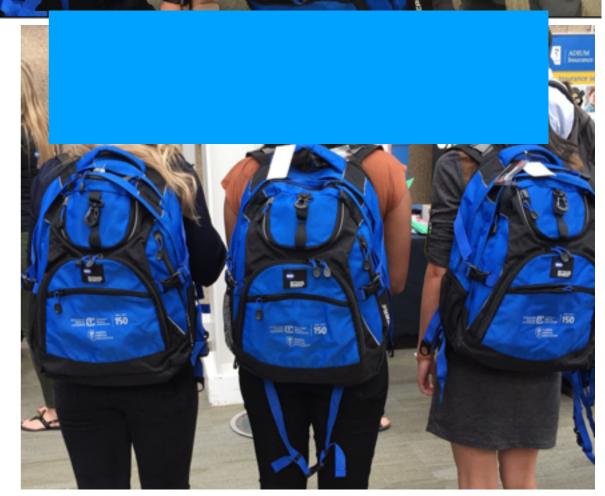
- A. Yes, I am confident that I could answer this question with ease.
- B. No, I honestly don't think I could confidently answer this question.
- C. Holy &H!7, please don't pick someone in the room at random to answer the question.

## Friends





# Medical Students And Residents

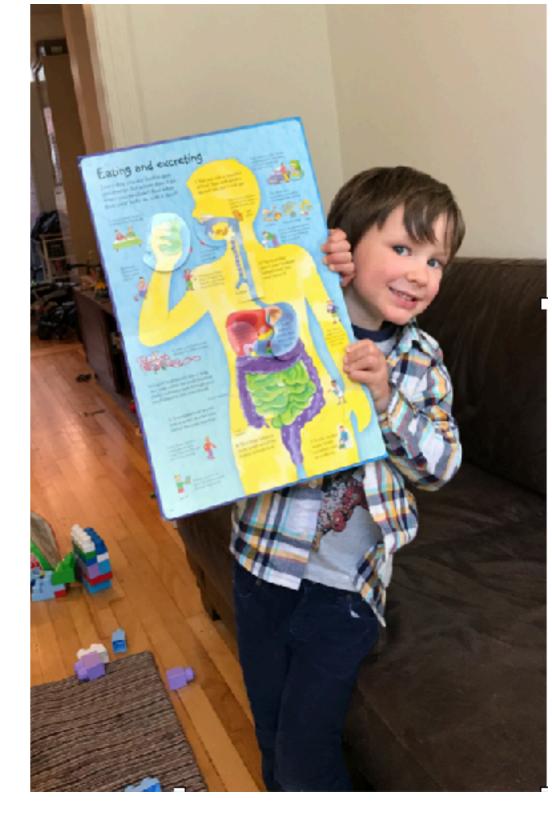


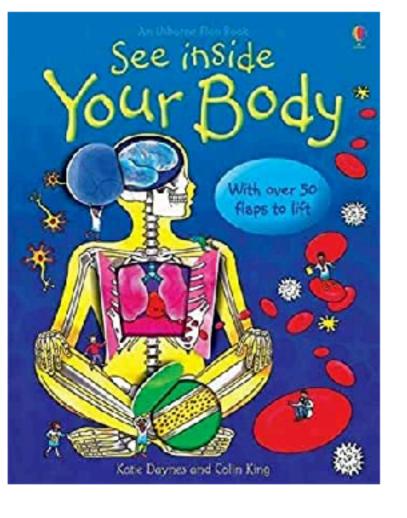
## 4 Year Old











#### See Inside Your Body

by Katie Daynes | Mar 14 2006



#### Paperback

 $^{\text{CDN}\$}16^{40} + ^{\text{CDN}\$18.95}$ 

**FREE Shipping** 

More buying choices

CDN\$ 2.98 (59 used & new offers)

#### **Board book**

More buying choices

CDN\$ 10.01 (54 used & new offers)







## What nerds argue about

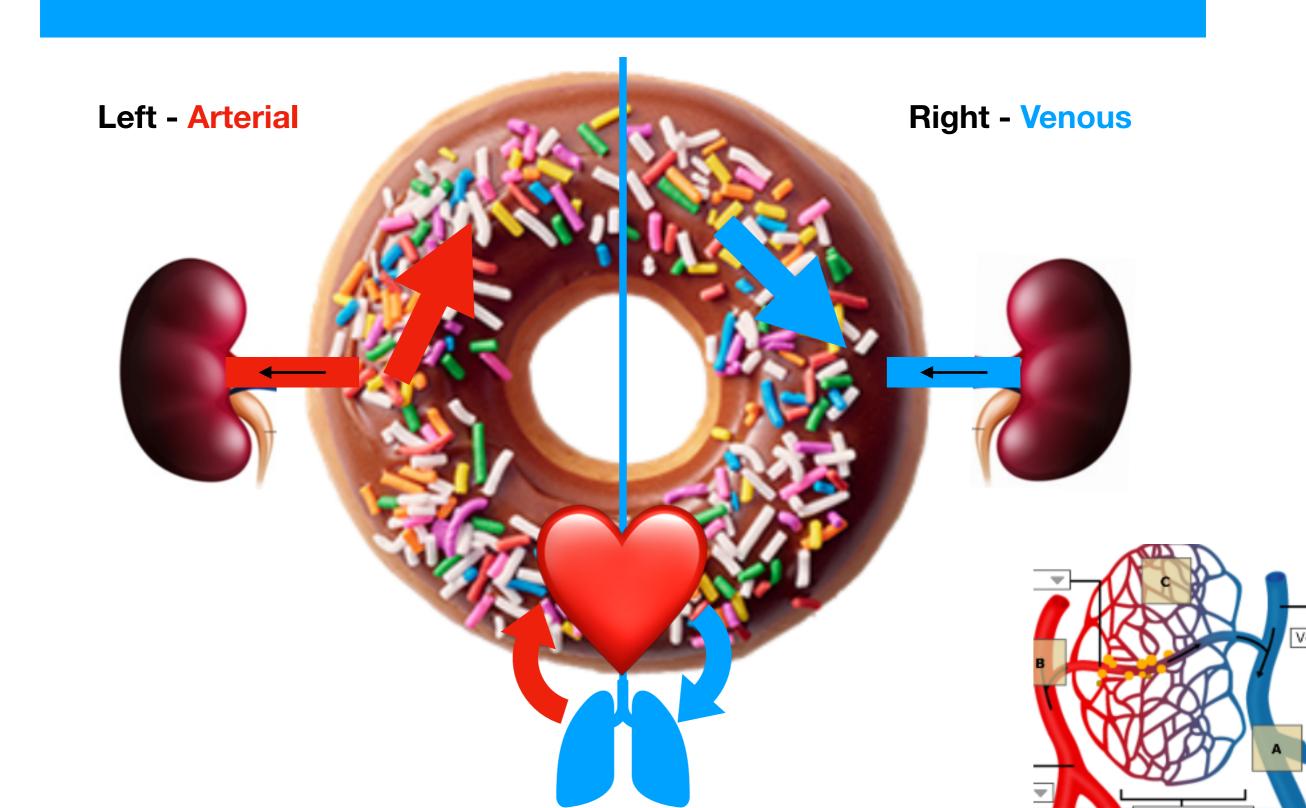
### Azotemia vs AKI



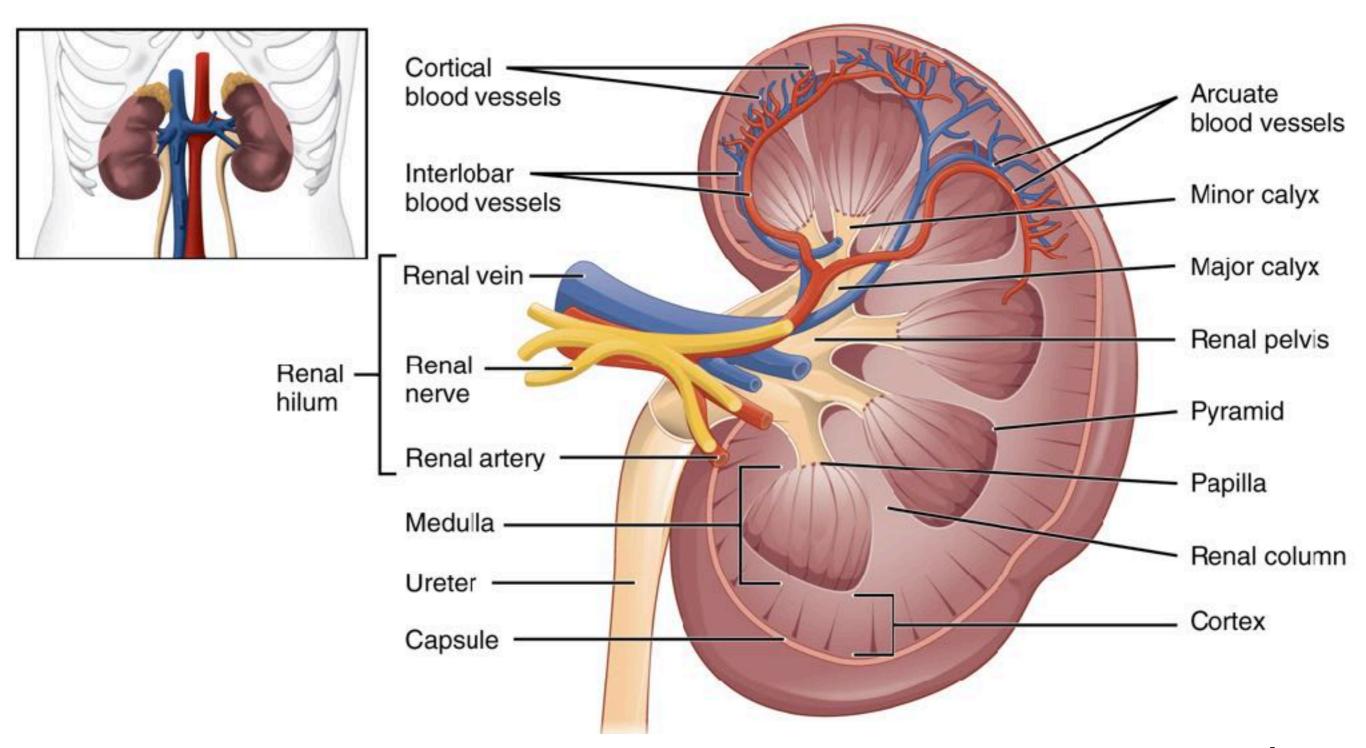
- Azotemia = Nitrogen "Azot" in blood "emia".
   Nitrogeneous waste build up in the blood... like urea and creatinine.
- AKI = Acute Kidney INJURY... Many different definitions. KDIGO is most accepted. Useful for studies...

# My way of thinking about things...

## The Lazy River

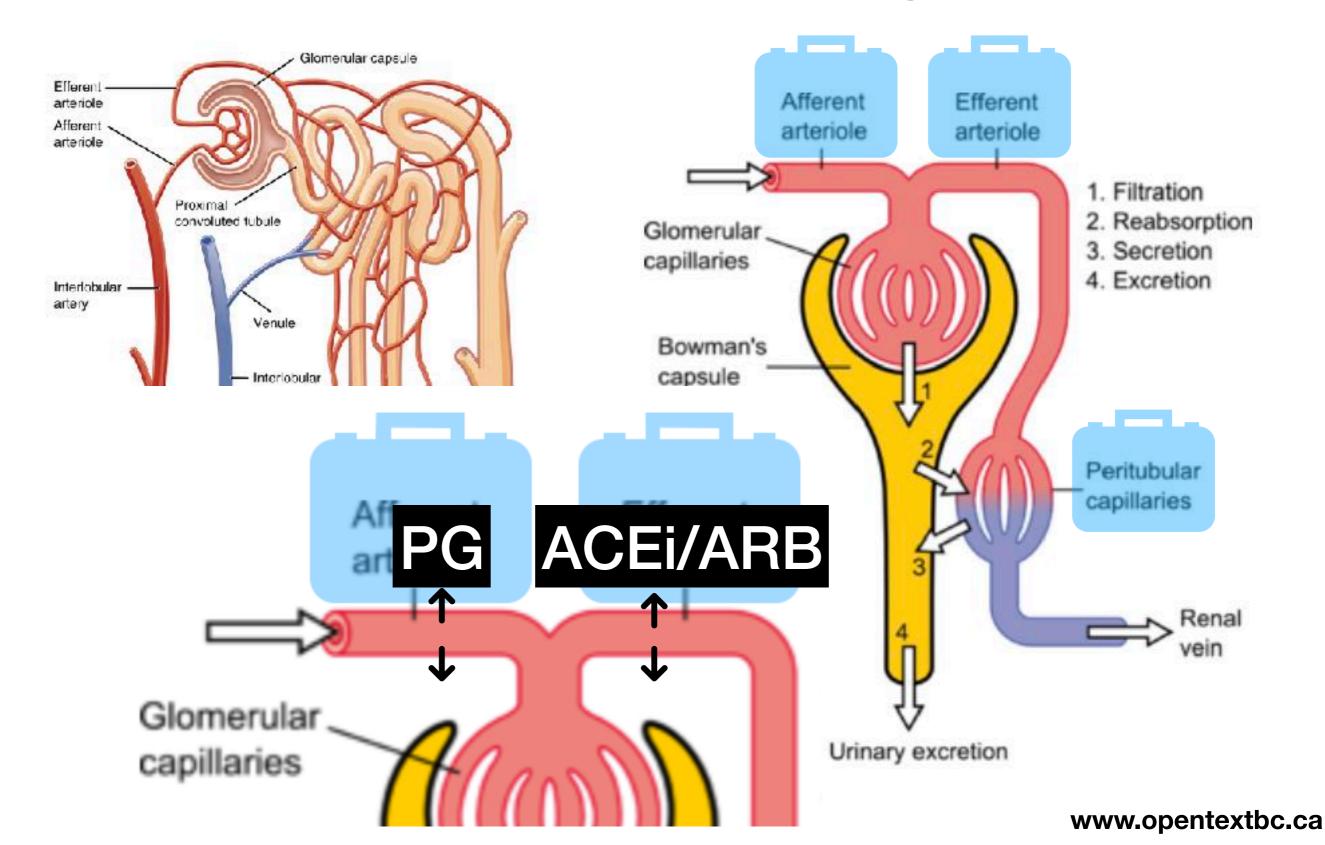


## Renal anatomy 101

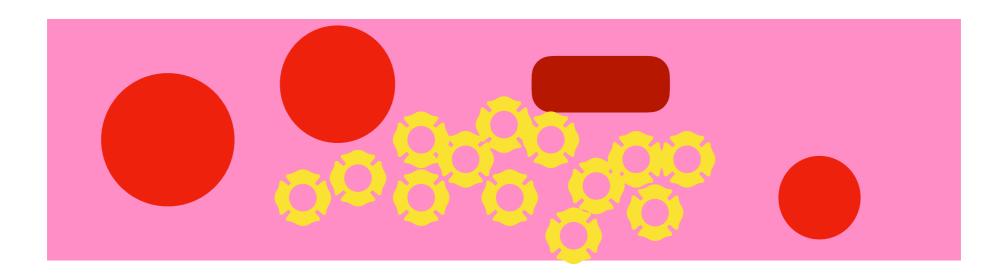


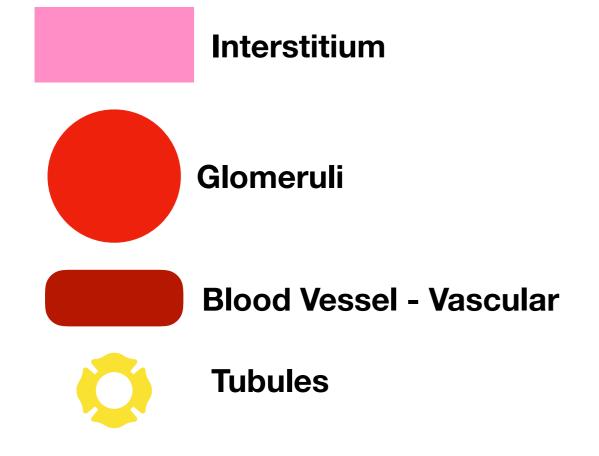
www.opentextbc.ca

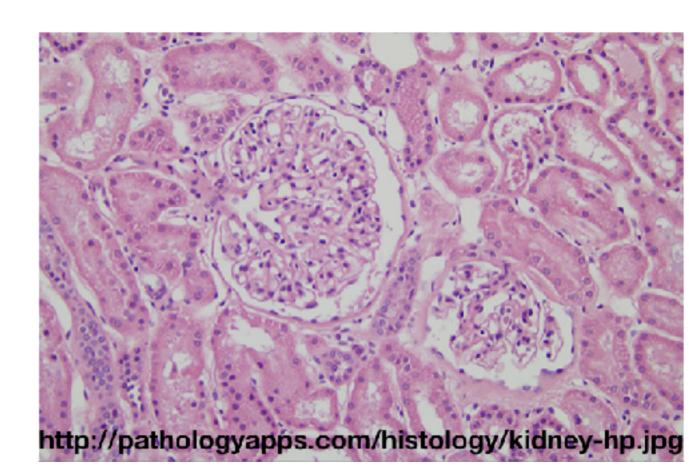
## Renal Anatomy 201



## Renal Anatomy 301







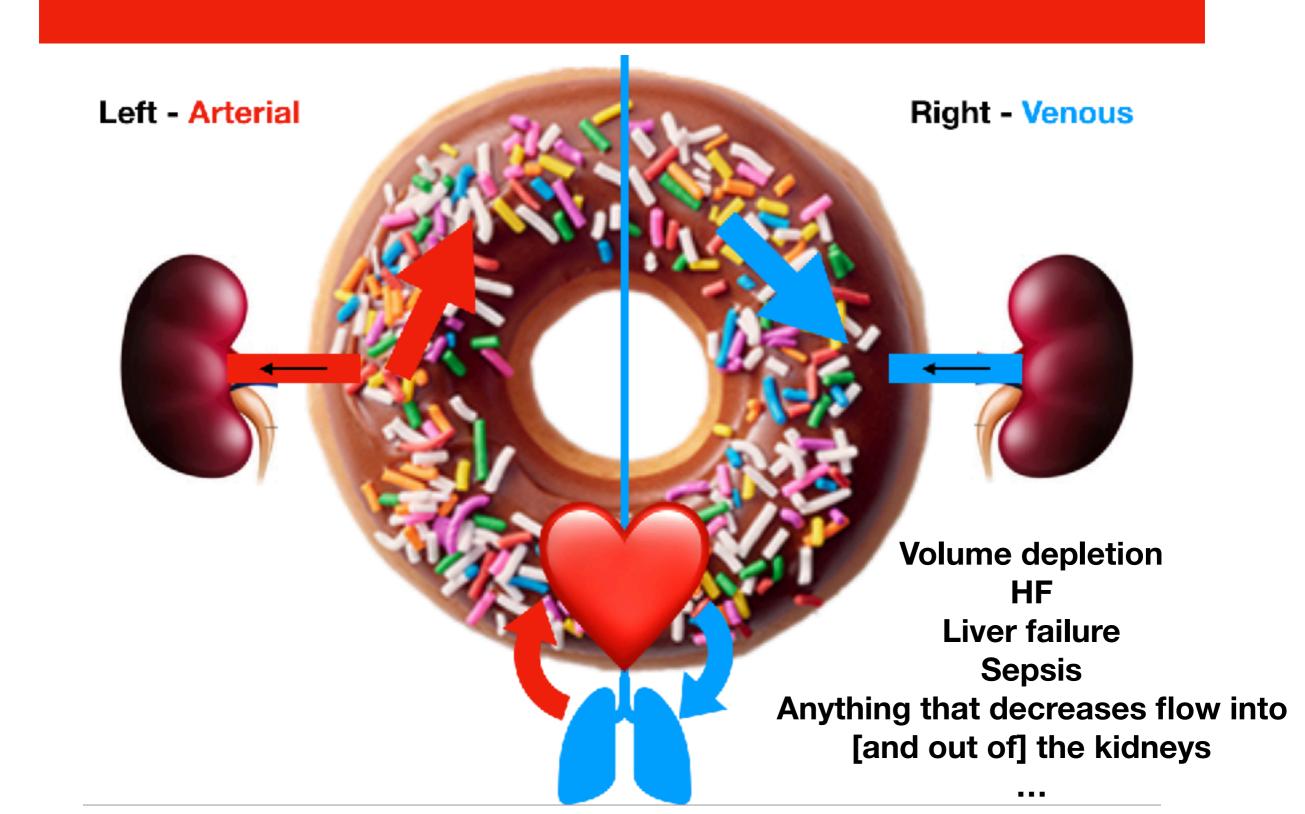
# The common approach to AKI [or maybe only azotemia:]

Pre-renal

Renal

Post-renal

### Pre-renal

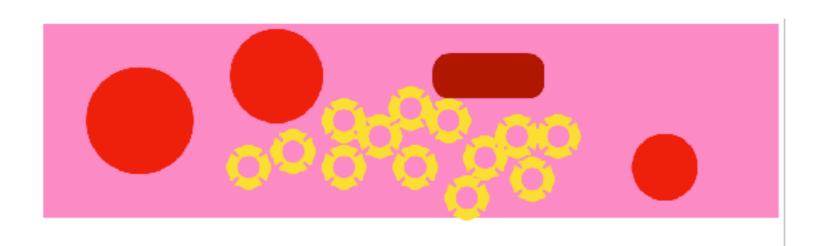


#### **Pop Quiz:**

#### Does furosemide [lasix] cause injury to the kidney?

- A. Yes, it directly injures the kidneys, especially when the Cr is high
- B. Yes, it has potential to indirectly injure the kidneys
- C. Nope, kidneys love the stuff
- D. Lasix lasts for 6 hours ... not a an answer choice but a cool fact
- E. Lasix makes people piss like a race horse. Yup!

### Renal



Interstitium

**AIN - Acute Interstitial Nephritis** 

Glomeruli

**GN - Glomerulonephropathy/Nephritis** 



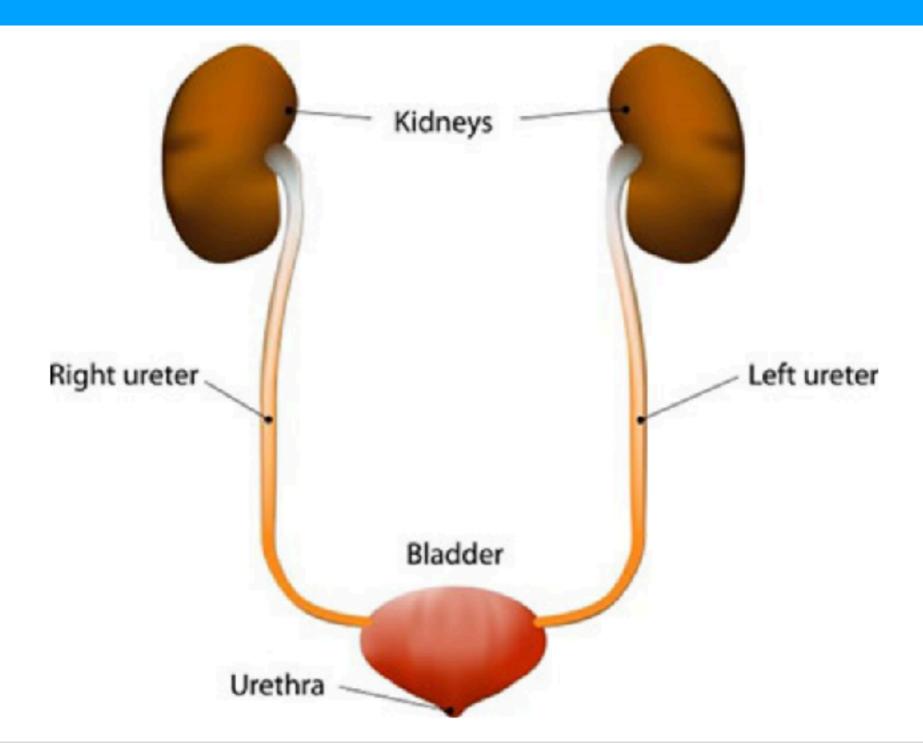
**Vasculitis** 



ATN - Acute Tubular Necrosis

**Tubules** 

### Post-renal



#### **POP QUIZ**

A lack of hydronephrosis on U/S and/or CT rules out obstruction?

A. Yes

B. No

# Lets get boring estimating renal function

## Question

Richard Head Trump is a 73M, in perfect health, except for diabetes and newly found proteinuria. PMHx: Type 2 DM, narcissistic personality disorder and small hands NYD. Cr 86 from baseline 70 as of one year ago. UA -ve for blood but is tracely +ve for protein, Urine ACR 56.

Which equation is best for predicting his GFR?

- A. Cockroft-Gault
- B. MDRD
- C. NRA
- D. CKD-Epi

## Estimating GFR

Cockcroft-Gault - ~200 inpatients at a VA hospital in the USA. Predominantly men... they weren't looking at GFR they were looking at CrCl. Multiply by 0.85 for women...

Cockcroft DW, Gault MH, Nephron. 1976;16(1):31.

**MDRD** - Modification of Diet in Renal Disease study... Does a low protein diet protect you from kidney disease? In mice yes. In humans...probably not. They gathered lots of info along with actual measurements of GFR (iothalamate...similar to inulin). All American. Not many AA in the study. *Had to have kidney disease to be enrolled*. **Not accurate with GFR > 60** 

Levey AS et al, Intern Med. 1999;130(6):461.

**CKD Epi** - much larger population. Patients without kidney disease included. More accurate in patients with GFR > 60. Not much of a difference below 60 but 60-70 you can see a big split. Also, customizable for different regions.

Levey AS et al, Ann Intern Med. 2009;150(9):604.

## Estimating GFR

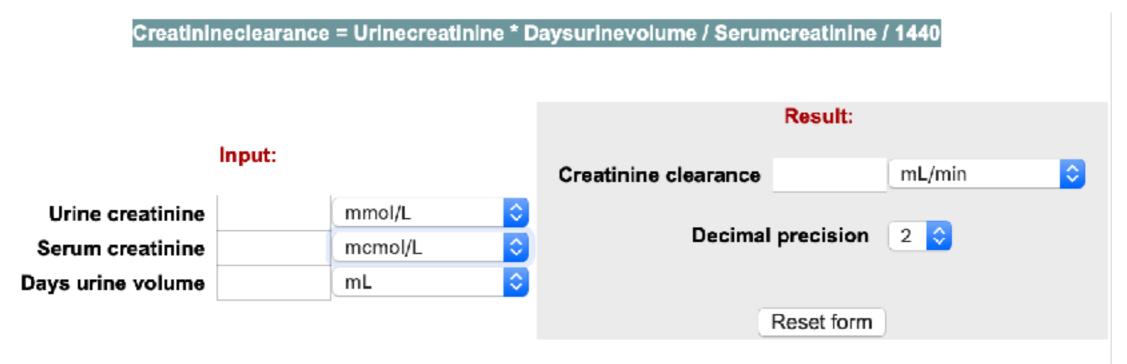
All of these count on a normal range of patient sizes. Not reliable for extremes of sizes. Ex. very small, CKC Epi will show better than actual renal function. Vice versa for large muscular people.

So...

Creatinine Clearance [CrCl] - 24h hour collection. 24h urine Cr and serum creatinine. Creatinine production is not related to renal function. It works in all circumstances. Just need a good sample.

CrCl does not equal GFR - it also includes creatinine secreted at the proximal tubule (trimethoprim and cimetidine block this)

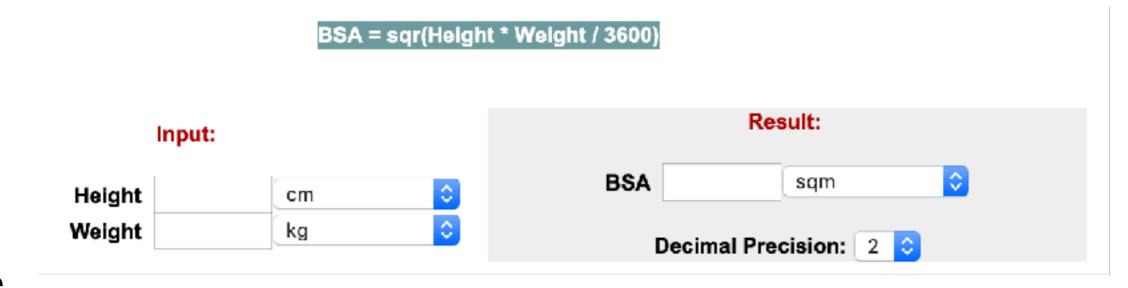
#### CrCl is based off of: GFR = [UCr x V] / SCr



#### Notes

 To calculate the creatinine clearance from a 24-hour urine collection, enter your patient's data into the appropriate data fields. The serum creatinine concentration must be stable for this formula to be valid. (See UpToDate topic reviews that discuss calculation of the creatinine clearance for a review of the factors that limit the accuracy of this test.)

#### CrCl x 1.73/BSA = CrCl normalized to a surface area of 1.73 m<sup>2</sup>



## Question

58M with bilateral RCC admitted for bilateral nephrectomies. Pre-Op Cr 80 and eGFR 100. Post op Cr is 90. What's his GFR?

A. 90

B. 80

C. 70

D. <60

E. What's a nephrectomy?

#### 58M with bilateral RCC admitted for bilateral nephrectomies. Pre-Op Cr 80 and eGFR 100. Post op Cr is 90. What's his GFR?

90

80

70

< 60

What's a nephrectomy?

# GFR is only part of the story...

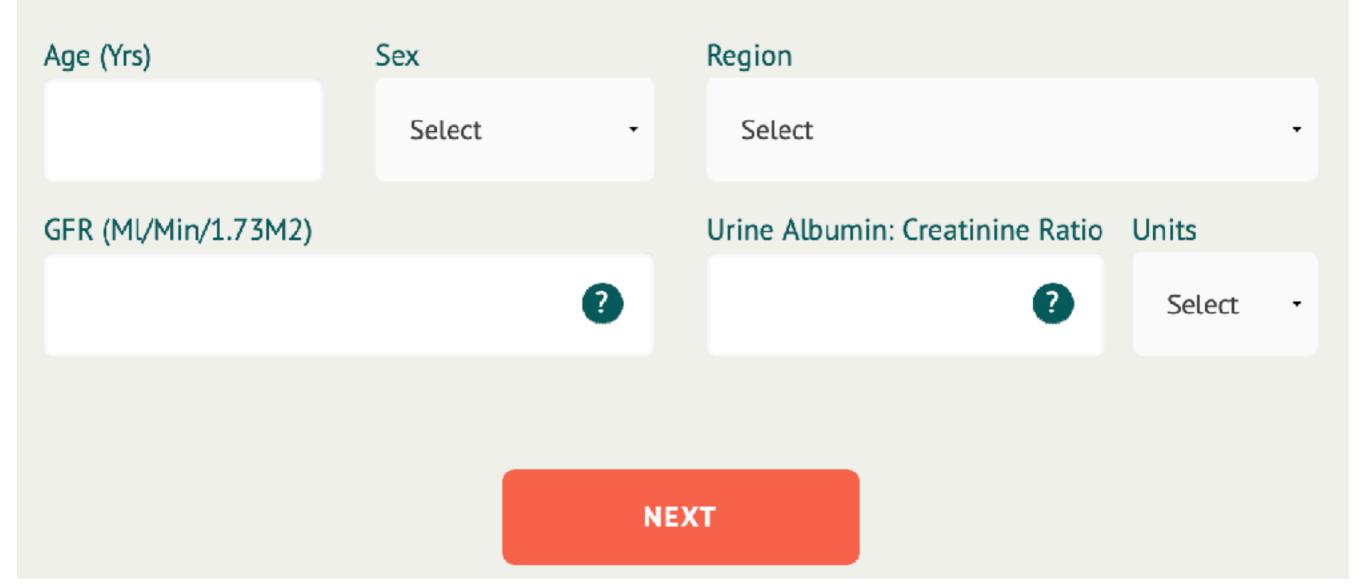
#### Prognosis of CKD by GFR and albuminuria category

				Persistent albuminuria categories, description and range		
Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012				A1	A2	А3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol
GFR categories (ml/min/1.73 m²), description and range	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.

# RISK CALCULATION

If you don't have the information required below talk to your doctor.



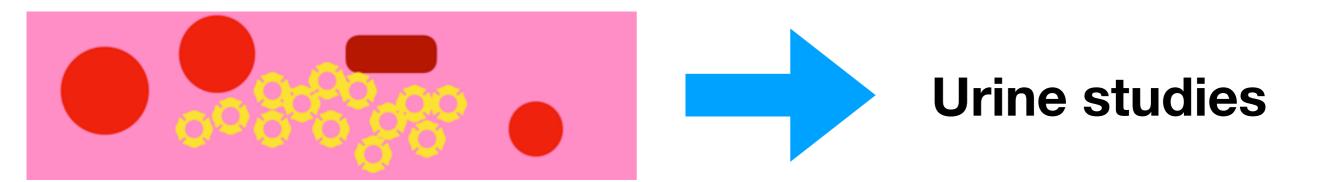
### First Encounter

HISTORY and PHYSICAL [pre-renal and post-renal...and even some renal!]

Rule out rapidly progressive kidney diseases: GNs/Autoimmune Diseases

Does the patient have renal disease because of HTN/Diabetes?

## First Encounter



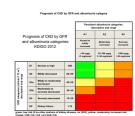
Check for proteinuria... Urine PCR vs ACR vs UA

Quantify the degree of proteinuria

Trend the proteinuria - DM is gradual. Membranous and FSGS can be very fast

Is there blood in the urine [urinary tract or kidneys]? RBC casts [kidneys]?

What's the Cr/eGFR? What's the trend?



Consider a renal U/S to rule out obstruction. It can also show a unilateral small kidney or evidence of chronic scarring [cortical thinning/increased echogenicity]

## The Referral

- Significant proteinuria
- GFR < 30 ml/min/1.73m2
- Red cells in the urine rule out urinary tract first
- HTN you can't control
- Whenever you're uncomfortable

# Let's get some things straight

## Contrast Induced Nephropathy

Is contrast risky on the kidneys? Controversial...



Estimating the Risk of Radiocontrast-Associated Nephropathy

**JASN 2017** 

Emilee Wilhelm-Leen, Maria E. Montez-Rath, and Glenn Chertow

Department of Medicine, Division of Nephrology, Stanford University School of Medicine, Palo Alto, California

## Dialysis patients do not need to have dialysis right after contrast studies!!!!!!!

Does IVF prevent it? It doesn't seem like it...



Prophylactic hydration to protect renal function from intravascular iodinated contrast material in patients at high risk of contrast-induced nephropathy (AMACING): a prospective, randomised, phase 3, controlled, open-label, non-inferiority trial.

Nijssen EC<sup>1</sup>, Rennenberg RJ<sup>2</sup>, Nelemans PJ<sup>3</sup>, Essers BA<sup>4</sup>, Janssen MM<sup>5</sup>, Vermeeren MA<sup>6</sup>, Ommen VV<sup>6</sup>, Wildberger JE<sup>5</sup>.

**AMACING - Lancet 2017** 

AMACING: 660 patients randomly assigned to either IV isotonic saline versus no IVF: Incidence of AKI: 2.7% vs 2.6%, respectively.

#### Review - NEJM, May 2019

### Contrast-Associated Acute Kidney Injury

Roxana Mehran, M.D., George D. Dangas, M.D., Ph.D., and Steven D. Weisbord, M.D.

## IV fluids



Crystalloids - salts in water [NS, RL, Plasma-lyte]

**Colloids** - Higher osmole content staying within the vasculature [albumin, hetastarch...]



## Colloids...are out

Human albumin administration in critically ill patients: systematic review of randomised controlled trials

Cochrane Injuries Group Albumin Reviewers

**Cochrane review 1998** 

A Comparison of Albumin and Saline for Fluid Resuscitation in the Intensive Care Unit

The SAFE Study Investigators<sup>4</sup>

**NEJM 2004** 

#### Colloids or crystalloids for fluid replacement in critically people

**Cochrane review 2018** 

Association of Hydroxyethyl Starch Administration With Mortality and Acute Kidney Injury in Critically III Patients Requiring Volume Resuscitation

A Systematic Review and Meta-analysis

**JAMA 2013** 

# Crystalloids The battle between balanced crystalloids [Ringers Lactate] and Normal Saline

Normal Saline - 9g/L of Sodium. 154 mmol/L of Na and Cl. pH 5.5

Ringers Lactate - 6g/L of Sodium, 130 mmol/L Na, Cl 109mmol/L, Calcium 1.4mmol/L, K 4 mmol/L, Lactate 3.1g/L, pH 6.5

#### **SALT-ED**

#### Balanced Crystalloids versus Saline in Noncritically Ill Adults

Wesley H. Self, M.D., M.P.H., Matthew W. Semler, M.D., Jonathan P. Wanderer, M.D., Li Wang, M.S., Daniel W. Byrne, M.S., Sean P. Collins, M.D., Corey M. Slovis, M.D., Christopher J. Lindsell, Ph.D., Jesse M. Ehrenfeld, M.D., M.P.H., Edward D. Siew, M.D., Andrew D. Shaw, M.B., Gordon R. Bernard, M.D., et al., for the SALT-ED Investigators\*

#### **SMART**

#### Balanced Crystalloids versus Saline in Critically Ill Adults

Matthew W. Semler, M.D., Wesley H. Self, M.D., M.P.H., Jonathan P. Wanderer, M.D., Jesse M. Ehrenfeld, M.D., M.P.H., Li Wang, M.S., Daniel W. Byrne, M.S., Joanna L. Stollings, Pharm.D., Avinash B. Kumar, M.D., Christopher G. Hughes, M.D., Antonio Hernandez, M.D., Oscar D. Guillamondegui, M.D., M.P.H., Addison K. May, M.D., et al., for the SMART Investigators and the Pragmatic Critical Care Research Group\*

#### MAKE-30 - New composite outcome

Major Adverse Kidney Events in 30 days [Death, New RRT, Final Cr > 200% of baseline

SALT-ED - Balanced [4.7%], NS [5.6%], p-value 0.01

SMART - Balanced [14.3%], NS [15.4%], p-value 0.04

## The IVF studies

MAKE 30 = major adverse kidney events within 30 days.

SMART - ICU patients: NS 15.4% RL 14.3%

SALT - ED - NS 5.6% vs RL 4.7%

NNT=100: 100 patients treated with a balanced solution to get 1 reduction in the MAKE 30 outcome...

# NS vs Balanced Crystalloids (RL or plasmalyte)

#### The common concerns:

- RL lactic acidosis and hyperkalemia... nope
  - NaLactate not H+Lactate
  - May give a higher lactate in cirrhotics but it is NOT contributing to the acidosis
  - NS has a pH of 5.5 (dissolved CO2) and RL 6.5. The higher acidity of NS actually causes a great increase in K than RL despite RL having 4 mmol/L of K.
- NS hyperchloremic non gap metabolic acidosis ... yup...
  - Normal Cl is ~ 110. NS is 154.
  - The macula densa is a CI sensor. MD tells the afferent arteriole to constrict... decreased GFR and possible AKI. Also get increased angiotensin and thromboxane release causing further vasoconstriction.

When not to use RL ... patients with metabolic alkalosis (emesis or overuse of diuretics) then use NS. These guys need the Cl.



CKD

## CKD - The issues

Renal function: Cr/eGFR and ACR

Blood Pressure: CHEP guidelines

Potassium: Within normal range

Acidosis of CKD: Target HCO3 > 24

**Bicarbonate supplementation slows progression of CKD and improves nutritional status**. de Brito-Ashurst et al. JASN, 2009. [CKD STAGE 4 with HCO3 16-20]

Also evidence for CKD patients with HCO3 22-24 and CKD patients with earlier CKD

CKD Mineral Bone Disease [Cai, PO4, PTH, Vitamin D] ... its a long story...

Anemia of CKD: Iron deficiency is most common cause of anemia in CKD. If iron stores are optimal and **Hb < 100**, then we will start an erythropoietin stimulating agent. **Target Hb in this case is 100-110**. [Level 1 evidence that ESA's should not be used to get Hb >130]. See next slide...

Other Issues:

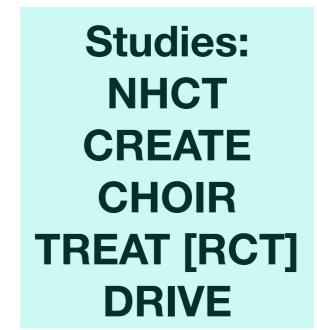
Glycemic control

**Heart Failure** 

... REVIEW MEDICATIONS...

# Erythropoetin Stimulating Agents [ESA]

- Benefits:
  - Reduction in transfusion requirements
  - Improvement in patients QOL
- Risks:
  - Cardiovascular events
  - HTN
  - Thromboembolism- HD access thrombosis [AVFs and grafts] risk increases with increasing Hb
  - Increased solid tumour growth
  - Increased mortality when Hb >130 in HD patients with symptomatic CVD and non-dialysis patients
  - Increased risk of stroke when Hb >130 in HD patients
  - Lower HD adequacy with increasing Hb



## Drug prescribing in CKD

# USE UpToDate for dose adjustments... that's often what we do

**Septra** - trimethoprim blocks ENac and also competes with proximal tubule for secretion of creatinine [hyperkalemia and elevated Cr ... remember this has nothing to do with the GFR]

**ACEI/ARB** - allow for up to 30% rise in Cr from baseline.

**NSAIDs** - PGs. With lower GFRs patient become dependent on the PG dilation of the afferent arteriole.

## Drug Prescribing in CKD

• **PPI** - in the past ~10 years we have recognized that PPIs are one of the top causes of AIN and a definite cause of CKD.

Proton Pump Inhibitors and Kidney Disease—GI Upset for the Nephrologist?

Stephanie M. Toth-Manikowski<sup>1</sup> and Morgan E. Grams<sup>1,2</sup>

**Kidney Int Rep 2017** 

• Metformin - down to a GFR of 30 ml/min/1.73m2

#### **POP QUIZ**

Richard Face Trump is a 74M with CKD related to DM-Nephropathy. His eGFR is 30 and ACR 40. He has pain in the right knee that you have diagnosed as being OA related. The pain reaches levels of up to 8/10 after long days on the golf course. He loves to golf. We all know that. What medication will you prescribe for his pain.

- **A.** T3
- **B.** Morphine
- C. Tylenol
- D. Ibuprofen [advil]
- E. Tramacet
- F. Hydromorphone [dilaudid]

## Pain Management in CKD

### VERY challenging issue



### DO NOT USE

Morphine

Metabolite M6G is potent and renally cleared

Codeine

Baclofen

### **USE WITH CAUTION**

Oxycodone

Tramadol

Gabapentinoids

SNRI metabolized to ODT [mu-1 agonist] by CYP2D6

CYP2D6 is highly variable patient to patient CYP2D6 is inhibited by many other medications

**Renally cleared** 

## Safest options...

#### Acetaminophen

**Hydromorphone** 

If you need an opiate
H6G metabolite IS renally cleared but is inert

**NSAIDS** 

May be safer than we think in mild CKD Less concern in anuric ESRD patients

## Pain Management in CKD

- NSAIDs on everyone's "do not give to CKD patients" list but may not be nearly as
  dangerous as we fear...
  - PHYSICIANS HEALTH STUDY: Cohort study, 1982-95 11000 men, self reported analgesic use >2500 pills RR for Cr increase to >133 umol/L: 0.83 for acetaminophen, 0.98 for ASA, and 1.07 for NSAIDs NO SIGNIFICANT DIFFERENCE

Analgesic Use and Renal Function in Men

**JAMA 2001** 

Kathryn M. Rexrode, MD: Julie E. Buring, ScD: Robert J. Glynn, ScD: et al.

PRECISION trial: celecoxib, ibuprofen, naproxen)... see next slide

Cardiovascular Safety of Celecoxib, Naproxen, or Ibuprofen for Arthritis

Steven E. Nissen, M.D., Neville D. Yeomans, M.D., Daniel H. Solomon, M.D., M.P.H., Thomas F. Lüsche, M.D., Peer Libby, M.D., M. Elaine Husni, M.D., David Y. Graham, M.D., Jeffrey S. Borer, M.D., Lisa M. Wisniewski, R.N., Katherine E. Wolski, M.P.H., Qiuqing Wang, M.S., Venu Menon, M.D., et al., for the PRECISION Trial Investigators\*

**NEJM December 2016** 

• NSAID vs ACEi + NSAID vs ACEi + NSAID + diuretic. Diuretics seem to tip things over

Celecoxib Group (N=8072)	Naproxen Group (N = 7969)	Ibuprofen Group (N=8040)	Celecoxib vs. Naproxen≄		Celecoxib vs. Ibuprofen*	
			Adjusted Hazard Ratio (95% CI)	P Value	Adjusted Hazard Ratio (95% CI)	P Value
number of patients (percent)						
188 (2.3)	201 (2.5)	218 (2.7)	0.93 (0.76-1.13)	0.45	0.85 (0.70-1.04)	0.12
337 (4.2)	346 (4.3)	384 (4.8)	0.97 (0.83-1.12)	0.64	0.87 (0.75-1.01)	0.06
86 (1.1)	119 (1.5)	130 (1.6)	0.71 (0.54-0.93)	0.01	0.65 (0.50-0.85)	0.002
55 (0.7)	56 (0.7)	72 (0.9)	0.97 (0.67–1.40)	0.86	0.76 (0.53-1.08)	0.12
33 (0.4)	69 (0.9)	64 (0.8)	0.47 (0.31-0.71)	<0.001	0.51 (0.33-0.77)	0.002
57 (0.7)	71 (0.9)	92 (1.1)	0.79 (0.56-1.12)	0.19	0.61 (0.44-0.85)	0.004
45 (0.6)	48 (0.6)	46 (0.6)	0.92 (0.62-1.39)	0.70	0.98 (0.65-1.47)	0.91
24 (0.3)	34 (0.4)	40 (0.5)	0.69 (0.41-1.17)	0.17	0.60 (0.36-0.99)	0.04
132 (1.6)	163 (2.0)	142 (1.8)	0.80 (0.63-1.00)	0.052	0.92 (0.73-1.17)	0.49
68 (0.8)	86 (1.1)	80 (1.0)	0.78 (0.57-1.07)	0.13	0.84 (0.61-1.16)	0.30
76 (0.9)	66 (0.8)	92 (1.1)	1.14 (0.82-1.59)	0.43	0.82 (0.61-1.11)	0.21
51 (0.6)	57 (0.7)	53 (0.7)	0.88 (0.61-1.30)	0.52	0.95 (0.65-1.40)	0.81
55 (0.7)	64 (0.8)	65 (0.8)	0.86 (0.60-1.23)	0.40	0.84 (0.59-1.21)	0.35
174 (2.2)	161 (2.0)	198 (2.5)	1.07 (0.87-1.33)	0.52	0.87 (0.71-1.07)	0.18
18 (0.2)	18 (0.2)	27 (0.3)	0.99 (0.51-1.90)	0.97	0.66 (0.37-1.20)	0.18
	(N=8072)  188 (2.3) 337 (4.2) 86 (1.1) 55 (0.7) 33 (0.4)  57 (0.7) 45 (0.6) 24 (0.3) 132 (1.6)  68 (0.8) 76 (0.9) 51 (0.6) 55 (0.7) 174 (2.2)	number of patients (percentage)  188 (2.3) 201 (2.5)  337 (4.2) 346 (4.3)  86 (1.1) 119 (1.5)  55 (0.7) 56 (0.7)  33 (0.4) 69 (0.9)  57 (0.7) 71 (0.9)  45 (0.6) 48 (0.6)  24 (0.3) 34 (0.4)  132 (1.6) 163 (2.0)  68 (0.8) 86 (1.1)  76 (0.9) 66 (0.8)  51 (0.6) 57 (0.7)  55 (0.7) 64 (0.8)  174 (2.2) 161 (2.0)	number of patients (percent)         188 (2.3)       201 (2.5)       218 (2.7)         337 (4.2)       346 (4.3)       384 (4.8)         86 (1.1)       119 (1.5)       130 (1.6)         55 (0.7)       56 (0.7)       72 (0.9)         33 (0.4)       69 (0.9)       64 (0.8)         57 (0.7)       71 (0.9)       92 (1.1)         45 (0.6)       48 (0.6)       46 (0.6)         24 (0.3)       34 (0.4)       40 (0.5)         132 (1.6)       163 (2.0)       142 (1.8)         68 (0.8)       86 (1.1)       80 (1.0)         76 (0.9)       66 (0.8)       92 (1.1)         51 (0.6)       57 (0.7)       53 (0.7)         55 (0.7)       64 (0.8)       65 (0.8)         174 (2.2)       161 (2.0)       198 (2.5)	(N=8072) (N=7969) (N=8040) Celecoxib vs. Napro Adjusted Hazard Ratio (95% CI)  number of patients (percent)  188 (2.3) 201 (2.5) 218 (2.7) 0.93 (0.76–1.13)  337 (4.2) 346 (4.3) 384 (4.8) 0.97 (0.83–1.12)  86 (1.1) 119 (1.5) 130 (1.6) 0.71 (0.54–0.93)  55 (0.7) 56 (0.7) 72 (0.9) 0.97 (0.67–1.40)  33 (0.4) 69 (0.9) 64 (0.8) 0.47 (0.31–0.71)  57 (0.7) 71 (0.9) 92 (1.1) 0.79 (0.56–1.12)  45 (0.6) 48 (0.6) 46 (0.6) 0.92 (0.62–1.39)  24 (0.3) 34 (0.4) 40 (0.5) 0.69 (0.41–1.17)  132 (1.6) 163 (2.0) 142 (1.8) 0.80 (0.63–1.00)  68 (0.8) 86 (1.1) 80 (1.0) 0.78 (0.57–1.07)  76 (0.9) 66 (0.8) 92 (1.1) 1.14 (0.82–1.59)  51 (0.6) 57 (0.7) 53 (0.7) 0.88 (0.61–1.30)  55 (0.7) 64 (0.8) 65 (0.8) 0.86 (0.60–1.23)  174 (2.2) 161 (2.0) 198 (2.5) 1.07 (0.87–1.33)	(N=8072)       (N=7969)       (N=8040)       Celecoxib vs. Naproxen*         Adjusted Hazard Ratio (95% CI)       P Value         number of patients (percent)       P Value         188 (2.3)       201 (2.5)       218 (2.7)       0.93 (0.76−1.13)       0.45         337 (4.2)       346 (4.3)       384 (4.8)       0.97 (0.83−1.12)       0.64         86 (1.1)       119 (1.5)       130 (1.6)       0.71 (0.54−0.93)       0.01         55 (0.7)       56 (0.7)       72 (0.9)       0.97 (0.67−1.40)       0.86         33 (0.4)       69 (0.9)       64 (0.8)       0.47 (0.31−0.71)       <0.001	(N=8072) (N=7969) (N=8040) Celecoxib vs. Naproxen® Celecoxib vs. Ibupr  Adjusted Hazard Ratio (95% CI) P Value (95% CI)  number of patients (percent)  188 (2.3) 201 (2.5) 218 (2.7) 0.93 (0.76-1.13) 0.45 0.85 (0.70-1.04)  337 (4.2) 346 (4.3) 384 (4.8) 0.97 (0.83-1.12) 0.64 0.87 (0.75-1.01)  86 (1.1) 119 (1.5) 130 (1.6) 0.71 (0.54-0.93) 0.01 0.65 (0.50-0.85)  55 (0.7) 56 (0.7) 72 (0.9) 0.97 (0.67-1.40) 0.86 0.76 (0.53-1.08)  33 (0.4) 69 (0.9) 64 (0.8) 0.47 (0.31-0.71) <0.001 0.51 (0.33-0.77)  57 (0.7) 71 (0.9) 92 (1.1) 0.79 (0.56-1.12) 0.19 0.61 (0.44-0.85)  45 (0.6) 48 (0.6) 46 (0.6) 0.92 (0.62-1.39) 0.70 0.98 (0.65-1.47)  24 (0.3) 34 (0.4) 40 (0.5) 0.69 (0.41-1.17) 0.17 0.60 (0.36-0.99)  132 (1.6) 163 (2.0) 142 (1.8) 0.80 (0.63-1.00) 0.052 0.92 (0.73-1.17)  68 (0.8) 86 (1.1) 80 (1.0) 0.78 (0.57-1.07) 0.13 0.84 (0.61-1.16)  76 (0.9) 66 (0.8) 92 (1.1) 1.14 (0.82-1.59) 0.43 0.82 (0.61-1.11)  51 (0.6) 57 (0.7) 53 (0.7) 0.88 (0.61-1.30) 0.52 0.95 (0.65-1.40)  55 (0.7) 64 (0.8) 65 (0.8) 0.86 (0.60-1.23) 0.40 0.84 (0.59-1.21)  174 (2.2) 161 (2.0) 198 (2.5) 1.07 (0.87-1.33) 0.52 0.87 (0.71-1.07)

 Celecoxib
 Naproxen
 Ibuprofen

 Renal events
 57 (0.7)
 71 (0.9)
 92 (1.1)



Table 2. Adjudicated Outcomes in the Intention-to-Treat Population.

Doses could be increased up to:
Celecoxib 200mg BID
Naproxen 500mg BID
Ibuprofen 800mg TID



## Statins

- No reliable evidence for benefit from statins in dialysis patients
- Only evidence for harm

4D - increase in strokes
AURORA - Increase in hemorrhagic strokes
SHARP - CV benefit in those with CKD who progressed to dialysis

DO NOT PRESCRIBE STATINS TO PATIENTS ON DIALYSIS

#### Microalbuminuria is not a good treatment surrogate

HOPE: Microalbuminuria was the highest predictor of poor CV outcomes [over DM, HTN, and Smoking]



ONTARGET: Combination ACE and ARB no better than either agent alone.

ASCEND - endothelin antagonists to reduce proteinuria in diabetic nephropathy. Worked great at reducing albuminuria but seemed to cause an increase in HF exacerbations.

ROADMAP, ORIENT, ALTITUDE... all succeeded in reducing albuminuria but at the cost of adverse outcomes and no benefit. [hyper K, HF, AKI...]

## SGLT2Ri

- Canvas
- Empa-REG
- CREDENCE

Very important and very impressive medications that you should know about.

GAME CHANGERS

But... we are out of time...

#### Recommendations/References:

Curbsiders Internal Medicine Podcast; NephMadness sessions with Dr. Joel Topf

Precious Bodily Fluids [Dr. Topf]: <a href="http://pbfluids.com">http://pbfluids.com</a>

UKidney [Dr. Jordan Weinstein]: <a href="https://www.ukidney.com">www.ukidney.com</a>