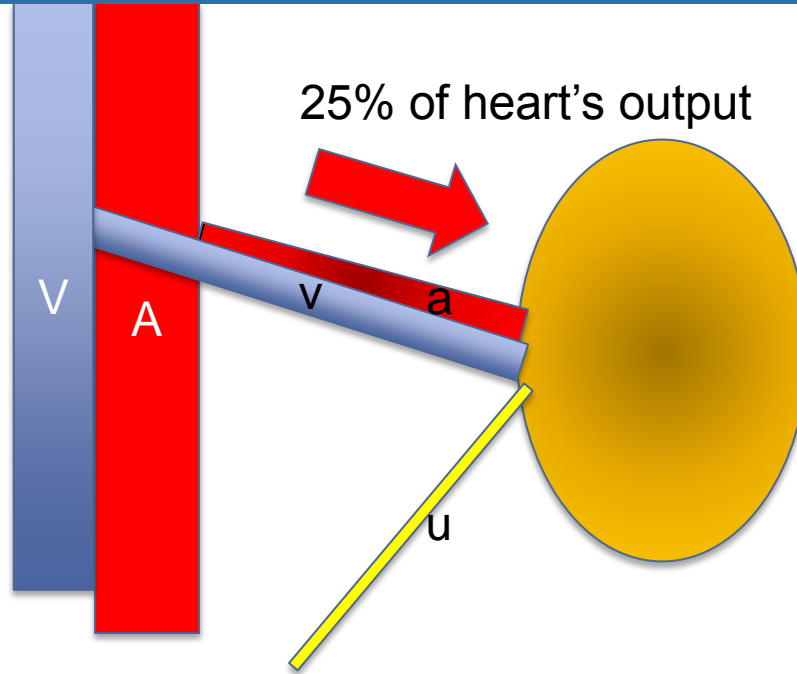




## Keeping your kidneys young

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The kidneys get a lot of blood from the heart, and they work 24 hours a day every day



# What do they do with all that blood for all that time?

- 1.Purifies blood from “nitrogenous” or nitrogen based wastes (BUN-blood urea nitrogen) and **creatinine** among others
- 2.Removes extra fluid from body (volume control)
- 3.Removes excess potassium, phosphorous, from body
- 4.Clears extra water and balances intake and output of various substances
- 5. Hormonal functions in red blood cell generation
- 6. Control of blood pressure by hormonal and neurological means
- 7. Hormonal functions in bone structure and calcium, phosphorous level maintenance

# Blood filtration 1

1-Measured by serum creatinine “normal” 0.5-1  
Range depends on age, weight, height, gender, ethnicity,  
Muscle mass etc.

2-Blood urea nitrogen “normal” is 8-15 (sometimes up to 20 depending on lab).

3-Cystatin C a novel “new creatinine” range up to 1 is “normal range”  
Both are breakdown products of protein metabolism

4-ALL these represent metabolic wastes removed by filter at a certain rate depending on blood flow to kidneys and proper kidney cell filtration function. They should not be removed or absorbed back to any appreciable extent.

# Blood filtration 2

The real measurement we use these “metabolic waste” levels for is

Estimated glomerular filtration rate

Normal is 90-120 (usually we say 100 is normal) units are milliliters / minute, or number of milliliters of plasma filtered by kidneys in 1 minute

-A single Cr number from blood along with weight, age, gender, ethnicity allows us to use various equations to estimate this parameter.

-Cystatin C is a more high tech measurement of the same parameter that is supposed to be less prone to error than creatinine

-Another strategy is to collect 24 hours of urine and compare level of urea and creatinine in it to the blood.

-more complex but impractical tests are available but not used clinically.

# How we grade kidney filtration defects

Guide to Frequency of Monitoring (number of times per year) by GFR and Albuminuria Category				Persistent albuminuria categories Description and range		
				A1	A2	A3
				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 >30mg/mmol
GFR categories (ml/min/1.73 m <sup>2</sup> ) Description and range	G1	Normal or high	≥90	1 if CKD	1	2
	G2	Mildly decreased	60–89	1 if CKD	1	2
	G3a	Mildly to moderately decreased	45–59	1	2	3
	G3b	Moderately to severely decreased	30–44	2	3	3
	G4	Severely decreased	15–29	3	3	4+
	G5	Kidney failure	<15	4+	4+	4+

# Volume control

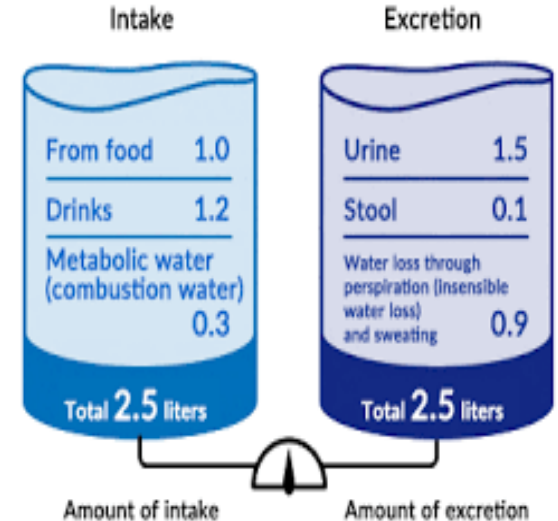
-Did you ever wonder why our body doesn't gain weight forever?

-because input and output into the human body are matched

-How is this done?

-when more blood volume exists, more is filtered and the pressure in the kidneys increases, prompting more urine formation and salt removal from body.

-Also hormonal control takes over when blood pressure goes up (see blood pressure slides)



# Balance of nutrients

-Kidneys ensure potassium level is not too high or too low-  
could be very dangerous if level  $<3$  or  $>6$

-Kidneys ensure balance of phosphorous too low and  
muscles fail, too high and blood vessels can become calcified  
and heart attack and stroke risk soar.

-This is done both by higher filtered and removed loads with  
higher concentrations and hormonal input.

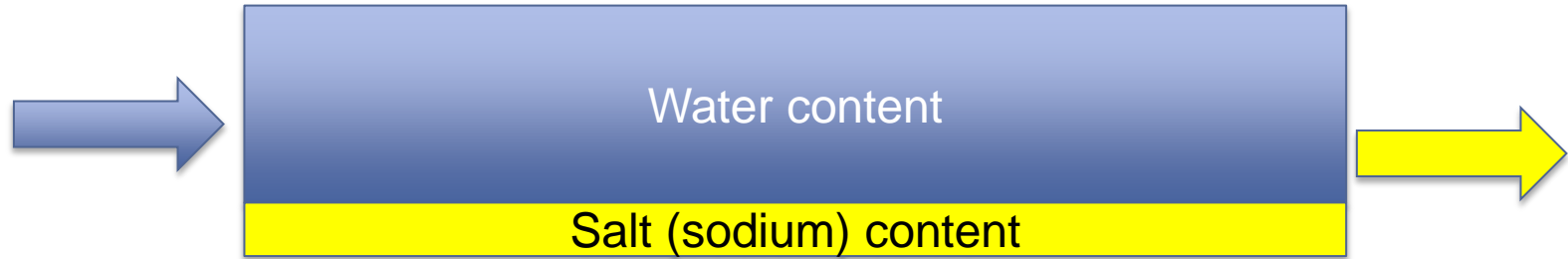
-For potassium hormone is aldosterone.

-For phosphorous hormone is called FGF-23.


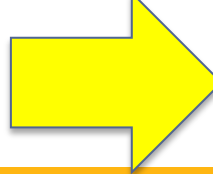


# Balance of water

Water intake = water clearance



 Kidneys need to concentrate urine output if low water intake  Concentrated urine

 Kidneys need to dilute urine and clear more water if excessive water intake 

Dilute urine

# Erythropoietin and red blood cell generation

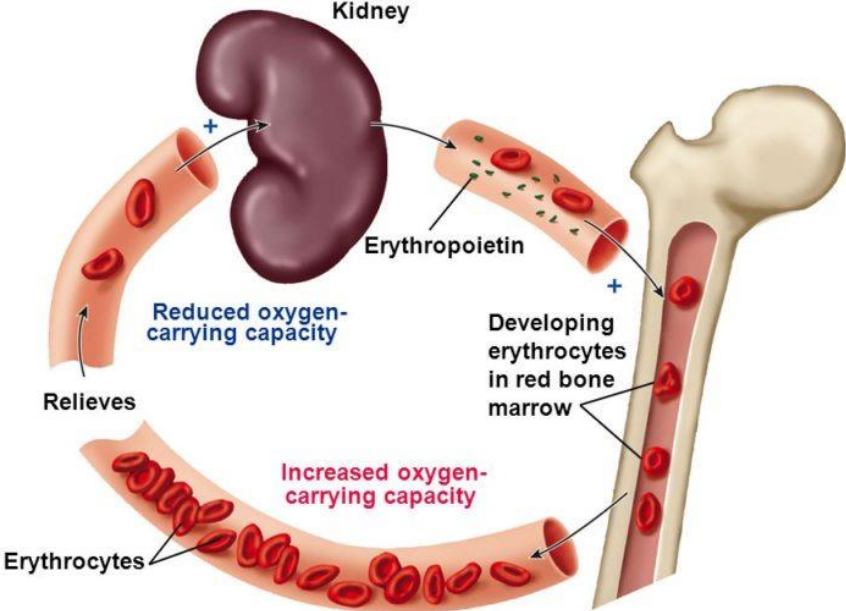
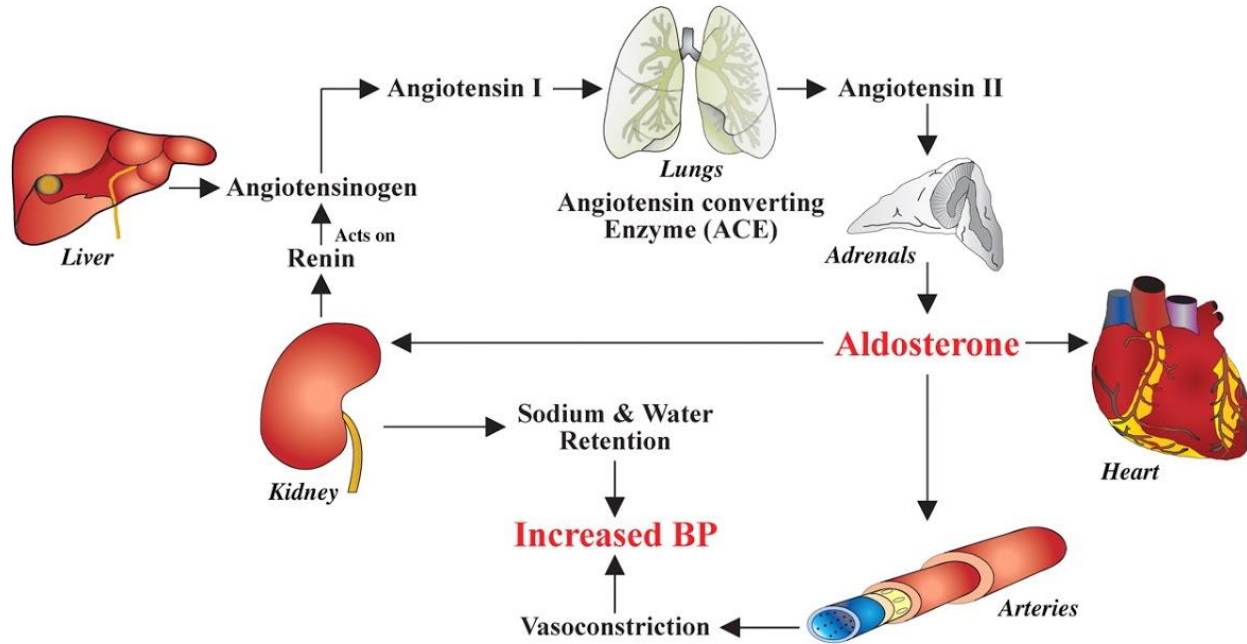
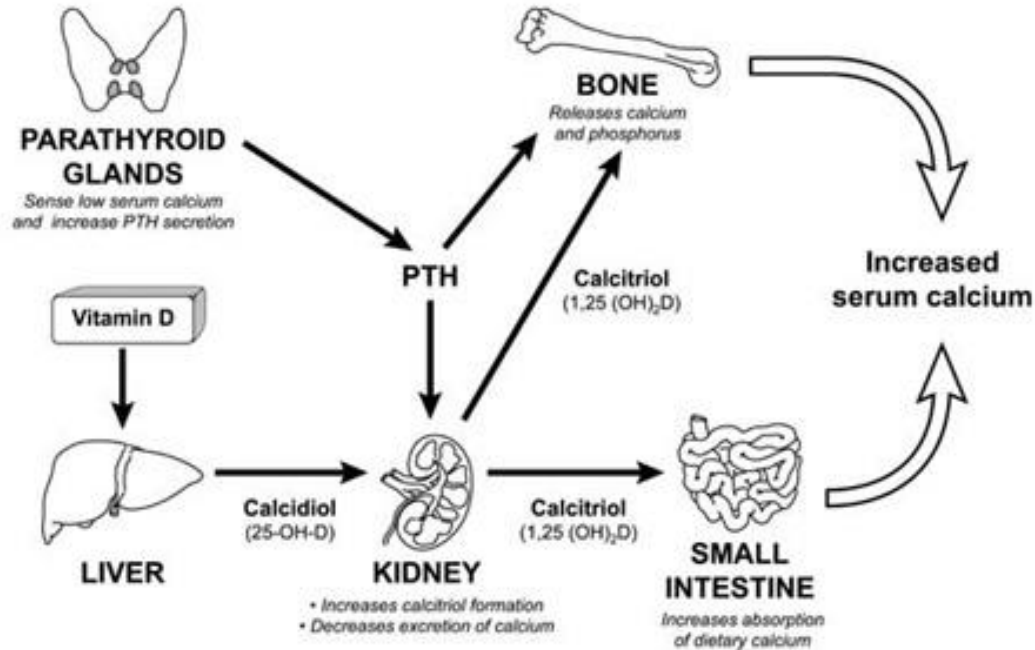


Figure 9-6 p393

# Blood pressure control by kidneys



# Vitamin D and Parathyroid hormone control

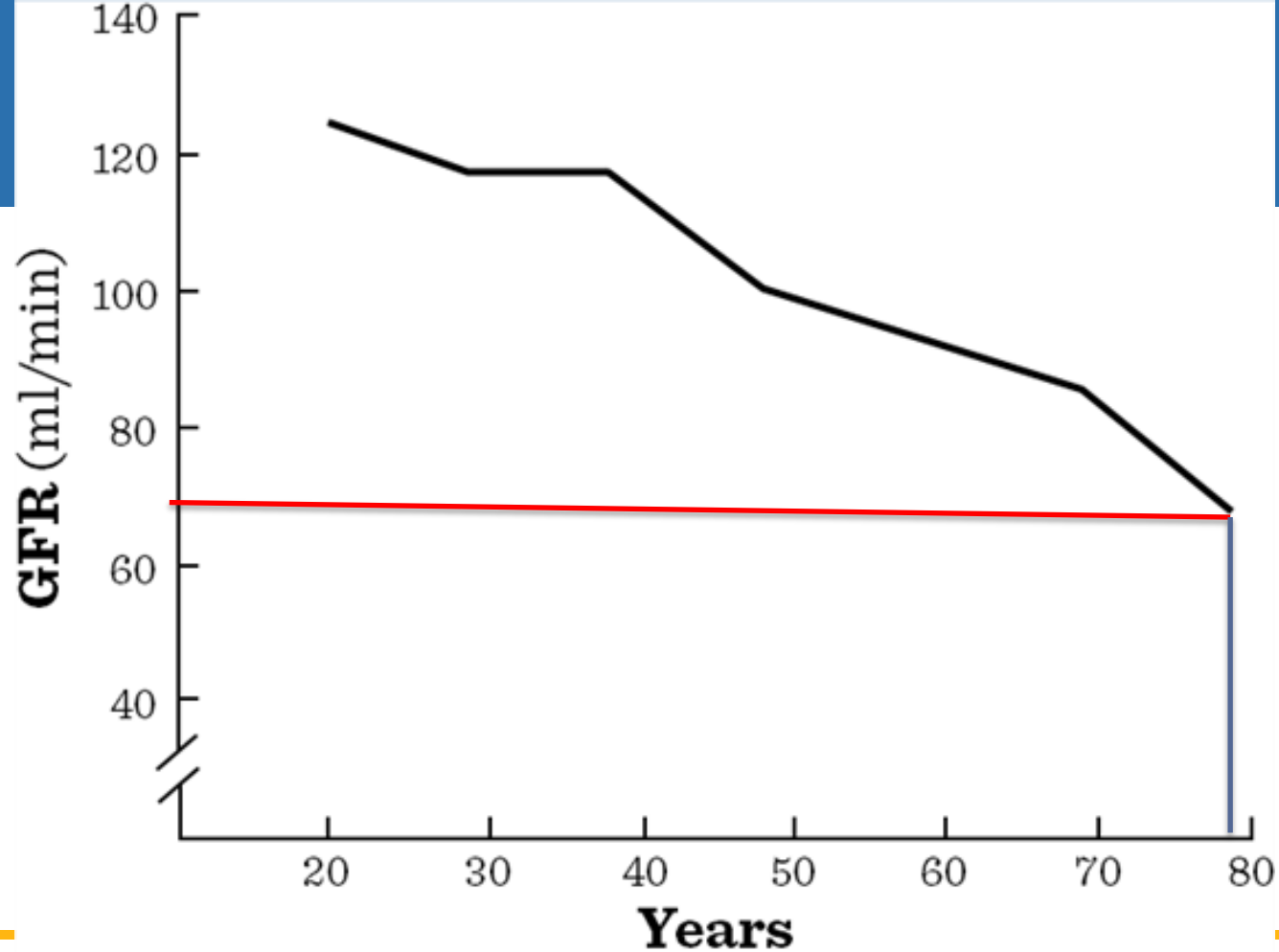


Aging affects each of these core functions of the kidneys

# Kidney filtration and aging

-The human body loses between 1 ml/min of glomerular filtration per year  
Rate of loss can be much higher in patients with other systemic diseases

-Those taking other medications that may affect kidneys are also at higher risk. We call medications that are bad for the kidney nephrotoxins. Non steroidal anti inflammatory drugs, (ibuprofen and it's cousins, contrast for computed tomography (CT) scans, certain antibiotics, and now proton pump inhibitors are common ones.



# So why does creatinine stay 1

- Patients also lose a certain amount of lean body mass, especially muscle with normal aging.
- This means that serum creatinine may stay “within normal limits” but this may reflect decreasing kidney function
- Normal renal function in elderly patient maybe reflected in those with a low serum creatinine
- Your doctor (s) should be paying attention to GFR
- If GFR number is less than 60 ml/min please go see a nephrologist, between 60-90 is not a bad idea either to come see a kidney specialist.



# Volume control and aging

- The kidneys remain able to remove excess volume, but.
- The heart may become damaged by heart attacks or go into heart failure. Long term high blood pressure may make heart stiff.
- These changes may make it harder for body to eliminate extra fluid and this may result in trips to ER with shortness of breath.
- Liver and heart failure both result in more hormones being put into blood stream promoting salt and water retention.
- If kidneys start to fail this compounds situation as well.

# Nutrient balance and aging

-Given tendency for kidney filtration to decrease with time, this may result in difficulty of kidney in removing potassium, phosphorous as well as creatinine and blood urea nitrogen.

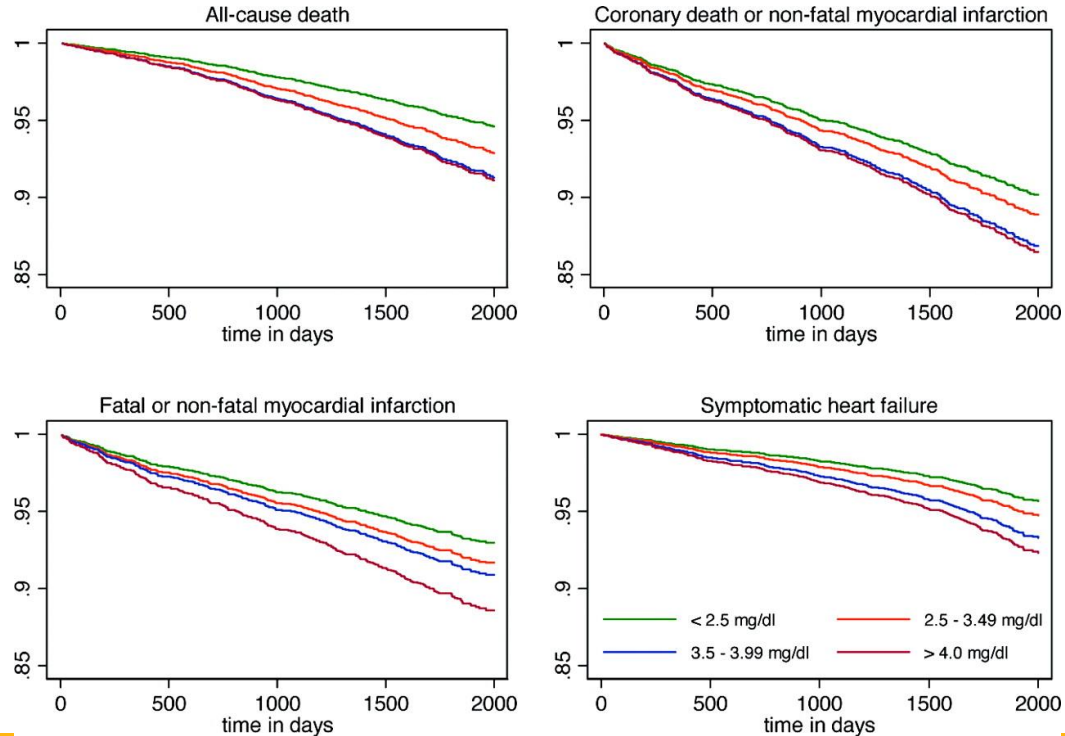
-Your doctor should monitor these levels and take medications to control them.

-Binders for potassium and phosphorous now exist.

-You may be asked to adjust your diet, a kidney dietician maybe very helpful in this process.

Any nutrient in excess or deficiency could be a toxin or cause serious organ dysfunction.

# Phosphorous level and risk of heart disease

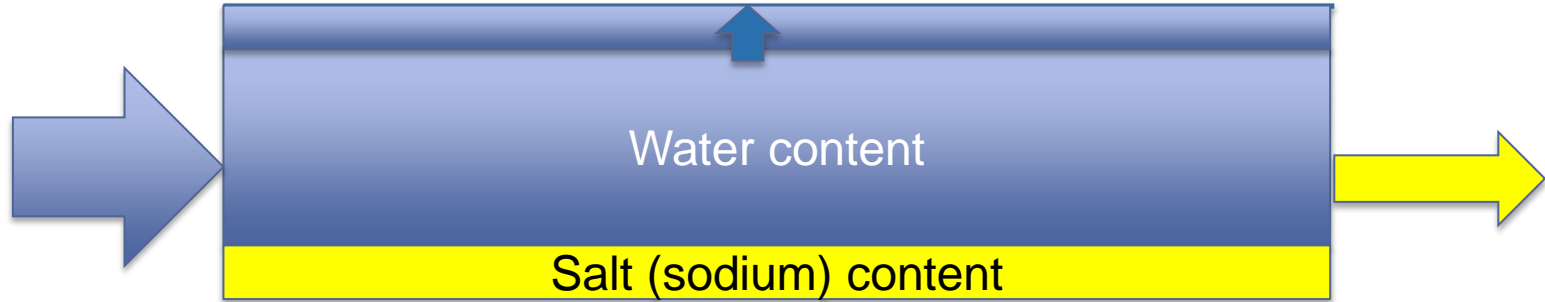


# Water control

- This is major
- As we age and kidney function declines quantitatively
- The ability of the kidneys to concentrate and dilute fluid is also diminished
- This means that the urine can be concentrated or diluted to a narrower range
- And the problem is more compounded in people with dysfunctional kidney (frank kidney failure), and with other organs (heart and liver) that aren't working well
- Certain diuretics become much more likely to cause issues (like hydrochlorothiazides) these can land someone in hospital with low sodium-which can cause life threatening brain swelling and brain injury if not corrected by an expert.

# Balance of water-problems

Water intake more than water clearance



Too much water intake

Urine not dilute enough

Too much water for level of filtration

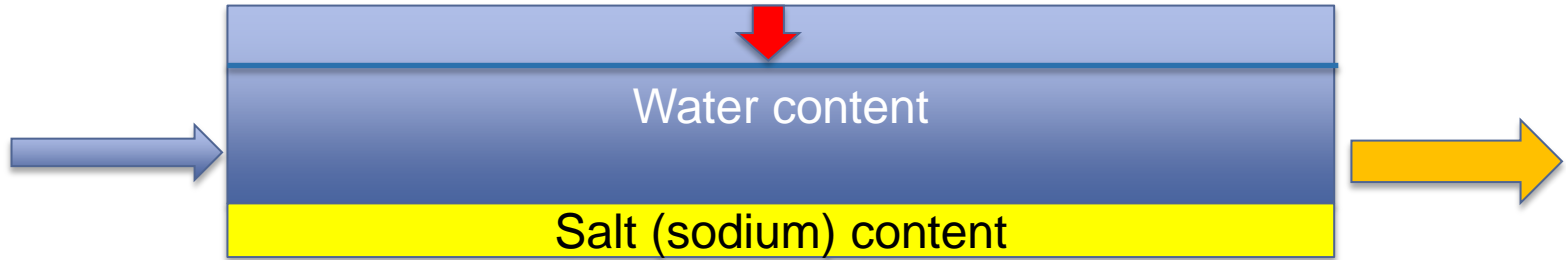
Water level goes up

Sodium concentration goes down  $140 \rightarrow 125$

Can also occur due to certain drugs, diseases

# Balance of water-problems

Water intake less than equal water clearance



Less water intake

Urine not concentrated enough

Poor concentration can result in wasting too much water  
Sodium 140 → 150

# 8 glasses of 8 oz is NOT the most up to date advice

- Drink when you are thirsty, your body comes with receptors for low volume and high concentration and these release vasopressin-so listen to your doctor.
- If your sodium level is low listen to your doctor (especially nephrologist)-They should tell you how much water to drink.

# Anemia and chronic kidney disease

- If your kidney disease reaches stage III b (45 ml/min) or stage IV (30 ml/min or less),
  - you may develop anemia due to chronic kidney disease
- In these cases your doctor should check your iron levels
  - Make sure you aren't bleeding from somewhere
  - That your bone marrow isn't missing another vitamin (b12 etc.)
  - That you don't have bone marrow failure or cancer causing bleeding
  - If all these are true he may prescribe erythropoietin to bring up red blood cell production.



# Blood pressure

- Standard JNC definitions for high blood pressures take age into account
- Different targets exist depending on
  - Age
  - Protein leakage
  - Kidney function

# JNC-8 blood pressure categories

**TABLE 1: JNC 8'S BLOOD PRESSURE GOALS**

Population	Start antihypertensive drugs when this parameter meets or exceeds		Target BP
	SBP (mm Hg)	DPB (mm Hg)	SBP/DPB
General population 60 years and older <sup>a</sup>	150	90	<150/90
General population 60 years and younger	140	90	<140/90
Adult with diabetes <sup>b</sup> or CKD <sup>c</sup>	140	90	<140/90

CKD = chronic kidney disease; DBP = diastolic blood pressure; SBP = systolic blood pressure.

<sup>a</sup>If patient's SBP is <140 mm Hg after treatment and he or she reports no adverse effects, treatment can be continued without adjustment.

<sup>b</sup>For the general non-black population, initial treatment should include a thiazide-type diuretic, calcium channel blocker (CCB), angiotensin-converting enzyme (ACE) inhibitor, or angiotensin II receptor blocker (ARB). In the general black population, including those with diabetes, initial treatment should include a thiazide-type diuretic or a CCB.

<sup>c</sup>In adults with comorbid CKD and hypertension regardless of race or diabetes status, initial (or add-on) treatment should include an ACE inhibitor or an ARB to improve kidney outcomes.

Adapted from reference 1.

# Why take age into account?

- In older patients better blood pressure control associated with lower risk of heart attack or stroke
- But also increased risk of kidney injury and falls
- As we get older our blood vessels become more stiff.
- To a certain degree a higher blood pressure maybe needed to perfuse brain and kidneys.
- If protein leakage occurring this should also be taken into account.

# Vitamin D-page 1

-In a nut shell:

-Vitamin D is eaten, activated in skin, and chemically modified first in liver then kidney.

-D2 is 25 hydroxy vitamin D after the liver finishes it. It is pro hormone for active vitamin D

-D3 is 1,25 di hydroxy vitamin D after kidney modifies it.

-D2 has different functions than D3, but both are involved in controlling calcium removal from body, phosphorous levels, and bone health.

-weak bones can result from vitamin D3 deficiency.

-Vitamin D2 deficiency is thought to contribute to heart and blood vessel problems.

# Vitamin D-page 2

- In normal aging D2 (25 hydroxy vitamin D) deficiency is a common problem
- In kidney disease D3 (1,25 dihydroxy vitamin D) deficiency occurs since there are fewer kidney cells available to perform necessary chemical modification
  - This results in high parathyroid hormone levels (PTH) that can damage bones by leeching calcium out
  - This is called secondary hyperparathyroidism

High phosphorous levels also increase PTH by a hormone called FGF-23

# Compounding the issue

- MOST patients (with or without kidney problems)
- Have vitamin D deficiency since we have become sedentary indoor dwellers
- So supplement careful (have doctor keep eye on calcium)
- And if you are outside wear sunscreen

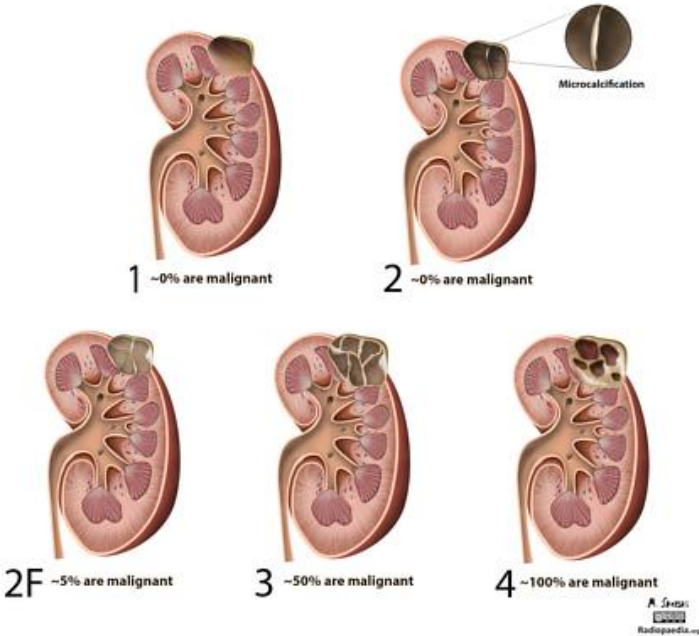
# Kidney Cysts

- Can be a part of normal aging
- Allowed 1 cyst/kidney/decade after 30 years of age without concern for other cystic diseases.
- If cyst is large or blood in urine further testing need to make sure no cancer.
  - This is really purview of urology but nephrologists deal with this enough to know when to refer. This problem requires a qualified urologist to see patient though.



# Bosniak score – on CT scan for large or concerning cysts

## Bosniak classification of renal cysts





# Protein leakage and inflammatory diseases of kidney

- NOT the usual causes of kidney decline in normal aging
- If protein leakage is approaching one gram or ½ gram with decreased kidney function.
- If unexplained blood in urine (no mass or cancer)
- If abnormal antibodies in blood
- See kidney doctor RIGHT away.

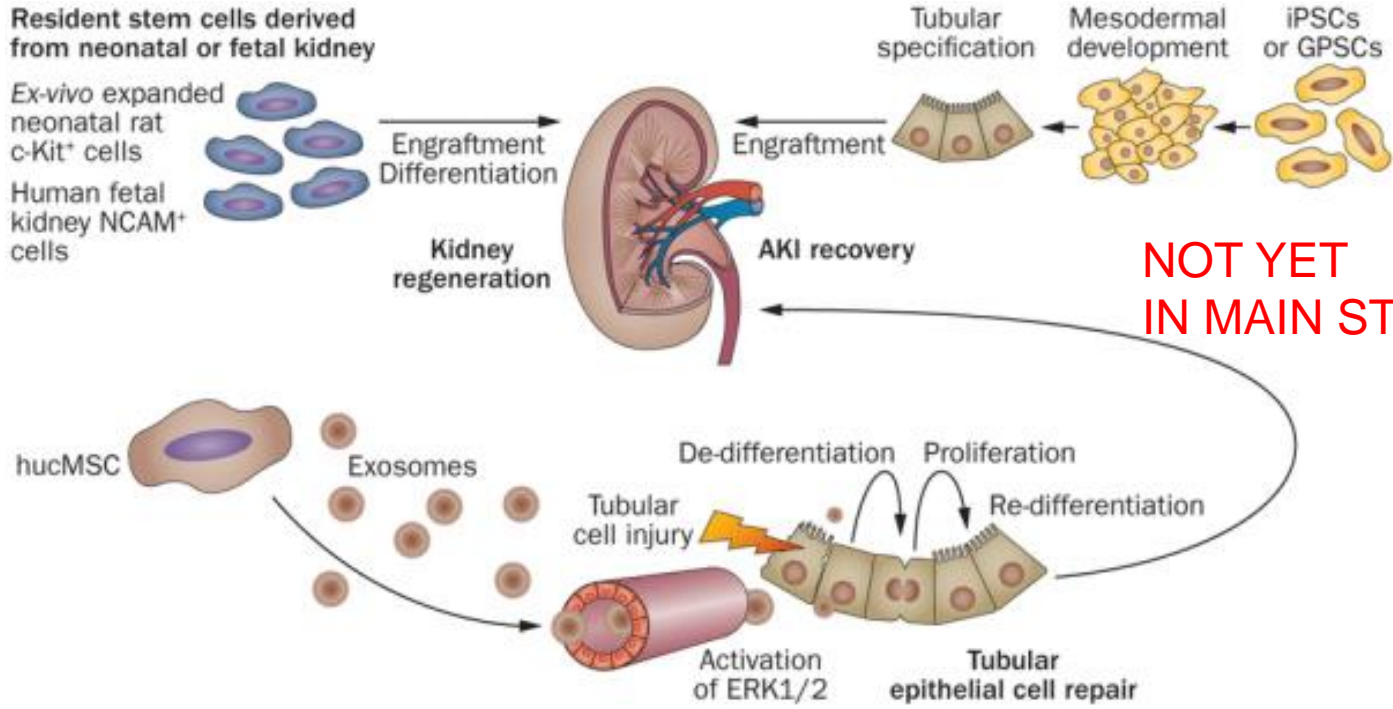
# Practical things to guard against

- Control your blood pressure to a safe level (definition changes depending on age, situation)
- Prevent or delay onset of diabetes
- Prevent or delay onset of being overweight or obese
- Eat a moderate protein diet (1g/kg) avoid atkin's style diets
- Avoid eating too much phosphorous
- Ask your doctor about your potassium level
- If your sodium level is low see a kidney doctor and remember
- Drink when you are thirsty is a good rule of thumb.

# Avoiding drugs Toxic to the kidneys

- NSAIDs
- Toxic medications to kidneys (antibiotics, certain blood pressure medications and diuretics *if* used inappropriately)
- Certain herbal medications
- Heavy metal exposure
- ?certain eye injections? (stay tuned)
- Any drug in wrong dose can be dangerous if dosing is not correct for level of kidney function

# Kidneys have self regenerative capacity



# Klotho

- FGF 23 and klotho are new markers that we have found correlate with kidney disease
- This is very new but suffice it to say that premature kidney damage is associated with premature aging
- Klotho is known to play a role in aging in mice
- Klotho for the classically inclined is known to be one of the three fates from greek mythology who weaves the thread of life
- This link between the kidney health and aging is not lost on anyone  
I am sure

# LIFE AND DEATH ARE IN THE KIDNEYS?



