Renal Physiology - Lectures

✓ Physiology of Body Fluids – PROBLEM SET, RESEARCH ARTICLE
✓ Structure & Function of the Kidneys
✓ Renal Clearance & Glomerular Filtration – PROBLEM SET
✓ Regulation of Renal Blood Flow - REVIEW ARTICLE
✓ Transport of Sodium & Chloride – TUTORIAL A & B
6. Transport of Urea, Glucose, Phosphate, Calcium & Organic Solutes
7. Regulation of Potassium Balance
8. Regulation of Water Balance
9. Transport of Acids & Bases
10. Integration of Salt & Water Balance
11. Clinical Correlation – Dr. Credo
12. **PROBLEM SET REVIEW – May 9, 2011**
13. **EXAM REVIEW – May 9, 2011**
14. **EXAM IV – May 12, 2011**

Renal Physiology Lecture 6
Transport of Urea, Glucose, Phosphate, Calcium, Organic Solutes by the Nephron
Chapter 9 & pg 52-62; 80-88 Koeppen & Stanton Renal Physiology

1. Urea - Filtered, Reabsorbed & Secreted
2. Glucose Tmax
3. Phosphate Reabsorption *Inhibited* by PTH
4. Calcium Reabsorption *Stimulated* by PTH & Vit D

** Renal Failure Patient **

Patient Data	Δ Normal
$Plasma_{K+}$	⇑
P_{Urea}	⇑
BP	⇑
P_{PO4-}	⇑
Hematocrit	⇓
P_{HCO3-}	⇓
P_{pH}	⇓
P_{Ca2+}	⇓

REVIEW - Filtration & Reabsorption

	Amount FILTER/d	Amount EXCRETE/d	% REABSORB
✓ Water (L)	**180**	**1.8**	**99.0**
K^+ (mEq)	**720**	**100**	**86.1**
** Ca^{2+} (mEq)	**540**	**10**	**98.2**
HCO_3^- (mEq)	**4,320**	**2**	**99.9+**
✓ Cl^- (mEq)	**18,000**	**150**	**99.2**
✓ Na^+ (mEq)	**25,500**	**150**	**99.5**
** Glucose (mmol)	**800**	**0**	***100***
** Urea (g)	**56**	**28**	**50**

UREA

- P_{Urea} varies protein diet
  - *endogenously* produced by liver primary end-product of *protein metabolism*
- Primary route of elimination = excretion by kidneys
- ~ 40% U_{Osm}

BUN – Blood Urea Nitrogen

- Plasma (serum) urea levels- mg elemental nitrogen/dl plasma

  Normal value 7-18 mg/dl

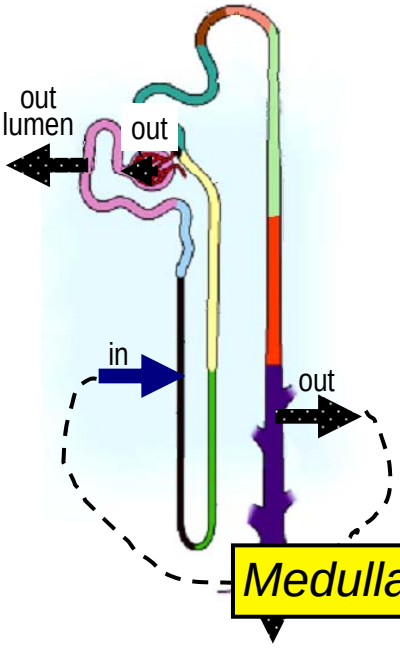
- Plasma levels vary *inversely* w/ GFR
- Elevated levels may indicate *reduced* kidney function

  >100 mg/dl = dialysis

BUN – Blood Urea Nitrogen

- Renal Failure Patient
- Colon can't compensate for loss of kidneys ability to excrete urea
- Treatment: Low protein diet to decrease plasma protein

UREA Handling – Pg 85-86



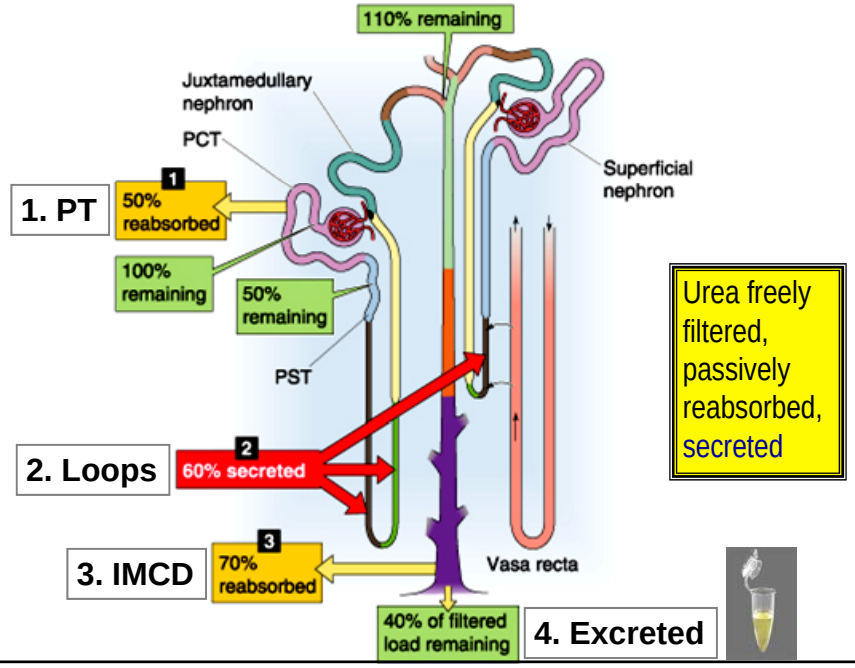
Urea freely filtered, passively reabsorbed, secreted

BIDIRECTIONAL TRANSPORT

- Net *reabsorption*
  - PT
  - IMCD
- Net *secretion*

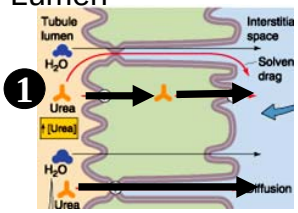
Medullary recycling of urea

UREA Handling by Nephron

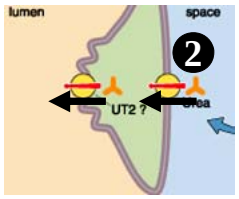


UREA Handling by Kidney

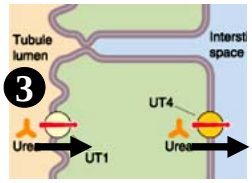
Lumen



1. Proximal tubule - reabsorption



2. Loop of Henle - *secretion*



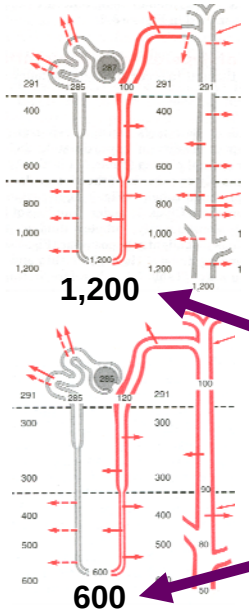
3. IMCD – reabsorption

Percentage Filtered UREA Handled Along Nephron

1.	Proximal tubules	50% reabsorb
2.	Loops of Henle	60% *secrete*
3.	Med collecting duct	70% reabsorb
4.	Excreted	40%

- High urine flow – kidneys excrete 70% filtered urea
- Low GFR – low urine flow – retain urea = ⇑ BUN

Urea Handling



Countercurrent system

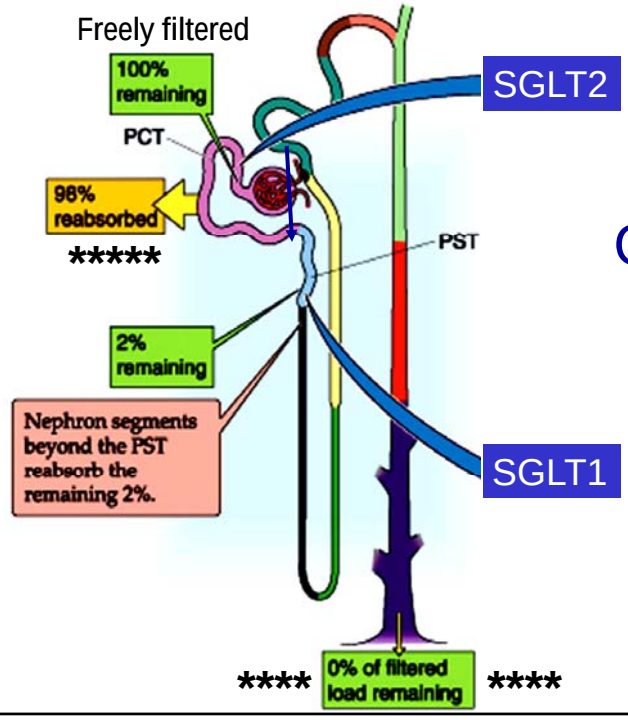
- Urea - 50% of inner medulla ISF Osm during *antidiuresis*
- < 10% during *water diuresis*

Renal Physiology Lecture 5

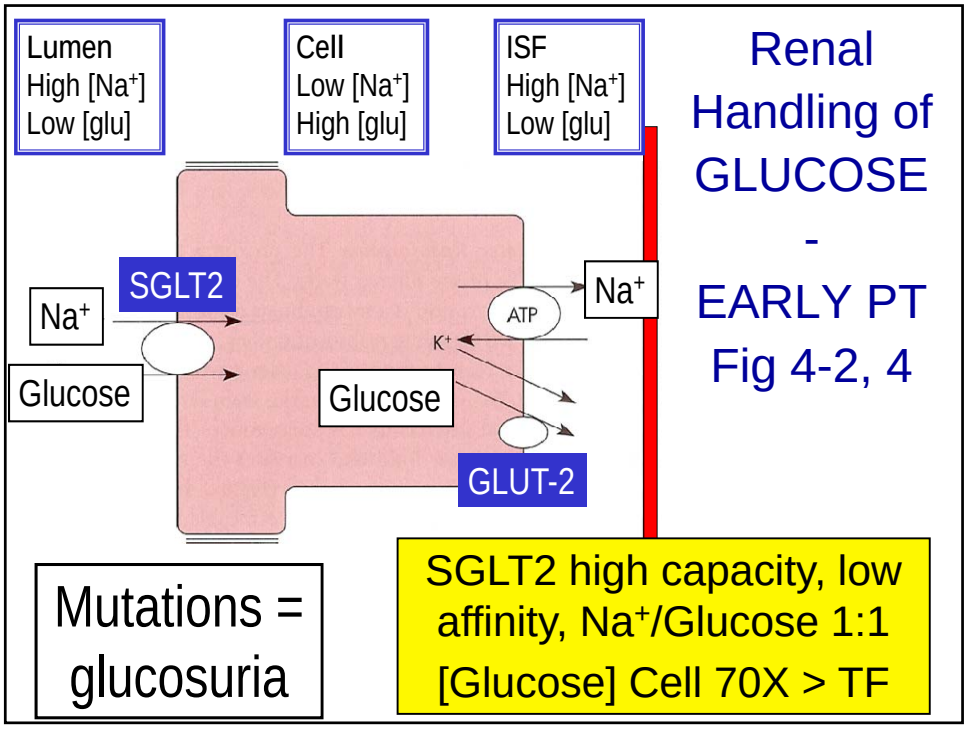
1. Urea - Filtered, Reabsorbed & Secreted
2. Glucose Tmax
3. Phosphate Reabsorption *Inhibited* by PTH
4. Calcium Reabsorption *Stimulated* by PTH & Vit D

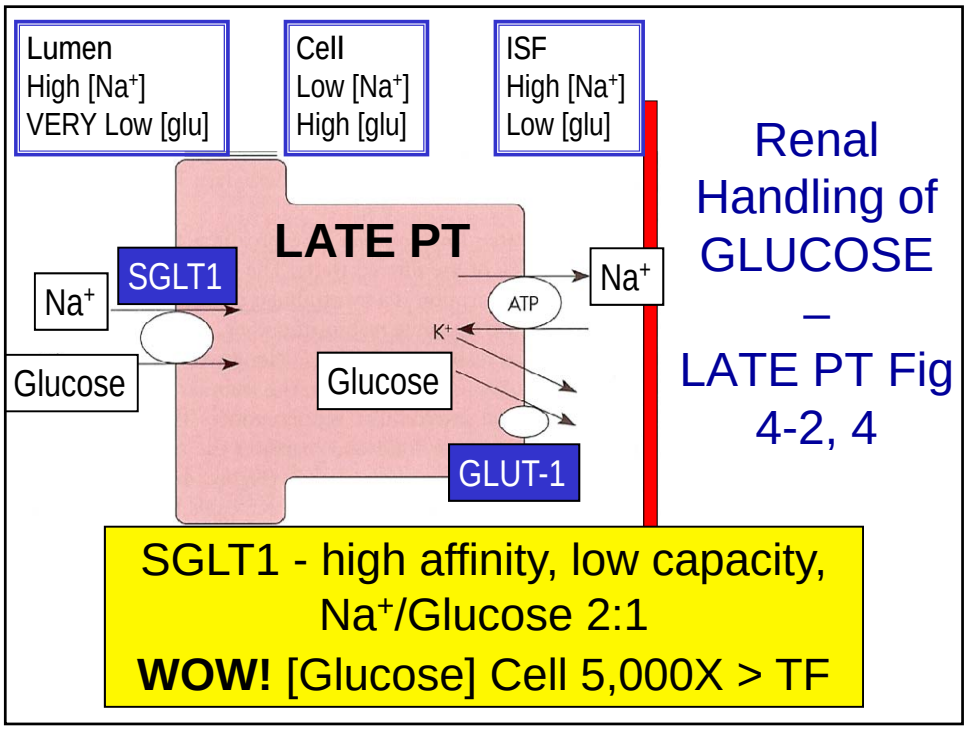
What causes glucose in urine?

1. plasma glucose concentration above the transport maximum for PT glucose reabsorption
2. mutations in apical or basolateral glucose transporters = glucosuria



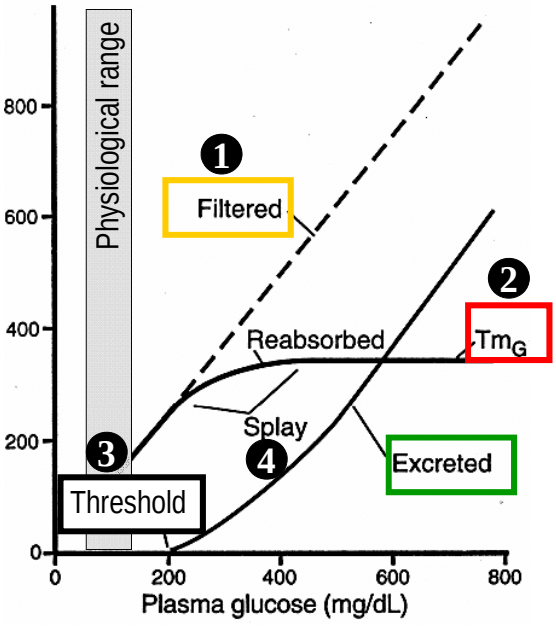
Renal Handling of GLUCOSE - PT


Lumen
High [Na+]
Low [glu]
Cell
Low [Na+]
High [glu]
ISF
High [Na+]
Low [glu]
Renal Handling of GLUCOSE - EARLY PT Fig 4-2, 4
SGLT2
Na+
Glucose
ATP
K+
Na+
Glucose
GLUT-2
Mutations = glucosuria
SGLT2 high capacity, low affinity, Na+/Glucose 1:1
[Glucose] Cell 70X > TF

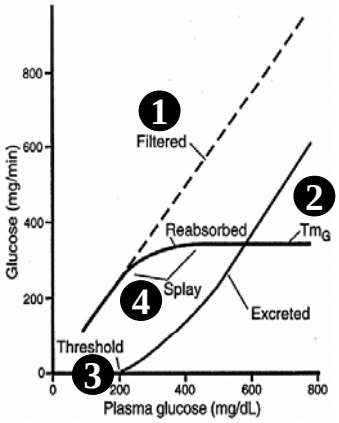

Lumen
High [Na+]
VERY Low [glu]
Cell
Low [Na+]
High [glu]
ISF
High [Na+]
Low [glu]
Renal Handling of GLUCOSE – LATE PT Fig 4-2, 4
LATE PT
SGLT1
Na+
Glucose
ATP
K+
Na+
Glucose
GLUT-1
SGLT1 - high affinity, low capacity, Na+/Glucose 2:1
WOW! [Glucose] Cell 5,000X > TF

GLUCOSE Titration Curve

Filtered load, reabsorption, or excretion of glucose (mg/min)

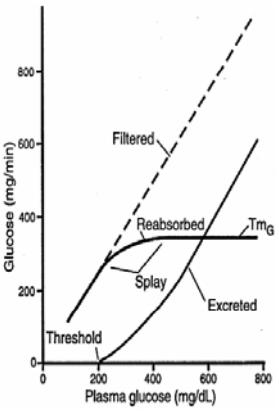


GLUCOSE Titration Curve



1. <u>Filtered load</u> = P_{Glu} X GFR
2. <u>Tm_G</u> - Max reabsorptive rate glucose – carriers saturated, P_{Glu} ~ 200 mg/dl
3. <u>Threshold</u> – P_{Glu} above, glucose excreted
4. <u>Splay</u> – *(rounding of reabsorption curve)* all nephrons don't have identical filtering & reabsorptive capacities

Normal GLUCOSE Handling



Filtered load glucose does NOT <u>normally</u> exceed renal Tm_G … ALL filtered glucose removed

Normal P_{Glu} = 100 mg/dl

- Glucose Threshold = 200 mg/dl

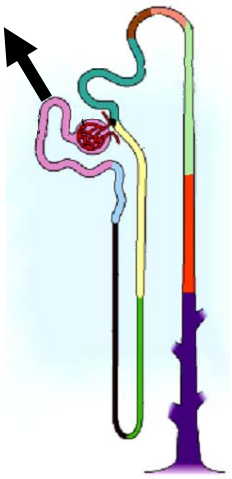
Kidney does NOT regulate P_{Glu}

Causes of Glucosuria (excretion GLUCOSE)

- *Diabetes Mellitus*

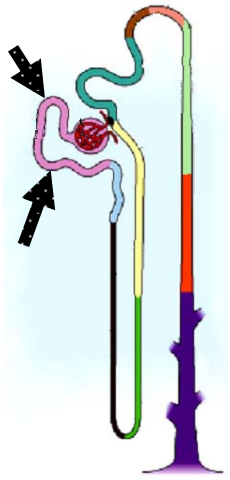
- P_{Glu} 500 mg/dl *exceeds* threshold =
- Glucose spills into urine = glucosuria
- Glucose-dependent osmotic diuresis

ORGANIC SOLUTES



- PT *reabsorbs 99-100% filtered*
  - Amino acids, Proteins (7 g/day filtered, < 30 mg/d excreted)
  - Mono-, di-, tricarboxylates
  - Urate

ORGANIC SOLUTES Box 4-1, 2



- PT *secretes*
  - Organic Anions
    - Penicillin
    - PAH
    - NSAIDS
  - Organic Cations
    - Creatinine
    - morphine
    - Amiloride
- Competition of Transporters

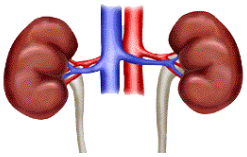
Renal Physiology Lecture 5

1. Urea - Filtered, Reabsorbed and Secreted
2. Glucose Tmax
3. Phosphate Uptake Inhibited by PTH
4. Calcium Uptake Stimulated by PTH & Vit D

PHOSPHATE Handling







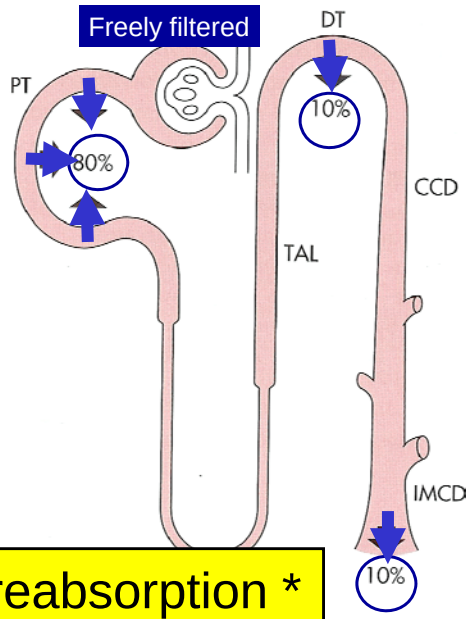
Metabolism of inorganic phosphate (Pi) depends on bone, GI tract, kidneys

86%

* Renal Pi *excretion* primary regulation Pi homeostasis *

PHOSPHATE Handling Fig 9-6

1. PT reabsorbs 80% filtered Pi (Na^+ / P_i cotransporter)
2. DT reabsorbs 10% filtered Pi
3. 10% filtered Pi excreted urine



* PTH *inhibits* Pi reabsorption *

PHOSPHATE Handling

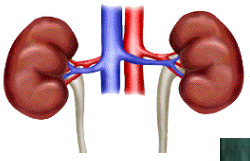
1. High serum phosphate = high serum PTH
2. **PTH** – inhibits phosphate reabsorption = increases renal phosphate excretion
3. Chronic renal failure CRF – high serum phosphate
   - Treatment: give oral phosphate binders (reduce GI phosphate absorption), avoid high phosphate intake

Renal Physiology Lecture 5

1. Urea - Filtered, Reabsorbed and Secreted
2. Glucose Tmax
3. Phosphate Reabsorption *Inhibited* by PTH
4. Calcium Reabsorption *Stimulated* by PTH & Vit D

Calcium Handling


Maintenance of plasma Ca^{++} depends on bone, GI tract, kidneys



200 mg/d

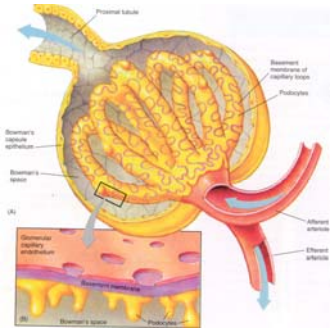
99%

Net 20% absorbed

* Kidneys play major role Ca^{++} homeostasis *

Regulation of CALCIUM Balance

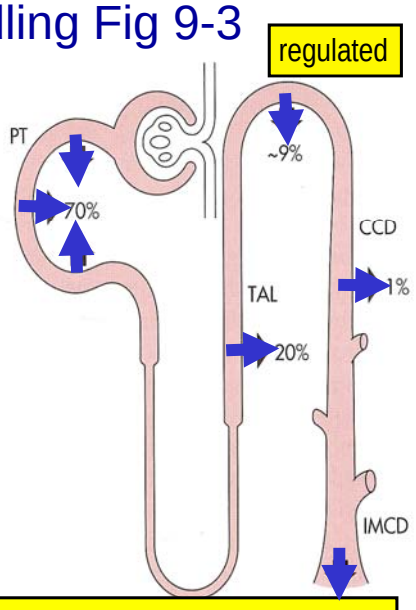
- 40% plasma Ca^{2+} <u>bound</u> to plasma proteins
- 60% plasma Ca^{2+} <u>filterable</u> at glomerulus
  - 15% complex (sulfate, citrate, phosphate)
  - 45% ionized
- 99% filtered Ca^{+2} reabsorbed, but NOT secreted



CALCIUM Handling Fig 9-3

Kidneys reabsorb 99% filtered Ca^{+2} by

1. PT - 70%
2. TAL - 20%
3. DCT - 9% (major *regulatory* site)
4. CD – 1%
5. Excreted – 1%



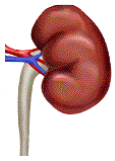
* PTH stimulates Ca^{2+} reabsorption *

Hypocalcemia: Regulation of Ca^{2+} Balance

⇓ $P[Ca^{2+}]$ stimulus

– ⇑ PTH (parathyroid hormone)

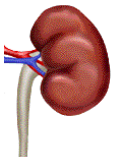
⇑ P $[Ca^{2+}]$ by stimulating:



- ⇑ Renal distal tubule reabsorption Ca^{2+}
- ⇑ bone resorption by osteoclasts
- ⇑ 1 alpha-hydroxylase = ⇑ formation 1,25-dihydroxy vitamin D3
  - » ⇑ Ca^{2+} absorption intestine

Hypercalcemia: Regulation of Ca^{2+} Balance

⇑ $P[Ca^{2+}]$ stimulus



– ⇑ Calcitonin

⇓ P $[Ca^{2+}]$ by:

- ⇓ Synthesis and release PTH
- ⇓ Renal distal tubule reabsorption Ca^{2+}
- ⇓ bone resorption by osteoclasts
- ⇓ Calcitriol production
  - » ⇓ Ca^{2+} absorption intestine

Chronic Renal Failure CRF

⇓ serum Ca^{++} & ⇑ serum Pi = ⇑ PTH

PTH *inhibits* Pi reabsorption by PT & stimulates Ca^{++} reabsorption by DT

CRF patient:

- ⇑ serum Pi = ⇑ PTH = ⇑ Ca^{++} mobilization from bone = bone loss = renal osteodystrophy
- ⇓ serum Ca^{++} is due to ⇓ Vit D production by kidney & ⇓ Ca^{++} absorption by gut

*Treatment: Avoid high Pi intake + Ca^{++} supplements + Vit D + Pi binders *

Summary

1. Kidney handles urea excretion
   - Bidirectional transport
   - Build up of excess urea = toxic
2. Kidney 1 of 3 organs regulating Ca^{++} balance
   - Regulate reabsorption
3. No glucose in urine if < Tmax glucose
4. Time for Questions