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 **

<table>
<thead>
<tr>
<th>Patient Data</th>
<th>△ Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma$_{K+}$</td>
<td>↑</td>
</tr>
<tr>
<td>P$_{Urea}$</td>
<td>↑</td>
</tr>
<tr>
<td>BP</td>
<td>↑</td>
</tr>
<tr>
<td>P$_{PO4^-}$</td>
<td>↑</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>↓</td>
</tr>
<tr>
<td>P$_{HCO3^-}$</td>
<td>↓</td>
</tr>
<tr>
<td>P$_{pH}$</td>
<td>↓</td>
</tr>
<tr>
<td>P$_{Ca2+}$</td>
<td>↓</td>
</tr>
</tbody>
</table>

** REVIEW - Filtration & Reabsorption **

<table>
<thead>
<tr>
<th></th>
<th>Amount FILTER/d</th>
<th>Amount EXCRETE/d</th>
<th>% REABSORB</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ Water (L)</td>
<td>180</td>
<td>1.8</td>
<td>99.0</td>
</tr>
<tr>
<td>K$^+$ (mEq)</td>
<td>720</td>
<td>100</td>
<td>86.1</td>
</tr>
<tr>
<td>** Ca$^{2+}$ (mEq)</td>
<td>540</td>
<td>10</td>
<td>98.2</td>
</tr>
<tr>
<td>HCO$_3^-$ (mEq)</td>
<td>4,320</td>
<td>2</td>
<td>99.9+</td>
</tr>
<tr>
<td>✓ Cl$^-$ (mEq)</td>
<td>18,000</td>
<td>150</td>
<td>99.2</td>
</tr>
<tr>
<td>✓ Na$^+$ (mEq)</td>
<td>25,500</td>
<td>150</td>
<td>99.5</td>
</tr>
<tr>
<td>** Glucose (mmol)</td>
<td>800</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>** Urea (g)</td>
<td>56</td>
<td>28</td>
<td>50</td>
</tr>
</tbody>
</table>
**UREA**

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

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**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
  - $>100 \ \text{mg/dl} = \text{dialysis}$
**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

1. PT
   - Urea freely filtered, passively reabsorbed

2. Loops
   - 60% secreted

3. IMCD
   - 70% reabsorbed

4. Excreted
   - 40% of filtered load remaining

UREA Handling by Kidney

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

SGLT1 - high affinity, low capacity, Na+/Glucose 2:1
WOW! [Glucose] Cell 5,000X > TF
GLUCOSE Titration Curve

1. **Filtered load** = \( P_{\text{Glu}} \times \text{GFR} \)

2. **\( T_{\text{mG}} \)** - Max reabsorptive rate glucose - carriers saturated, \( P_{\text{Glu}} \sim 200 \text{ mg/dl} \)

3. **Threshold** - \( P_{\text{Glu}} \) above, glucose excreted

4. **Splay** - (rounding of reabsorption curve) all nephrons don’t have identical filtering & reabsorptive capacities
Normal GLUCOSE Handling

Filtered load glucose does NOT normally exceed renal $Tm_G$ ... ALL filtered glucose removed

Normal $P_{Glu} = 100 \text{ mg/dl}$

- 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

* Renal Pi excretion primary regulation Pi homeostasis *

86%
PHOSPHATE Handling

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

* PTH inhibits Pi reabsorption *

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

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3. Phosphate Reabsorption
   *Inhibited* by PTH

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   *Stimulated* by PTH & Vit D

Calcium Handling

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

* Kidneys play major role in Ca++ homeostasis *

Net 20% absorbed
Regulation of CALCIUM Balance

- 40% plasma Ca\(^{2+}\) bound to plasma proteins
- 60% plasma Ca\(^{2+}\) filterable 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

\(\downarrow\) P[Ca\(^{2+}\)] stimulus

- \(\uparrow\) PTH (parathyroid hormone)
- \(\uparrow\) P [Ca\(^{2+}\)] by stimulating:
  - \(\uparrow\) Renal distal tubule reabsorption Ca\(^{2+}\)
  - \(\uparrow\) bone resorption by osteoclasts
  - \(\uparrow\) 1 alpha-hydroxylase = \(\uparrow\) formation 1,25-dihydroxy vitamin D3
    » \(\uparrow\) Ca\(^{2+}\) absorption intestine

Hypercalcemia: Regulation of Ca\(^{2+}\) Balance

\(\uparrow\) P[Ca\(^{2+}\)] stimulus

- \(\uparrow\) Calcitomin

\(\downarrow\) P [Ca\(^{2+}\)] by:
  - \(\downarrow\) Synthesis and release PTH
  - \(\downarrow\) Renal distal tubule reabsorption Ca\(^{2+}\)
  - \(\downarrow\) bone resorption by osteoclasts
  - \(\downarrow\) Calcitriol production
    » \(\downarrow\) 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