Renal Physiology 2011
Lisa M. Harrison-Bernard, PhD
Contact me at lharris@lsuhsc.edu
Renal Physiology Lecture 3
Renal Clearance and Glomerular Filtration

### Filtration and Reabsorption

<table>
<thead>
<tr>
<th>Substance</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>Ca²⁺ (mEq)</td>
<td>540</td>
<td>10</td>
<td>98.2</td>
</tr>
<tr>
<td>HCO₃⁻ (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⁺ (g)</td>
<td>630</td>
<td>3.2</td>
<td>99.5</td>
</tr>
<tr>
<td>Glucose (g)</td>
<td>180</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Urea (g)</td>
<td>54</td>
<td>30</td>
<td>44</td>
</tr>
</tbody>
</table>
Tubular Secretion

Most important:
- $\text{H}^+$
- $\text{K}^+$
- Organic anions: choline, creatinine
- Foreign chemicals: penicillin

Handling of Substance L by Kidney

- **Filtered Load**
  
  \[
  \text{GFR} \times \text{Plasma } [L]
  \]
  \[
  \text{GFR} \times \text{P}_L
  \]

- **Excretion Rate**
  
  \[
  \text{Urine } [L] \times \text{Urine flow}
  \]
  \[
  U_L \times V
  \]
Summary

1. Kidney is a very important organ.
2. Juxtaglomerular apparatus is coolest.
3. 3 basic renal processes
   - Filtration, reabsorption, secretion
4. Damage to filtration barrier results in glomerular disease

Renal Physiology - Lectures

- Physiology of Body Fluids
- Structure & Function of the Kidneys
- Renal Clearance & Glomerular Filtration
- Regulation of Renal Blood Flow
- Transport of Sodium & Chloride
- Transport of Urea, Glucose, Phosphate, Calcium & Organic Solutes
- Regulation of Potassium Balance
- Regulation of Water Balance
- Transport of Acids & Bases
- Integration of Salt & Water Balance
- 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 3
Renal Clearance and Glomerular Filtration
Chapter 3 Koeppen & Stanton Renal Physiology

1. Starling Forces
2. Control of GFR
3. Concept of Renal Clearance
4. Clearance of Inulin & Creatinine = Estimates of GFR
5. PAH = Estimate of RPF

Fluid Movement Out of Glom Cap – Into Bowman’s Space
Glomerular Ultrafiltration - Eq 3-10

\[ J_v = K_f \left[ (P_{GC} - P_{BS}) - \sigma (\pi_{GC} - \pi_{BS}) \right] \]

\( J_v \) – volume flux across the capillary wall

\( \sigma \) – reflection coefficient for protein

\( \sigma = 1 \)

protein cannot cross glomerular membrane
Kf – Ultrafiltration Coefficient

\[ GFR = K_f [ (P_{GC} - P_{BS}) - (\pi_{GC} - \pi_{BS}) ] \]

- Intrinsic permeability glom capillary
- Product of hydraulic conductivity \((L_p)\) & surface area \((S_f)\)
- \(L_p\) & \(S_f\) 10-100 X > other beds

Kf = Lp x A

- Area - total capillary surface area
- ~ 1 cm length/glom cap
- ~ 12 miles total length (2 mil glom)
- 6,000 cm\(^2\) total surface area
- filtration area ~10% (Fenestrae)

Boyle et al. *Kidney International* 1998
Ultrafiltration Coefficient

\[
GFR = (K_f)(P_{UF})
\]

\[K_f \text{ ml/min/mmHg}\]

125 ml/min = 
8.3 ml/min/mmHg (15 mmHg)

Forces Involved in Glomerular Filtration – Fig 3-6

2 forces favor fluid filtration

2 forces oppose fluid filtration
Forces Involved in Glomerular Filtration – Fig 3-6

Two forces favor fluid filtration.

Two forces oppose fluid filtration.

\[ \text{Net Filtration Pressure} = P_{GC} - P_{BS} - \pi_{GC} + \pi_{BS} \]

\[ P_{GC} = \text{Glomerular capillary hydrostatic pressure} \]
\[ \pi_{BS} = \text{Bowman’s space oncotic pressure} \]
\[ P_{BS} = \text{Bowman’s space hydrostatic pressure} \]
\[ \pi_{GC} = \text{Glomerular capillary oncotic pressure} \]
Net Glomerular Filtration Pressure - Glomerular Capillary

\[ P_{GC} - P_{BS} - \pi_{GC} + \pi_{BS} \]

\( P_{GC} = 50, P_{BS} = 10, \pi_{GC} = 25, \pi_{BS} = 0 \text{ mmHg} \)

\[ 50 - 10 - 25 + 0 \text{ mmHg} = 15 \text{ mmHg} \]

\( P_{GC} - \) only force favors filtration

\[ 2X > \text{most capillaries} \]

Glomerular Ultrafiltration - Eq 3-10

\[ \text{GFR} = K_f \left[ (P_{GC} - P_{BS}) - (\pi_{GC} - \pi_{BS}) \right] \]

Rate of glomerular ultrafiltration

\[ = \text{ultrafiltration coefficient (} K_f \text{) } \times \text{ net Starling forces (} P_{UF} \text{)} \]
Starling Forces Change Along the Length of Capillaries: Skeletal Muscle (Non-Renal Capillary)

Net Filtration

Net Absorption

Equilibration Point

Overall: Filtration ~ Absorption

Starling Forces Along Glomerular Capillaries

\[ \pi_{GC} \text{ increases along glom capillary} \]

NEVER Absorptive flux
Forces Involved in ABSORPTION by Peritubular Capillaries

Net peritubular capillary pressure

\[ \text{Net peritubular capillary pressure} = P_{PC} - P_O - \pi_{PC} + \pi_O \]

Net Glomerular Filtration Pressure - Peritubular Capillary

\[ \text{Net Glomerular Filtration Pressure - Peritubular Capillary} = P_{PC} - P_O - \pi_{PC} + \pi_O \]

\[ P_{PC} = 20, \quad P_O = 8, \quad \pi_{PC} = 35, \quad \pi_O = 6 \text{ mmHg} \]

\[ 20 - 8 - 35 + 6 \text{ mmHg} = \text{minus 17 mmHg} \]

Negative filtration \(\equiv\) absorption

Forces favor reabsorption of fluid
Renal Physiology Lecture 3

✓ Starling Forces

2. Control of GFR

3. Concept of Renal Clearance

4. Clearance of Inulin & Creatinine

5. Clearance of PAH

What would happen to GFR if ↑ RAP?
Control of GFR

\[ P_{UF} = P_{GC} - P_{BS} - (\pi_{GC} - \pi_{BS}) \]

\[ GFR = K_f (P_{UF}) \]

- \( \uparrow \) Renal Artery Pressure (RAP) = \( \uparrow \) GFR
- \( \uparrow \) AA resistance = \( \downarrow \) GFR

Control of GFR

\[ P_{UF} = P_{GC} - P_{BS} - (\pi_{GC} - \pi_{BS}) \]

\[ GFR = K_f (P_{UF}) \]

- \( \downarrow \) AA resistance = \( \uparrow \) GFR
- \( \downarrow \) EA resistance = \( \downarrow \) GFR
Control of GFR

\[ P_{UF} = P_{GC} - P_{BS} - (\pi_{GC} - \pi_{BS}) \]

\[ GFR = K_f (P_{UF}) \]

- \( \downarrow \pi_{GC} \) - \( \uparrow \) GFR
  - \( \downarrow \) protein metabolism - malnutrition, hepatic disease, GI losses
  - \( \uparrow \) protein excretion - kidney disease = proteinuria

Control of GFR

\[ P_{UF} = P_{GC} - P_{BS} - (\pi_{GC} - \pi_{BS}) \]

\[ GFR = K_f (P_{UF}) \]

- \( \uparrow P_{BS} \) - \( \downarrow \) GFR
  - acute obstruction – stone, enlarged prostate
- \( \uparrow \pi_{BS} \) - \( \uparrow \) GFR
  - filter protein - proteinuria
Control of GFR

\[ P_{UF} = P_{GC} - P_{BS} - (\pi_{GC} - \pi_{BS}) \]

\[ GFR = K_f (P_{UF}) \]

\[ K_f = L_p \times S_f \]

\[ \downarrow K_f = \downarrow GFR \]

reduce surface area or # filtering glomeruli

- hypertension
- diabetes
- glomerulosclerosis

Decreases in GFR - Disease

\[ GFR = K_f \left[ (P_{GC} - P_{BS}) - (\pi_{GC} - \pi_{BS}) \right] \]

• Acute Renal Failure

\[ \downarrow \text{RAP, } \uparrow R_A, \downarrow R_E, \downarrow P_G, \downarrow GFR \]
Renal Physiology Lecture 3

✓ Starling Forces
✓ Control of GFR

3. Concept of Renal Clearance

4. Clearance of Inulin & Creatinine

5. Clearance of PAH

Renal Plasma Clearance

• Renal CLEARANCE of any substance

volume of plasma from which a substance is completely removed (cleared) by kidneys per unit time

Units = Volume plasma per time

ml/min

• QUANTITATIVE evaluation: how kidney handles specific substance
Clearance $S =$
\[
\frac{\text{Mass } S \text{ excreted}}{\text{time}}
\]
\[
\text{Plasma } [S]
\]
\[
\text{Cl}_S \cdot P_S = U_S \cdot V
\]
\[
\text{Cl}_S = \frac{U_S \cdot V}{P_S}
\]

What is the renal clearance of glucose?
<table>
<thead>
<tr>
<th>Substance</th>
<th>CLEARANCE (ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>0</td>
</tr>
<tr>
<td>Na⁺</td>
<td>0.9</td>
</tr>
<tr>
<td>K⁺</td>
<td>12</td>
</tr>
<tr>
<td>Inulin</td>
<td>125</td>
</tr>
<tr>
<td>Creatinine</td>
<td>140</td>
</tr>
<tr>
<td>PAH</td>
<td>560</td>
</tr>
</tbody>
</table>

Renal Physiology Lecture 3

- Starling Forces
- Control of GFR
- Concept of Renal Clearance
- Clearance of Inulin & Creatinine
- Clearance of PAH
Inulin

$\text{Cl}_{\text{IN}} = \text{GFR}$

- MW 5,000 Da
- Freely filterable
- NOT reabsorbed
- NOT secreted
- NOT metabolized, synthesized, stored
- NOT alter GFR
- NONtoxic
- Infusion required
- $P_{\text{IN}} \cdot U_{\text{IN}}$ - analytic method
Inulin
Measurement of GFR
Amount Filtered = Amount Excreted

\[ \text{GFR} \cdot P_{\text{IN}} = U_{\text{IN}} \cdot \dot{V} \]

\[ \text{GFR} = \frac{U_{\text{IN}} \cdot \dot{V}}{P_{\text{IN}}} = \text{Cl}_{\text{IN}} \]

Creatinine
\[ \text{Cl}_{\text{Cr}} \sim \text{GFR} \]
Creatinine

Rate of Production  =  Rate of Excretion
1 g/day = 1 g/day

Index of GFR

\[ \text{GFR (Clearance}_{Cr}) = \frac{U_{Cr} \cdot \dot{V}}{P_{Cr}} \]

\( Cl_{Cr} \) is inversely related to \( P_{Cr} \)

Creatinine ~Fig 3-2

- Metabolism of creatine phosphate - muscle
- Produced continuously
- Freely filtered
- NOT reabsorbed
- Small amount secreted
- NO infusion required
- Stable \( P[Cr] \)
- \( P[Cr] \) & \( U[Cr] \) – colorimetric method
Plasma \( \text{Cr} \) Inversely Related to GFR ~Fig 3-3

Plasma creatinine concentration (mg/dl)

\[ \begin{array}{c|c}
\text{GFR (ml/min)} & \text{\( P_{\text{Cr}} \) (mg/dl)} \\
120 & 1 \\
60 & 2 \\
30 & 4 \\
15 & 8 \\
\end{array} \]

Normal
\( P_{\text{Cr}} = 1 \text{mg/dl} \)

Normal GFR

\( P_{\text{Cr}} = 2 \text{mg/dl} \)
GFR ½

\( P_{\text{Cr}} = 6 \text{mg/dl} \)
GFR 1/6

Plasma Creatinine Concentrations

\( P_{\text{Cr}} = 0.8 – 1.2 \text{ mg/dl (1.0mg/dl)} \)

normal range for adult

\( \text{Plasma}_{\text{Cr}} \) inversely related to GFR
Normal Values GFR

GFR corrected to body surface area 1.73 m²

- Newborns 20 ml/min
- ♀ 120 ml/min
- ♂ 130 ml/min

Declines after age 40
- ~ 1 ml/min/yr

Current Recommendations for Routine Estimation of GFR in Clinical Setting

**MDRD Study Equation:**

\[
GFR \text{ (ml/min/1.73 m²)} = \\
175 \times (S_{Cr})^{-1.154} \times \text{(Age)}^{0.203} \times (0.742 \text{ if female}) \times (1.212 \text{ if African American})
\]

**Cockcroft-Gault Equation:**

\[
\text{Clearance \(Cr\) (ml/min) = } \\
(140 \text{ – age}) \times \text{(Wt in kg)} \times (0.85 \text{ if female}) / (72 \times S_{Cr})
\]

MDRD = Modification of Diet in Renal Disease; SCr = serum creatinine, mg/dl
GFR Calculators Are Available Online:
National Kidney Disease Education Program (NKDEP) of NIH
Kidney Disease Outcomes Quality Initiative (KDOQI) of National Kidney Foundation
Renal Physiology Lecture 3

- Starling Forces
- Control of GFR
- Concept of Clearance
- Clearance of Inulin & Creatinine

5. Clearance of PAH

PAH
Para-amino hippuric acid

$\text{Cl}_{\text{PAH}} \sim \text{RPF}$
Para-amino hippuric acid (PAH)

- Organic anion
- Freely filtered
- Vigorously secreted PT
- ≥ 90% removed single circuit
- ~ 10% RV
- NOT produced
- Infusion required

Para-amino hippuric acid (PAH)

**PAH Clearance ~ Renal Plasma Flow**

**Amount Entering Kidney ~ Excretion Rate**

\[ \text{RPF} \cdot \text{P}_{\text{PAH}} = \text{U}_{\text{PAH}} \cdot \dot{V} \]

**Rearrange**

\[ \text{RPF} = \frac{\text{U}_{\text{PAH}} \cdot \dot{V}}{\text{P}_{\text{PAH}}} \]
Summary

1. Glomerular filtrate formation - *filtration barrier* & *Starling forces*

2. *Clearance* of certain substances – index of renal function

3. Plasma *creatinine* - tool for diagnosing and following renal function

THE END
Calculate Renal Plasma Flow

\[ \text{RPF} = \frac{U_{\text{PAH}} \cdot \mathbf{V}}{P_{\text{PAH}}} \]

\[ \text{R ‘Plasma’ F = RPF} = 600 \text{ ml/min} \]

\[ \text{R ‘Blood’ F = RBF} = 1,200 \text{ ml/min} \]

Review Clearance Principles

- \( \text{Cl}_X < \text{GFR} \) net reabsorption \( X \)
- \( \text{Cl}_X > \text{GFR} \) net secretion \( X \)
- \( \text{Cl}_X < \text{Cl}_{\text{IN}} \) reabsorbed - glucose
- \( \text{Cl}_X > \text{Cl}_{\text{IN}} \) secreted - PAH
- \( \text{Cl}_X = \text{Cl}_{\text{IN}} \) only filtered - creatinine
- filtered load > rate of excretion = reabsorption \( X \)