Regulation of Glomerular Filtration Rate and Renal Blood Flow – 2 Hrs
Chapters 3 Koeppen & Stanton Renal Physiology

1. Starling Forces
2. Control of GFR
3. Oxygen Consumption
4. Autoregulation
   • Myogenic
   • Tubuloglomerular Feedback
5. Control of Renal Circulation
   • AngII, ANP, SNS, AVP

Terminology
• Oncotic pressure – pressure generated by large molecules (especially proteins) in solutions
• Hydrostatic pressure – pressure exerted by liquids
• Renal artery pressure - RAP
• Renal plasma flow - RPF

Which of the following is the most important in regulating water balance in the body?

a) Water lost through skin and lungs
b) Water lost in feces
c) Water lost in sweat
d) Urine production

Functions of the Kidney
Kidneys - major regulation of body water and inorganic ions = extracellular fluid (ECF)
Body fluid
   osmolality
   volume

What are some of the functions of the kidney???
Functions of the Kidney
• Regulate water & inorganic-ion balance \( \equiv \text{BP} \)
  \( \text{H}_2\text{O}, \text{Na}^+, \text{K}^+, \text{Ca}^{2+}, \text{Cl}^-, \text{Mg}^{2+}, \text{etc.} \)
• Acid-base balance
• Remove metabolic waste products
  Urea, uric acid, creatinine

Functions of the Kidney
• Remove foreign chemicals
  Drugs, toxins, pesticides
• Secrete hormones
  Erythropoietin
  Renin
  Vitamin D

Starling Forces Change Along the Length of Capillaries: Skeletal Muscle
Arteriole
Venule
Net Filtration
Net Absorption
Equilibration Point

Fluid Movement Out of Glom Cap – Into Bowman’s Space

Filtration
• Net filtration of fluid across all capillaries (except kidney)
  \( = 4 \text{ L/d} \)
• Glomerular Filtration Rate - GFR
  \( = 125 \text{ ml/min} \) (both kidneys)
  \( = 180 \text{ L/day} \)
• Plasma volume - PV
  \( = 3\text{L} \) = filtered 60X /d
• ECFV
  \( = 17\text{L} \) = filtered 10X /d

Glomerular Filtration
• 1st step in urine formation
• Ultrafiltration of plasma by glomerulus
• Devoid of cellular elements
• Essentially protein free
• Conc salts, glucose, amino acids = plasma
• Driven by Starling forces
Glomerular Ultrafiltration - Eq 3-10

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

\( \sigma \) – reflection coefficient for protein

= 1

protein cannot cross glomerular membrane

Glomerular Ultrafiltration - Eq 3-10

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

Rate of glomerular ultrafiltration = product of ultrafiltration coefficient \( (K_f) \) and net Starling forces \( (P_{UF}) \)

Ultrafiltration Coefficient

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

\( K_f \) ml/min/mmHg

- Intrinsic permeability of glom capillary
- Product of hydraulic conductivity & surface area
- 10-100X > other beds

Forces Involved in Glomerular Filtration – Fig 3-6

Net glomerular filtration pressure - beginning of capillary

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

Net Filtration Pressure = \( P_{GC} - P_{BS} - \pi_{GC} + \pi_{BS} \)
Net glomerular filtration pressure - beginning of capillary

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

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

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

\( P_{GC} \) – only force that favors filtration

2X > most capillaries

Ultrafiltration Coefficient

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

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

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

Net peritubular capillary pressure - beginning of the capillary

\[ P_{PC} - P_{O} - \pi_{PC} + \pi_{O} \]

\( P_{PC} = 20 \), \( P_{O} = 8 \), \( \pi_{PC} = 35 \), \( \pi_{O} = 6 \) mmHg

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

Negative filtration \( \equiv \) absorption

Forces favors reabsorption of fluid
Control of GFR

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

- \( \uparrow \) Renal Artery Pressure (RAP) = \( \uparrow P_{GC} = \uparrow GFR \)
- \( \uparrow \) AA resistance
  - \( \downarrow P_{GC} = \downarrow GFR \)

\[ \Delta \text{ protein metabolism, protein loss in urine} \]
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

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

- \(\downarrow K_f\)
  - hypertension
  - diabetes
  - glomerulosclerosis

Renal Parameters

- Cardiac Output (CO) = 5,000 ml/min
- Renal Blood Flow (RBF) =
  - 1,000 ml/min
  - 350 ml/min/100gKW
  - 4 ml/min/g (1% BW)
- Brain = 50 ml/min/100g
- Skeletal muscle = 0.08 ml/min/g

Renal Fraction (RF) = RBF/CO

\[
1,000 \text{ ml/min} \div 5,000 \text{ ml/min} = 0.20 = 20\%
\]

Hematocrit (Hct) = 0.40

\[
40\% \text{ BV} = \text{RBC}
\]

Renal Plasma Flow (RPF) =

\[
RBF \times (1 - Hct)
\]

\[
1,000 \text{ ml/min} \times (1 - 0.40) = 600 \text{ ml/min}
\]

\[
\text{Filtration Fraction (FF)} = \frac{GFR}{RPF} = \frac{125 \text{ ml/min}}{600 \text{ ml/min}} = 0.20
\]

\[
\text{Urine flow} (V) = 1 \text{ ml/min}
\]

Fluid reabsorbed =

\[
125 \text{ ml/min} - 1 \text{ ml/min} = 124 \text{ ml/min} > 99\%
\]

*Filtration >>> Urine Output*
Time for a Break

O₂ Consumption by Kidneys
- O₂ consumption/g tissue > any organ except heart
- Arterial - Venous O₂ difference lowest
- O₂ consumption relative to RBF is not very high
- O₂ is not the critical factor for RBF

O₂ Consumption & Na⁺ Transport
- O₂ consumption is LARGE and parallels Na⁺ reabsorption
- RBF large – Arterial - Venous PO₂ difference is SMALL

Regulation of RBF
- Intrinsic mechanisms
  - Renal autoregulation
    - Myogenic mechanism
    - Tubuloglomerular feedback mechanism (TGF)
- Extrinsic control mechanisms
  - Role of renal nerves
  - Circulating vasoactive hormones – ANP, AVP, RAS

Hydrostatic Pressure Profile
Note the sharp decreases in pressure across the afferent and efferent arterioles.
Relatively high hydrostatic pressure is maintained along the glomerular capillary.
Renal Blood Flow Autoregulation

- Autoregulation – vascular bed maintains BF with Δ Blood Pressure
- RAP ~ 80 – 170 mmHg (posture, exercise, sleep)
  RBF & GFR constant
* Intrinsic phenomenon *

Myogenic Mechanism
Responds to Change AP

- Intrinsic property of arterial smooth muscle
  ↑ vascular wall tension - contract
  or
  ↓ vascular wall tension - relax

Tubuloglomerular Feedback (TGF)

- Balance filtration (hemodynamic) & reabsorption (metabolic)
- Tubulo-vascular crosstalk preservation of electrolyte balance
  * Limits UNaV

Handout

Initial ↑ MAP Above normal
↓ RBF & GFR To return to normal
* Renal Blood Flow Autoregulation *

Distend Afferent Arteriole

↑ AA Wall Tension

Stretch AA VSMC Open Stretch Activated Channels Influx Calcium

↑ AA RESISTANCE

Smooth Muscle Cell Contraction

* Renal Blood Flow Autoregulation *

Autoregulation of RBF K&S Fig 3-7

Relative vascular resistance

Renal blood flow (m/min)

GFR (m/min)

Renal arterial pressure (mm Hg)

80 - 170 mmHg

* Intrinsic phenomenon *
Tubuloglomerular Feedback Mechanism K&S Fig 3-8

Control of Renal Circulation
- Sympathetic nervous system
- Hormones
- Endothelial factors

Affect AA & EA resistance
Alter RBF & GFR
Autoregulation RBF & GFR can be overridden

Sympathetic Nervous System
- AA & EA
- Juxtaglomerular cell
- Tubule
  - ↑ firing rate = vasoconstriction
  - Trauma/shock – strong SNS output
    ↓ RBF cease GFR

Renin-Angiotensin System - RAS
- RAS regulates Na+ balance, plasma volume
  control of arterial blood pressure
- Renin - rate limiting step AngII formation
  * Major concern = ↑ ECFV ↑ BP *

HEMODYNAMIC Actions of Angiotensin II
- vasoconstriction ↑ TPR
  ↑ BP
- constrict afferent & efferent arterioles
  ↓ RBF
- contract mesangial cells -
  ↓ Kf ↓ GFR
  * Reduce RBF & GFR *
Mouse In Vitro Blood Perfused Juxtamedullary Nephron

AVP – Arginine Vasopressin = ADH – AntiDiuretic Hormone

Identical Peptide

Actions of AVP (ADH)
- Constriction of afferent and efferent arterioles
- ↓ BF to renal medulla
- Systemic vasoconstriction ↑ BP

* Reduce H₂O Excretion ↑ BP *

Nitric Oxide
- Endothelia generate nitric oxide – acetylcholine, histamine, bradykinin
- Relax vascular smooth muscle
  ✓ afferent & efferent arterioles
- Buffer excessive vasoconstriction of AngII & NE

Atrial Natriuretic Peptide (ANP)
- Synthesized, secreted - cardiac atria
  Stimulus
    ✓ ↑ atrial distention
    ✓ ↑ plasma volume
    ✓ Severe volume expansion

Atrial Natriuretic Peptide (ANP)
- Dilates afferent arteriole ↑ GFR

↓ Plasma Na⁺ & Volume
Renal Prostaglandins

- VSMC, endothelial cells, mesangial cells, tubule, interstitial cells synthesize PG
- vasodilate afferent & efferent arteriole
  \[\uparrow \text{RBF and } \uparrow \text{GFR}\]

\[\uparrow \text{Severe volume depletion (dehydration), salt depletion, blood loss (hemorrhage), low BP, surgery, anesthesia, stress, SNS, RAS}\]

Prevents severe and potential harmful vasoconstriction and renal ischemia

\[\text{Buffer Excessive Vasoconstriction}\]

Summary Major Renal Hormones

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<thead>
<tr>
<th>Vasconstrictors</th>
<th>(\downarrow \text{RBF} \downarrow \text{GFR})</th>
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<tbody>
<tr>
<td>Sympathetic nerves</td>
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<tr>
<td>Angiotensin II</td>
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<tr>
<td>Endothelin</td>
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<td>AVP</td>
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<td>Norepinephrine</td>
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<tr>
<th>Vasodilators</th>
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<tr>
<td>Prostaglandins</td>
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<td>Bradykinin</td>
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<td>ANP</td>
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Summary

1. Glomerular filtrate formation - dependent on filtration barrier & Starling forces
2. \(O_2\) consumption is NOT regulator of RBF
3. RBF autoregulation – AFFERENT ARTERIOLE RESISTANCE
   - TGF & Myogenic
4. Hormonal regulation of RBF and GFR to maintain BV & BP

Time for Questions