Renal Physiology - Lectures

✓ Physiology of Body Fluids – PROBLEM SET, RESEARCH ARTICLE
✓ Structure & Function of the Kidneys
✓ Renal Clearance & Glomerular Filtration – PROBLEM SET
4. Regulation of Renal Blood Flow - REVIEW ARTICLE
5. Transport of Sodium & Chloride
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 4
Regulation of Renal Blood Flow
Chapter 3 Koeppen & Stanton Renal Physiology

1. Renal Parameters
2. Oxygen Consumption
3. Resistance of Arterioles
4. Regulation of RBF
   • Intrinsic & Extrinsic
   • Hormonal
   AngII, ANP, SNS, AVP
Renal Parameters

• Cardiac Output (CO) = 5,000 ml/min

• Renal Blood Flow (RBF) =
  - 1,000 ml/min
  - 350 ml/min/100 g
  - 4 ml/min/g (1% BW)

• Brain = 0.5 ml/min/g

• Skeletal muscle (rest) = 0.08 ml/min/g

• Renal Fraction (RF) = RBF/CO =
  - 1,000 ml/min ÷ 5,000 ml/min =
  - 0.20 = 20%

• Hematocrit (Hct) = 0.40
  - 40% BV = RBC
  - 60% BV = Plasma
Renal Parameters

• RBF =
  - Renal Plasma Flow (RPF) ÷ (1 – Hct)
  - 600 ml/min ÷ (1 – 0.50) = 1,200 ml/min

• Filtration Fraction (FF) =
  GFR ÷ RPF =
  125 ml/min ÷ 600 ml/min = 0.20

Renal Parameters

• Urine flow (\(\dot{V}\)) = 1 ml/min

• Fluid reabsorbed =
  - 125 ml/min – 1 ml/min = 124 ml/min > 99%

* Fluid Filtration >>> Urine Output *
**Normal Adult Values GFR**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal range</td>
<td>100 – 140 ml/min</td>
</tr>
<tr>
<td>Moderately impaired</td>
<td>60 – 90 ml/min</td>
</tr>
<tr>
<td>Chronic renal disease</td>
<td>&lt; 60 ml/min</td>
</tr>
<tr>
<td>Dialysis</td>
<td>10 – 20 ml/min</td>
</tr>
</tbody>
</table>

**Renal Physiology Lecture 4**

- Renal Parameters
  - 2. Oxygen Consumption
  - 3. Resistance of Arterioles
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    - Intrinsic & Extrinsic
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O₂ Consumption by KIDNEYS

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

O₂ Consumption & Na⁺ Transport

- O₂ consumption LARGE & parallels Na⁺ reabsorption
- RBF LARGE
- Arterial - Venous PO₂ difference is SMALL
Renal Physiology Lecture 4

✓ Renal Parameters
✓ Oxygen Consumption

3. Resistance of Arterioles

4. Regulation of RBF
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Hydrostatic Pressure Profile

Vascular pressure (mm Hg) vs. Blood vessel

- Relatively high hydrostatic pressure is maintained along the glomerular capillary.
- Note the sharp decreases in pressure across the afferent and efferent arterioles.
What would happen to GFR if AA contracted?
Changing Resistance of Renal ARTERIOLES

GFR mainly driven by $P_{GC}$

$\Delta R_A$ – RBF & GFR $\Delta$ in **parallel**

$\Delta R_E$ – RBF & GFR $\Delta$ in **opposite** directions

Renal Physiology Lecture 4

- Renal Parameters
- Oxygen Consumption
- Resistance of Arterioles

4. Regulation of RBF
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Intrinsic: Renal Blood Flow Autoregulation

- **Autoregulation** – vascular bed maintains BF with $\Delta$ BP
- No metabolic component
- RAP $\approx$ 90 – 180 mmHg
- RBF & GFR constant

* $\Delta$ AFFERENT ARTERIOLE RESISTANCE *

![Diagram](image)

**Autoregulation of RBF ~ Fig 3-7**

- **Relative vascular resistance**
- **Renal blood flow (ml/min)**
- **GFR (ml/min)**

Graph showing the relationship between renal arterial pressure (mm Hg) and renal blood flow (ml/min) with RBF constant in the range of 90 to 180 mmHg.
Renal Blood Flow Autoregulation

* △ AFFERENT ARTERIOLE RESISTANCE *

• w/o renal nerves, circulating hormones, occurs isolated kidney perfused in vitro

* Intrinsic phenomenon *

Myogenic Mechanism
Pressure-Sensitive

• Intrinsic property of arterial vascular smooth muscle cell
  ▲ vascular wall stretch = contract
  OR
  ▼ vascular wall stretch = relax

* Renal Blood Flow Autoregulation *
SHOW AND TELL: Tubuloglomerular Feedback Mechanism

• New Zealand rabbit
• Isolated afferent arteriole, glomerulus, TAL
• Effects of increased tubular salt/flow in the MD segment causing the propagating TGF vasoconstriction
• Peti-Peterdi 2006

Extrinsic: Sympathetic Nervous System
(NO Parasympathetic Innervation)

➢ Renal arteries, AA & EA
➢ Juxtaglomerular cell
➢ Tubules – PT, LOH, DT, CD
➢ Norepinephrine release

↑ firing rate = vasoconstriction
↓ RBF cease GFR

Affect AA & EA Resistance = Alter RBF & GFR
Autoregulation RBF & GFR can be overridden by SNS & Hormones
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Renin-Angiotensin System - RAS

- RAS regulates Na\(^+\)
  balance, plasma
  volume
  control of arterial
  blood pressure
- Renin - rate limiting
  step AngII formation

* Major concern = \(\uparrow\) ECFV \(\uparrow\) MAP *
Renin-Angiotensin System

Angiotensinogen (α-2 globulin; 452 aa) → Renin – Proteolytic Enzyme

Angiotensin I (10 aa) → Angiotensin Converting Enzyme

Angiotensin II (8 aa) → Aldosterone

- Vasoconstriction
- Sodium reabsorption

Constrict afferent & efferent arterioles
- RBF
- Contract mesangial cells - Kf
- GFR
- TGF - sensitivity
- Medullary BF - reduced

* Reduce RBF & GFR *
SHOW AND TELL
Mouse In Vitro Blood Perfused Juxtamedullary Nephron

Efferent Arteriole
Response to AngII

TUBULAR Actions of Angiotensin II

- AngII acts directly on tubules
  \[ \uparrow \text{Na}^+ \text{ reabsorption} \]
- Aldosterone release from adrenal
  \[ \uparrow \text{Na}^+ \text{ reabsorption} \]

* Reduce Salt & H₂O Excretion *
Which patients would benefit from drugs that block RAS?

Patients with:
- Hypertension
- Heart failure
- Kidney failure in diabetes
- Coronary artery disease
- Chronic kidney disease
- Migraines
- Heart attacks
**AVP** – Arginine Vasopressin = **ADH** – Antidiuretic Hormone

- Collecting duct $\uparrow$ H$_2$O absorption
- Constriction AA & EA
- $\downarrow$ BF renal medulla

*Reduce H$_2$O Excretion $\uparrow$ BP*

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**Nitric Oxide**

- Endothelial generated
  - shear force, acetylcholine, histamine, bradykinin

- **Relax** vascular smooth muscle
  - AA & EA

- **Buffer** excessive vasoconstriction of AngII & NE
Atrial Natriuretic Peptide (ANP)

- Dilates AA
- ↑ GFR
- ↑ Na⁺ excretion
- Inhibits Na⁺ reabsorption tubules

* ↓ Plasma Sodium & Volume *

Renal Prostaglandins

- vasodilation AA & EA
- ↑ RBF ↑ GFR

↑ Severe volume depletion - dehydration, salt depletion, blood loss = hemorrhage, low BP, surgery, anesthesia, stress, activation of SNS, RAS

* Buffer Excessive Vasoconstriction *
Renal Prostaglandins
• Inhibited by non-steroidal anti-inflammatory agents (NSAID)
  Ex. Motrin, Ibuprofen, Aspirin

Surgery + NSAID =
  unopposed vasoconstriction
  ↓ RBF  ↓ GFR = 0  ↓ Na⁺ excretion, ischemia, cell death
  = Acute Renal Failure
  = BAD NEWS

Summary Major Renal Hormones ~ Table 3-1

<table>
<thead>
<tr>
<th>Vasoconstrictors</th>
<th>↓ RBF  ↓ GFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sympathetic nerves</td>
<td></td>
</tr>
<tr>
<td>Angiotensin II</td>
<td></td>
</tr>
<tr>
<td>Endothelin</td>
<td></td>
</tr>
<tr>
<td>AVP</td>
<td></td>
</tr>
<tr>
<td>Norepinephrine</td>
<td></td>
</tr>
<tr>
<td>Vasodilators</td>
<td>↑ RBF  ↑ GFR</td>
</tr>
<tr>
<td>Prostaglandins</td>
<td></td>
</tr>
<tr>
<td>Nitric Oxide</td>
<td></td>
</tr>
<tr>
<td>Bradykinin</td>
<td></td>
</tr>
<tr>
<td>ANP</td>
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Summary

1. O₂ consumption by kidney is NOT the regulator of RBF

2. Renal autoregulation – alterations in AFFERENT ARTERIOLE RESISTANCE
   • TGF & Myogenic

3. Hormonal regulations of RBF and GFR to maintain BV & BP

The End