Renal Physiology - Lectures

1. ✓ Physiology of Body Fluids – PROBLEM SET, RESEARCH ARTICLE
2. ✓ Structure & Function of the Kidneys
3. ✓ Renal Clearance & Glomerular Filtration – PROBLEM SET
4. ✓ Regulation of Renal Blood Flow – REVIEW ARTICLE
5. ✓ 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– **REVIEW ARTICLE**
11. Clinical Correlation – Dr. Credo – 9 am - **HANDOUT**
12. **PROBLEM SET REVIEW – May 9, 2011 at 9 am**
13. **EXAM REVIEW – May 9, 2011 at 10 am**
14. **EXAM IV – May 12, 2011**

Renal Physiology Lecture 10
Integration of Salt & Water Balance
Chapter 6 & 10 Koeppen & Stanton Physiology
Review Article: Renal Renin Angiotensin System

1. Regulation ECFV
2. RAS & Control of Renin Secretion
3. SNS, ANP, AVP
4. Response to Δ ECFV
5. Kidney Diseases

Control System

Rates subject to
physiological control

KIDNEY - Δ rate of filtration, reabsorption, and/or secretion to maintain *homeostasis*

Integration of Salt and Water Balance

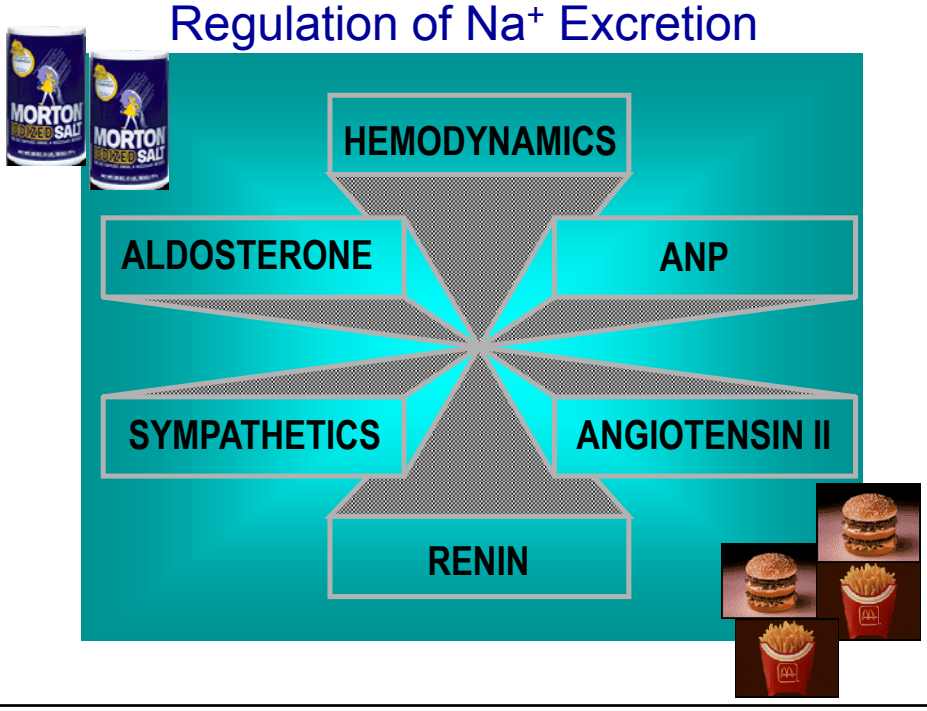
Important to regulate ECFV to maintain BP – tissue perfusion

- Regulation ECF Volume = monitor '*effective circulating volume*' = functional blood volume evidenced by fullness or pressure w/i blood vessels, NOT ECFV
- Adjust total-body content **NaCl**
- *Modulate urinary Na^+ excretion*

Integration of Salt and Water Balance

- Regulation ECF Osmolality – hypotonic or hypertonic = Δ cell volume – alter cell function – brain
- *modulate urinary H_2O excretion*
- manifest Δ $\mathbf{P_{Osm}}$

Regulation of Na^+ Excretion



ECF *Volume* Receptors Table 6-1

Vascular sensors	* Low-pressure * Cardiac atria Pulmonary vasculature
Sense effective circulating volume	High-pressure - arterial Carotid sinus Aortic arch JGA – afferent arteriole
Sensors in CNS	CSF, arteriole [Na^+]
Sensors in Liver	Pressure, [Na^+]

Regulation of **ECFV**

What is sensed?	Effective Circulating Volume
Sensors	Carotid sinus, aortic arch, renal afferent arteriole, atria
Efferent pathway	RAS, SNS, AVP, ANP
Effector	Short term: Heart, blood vessels Long term: **Kidney**
What is Affected?	Short term: Blood pressure Long term: **Na^+ excretion**

Control Renal Sodium and Water Excretion
Table 6-2

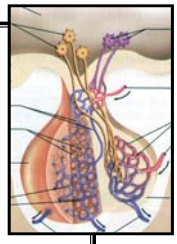
Δ Effective circulating volume affects 4 systems:

1. **RAS**
2. **SNS**
3. **AVP**
4. **ANP**

Regulation of **Osmolality**

What is sensed?	Plasma Osmolality	
Sensors	Hypothalamic Osmoreceptors	
Efferent pathways	AVP	Thirst
Effector	Kidney	Brain-drinking
What is Affected?	**H_2O excretion**	**H_2O intake**

Stimuli for ADH Release



** Osmolality of Plasma **

- Osmoreceptors
  - ⇑ P_{Osm} 1%
    - steep slope P[ADH] for 280-300 mOsm/kg H_2O
  - ⇑ ADH – *most sensitive*
- Baroreceptors
  - ⇓ pressure > 10% fall BV or BP
  - ⇑ ADH – *most powerful*

Renal Physiology Lecture 10

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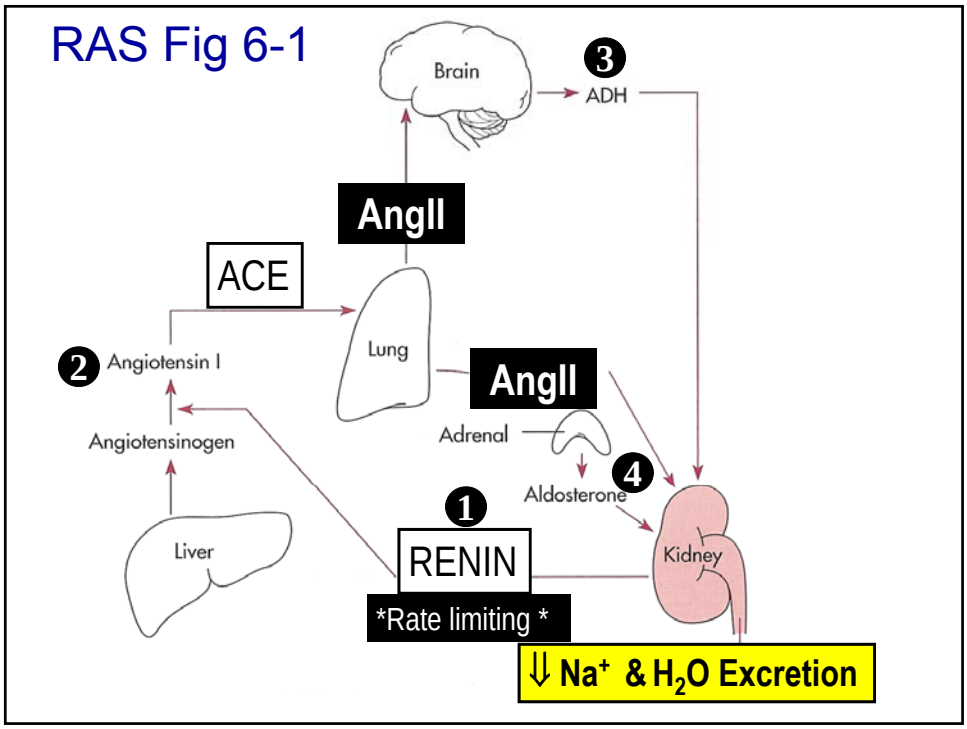
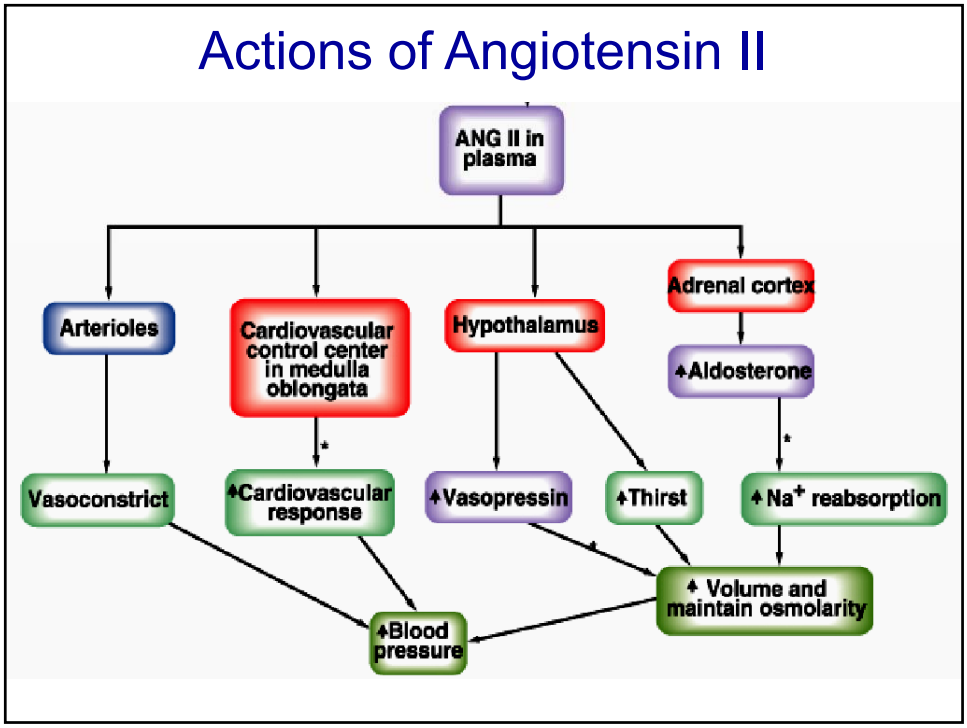

RAS Fig 6-1
Brain
3
ADH
AngII
ACE
Lung
2
Angiotensin I
AngII
Angiotensinogen
Adrenal
4
Aldosterone
1
Liver
RENIN
Kidney
*Rate limiting *
⇓ Na+ & H2O Excretion

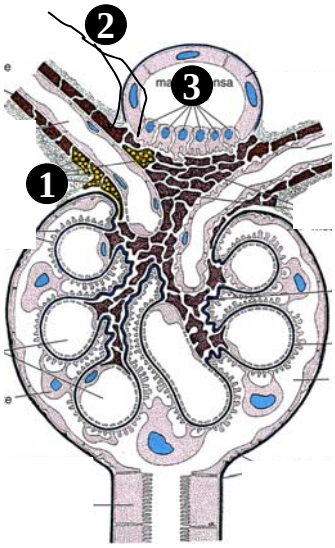

Actions of Angiotensin II
ANG II in plasma
Arterioles
Cardiovascular control center in medulla oblongata
Hypothalamus
Adrenal cortex
Aldosterone
Vasoconstrict
Cardiovascular response
Vasopressin
Thirst
Na+ reabsorption
Volume and maintain osmolarity
Blood pressure

Control of RENIN Release pg 96

Production of renin - ***rate limiting*** step AngII formation

≡ importance of regulation

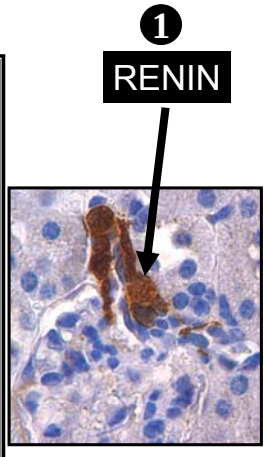
1. Perfusion pressure - Intrarenal baroreceptors - afferent arterioles
2. Sympathetic nerves – input to JG cells
3. Delivery NaCl to Macula densa cells



JGA

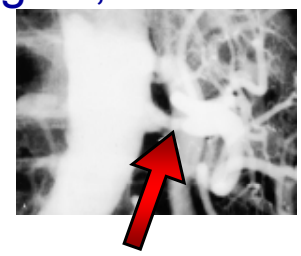
Control of RENIN Release

1. "Renal" baroreceptors – JG cells afferent arteriole
   - ⇑ RAP ⇑ stretch ⇓ renin release
   - ⇓ RAP ⇓ stretch ⇓ Ca^{2+} ⇑ renin release

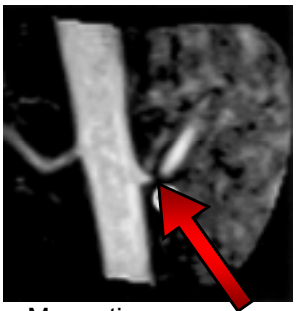


Renal Artery Stenosis – pg 41, 94

1. "Renal" baroreceptors – JG cells afferent arteriole detect ⇓ pressure
   - Constriction aorta above renal arteries = stenosis (narrowing of renal artery) due to *atherosclerosis (90%)*
   - Stenosis of preglomerular arteries or arterioles by *fibrosis*
   - = Renal hypertension ⇑ renin
   - Treat patient w/ ACE inhibitor or ARB with or w/o diuretic and a statin



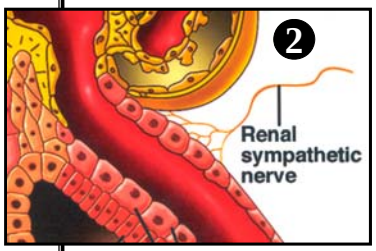
Renal angiogram



Magnetic resonance angiography

Control of RENIN Release

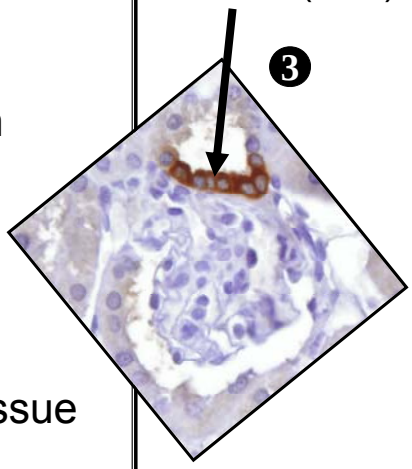
2. Influence of sympathetic nerves on JG cells
   - ⇑ activity of nerves
     ⇑ renin secretion
   - ⇓ activity of nerves
     ⇓ renin secretion



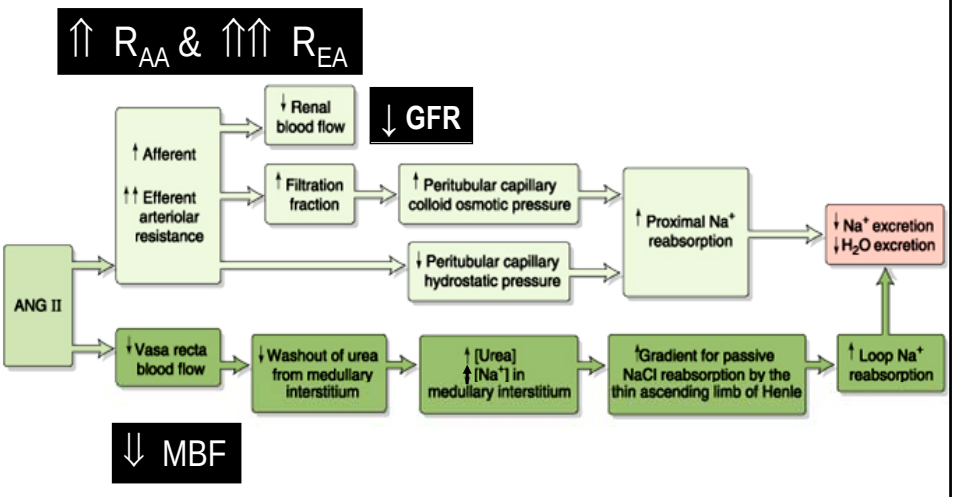
Control of RENIN Release

3. Influence of distal delivery of NaCl

- ⇑ **NaCl**
  - ⇓ renin secretion
- ⇓ **NaCl**
  - ⇑ renin secretion
  - ⇑ AngII
  - ⇑ BP - maintain tissue perfusion



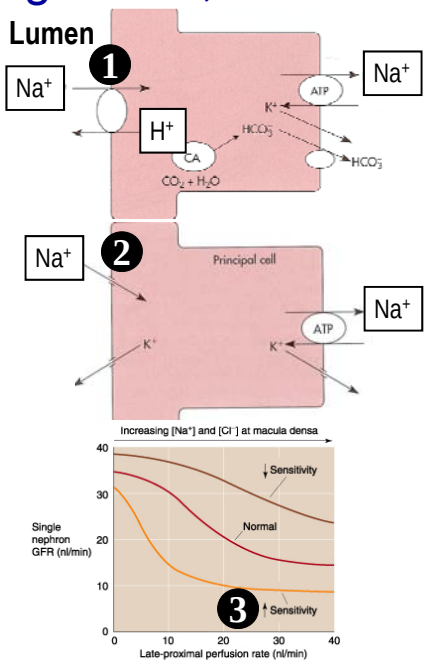
Hemodynamic Actions AngII



Tubular Actions AngII – 4-2, 10

1. Enhance Na^+-H^+ exchanger PT & TAL = ⇑ Na^+ reabsorption
2. Enhance NCC in DT & ENaC in CD = ⇑ Na^+ reabsorption
3. ⇑ TGF Sensitivity

Net effect = ⇓ Na^+ excretion



Renal Physiology Lecture 10

1. Regulation ECFV
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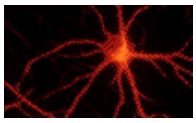
4. Response to Δ ECFV
5. Kidney Diseases

2. SNS Activity

1. ⇑ AA & EA renal vascular resistance = ⇓ GFR
2. ⇑ Renin release = ⇑ AngII
3. ⇑ Tubular Na^+ reabsorption – PT *

⇑ Activity during low Na^+ intake, hemorrhage

Net effect = ⇓ Na^+ excretion



3. Actions AVP = ADH

1. ⇑ H_2O retention – distal nephron – AQP2
2. ⇑ Na/K/Cl cotransporter TAL
3. ⇑ ENaC open probability – CD

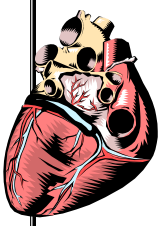
Generation of *hypertonic* medullary interstitium

⇑ low Na^+ intake, hemorrhage

Net effect = ⇓ Na^+ excretion

4. Actions ANP

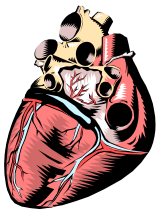
1. ⇑ ANP (atria) & BNP (ventricle)
2. Dilation of AA = Renal vasodilation - ⇑ CBF, ⇑ GFR, ⇑ MBF – medullary washout interstitium
3. ⇓ Renin & Aldosterone
4. ⇑ Na^+ load to PT & TAL = ⇑ Na^+ excretion
5. ⇓ NaCl reabsorption by ENaC in CD
6. ⇓ ADH secretion = ⇑ H_2O excretion
7. **Net effect = ⇑ Na^+ & H_2O excretion**



4. Actions ANP

BUT REMEMBER:

1. ⇓ effective circulating volume
2. ⇓ **ANP/BNP** release
3. Net effect = ⇓ Na^+ excretion



Renal Physiology Lecture 10

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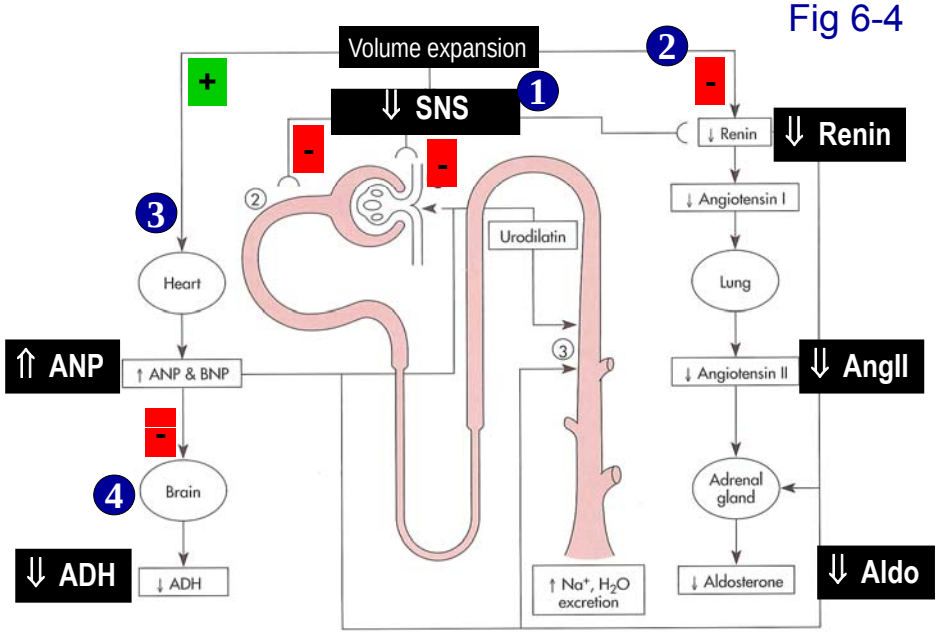
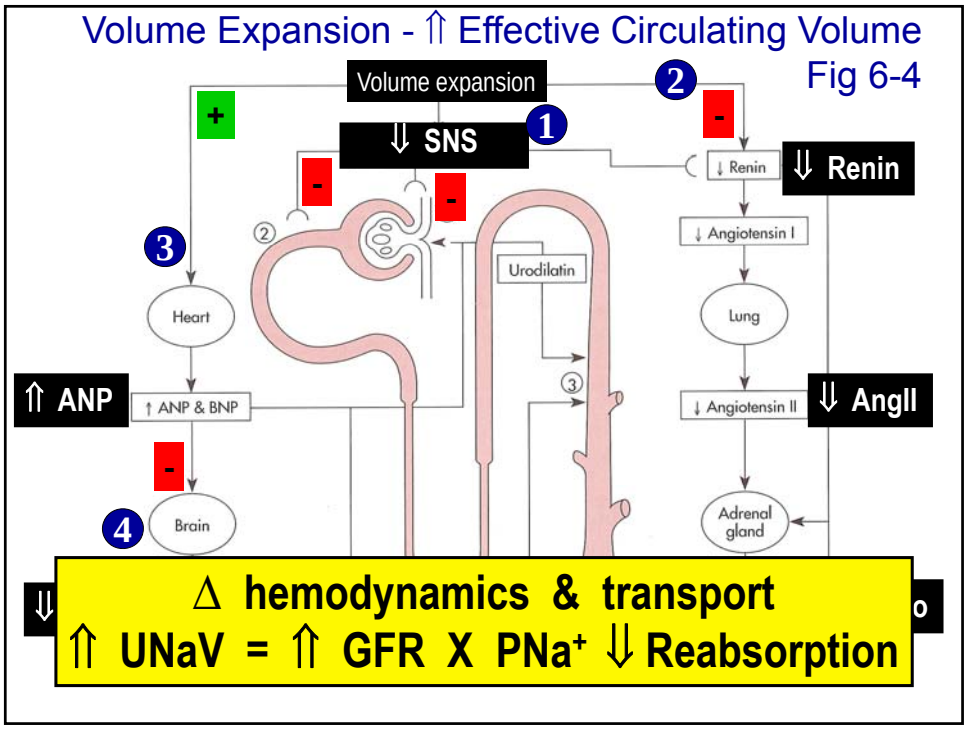
Volume Expansion - ⇑ Effective Circulating Volume

Fig 6-4





Volume Expansion

Δ Effective circulating volume affects 4 systems:

1. **⇓ RAS = ⇓ Renin ⇓ AngII ⇓ Aldosterone**
2. **⇓ SNS**
3. **⇓ AVP**
4. **⇑ ANP & BNP**

Volume Expansion

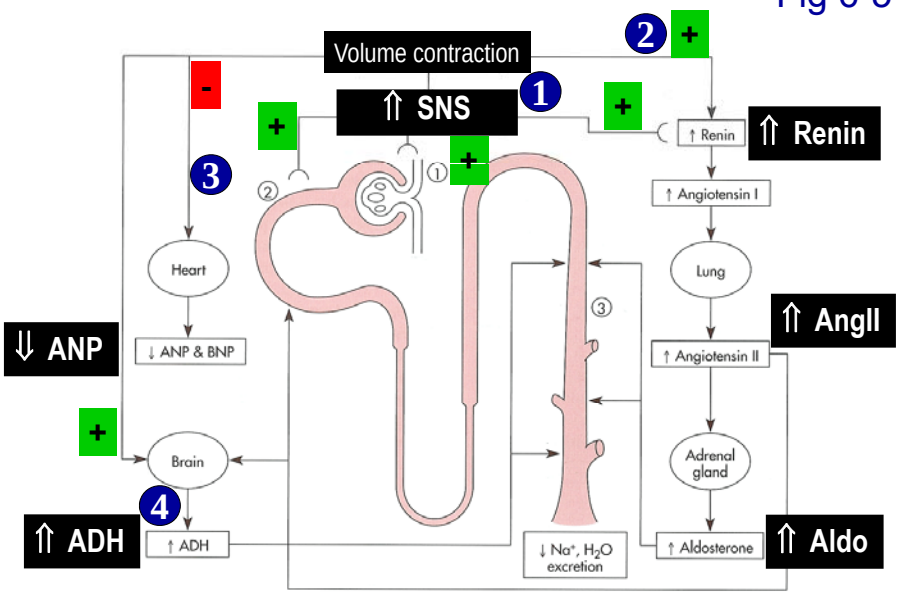
1. ⇑ GFR = ⇑ filtered load Na^+
2. ⇓ PT & loop of Henle Na^+ reabsorption
3. ⇑ Na^+ delivery to distal nephron = ⇓ Na^+ reabsorption

Net effect:

= ⇑ Na^+ & H_2O excretion

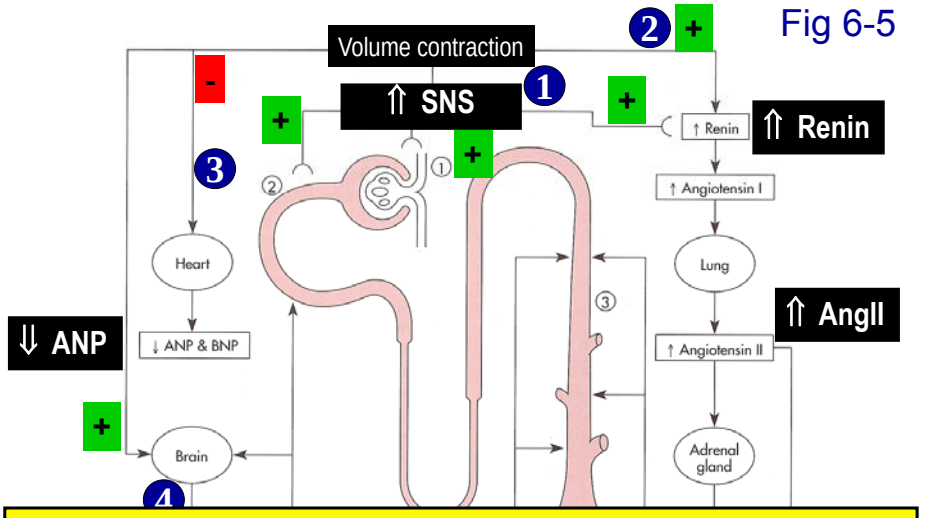
Volume Contraction - ⇓ Effective Circulating Volume

Fig 6-5



Volume Contraction - ⇓ Effective Circulating Volume

Fig 6-5



Δ hemodynamics & transport
⇓ UNaV = ⇓ GFR X PNa⁺ ⇑ Reabsorption

Volume Contraction

Δ Effective circulating volume affects 4 systems:

1. **⇑ RAS = ⇑ Renin ⇑AngII Aldosterone⇑**
2. **⇑ SNS**
3. **⇑ AVP**
4. **⇓ ANP & BNP**

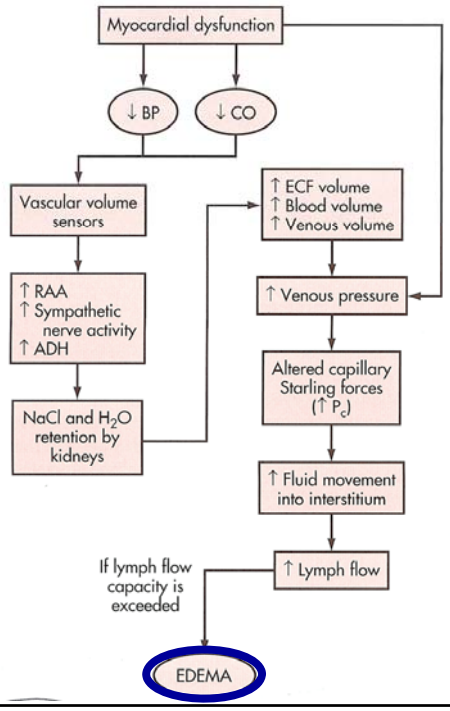
Volume Contraction

1. ⇓ **GFR** = ⇓ filtered load Na^+
2. ⇑ PT & loop of Henle Na^+ reabsorption
3. ⇓ Na^+ delivery to distal nephron = ⇑ Na^+ reabsorption

Net effect

= ⇓ Na^+ & H_2O excretion

CHF Fig 6-6



$U_{NaCl}V$ does not reflect ECFV; Reflects vascular volume

Treatment
⇓ Na^+ Intake
+
Diuretics

What Does a Nephrologist Expect a Medical Student to Know?

1. What is GFR?
   - How is it determined?
   - How is it estimated?
2. Body Fluid Compartments
3. Regulation of Sodium and Water Balance
4. Potassium Homeostasis
5. Acid/Base Physiology

Renal Physiology Lecture 10

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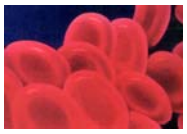
** Renal Failure Patient **

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

Renal Disease

- **Anemia**
  - ⇓ Secretion of erythropoietin
  - Treatment:
  - recombinant human erythropoietin (epoetin alpha; Epogen – Amgen) iv/sc injection
  - Oral or iv iron supplements



Renal Disease

- Uremia
  - –retention of excessive by-products of protein metabolism in the blood
  - –toxic condition

- Kidney stones
  - –block ureter
  - –tubular pressure increases

ESRD
End Stage Renal Disease

ESRD - < 10% total glomerular filtration renal function

- Normal Patient

  GFR = 125 ml/min

- ESRD

  GFR = 10 - 20 ml/min

Segment	Apical Na^+ Transporter	Drugs (Chapter 10)
Proximal tubule **PT**	Na^+ cotransporter (glucose, amino acids, phosphate, sulfate, etc) Na^+/H^+ exchanger (**NHE3**)	carbonic anhydrase inhibitor (Acetazolamide)
Thick ascending limb **TAL**	$Na^+/K^+/2Cl^-$ cotransporter (**NKCC2**)	Loop Diuretics (Furosemide, Lasix, Bumetanide)
Distal tubule **DT**	Na^+/Cl^- cotransporter (**NCC**)	Thiazides (Hydrochlorothiazide)
Collecting duct **CD**	Epithelial Na^+ channel (**ENaC**)	(Amiloride, Triamterene)

Apical Transporter	Loss of Function	Gain of Function
NKCC2 **TAL**	**Bartter's Syndrome** • Salt wasting • Hypokalemia • Alkalosis	
NCC **Distal tubule**	**Gitelman's Syndrome** • Salt wasting • Hypokalemia • Alkalosis	
ENaC **Collecting duct**	**Pseudohypoaldosteronism** (type 1) • Salt wasting • Hyperkalemia • Acidosis • Hypotension	**Liddle's Syndrome** • Salt retention • Early onset severe hypertension

What Did We Learn Today

1. Kidneys are *very* important for maintaining ECFV
2. Thank you kidneys for allowing us to eat at McDonalds.
3. KIDNEY IS AN AMAZING ORGAN!

Renal Physiology Problem Sets Review

on

Monday, May 9th @ 9 am

EXAM IV REVIEW

on

Monday, May 9th @ 10 am

Good Luck on the Exam!
Clinical Correlation Tomorrow