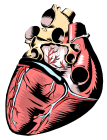
Renal Physiology - Lectures

✓ 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**

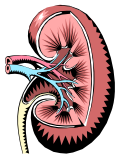
Renal Physiology Lecture 4
Regulation of Renal Blood Flow
Chapter 3 Koeppen & Stanton Renal Physiology

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

Renal Parameters



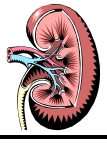
- Cardiac Output (CO) = 5,000 ml/min
- Renal Blood Flow (RBF) =
  - 1,000 ml/min
  - 350 ml/min/100 g
  - **4** ml/min/g (1% BW)

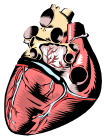


- Brain = **0.5** ml/min/g
- Skeletal muscle (rest) = **0.08** ml/min/g

Renal Parameters

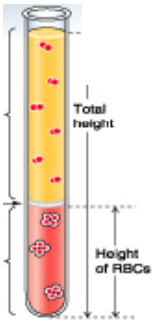
- Renal Fraction (**RF**) = RBF/CO =





  - 1,000 ml/min ÷ 5,000 ml/min =

    0.20 = 20%
- Hematocrit (**Hct**) = 0.40
  - 40% BV = RBC
  - 60% BV = Plasma

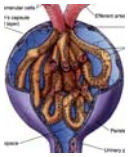


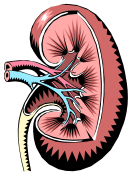
Renal Parameters

- **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 ($\dot{\mathbf{V}}$) = 1 ml/min

- Fluid reabsorbed =
  - 125 ml/min – 1 ml/min =

    124 ml/min > 99%

*** Fluid Filtration >>> Urine Output ***

Normal Adult Values GFR

Normal range 100 – 140 ml/min

Moderately impaired 60 – 90 ml/min

Chronic renal disease < 60 ml/min

Dialysis 10 – 20 ml/min

Renal Physiology Lecture 4

1. ✓ Renal Parameters
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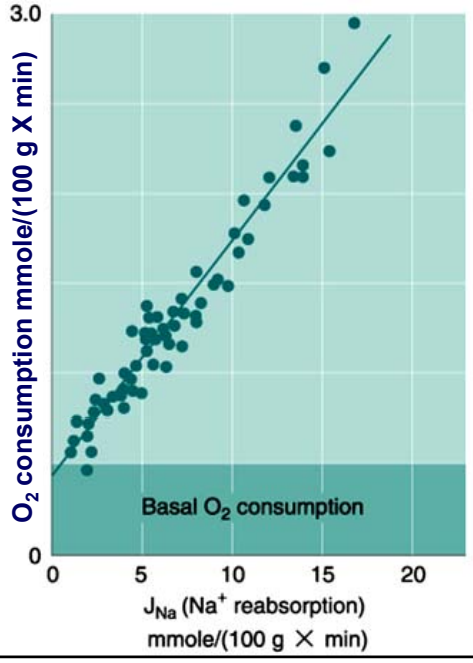
   - Intrinsic &Extrinsic
   - Hormonal

     AngII, ANP, SNS, AVP

O_2 Consumption by KIDNEYS

- O_2 consumption/**g tissue** > any organ except heart
- Arterial - Venous O_2 difference lowest
- O_2 consumption relative to RBF **not** very high
- O_2 is not critical factor for regulating RBF

O_2 Consumption & Na^+ Transport



- O_2 consumption **LARGE** & parallels Na^+ reabsorption
- RBF **LARGE**
- Arterial - Venous PO_2 difference is **SMALL**

Renal Physiology Lecture 4

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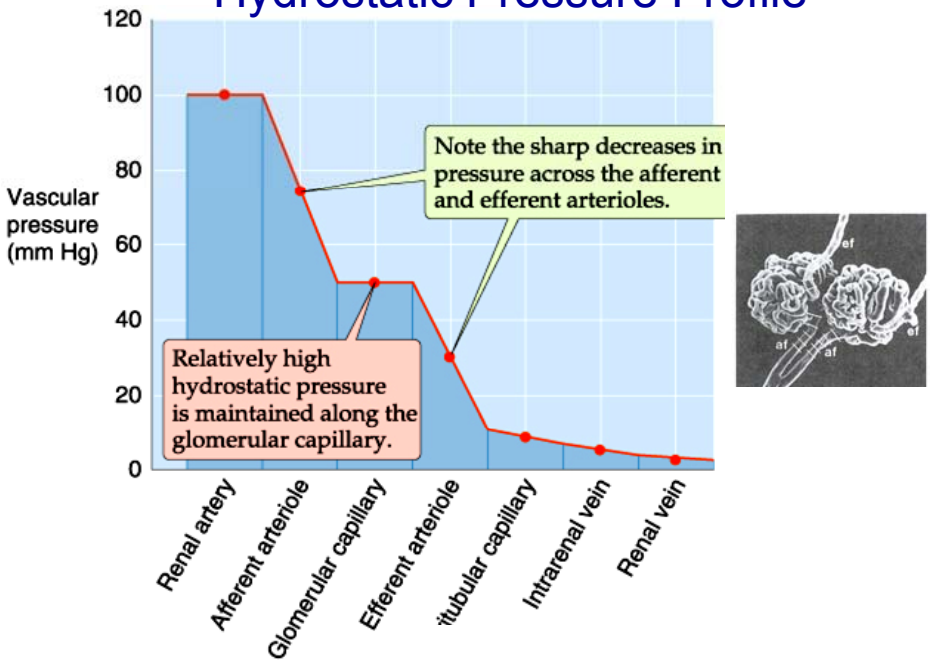
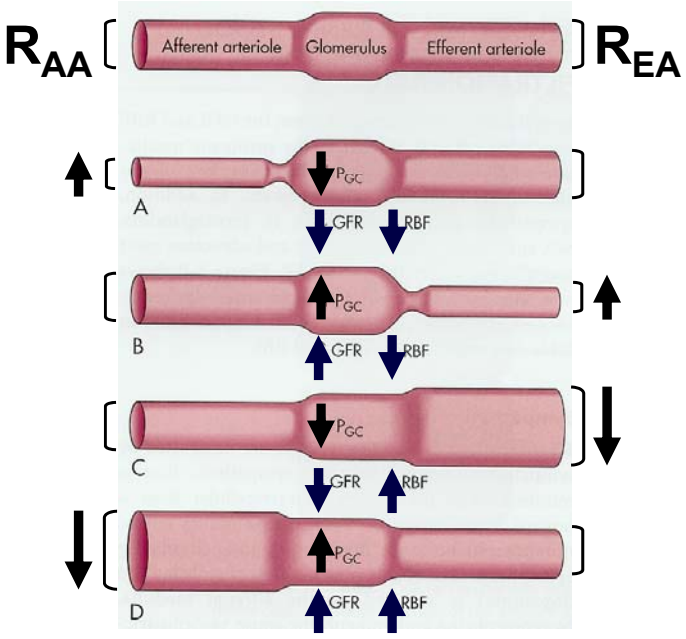
Hydrostatic Pressure Profile



What would happen to GFR if AA contracted?

Changing Resistance Fig 3-9



Changing Resistance of Renal ARTERIOLES

GFR mainly driven by P_{GC}

ΔR_A – RBF & GFR Δ in ***parallel***

ΔR_E – RBF & GFR Δ in ***opposite*** directions

Renal Physiology Lecture 4

- ✓ Renal Parameters
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- 4. Regulation of RBF
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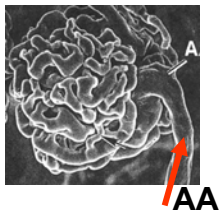
    AngII, ANP, SNS, AVP

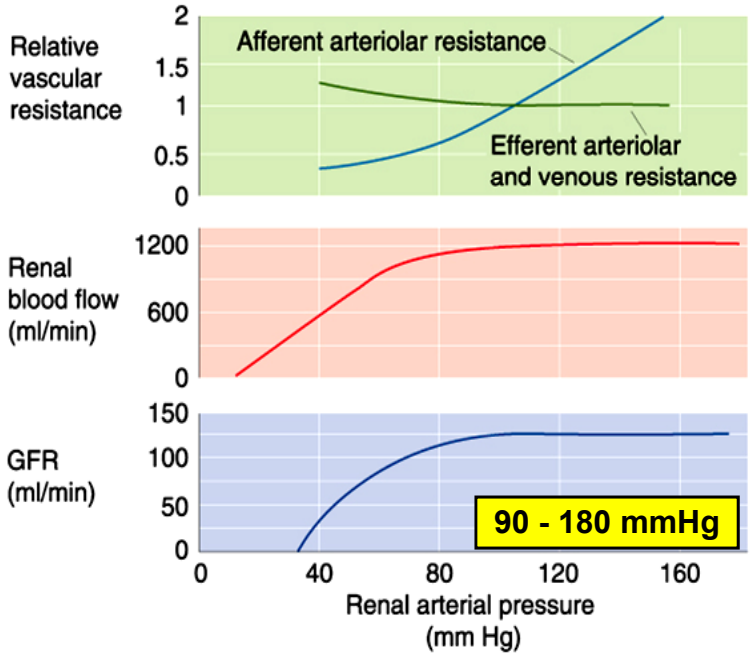
Intrinsic: Renal Blood Flow Autoregulation

- Autoregulation – vascular bed maintains BF with Δ BP
- No metabolic component
- RAP ~ 90 – 180 mmHg
- RBF & GFR constant



*** Δ AFFERENT ARTERIOLE RESISTANCE ***

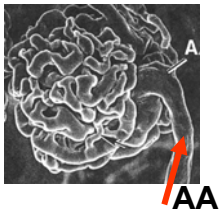
Autoregulation of RBF ~ Fig 3-7



Renal Blood Flow Autoregulation

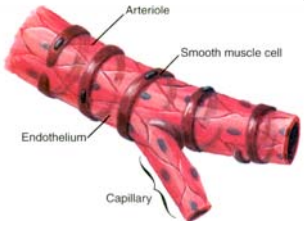
* **<u>Δ AFFERENT ARTERIOLE RESISTANCE</u>** *

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



* *Intrinsic phenomenon* *

Myogenic Mechanism
Pressure-Sensitive



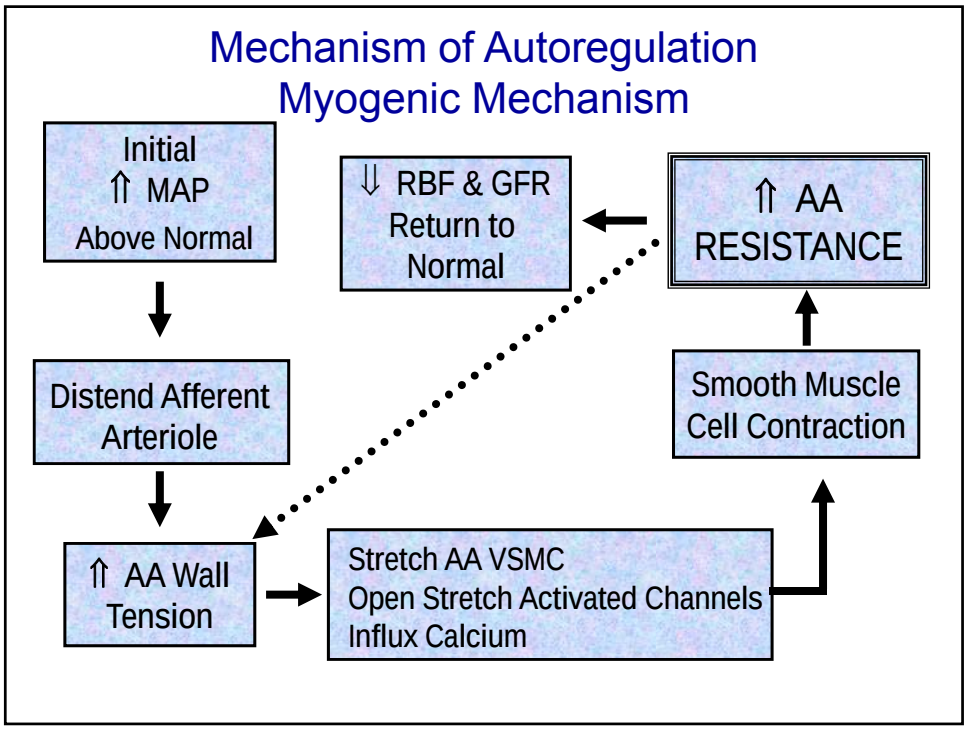
- *Intrinsic property* of arterial vascular smooth muscle cell

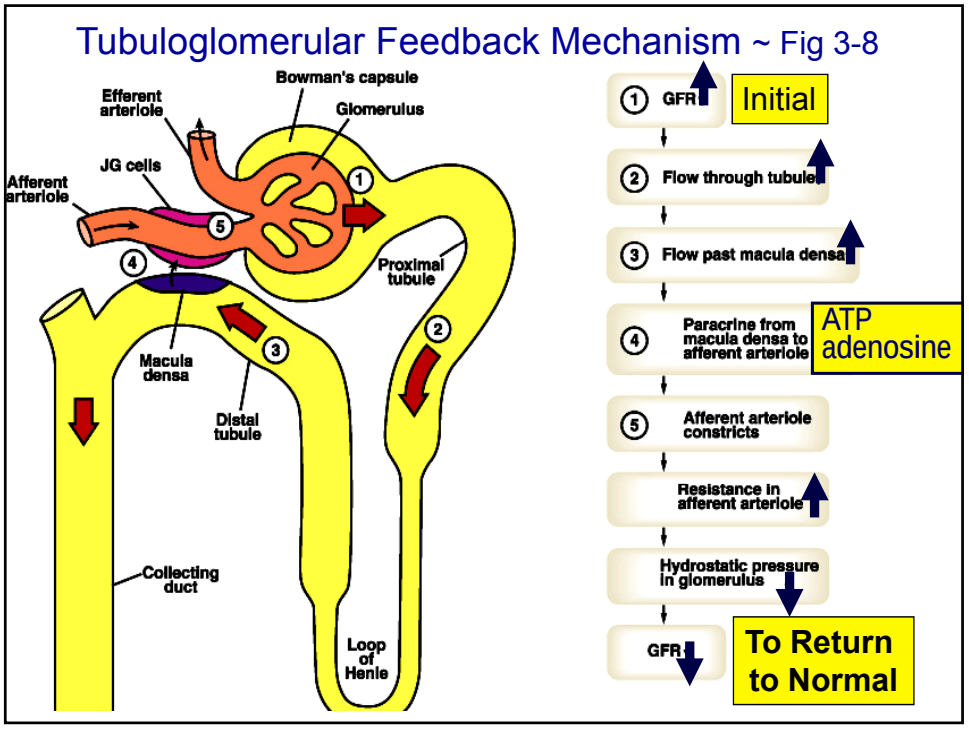
⇑ vascular wall stretch = <u>contract</u>

OR

⇓ vascular wall stretch = <u>relax</u>

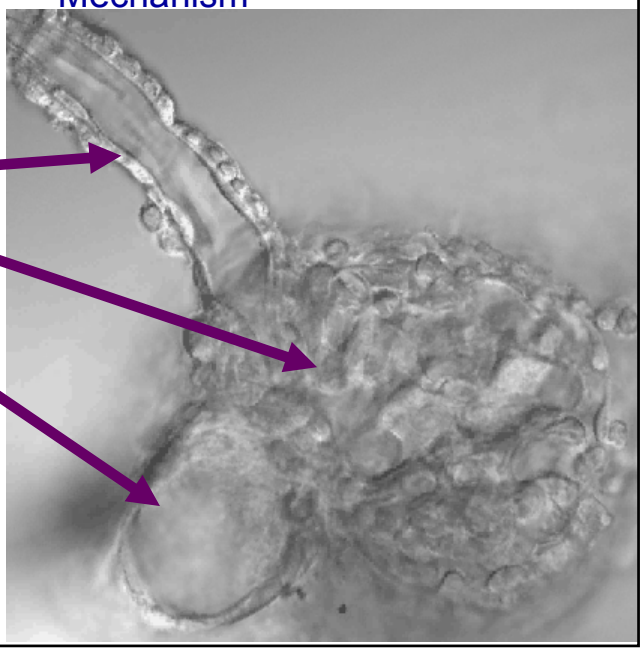
* Renal Blood Flow Autoregulation *


Mechanism of Autoregulation
Myogenic Mechanism
Initial
⇑ MAP
Above Normal
⇓ RBF & GFR
Return to
Normal
⇑ AA
RESISTANCE
Distend Afferent
Arteriole
Smooth Muscle
Cell Contraction
⇑ AA Wall
Tension
Stretch AA VSMC
Open Stretch Activated Channels
Influx Calcium


Tubuloglomerular Feedback Mechanism ~ Fig 3-8
Bowman's capsule
Efferent arteriole
Glomerulus
JG cells
Afferent arteriole
Proximal tubule
Macula densa
Distal tubule
Collecting duct
Loop of Henle
1 GFR
Initial
2 Flow through tubule
3 Flow past macula densa
4 Paracrine from macula densa to afferent arteriole
ATP adenosine
5 Afferent arteriole constricts
Resistance in afferent arteriole
Hydrostatic pressure in glomerulus
GFR
To Return to Normal

SHOW AND TELL: Tubuloglomerular Feedback Mechanism

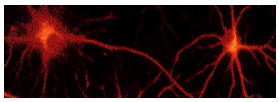
- New Zealand rabbit
- Isolated afferent arteriole, glomerulus, TAL
- Effects of increased tubular salt/flow in the MD segment causing the propagating TGF vasoconstriction
- Peti-Peterdi 2006



Extrinsic: Sympathetic Nervous System

(**NO** Parasympathetic Innervation)

- Renal arteries, AA & EA
- Juxtaglomerular cell



- Tubules – PT, LOH, DT, CD
- Norepinephrine release

⇑ firing rate = <u>vasoconstriction</u>

⇓ RBF cease GFR

Affect AA & EA Resistance = Alter RBF & GFR
Autoregulation RBF & GFR can be overridden by SNS & Hormones

Renal Physiology Lecture 4

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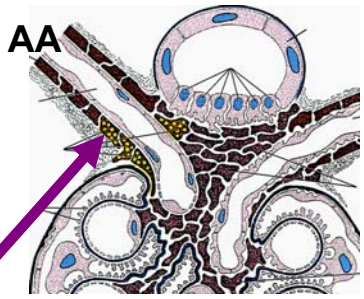
Renin-Angiotensin System - RAS

- RAS regulates Na^+ balance, plasma volume

  control of <u>arterial blood pressure</u>

- <u>Renin</u> - rate limiting step AngII formation



*** Major concern = ⇑ ECFV ⇑ MAP ***

Renin-Angiotensin System

Angiotensinogen (α-2 globulin; 452 aa)

↓ ← **Renin – Proteolytic Enzyme**

Angiotensin I (10 aa)

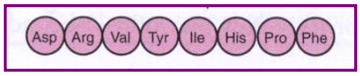
↓ ← **Angiotensin Converting Enzyme**

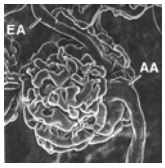
Angiotensin II (8 aa)

↓

Receptor AT_1 – Aldosterone
Vasoconstriction
↑ Sodium reabsorption

HEMODYNAMIC Actions of Angiotensin II

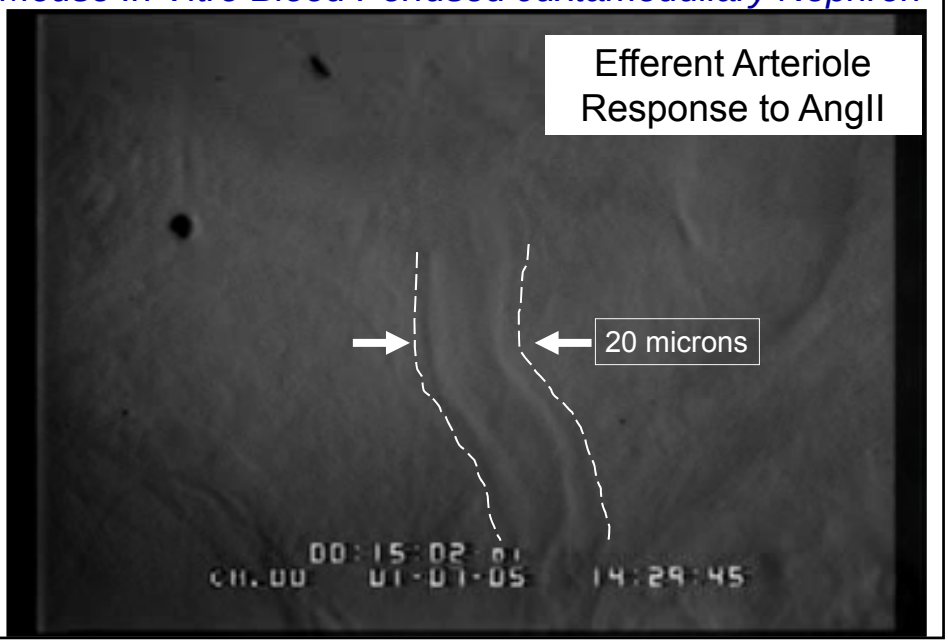




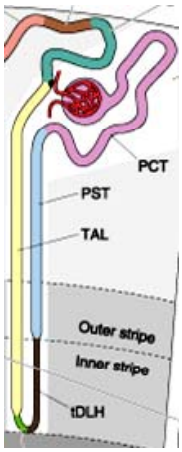
- constrict afferent & efferent arterioles
  ⇓ RBF
- contract mesangial cells - ⇓ K_f ⇓ GFR
- TGF - ⇑ sensitivity
- Medullary BF - reduced

*** Reduce RBF & GFR ***

SHOW AND TELL
Mouse In Vitro Blood Perfused Juxtamedullary Nephron



TUBULAR Actions of Angiotensin II



- AngII acts directly on tubules
  - ⇑ Na^+ reabsorption
- Aldosterone release from adrenal
  - ⇑ Na^+ reabsorption

*** Reduce Salt & H_2O Excretion ***

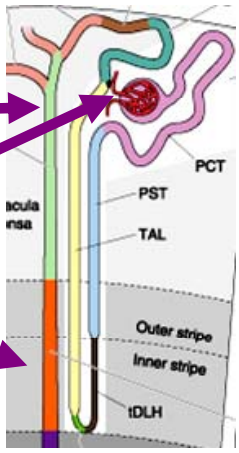
Which patients would benefit from drugs that block RAS?

Patients with:

- Hypertension
- Heart failure
- Kidney failure in diabetes
- Coronary artery disease
- Chronic kidney disease
- Migraines
- Heart attacks

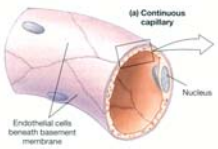
AVP – Arginine Vasopressin = **ADH** – Antidiuretic Hormone

- Collecting duct ⇑ H_2O absorption
- Constriction AA & EA
- ⇓ BF renal medulla



*** Reduce H_2O Excretion ⇑ BP ***

Nitric Oxide



- Endothelial generated

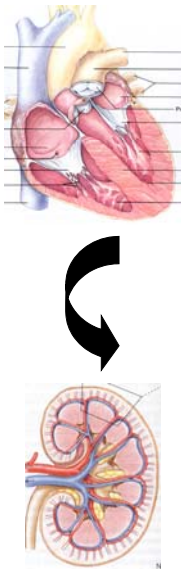
  shear force, acetylcholine, histamine, bradykinin

- <u>Relax</u> vascular smooth muscle

  AA & EA

- <u>Buffer</u> 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

↑ <u>Severe volume depletion -</u> 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

Vasoconstrictors	⇓ RBF ⇓ GFR
Sympathetic nerves	
Angiotensin II	
Endothelin	
AVP	
Norepinephrine	
Vasodilators	**⇑ RBF ⇑ GFR**
Prostaglandins	
Nitric Oxide	
Bradykinin	
ANP	

Summary

1. O_2 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