1. Control of renal blood flow and GFR

1. Autoregulation
   a) Myogenic
   b) Tubular feedback
2. Sympathetic nervous system
3. Hormonal
   a) Angiotensin II
   b) Atrial natriuretic peptide

Control mechanisms
1. Renal Blood Flow and GFR
2. Na⁺ and water
• Autoregulation
  1a. Myogenic – same as discussed in cardiovascular section
  • As flow ↑, stretches arterioles and the smooth muscles contract, ↑ resistance leads to ↓ flow

Tubular Feedback

• Autoregulation
  1b. Tubular feedback
  1. If GFR is High
  2. ↑ NaCl in tubule
  3. High Na, Cl detected by signal generated by macula densa
     4. Contraction of afferent arteriole – ↓ GFR

2. Sympathetic nervous system
  • innervates afferent arteriole
    – therefore SNS activity ↓ GFR by ↓ blood flow into glomerular capillaries
    – Circulating epinephrine also preferentially constricts afferent arteriole
• 3. Hormonal
  – Angiotensin II
  – Atrial Natriuretic Peptide

Angiotensin II

- Renin
  - Angiotensinogen
  - Angiotensin I
  - Angiotensin II

• General vasoconstriction
• Efferent arteriole more sensitive than afferent arteriole

Low AngII → efferent constriction > afferent
High AngII → both constricted, ↓ renal blood flow & ↓ GFR

Atrial Natriuretic Peptide

Eg, you drink 1 liter of water

↑ Blood volume → ↑ atrial stretch

↑ ANP released from atria

Renal arterioles
  1. Afferent dilation
  2. Efferent constriction

↑ GFR, without changing blood flow

• Summary for renal Blood Flow and GFR
  – Renal blood flow is the main determinant of GFR
  – Autoregulation helps maintain GFR over a range of arterial blood pressure
  – SNS, AngII major regulators of renal blood flow
  – In major crisis (bleeding) renal blood flow can be shut down to preserve arterial pressure
Na\(^+\) & Water reabsorption

Since Na\(^+\) is the main ion which generates osmotic forces, regulation of Na and water are directly linked.

Examples,
- if blood volume is low, Na\(^+\) reabsorption is increased to draw water back into the system
  - Concentrated urine
- If Na\(^+\) concentration is low, extra water is allowed to be excreted to return Na\(^+\) to normal
  - Dilute urine

Main factors controlling Na\(^+\) and water

1. Sympathetic nervous system
2. Renin-Angiotensin-Aldosterone
3. Atrial Natriuretic peptide
4. Anti-diuretic hormone/vasopression

Control of Na\(^+\) and water

1. SNS
   a) Vasoconstriction of afferent arteriole ↓ GFR, therefore ↓ filtration
   b) ↑ SNS activity → ↑ Renin secretion

Control of Na\(^+\) and water

2. Renin-Angiotensin II-Aldosterone

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renin
Angiotensin converting enzyme
Angiotensinogen → Angiotensin I → Angiotensin II
↓ vasoconstriction
↓ Renal blood flow & ↓ GFR
↑ ADH secretion from Pituitary
↑ Aldosterone secretion from adrenal cortex
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Renin-Angiotensin II-Aldosterone

2. Renin-Angiotensin II-Aldosterone

- Angiotensin II is the major factor controlling Aldosterone secretion from adrenal cortex.

- Effects of Aldosterone
  - Increase of Na⁺ channels on apical membrane of tubular epithelial cells
  - Increase ability to reabsorb sodium
3. Atrial Natriuretic Peptide

Stimulus for secretion is atrial stretch (i.e. ↑ blood volume)

- Dilation of afferent arterioles, constriction of efferent arterioles
- Reduces renin secretion
- Inhibits aldosterone secretion
- Inhibits NaCl reabsorption by collecting duct
- Inhibits ADH release

Since the stimulus for ANP is high blood volume/atrial stretch
- The effect of ANP is to increase GFR and allow more water to be excreted

4. ADH/vasopressin

ADH is secreted by hypothalamic neurons at the posterior pituitary

Factors regulating ADH secretion

Normal Physiological Control:
- Osmoreceptors in the hypothalamus

Big Changes in Blood Pressure (bleeding)
- Cardiovascular baroreceptors

Other:
- Angiotensin II stimulates ADH release
- ANP inhibits ADH release

Osmoreceptors (cells of the hypothalamus)

Respond to osmolarity changes occurring due to gain or loss of water

Recall changes in water volume redistribute both intra- and extracellular fluid
Plasma osmolarity (mOsm)

So what does ADH/vasopressin do?

• AQP-2 channels are constantly cycling to and from the apical cell surface of **collecting duct** epithelial.

• AQP-3/4 normally present on baso-lateral membrane

• The activity of the ADH/vasopressin receptor leads to phosphorylation of AQP-2
  – Increases rate of exocytosis, reduces the rate of endocytosis, or both

• Therefore more AQP-2 remains at the cell surface, increasing H₂O permeability

**Thirst**

• Thirst center is in the hypothalamus

  ↓ Plasma volume  ↑ Osmolarity
  ↓ baroreceptors  ↓ osmoreceptors  ↓ Angiotensin II

  Thirst center

  ↓ Regulate fluid intake

  ↑ Plasma volume  ↓ Osmolarity  ↓ Dry mouth
Summary
Water only moves by osmosis, so regulating the reabsorption or excretion of Na⁺ is the key factor in water volume regulation
- SNS and hormones are major factors by controlling GFR and permeability

K⁺ regulation
- K⁺ the major intracellular cation
- Changes in extracellular [K⁺] have major impact on nerve and muscle function by altering resting membrane potential

[ECF]
4 mM Normal
>5mM hyperkalemia
<3.5 mM hypokalemia

K⁺ distribution
Main factors controlling K⁺ uptake into cells:
1. Hormonal
   a) Insulin
   b) Aldosterone
   c) Epinephrine
2. [K⁺] in extracellular fluid

All can upregulate Na/K pump ability to move K into cells
K+ secretion

Main factors controlling K+ secretion in collecting duct
1. Aldosterone
2. [K⁺] in extracellular fluid