1. **Descending Limb:** Carries filtrate toward medulla
2. **Ascending Limb:** Returns filtrate to cortex
Functions:

1. **Primary Function**: Concentrate Interstitium
   - **Create concentration gradient**:
     - Increases toward medulla: ~5x more conc.
   - **Result**: Produces an Osmotic Gradient
     - Provides driving force for additional Water Re-absorption
   - Necessary for URINE CONCENTRATION

- **Re-absorption Location**: Collecting Duct
  - Collecting duct passes through concentrated medullary interstitium
  - Created by Loop of Henle
  - Draws water OUT of the Collecting Duct
  - Creating more concentrated URINE
  - Loop of Henle Concentrating Mechanism: Counter Current Multiplier
2. **Secondary Function**: **Reabsorb additional 20% water & Salts**
   - Total re-absorption **85% of total filtrate**

**Countercurrent Multiplier:**
- **Counter current filtrate flow multiplies concentration**
1. **Descending Limb** (Thin Segment)
   - ONLY water allowed to diffuse OUT
   - NO salt channels (Na\(^+\) & Cl\(^-\))
   - Aquaporins: WATER permeable

   ![Diagram of Descending Limb](image)

   - a. **Filtrate is concentrated on Descent:**
     - Water drawn out into surrounding CONCENTRATED interstitium
   - b. Result: Descending limb “delivers” concentrated filtrate to ascending limb ~1400mOsm

2. **Ascending Limb** (Thick segment)
   - ONLY SALT is pumped OUT
   - Primary Active Salt Channels (Na\(^+\) & Cl\(^-\))
   - Glycoprotein Layer: WATER Impermeable

   ![Diagram of Ascending Limb](image)
1. Filtrate is diluted upon ascent ~100mOsm

2. Interstitium is concentrated ~1400mOsm

Result: Ascending limb produces interstitial concentration gradient need to draw water from descending limb.

Significance of Countercurrent System:
- Provides OSMOTIC GRADIENT needed to concentrate URINE
- Location: Collecting Duct
• **Collecting Duct**: Variable water permeability
  - Permeability: Hormonally regulated
  - Antidiuretic Hormone: ADH

÷ **Systemic Affect**:
  - Increased **BLOOD VOLUME/PRESSURE**
  - Decreased **BLOOD OSMOLALITY**

- High ADH
- High Aquaporin number
- High water re-absorption
- High urine concentration
- Low urine volume
Low ADH
Low Aquaporin concentration
Low re-absorption
Low urine Concentration
High urine volume

High ADH
High Aquaporin concentration
High re-absorption
High urine Concentration
Low urine volume

Regulation of Body Fluid Volume:
A. Antidiuretic Hormone (ADH) or Vasopressin
"Urine concentrating Hormone"

• Location of Effect: Collecting Duct
• Pituitary Gland Hormone:

Stimuli: ▲ Blood Osmolality
* Sensor: Osmoreceptors in Hypothalamus

High Osmolality
Nephron
ADH
Action: \( \uparrow \) \( \text{H}_{2}\text{O} \) re-absorption
* Increase Collecting duct Aquaporins
* Utilizes Second messenger cAMP

1° Effect: Blood Osmolality
2° Effect: Blood Volume & Pressure

B. Aldosterone: “Salt retaining Hormone”

• Location of effect: Distal convoluted tubule and collecting duct

Sodium & Chloride retained
Potassium Secreted
• Adrenal Gland Hormone

1° Stimuli: \(\text{Blood } K^+\)
2° Stimuli: \(\downarrow\text{Blood Volume (Indirect)}\)

Action: Stimulates activity of \(\text{Na}^+ / K^+\) pump
⇒ Secretes: \(K^+\) into filtrate
⇒ Reabsorbs: \(\text{Na}^+ & \text{WATER}\)
1° Effect: ↓ Blood K⁺ & ↑ Blood Na⁺

2° Effect: ↑ Blood Volume

- BUT does NOT affect osmolality
- Uptakes BOTH Na⁺ (Cl⁻) and water

C. Renin–Angiotension Aldosterone System (RAS)

- Alternate method of Aldosterone secretion

Stimuli: ↓ Blood Volume

- Stretch of Juxtaglomerular Apparatus
- Stimulated decreased flow rate
**Actions:**
1. **JGA sense Decreased FLOW**
   - Release: Renin into blood
2. **Renin: Enzyme**
   - Converts plasma proteins:
     - Angiotensinogen → Angiotensin I
3. **Angiotensin Converting Enzyme: ACE**
   - Converts:
     - Angiotensin I → Angiotensin II

4. **Angiotensin II:**
   - a. Stimulates: Aldosterone secretion
   - b. Stimulates: Vasoconstriction of arterioles

**Diagram:**
- Renin released from the kidney
- Angiotensinogen binding to renin
- Formation of Angiotensin I
- Conversion to Angiotensin II
- Binding to AT receptor
- Vasoconstriction
- Increased blood volume
D. **Atrial Naturetic Factor (Peptide) ANP:**

"Anti-aldosterone" & "Na+ Excreter"

- **Atrial Hormone**

**Stimuli:** ↑ **Blood Volume**

- Sensor: *Atrial muscle stretch*

**Action:**

a. ↑ **Na+ & Water excretion**

\[ \text{Naturesis:} \]

\[ \text{Natrium} = \text{"Na+" Uresis} = \text{"making H}_2\text{O"} \]

b. ↑ **Urine production (H}_2\text{O loss)"**
Effect:

a. ↓ Blood Na⁺ concentration
b. ↓ Blood Pressure & Volume

Clinical Applications:

- Hypertension: Elevated blood pressure

Treatments:

a. ACE Inhibitors: Block conversion of Angiotensin I into Angiotensin II

C. ↓ Concentration of Angiotensin II
   * ↓ Vasoconstriction
   * ↓ Aldosterone & Na⁺ Retention
   ↓ Blood volume & PRESSURE

How ACE Inhibitors Act

ACE inhibitors inhibit formation of angiotensin II and thereby lower blood pressure.
b. **Diuretics: Increase URINE output**
   - Lower blood volume and pressure
   - **Mechanisms:** Varied
   - Most powerful: 
     
     *Inhibit Salt & Water re-absorption*

Caution: Stimulates $K^+$ secretion & increase $K^+$ loss!
- $\uparrow$ Na$^+$ delivery to Distal convoluted tubule
- $\uparrow$ K$^+$ secretion = LOSS

1. Inhibit Na$^+$ excretion
2. Deliver more Na$^+$ to DCT
3. Reabsorb Na$^+$ from a more conc. pool in exchange for K$^+$ secretion

The End