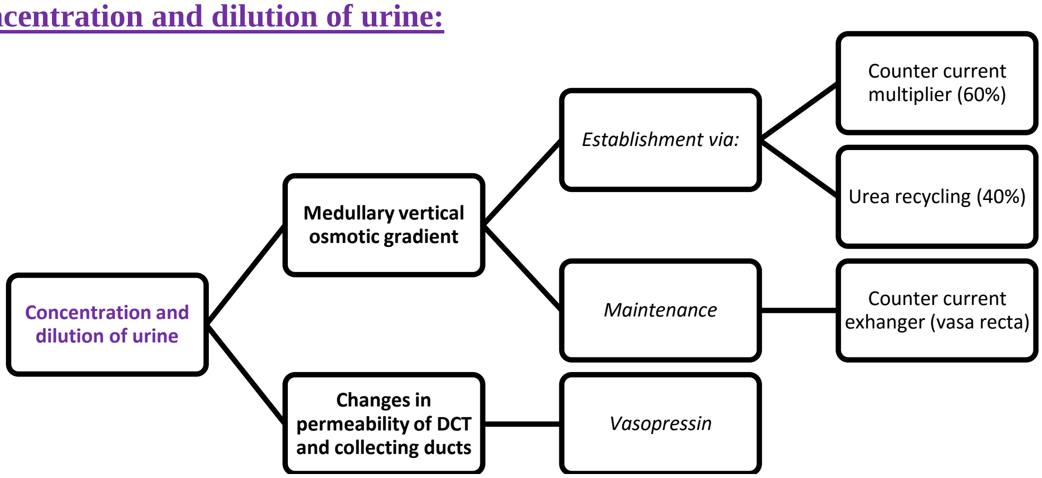
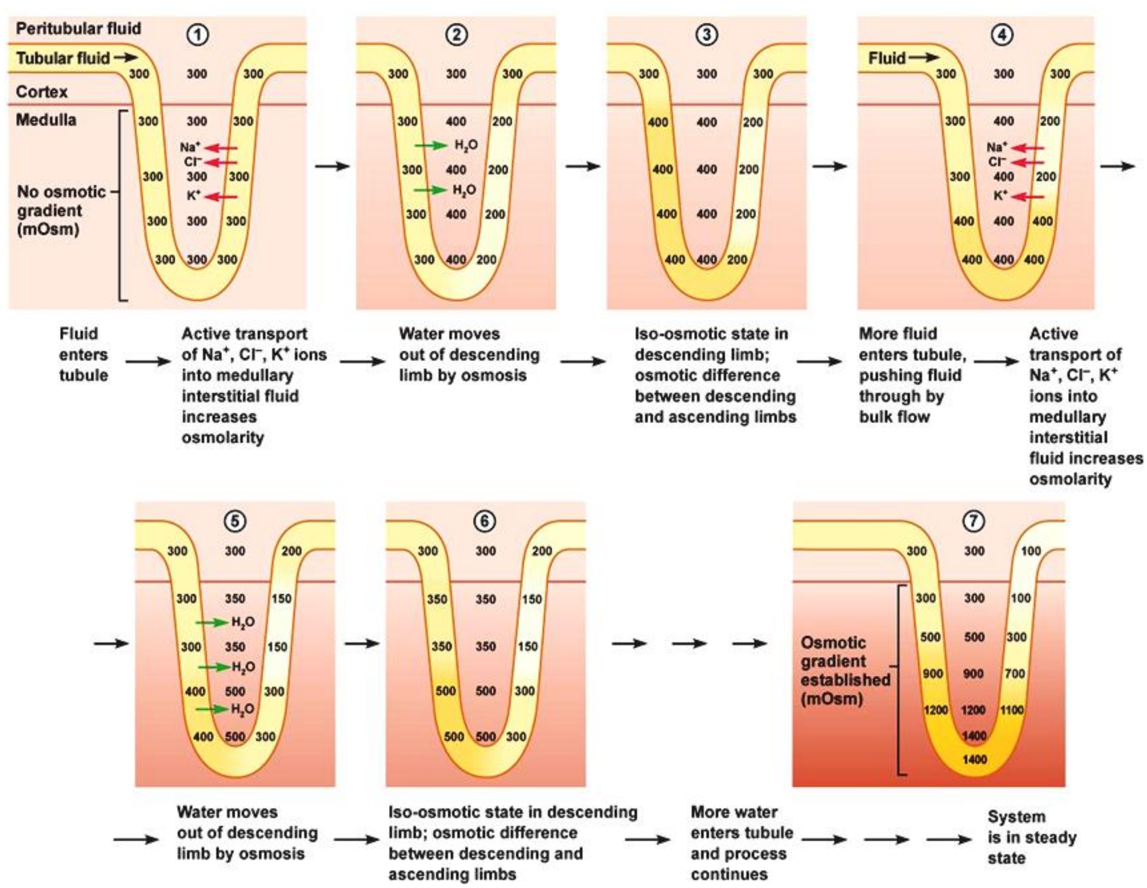
Unit V – Problem 11 – Physiology: Renal Mechanisms of Urine Concentration and Dilution

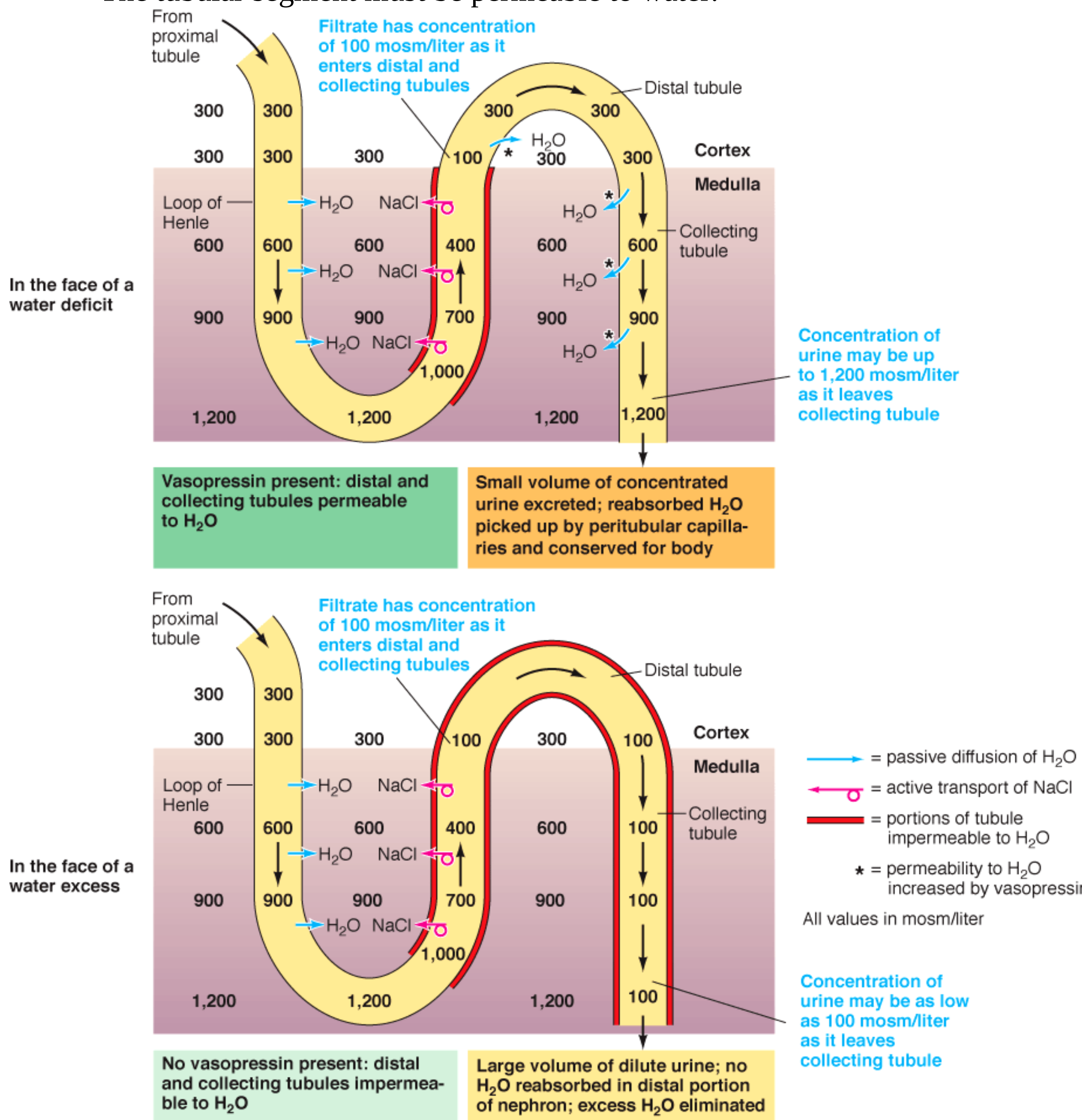
- **Urine volume:**
  - A human body in ideal fluid balance will produce 1 ml/min of isotonic (300 mOsm/l) urine.
  - Excessive intake of fluids (overhydration) will lead to production of dilute hypotonic (100 mOsm/l) urine.
  - Reduced intake of fluids (dehydration) will lead to production of concentrated hypertonic (1200 mOsm/l) urine.

    Notice that obligatory urine flow is the minimal volume of urine which must be excreted to remove 600 mOsm of daily waste solutes and this is equal to 0.5 L/day.
- **Kidney countercurrent system is represented by:**
  - **Juxtamedullary nephrons**: the long loop of Henle establishes a vertical osmotic gradient.
  - **Collecting tubules**: they use the gradient in conjugation with antidiuretic hormone (ADH) which is also known as vasopressin.
  - **Vasa recta**: prevents dissolution (إنحلال) of this gradient.
- **Concentration and dilution of urine:**

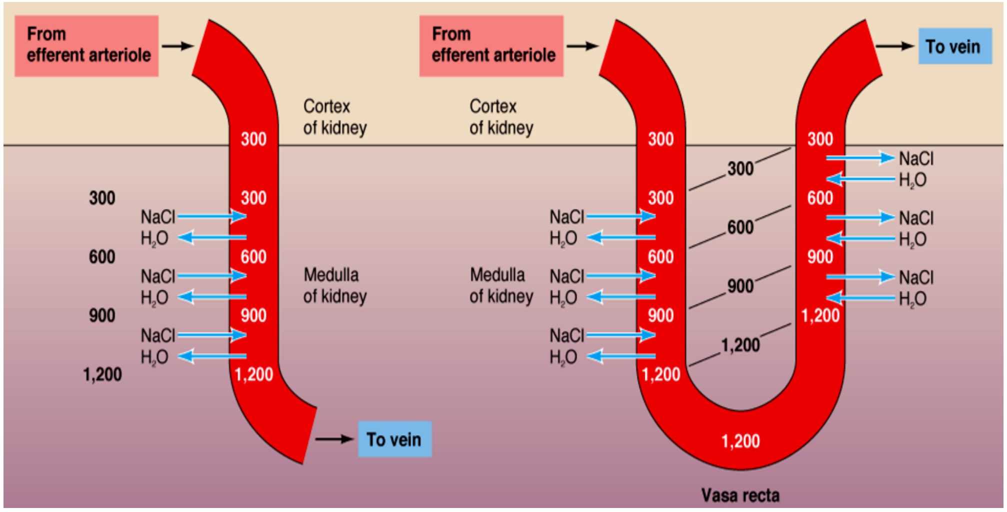


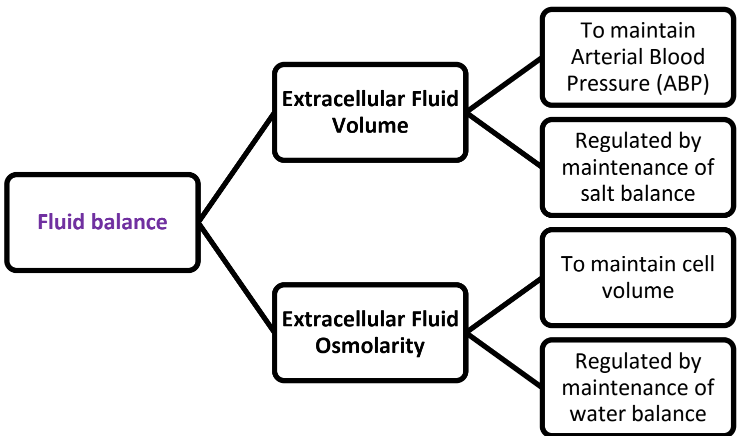


- **Loop of Henle-countercurrent multiplication:**
  - A 200 mOsm/l gradient between the ascending limb and the surrounding fluids at each medullary horizontal level.
  - There is large vertical gradient from the top to the bottom of renal medulla.
  - An isotonic fluid (300 mOsm/l) enters the loop of Henle → a maximum concentration of 1200 mOsm/l is found at the tip of the loop → a minimum concentration of 100 mOsm/L is generated as fluid enters distal parts of the tubule.
- **Water reabsorption from final tubular segments:**
  - There is reabsorption of 20% of water entering the Distal Convoluted Tubule (DCT) and collecting tubules. It is very important to know that (DCT) and collecting tubules are impermeable to water except in the presence of (ADH: vasopressin).
  - **There are two criteria for water reabsorption:**
    - ✓ An osmotic gradient must exist across the tubule segment.
    - ✓ The tubular segment must be permeable to water.

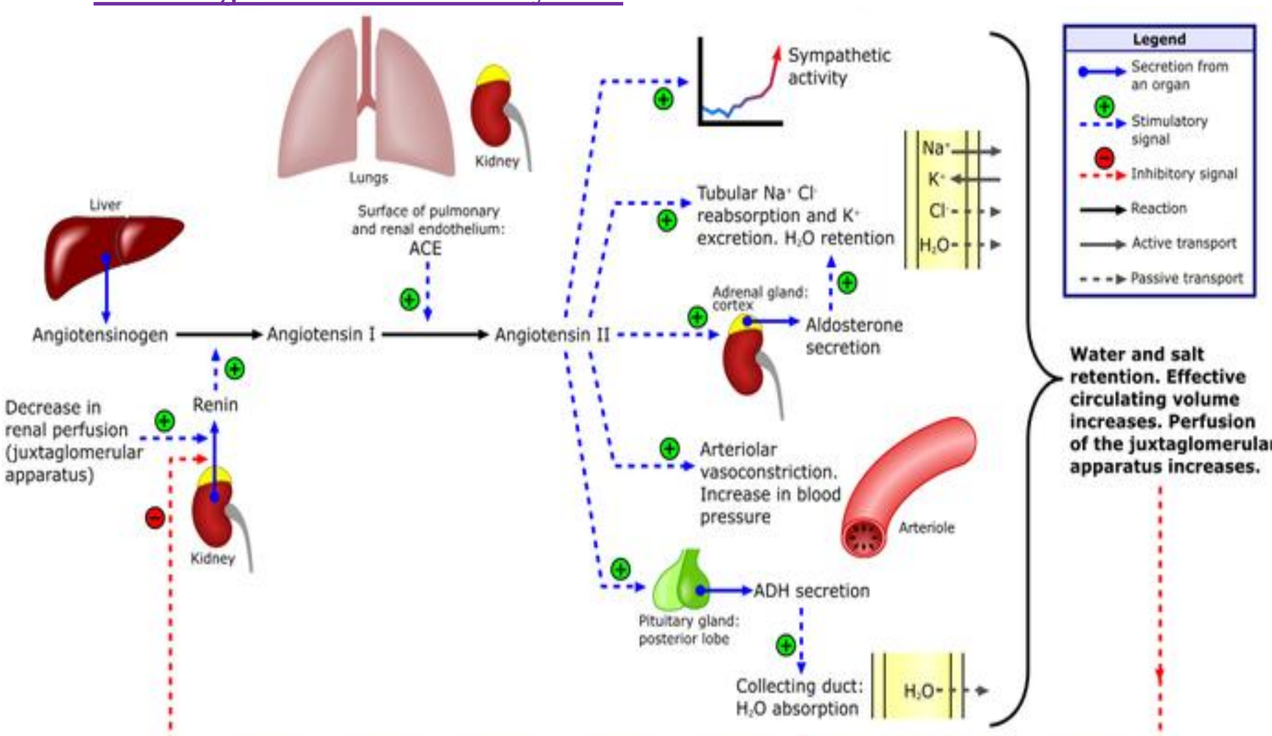


- **Urea excretion and recycling:**
  - Under conditions of water restriction, kidneys excrete nearly 20% of the filtered urea.
  - Urea contributes about 40% of the medullary interstitial fluid osmolarity (500 mOsm/l).
- **Countercurrent exchange in vasa recta:**
  - Slow blood flow and hairpin structure prevent the dissolution of the medullary osmotic gradient.





- <u>**Renin-angiotesnin-aldosterone system:**</u>



- **Angiotensin-II**: affects baroreceptor function; limits reflex bradycaria which would normally accompany its pressor effects. Helps maintain blood volume and blood pressure.
- **Atrial Natriuretic Peptide (ANP):** Rleased from atria in response to increased blood volume; may act as a 'check' on renin-angiotensin-aldosterone system. Relaxes vascular smooth muscle via cGMP, causing ↑GFR and ↓renin.

- **Antidiuretic Hormone (ADH):** primarily regulates osmolarity (by causing pure water retention from collecting tubules); also responds to low blood volume states.
- **Aldosterone**: Primarily regulates extracellular fluid sodium content and volume (by causing retention of sodium and water + secretion of potassium and hydrogen); responds to low blood volume states.
- **Juxtaglomerular apparatus:**
  - ✓ Consisting of Juxtaglomerular cells (modified smooth muscle of afferent arteriole) and the macula densa (NaCl sensor, part of the distal convoluted tubule).
  - ✓ Juxtaglomerular cells secrete renin in response to ↓ renal blood pressure, ↓NaCl delivery to distal tubule and ↑sympathetic tone (β_1).
  - ✓ Notice that β-blockers can decrease blood pressure by inhibiting β_1-receptors of the juxtaglomerular apparatus, causing ↓renin release.

- **Water reabsorption and excretion:**

Mandatory water reabsorption	Free water reabsorption
Linked to solute (Na^+) reabsorption	Not linked to solute reabsorption
Due to osmotic considerations	Under the effect of osmoreceptor-controlled vasopressin (ADH)
In tubular segments that are always permeable to water	In the distal part of the nephron

- **Free water clearance:**
  - ✓ Definition: it represents the rate at which solute free water is excreted by the kidneys.
  - ✓ $C_{H2O} = V - \frac{U_{osm}}{P_{osm}} V$
  - ✓ Example: for an individual with a urine osmolality of 140 mOsm/l, plasma osmolality of 280 mOsm/l, and a urine production of 4 ml/min, the free water clearance is 2 ml/min obtained from:
    - ❖ $C_{H2O} = 4\text{ml/min} - \frac{140\ mOsm/l}{280\ mOsm/l} \times 4\text{ml/min} = 2\text{ ml/min}$

- **Disorders of urinary concentrating ability:**
- **Diabetes insipidus**: characterized by intense thirst, polyuria and inability to concentrate urine due to lack of ADH.

	Central diabetes insipidus	Nephrogenic diabetes insipidus
Etiology	Pituitary tumor, autoimmune or surgery	Hereditary (ADH receptor mutation)
Findings	↓ ADH; serum osmolarity > 300 mOsm/L	Normal ADH levels; serum osmolarity > 300 mOsm/L
Diagnosis	Water restriction test: > 50% ↑ in urine osmolarity.	Water restriction test: no change in urine osmolarity
Treatment	Intranasal desmopressin and hydration	Hydrochlorothiazide and hydration