Urine Concentration Mechanism

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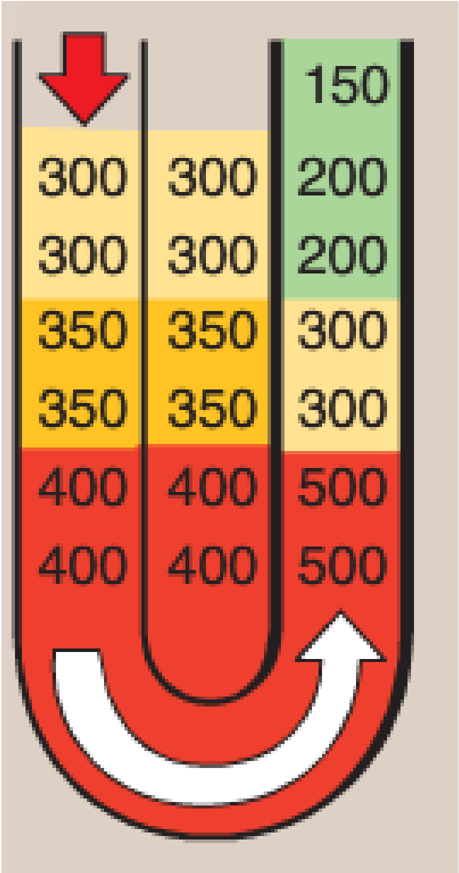
Learning Objectives:

- Identify and describe that the loop of Henle is referred to as countercurrent multiplier and the loop and vasa recta as countercurrent exchange systems in concentrating and diluting urine
- Explain what happens to osmolarity of tubular fluid in the various segments of the loop of Henle when concentrated urine is being produced.
- Explain the factors that determine the ability of loop of Henle to make a concentrated medullary gradient
- Differentiate between water diuresis and osmotic diuresis
- Appreciate clinical correlates of diabetes mellitus and diabetes insipidus

Countercurrent System

- A system in which inflow runs parallel and in close proximity but opposite to the outflow.
- The operation of such a system allows the outgoing fluid to heat the incoming fluid.



Mechanism for urine concentration/dilution

- While the loop of Henle reabsorbs another 20% of the salt/water in tubular fluid, primary function is to determine osmolarity of urine (i.e. whether concentrated or diluted) using

countercurrent multiplier system

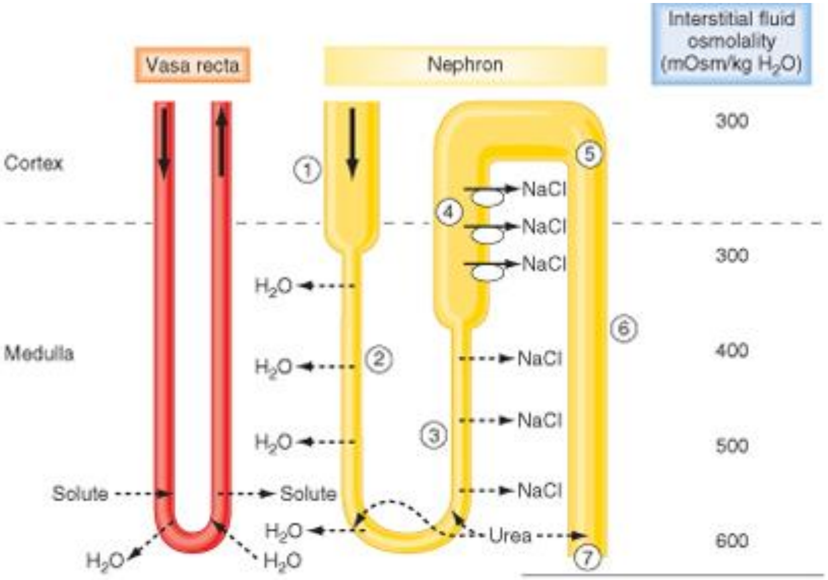
- While collecting duct is where urine concentration is determined, osmolarity of interstitial fluid in medulla must be high and osmolarity of tubular fluid must be low
  – Countercurrent multiplier system achieves this

Countercurrent multiplier system

- Is the repetitive reabsorption of NaCl by the thick ascending loop of Henle and continued inflow of new NaCl from PCT into LOH
- The NaCl reabsorbed from the ascending LOH keeps adding newly arrived NaCl (into LOH from PCT), thus multiplying its concentration in the medulla

How the kidney excrete dilute urine ?

- Dilution (low or no ADH):
- Reabsorb solute don't absorb water
- 1) Isoosmotic fluid from PCT
- 2) Thin descending limb permeable to water, less for NaCl
- ∴ water reabsorbed, tubule osomolality = medulla (i.e. high)



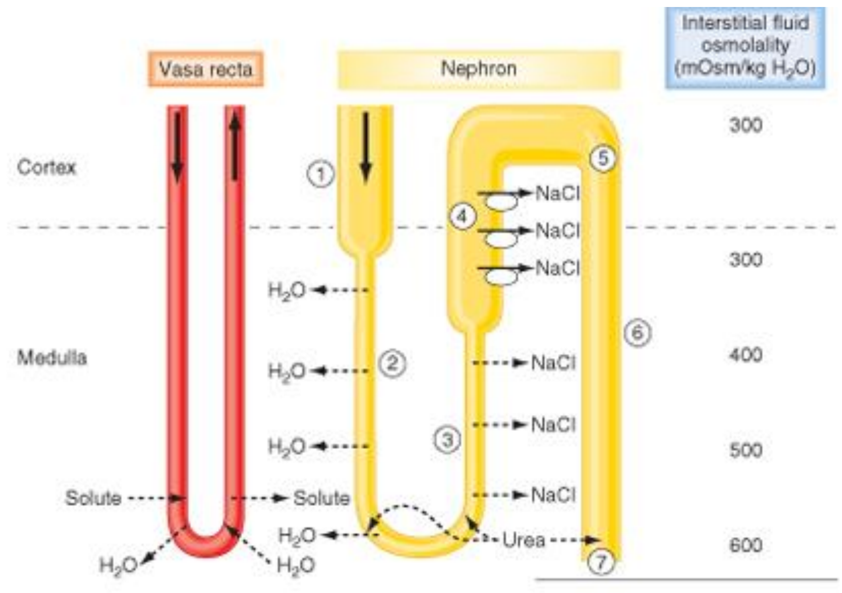
How the kidney excrete dilute urine ?

3) Thin ascending limb impermeable to water, permeable to NaCl (passive)

- tubule volume unchanged, [NaCl] ↓

4) TAL impermeable to water, NaCl actively reabsorbed (diluting segment of nephron)

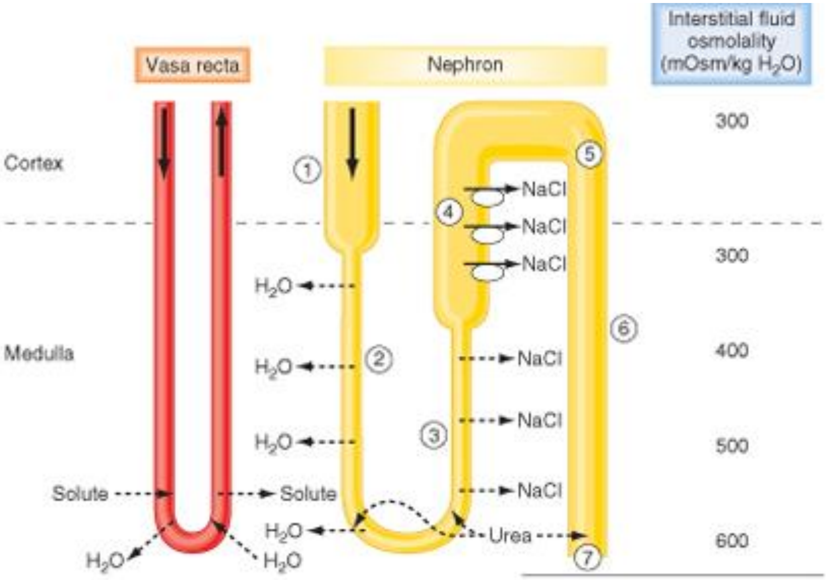
- diluting tubule fluid 150 mOsm/kg water



How the kidney excrete dilute urine ?

5) Collecting duct reabsorb NaCl

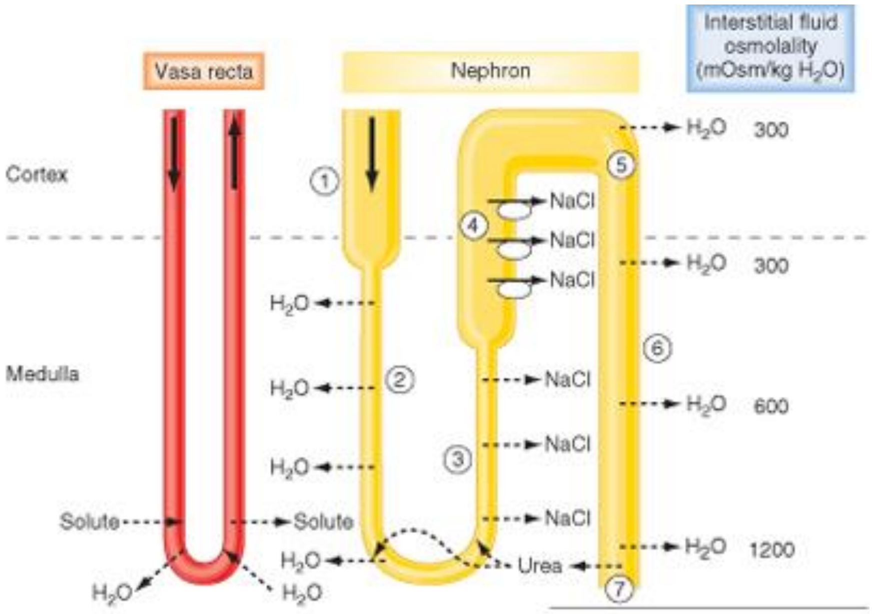
- ↓ osmolality, may reach 50 mOsm/kg water



How the kidney excrete concentrated urine ?

- Concentration of urine (ADH dependent):

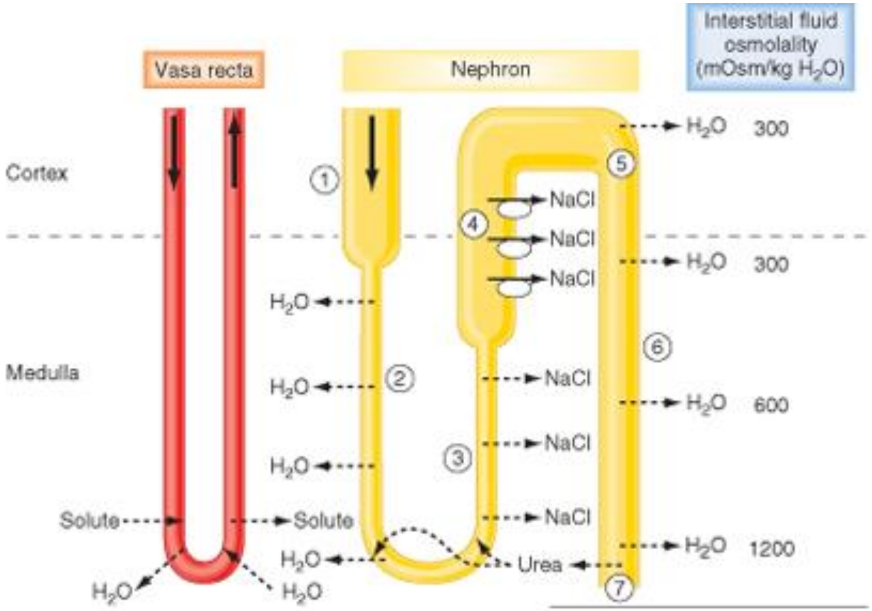
- 1-4 same as dilution
- Reabsorbed NaCl in loop of Henle ⇒ ↑ osmolality of interstitium
- Generated by **Countercurrent Multiplication**



How the kidney excrete concentrated urine ?

5) Fluid reaching CD hypoosmotic (osm due urea)

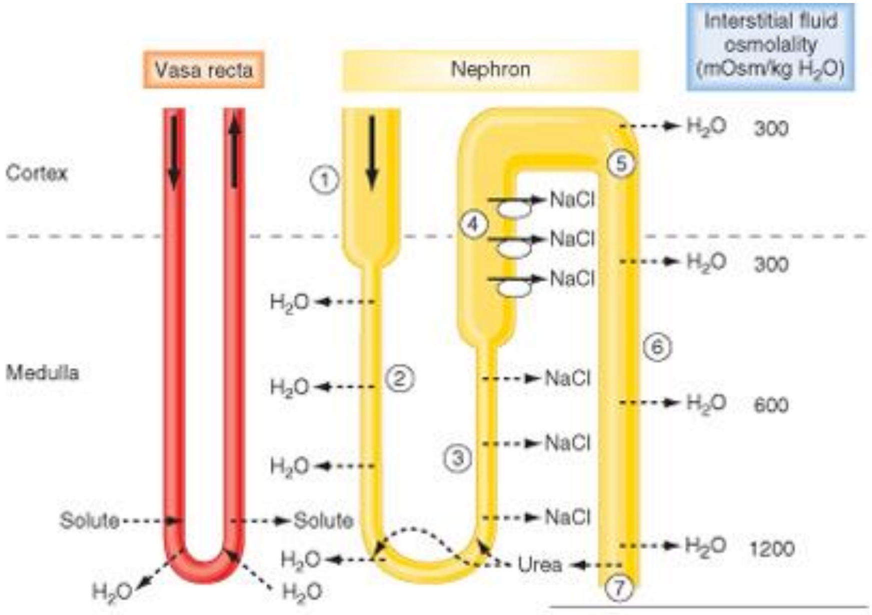
- ADH causes water to diffuse out up to a max of 300 mOsm/kg water



How the kidney excrete concentrated urine ?

6) Osmolality of medullary tissue high up to 1200 mOsm/kg water

- due to NaCl (accounts for 600)
- urea (accounts for 600)
- early CD impermeable to urea
- ADH allows water reabsorption passively



How the kidney excrete concentrated urine ?

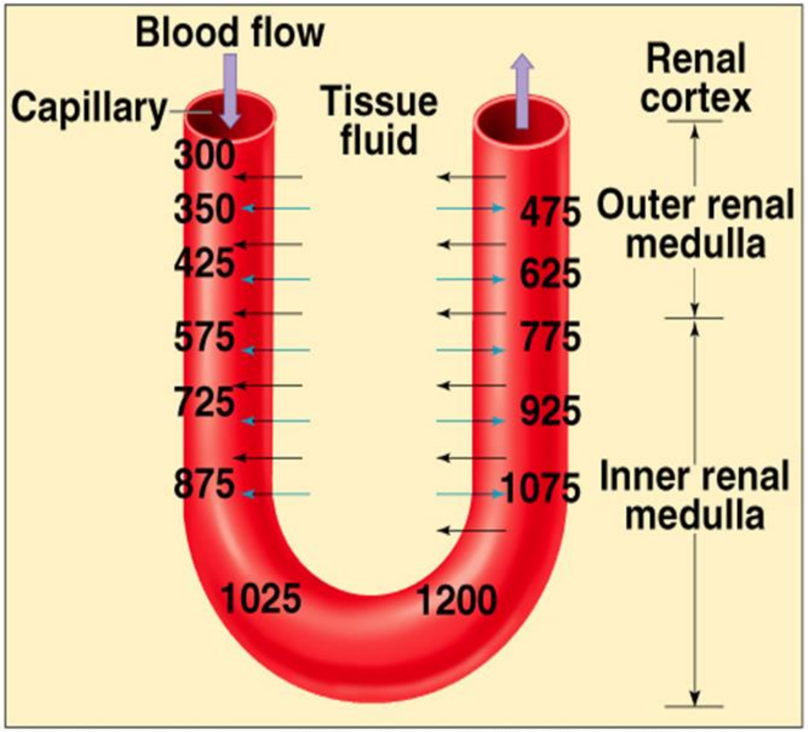
- When ADH levels high urea levels in medullary CD & interstitium equilibrate
- Most water absorbed in presence of ADH is in the cortical collecting duct

Countercurrent exchange in the Vasa Recta

- There are two special features of the renal medullary blood flow that contribute to the preservation of the high solute concentration:

1. The medullary blood flow is low, accounting for less than 5% of the renal blood flow. This sluggish blood flow is sufficient to supply the metabolic needs of the tissues but helps to minimize solute loss from the medullary interstitium
2. The vasa recta serve as countercurrent exchanger, minimizing washout of solutes from the medullary interstitium.

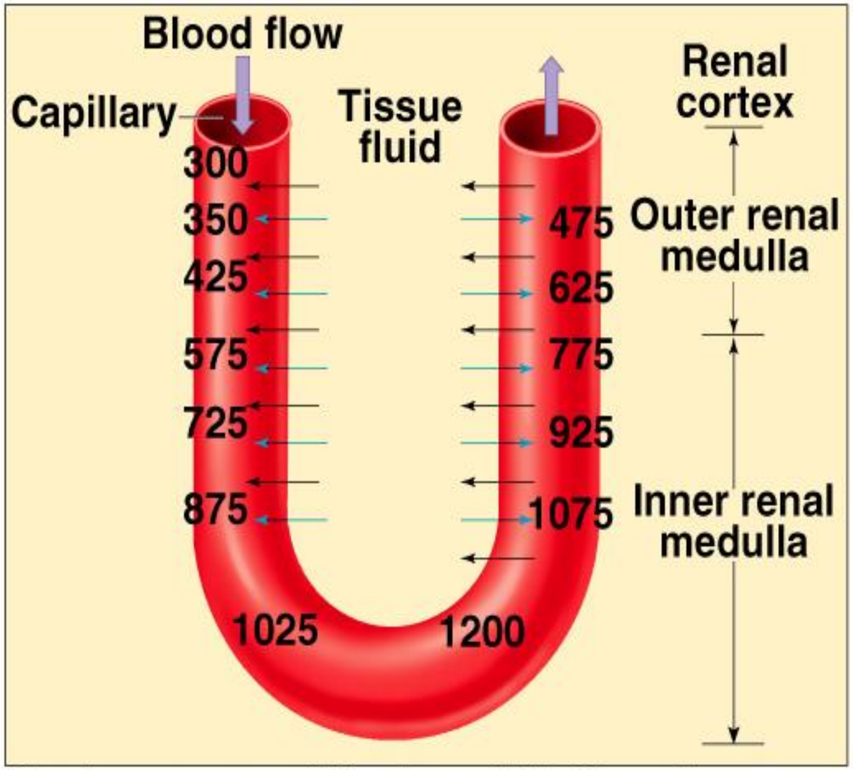
- **<u>The vasa recta do not create the medullary hyperosmolarity, but they do prevent from being dissipated</u>**



Black arrows = diffusion of NaCl and urea
Blue arrows = movement of water by osmosis

Countercurrent exchange in the Vasa Recta

- Recycles NaCl in medulla.
- Transports H_20 from interstitial fluid.
- Descending limb:
  - Urea transporters.
  - Aquaporin proteins (H_20 channels).
- Ascending limb:
  - Fenestrated capillaries.



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Vasa Recta

- Vasa recta maintains hypertonicity by countercurrent exchange.
- NaCl and urea diffuse into descending limb and diffuse back into medullary tissue fluid.
- At each level of the medulla, [solute] is higher in the ascending limb than in the interstitial fluid; and higher in the interstitial fluid than in descending vessels.
- Walls are permeable to H_20, NaCl and urea.
- Colloid osmotic pressure in vasa recta > interstitial fluid.

Factors affecting urine concentration

1. ADH: causes an increase in permeability of DCT, CT, and CD for water. It also increase the permeability of medullary CD to urea.

2. Length of the loop of Henle: the longer the loop of Henle, the greater the countercurrent multiplication effect and more urine concentration.
   - The new born baby having shorter loop of Henle can not concentrate as same as the adult.

Factors affecting urine concentration

3. Delivery of salt to ALH:
   - due to a decrease in GFR (Hemorrhage) the filter load of solute is decreased.
   - This leads to a decrease in the delivery of salt to ALH resulting in decreased reabsorption of salt from ALH.
   - Thus there is decreased addition of salts to the medullary ISF, leading to decreased medullary longitudinal osmotic gradient and decreased urine concentration.

Factors affecting urine concentration

4. Reabsorption of salt out of ALH: Diuretic drugs (Lasix) prevents NaCl reabsorption from thick ALH, leading to decreased addition of salts to the medullary ISF, decreased medullary longitudinal osmotic gradient and finally decreased urine concentration.

5. Delivery of fluid to medullary CT and CD:
   – Maximum urine concentration occures when only a small amount of fluid enters the medullary CT and CD

Factors affecting urine concentration

- Even during an osmotic diuresis, the increased fluid volume delivered to the medullary CT and CD leads to wash out of medullary longitudinal osmotic gradient and cause decreased urine concentration.

6. Medullary blood flow:
   - Normally very low blood flow (about 5% of total RBF) to the medulla
   - Increased blood flow to the medulla may cause wash out of the medullary longitudinal osmotic gradient, decreased effectiveness of the countercurrent exchange system and decreased urine concentration

Factors affecting urine concentration

7. Urea:
   - Urea recycling contributes significantly to the medullary longitudinal osmotic gradient and is essential for the countercurrent system.
   - A person on a protein free diet loses the ability to concentrate urine due to lack of urea in the medulla.

Water Diuresis and Osmotic Diuresis

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Causes: - Excess ingestion of water - Lack of ADH - Defect in ADH receptors in Distal segment of nephron (nephrogenic Diabetes Insipidus)	Causes: - Increase plasma glucose level (DM) - Increase level of poorly reabsorbed solutes/ anions - Diuretic drugs (Lasix)

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Diuresis is mainly due to decrease in water reabsorption in distal segment of nephron. No change to the water reabsorbed proximally	Diuresis is mainly due to decrease reabsorption of solute in PCT or LOH. Decrease solute reabsorption results in decrease in water reabsorption proximally as well as distally

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ADH administration will stop diuresis if it is due to lack of ADH or excess ingestion of water. ADH administration will not be effective in Nephrogenic Diabetes Insipidus.	ADH administration will not stop diuresis.

Disorders of urinary concentrating ability

Diabetes insipidus

- Cause: inability to produce or release ADH
- Urine: low fixed specific gravity (diluted urine)
- Polyuria
- Polydipsia.

Nephrogenic diabetes insipidus:

- Cause: inability of kidney to respond to ADH

Diabetes mellitus:

- High specific gravity urine.

Thanks