63. Concentration and Dilution of Urine

INTRODUCTION

The normal kidney has tremendous capability to vary the relative proportions of solutes and water in the urine. They can excrete urine with an osmolarity as low as 50 mOsm/L, when there is excess water in the body and ECF osmolarity low. They can also excrete urine with a concentration of 1200–1400 mOsm/L, when there is a deficit of water and extracellular fluid osmolarity high.

OBLIGATORY URINE VOLUME (OUV)

The maximal concentrating ability of the kidney depends on how much urine volume must be excreted each day, to void the body of waste products of metabolism and ions that are ingested. A normal 70 kg human must excrete about 600 mOsm of solute each day. If maximum urine concentrating ability is 1200 mOsm/L, the minimal volume of urine is OUV can be calculated as:

$$\frac{600 \text{ mOsm/day}}{1200 \text{ mOsm/L}} = 0.5 \text{ L/day}$$

REQUIREMENTS FOR EXCRETING A CONCENTRATED URINE

1. High ADH levels
2. Hyperosmotic renal medulla.

High ADH Levels

When osmolarity of the body fluids increases above normal the posterior pituitary secretes more ADH.

This increases the permeability of the distal tubule and collecting duct to water. So, more water is reabsorbed and concentrated urine is formed.

When there is excess water and ECF osmolarity is reduced, ADH from posterior pituitary decreases, thereby reducing permeability of distal tubule and collecting duct to water causing a dilute urine.

Hyperosmotic Renal Medullary Interstitium

Hyperosmotic renal medullary interstitium is produced by counter- current mechanism and urea.

The renal medullary interstitium surrounding the collecting duct is very hyperosmotic. So, when ADH levels are high, the water moves through the tubular membrane by osmosis into the renal interstitium, from there into vasa recta back into blood.

The countercurrent mechanism depend on the special anatomical arrangement of the long loops of Henle of juxtamedullary nephrons and the vasa recta, the specialized peritubular capillaries of the renal medulla. Loop of Henle is called countercurrent multiplier and vasa recta as countercurrent exchanger.

The corrected osmolar activity which accounts for intermolecular attraction and repulsion is about 282 mOsm/L. The osmolarity of renal interstitium is about 1200 to 1400 mOsm/L in the tip of medulla.

The major factors that contribute to high solute concentration into the renal medulla are:

1. Active transport of sodium ions and cotransport of potassium chloride out of the thick ascending limb of LOH into medullary interstitium.
2. Active transport of ions from the collecting ducts into the medullary interstitium.
3. Passive diffusion of large amounts of urea from inner medullary CD into the medullary interstitium.
4. Diffusion of only small amounts of water from tubules into interstitium.

COUNTERCURRENT MULTIPLIER SYSTEM IN THE LOOP OF HENLE (Fig. 8.24)

Step 1: Assume the loop of Henle (LOH) is filled with fluid with a concentration of 300 mOsm/L, the same concentration as in proximal tubule.

Step 2: The active transport of Na^+ and other ions out of thick ascending limb of LOH reduces the concentration of solute inside tubule but raising in interstitium.

Step 3: The tubular fluid in the descending limb of LOH and interstitium reaches osmotic equilibrium because of osmosis of water out of descending limb. The osmolarity in interstitium maintained at 400 mOsm/L.

Step 4: It is additional flow of fluid into LOH from proximal tubule which causes hyperosmotic fluid in descending limb to move into ascending limb.

Step 5: When fluid is in ascending limb, additional ions are pumped into interstitium with water remaining behind until a 200 mOsm/L osmotic gradient is reached, with interstitium fluid osmolarity raising to 500 mOsm/L.

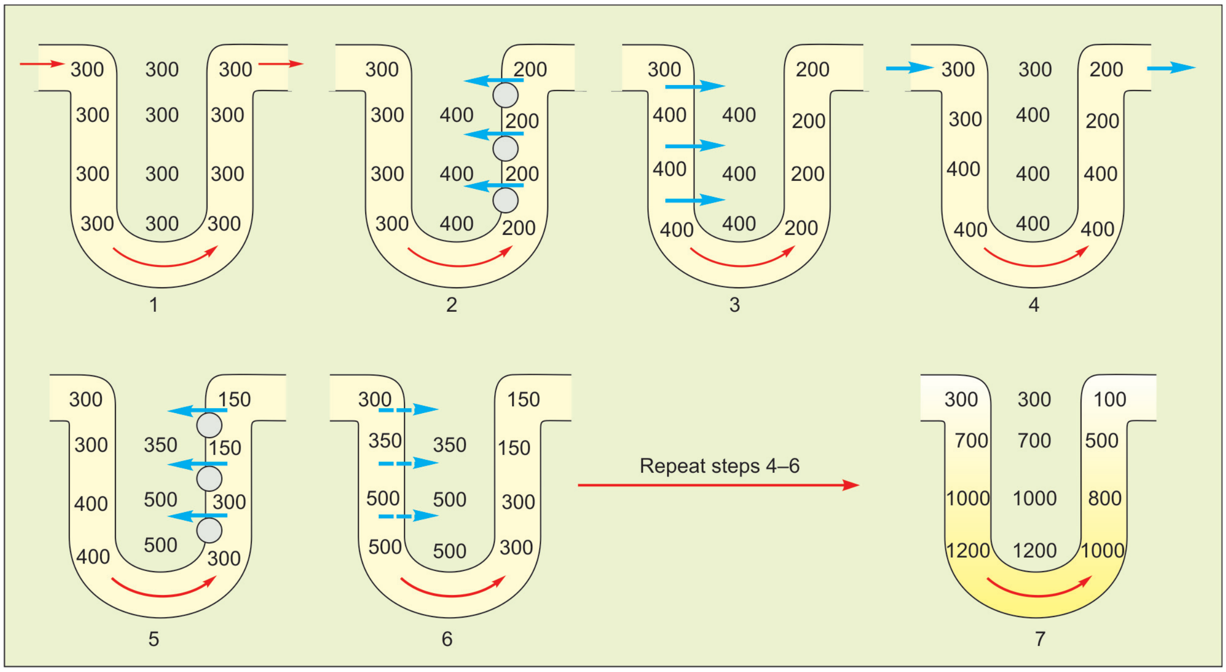

Fig. 8.24: Operation of loop of Henle as a countercurrent multiplier producing a gradient of hyperosmolarity in the medullary interstitium

Step 6: Once again the fluid in descending limb reaches equilibrium with hyperosmotic interstitial fluid. This fluid moves from descending limb to ascending limb so more solute is pumped out of the tubules and deposited in interstitium. These steps are repeated again and again till interstitium osmolarity reaches 1200–1400 mOsm/L.

UREA CONTRIBUTION TO HYPEROSMOTIC RENAL MEDULLARY INTERSTITIUM (Fig. 8.25)

Urea contributes about 40% (500 mOsm/L) of osmolarity of the renal medullary interstitium. When there is water deficit and ADH levels in blood are high, large amounts of urea are passively released from inner medullary collecting duct into interstitium which is highly permeable to urea.

Urea can also be recirculated from collecting duct into interstitium. The thick ascending limb of LOH, distal tubule and cortical collecting duct are impermeable to urea. A person usually excretes 40–60% of filtered urea. Excretion depends on two factors:

a. Concentration of urea in plasma
b. GFR.

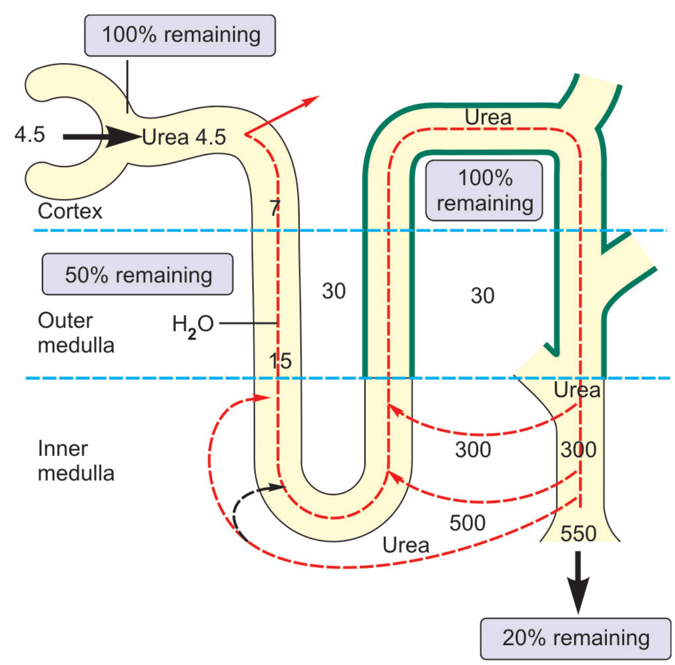

Fig. 8.25

COUNTERCURRENT EXCHANGE IN THE VASA RECTA PRESERVES HYPEROSMOLARITY (Fig. 8.26)

The vasa recta are highly permeable to solutes in the blood, except for the plasma proteins. Plasma flowing down the descending limb of vasa recta becomes more hyperosmotic because of diffusion of solutes from interstitial fluid into blood. In the ascending limb LOH, solutes diffuse back into interstitial fluid and water diffuses back into vasa recta.

Key Box

Countercurrent System:
- Countercurrent multiplier: Loop of Henle (thin descending limb, thin and thick ascending limbs)
- Countercurrent exchanger: Vasa recta

Osmolar Clearance (C_{osm})

It is the volume of plasma cleared of solutes each minute. It is expressed in ml/minute.

$$C_{osm} = \frac{U_{osm} \times V}{P_{osm}}$$

U_{osm} is urine osmalarity. V is urine flow rate. P_{osm} is plasma osmolarity.

Free Water Clearance (C_{H_2O})

The rate at which solute-free water is excreted by the kidneys. It is expressed in ml/minute.

$$C_{H_2O} = V - C_{osm} = V - \frac{(U_{osm} \times V)}{(P_{osm})}$$

It is calculated as the difference between urine flow rate and osmolar clearance. When C_{H_2O} is positive, excess water is being excreted by kidney. When C_{H_2O} is negative excess solutes are being removed from the blood by kidneys.

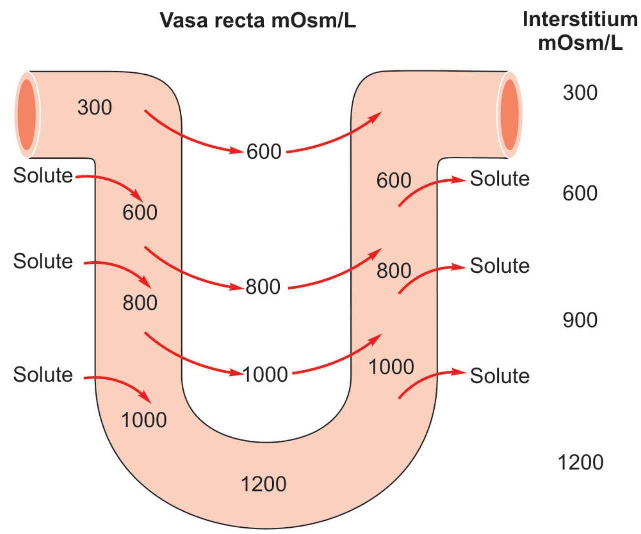

Fig. 8.26: Operation of the vasa recta as counter exchanger in the kidney

Disorders of Urine Concentrating Ability

It can be due to:
1. Inappropriate secretion of ADH as in central diabetes insipidus, cause being congenital infections or head injuries.
2. Impairment of countercurrent mechanisms.
3. Inability of DT, CD to respond to ADH: In conditions like nephrogenic diabetes insipidus and in usage of various drugs like lithium and tetracyclines, even if ADH is produced in normal amounts, abnormality of kidneys makes them to fail to respond to ADH.