SUBSTANCES SECRETED IN DIFFERENT SEGMENTS OF RENAL TUBULES.

- Potassium is secreted actively by sodium potassium pump in proximal and distal convoluted tubules and collecting ducts.
- Ammonia is secreted in the proximal convoluted tubule.
- Hydrogen ions are secreted in the proximal and distal convoluted tubules. Maximum hydrogen ion secretion occurs in proximal tubule.
- URINE IS FORMED IN THE NEPHRON BY THE PROCESSES OF GLOMERULAR FILTRATION,SELECTIVE REABSORPTION AND TUBULAR SECRETION.

CONCENTRATION OF URINE

- Osmolarity of glomerular filtrate is same as that of plasma and it is 300mOsm/L.
- Normally urine is concentrated and its osmolarity is four times more then that of plasma for example 1200mOsm/L.

Osmolarity of urine depends upon two factors

1. Water content in the body.
2. Antidiuretic hormone.

FORMATION OF CONCENTRATED URINE

- When the water content in the body decreases, kidney excretes concentrated urine.

It involves two important processes

- Medullary gradient which is developed and maintained by countercurrent system.
- Secretion of ADH.

- **Counter-Current Mechanisms**
- The mechanisms shown here are traditionally called the 'counter-current multiplier' and the 'counter-current exchanger'. The first takes place in the region of the nephron called Henle's loop; the second occurs in a region of the peritubular capillary bed called the 'vasa recta'. Both are involved in establishing an osmotic gradient throughout this region.

Counter-Currents

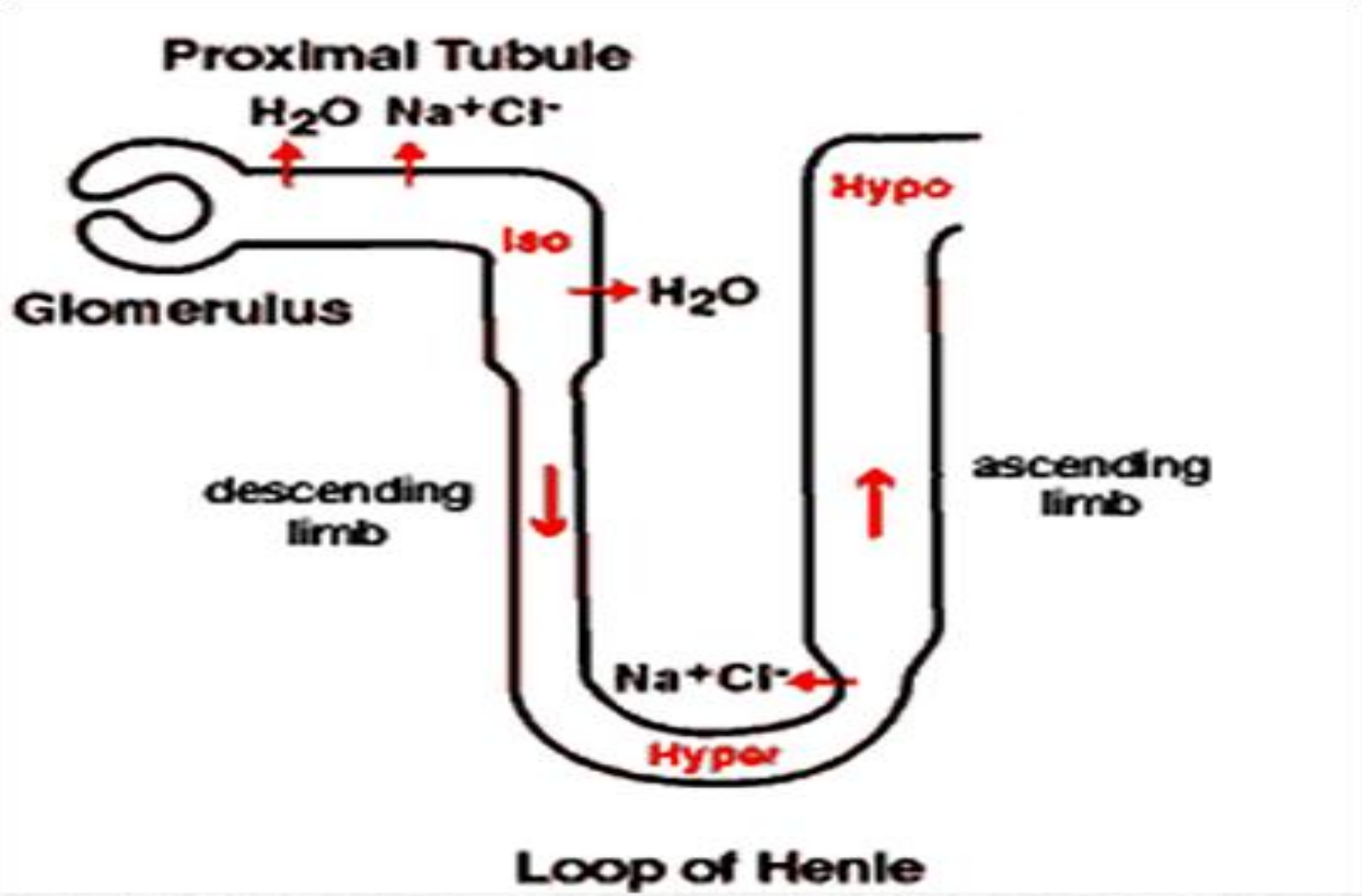
- Counter-currents exist when fluids flow in opposite directions in parallel and adjacent tubes. The two limbs of Henle's loop are a counter-current. The two limbs of the vasa recta are also a counter-current. It is apparent that these two sets of tubes are parallel and adjacent. Not apprent in the mind map is the fact that the descending limb of Henle is also counter-current with the ascending limb of the vasa recta; the same is true of the ascending limb of Henle and the descending vasa recta.

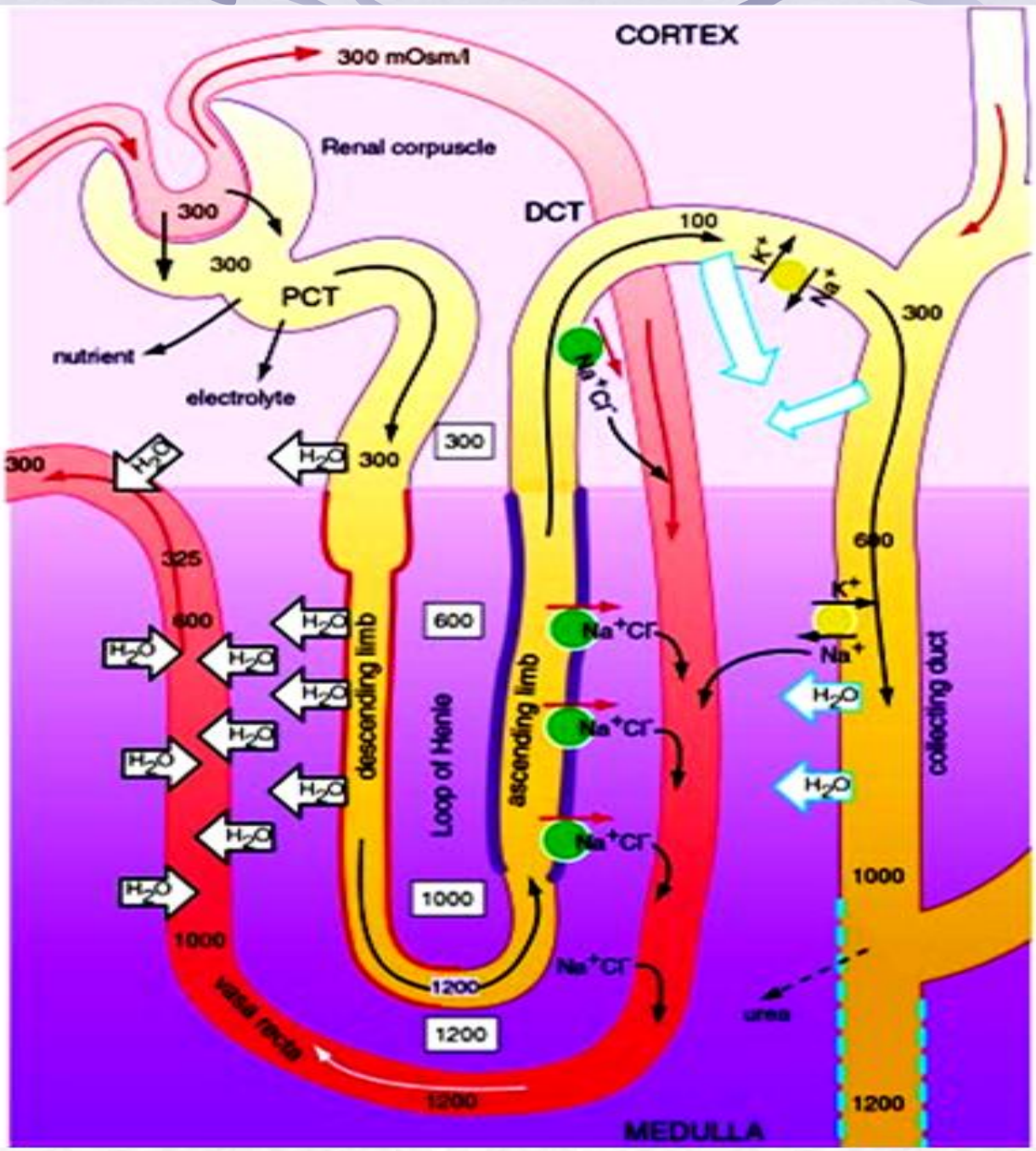
- The term derives from the form and function of the loop of Henle, which consists of two parallel limbs of renal tubules running in opposite directions, separated by the interstital space of the renal medulla.
- The descending limb of the loop of Henle is permeable to water but impermeable to solutes, due to the presence of aquaporin 1 in its tubular wall. Thus water moves across the tubular wall into the medullary space, making the urine hypertonic

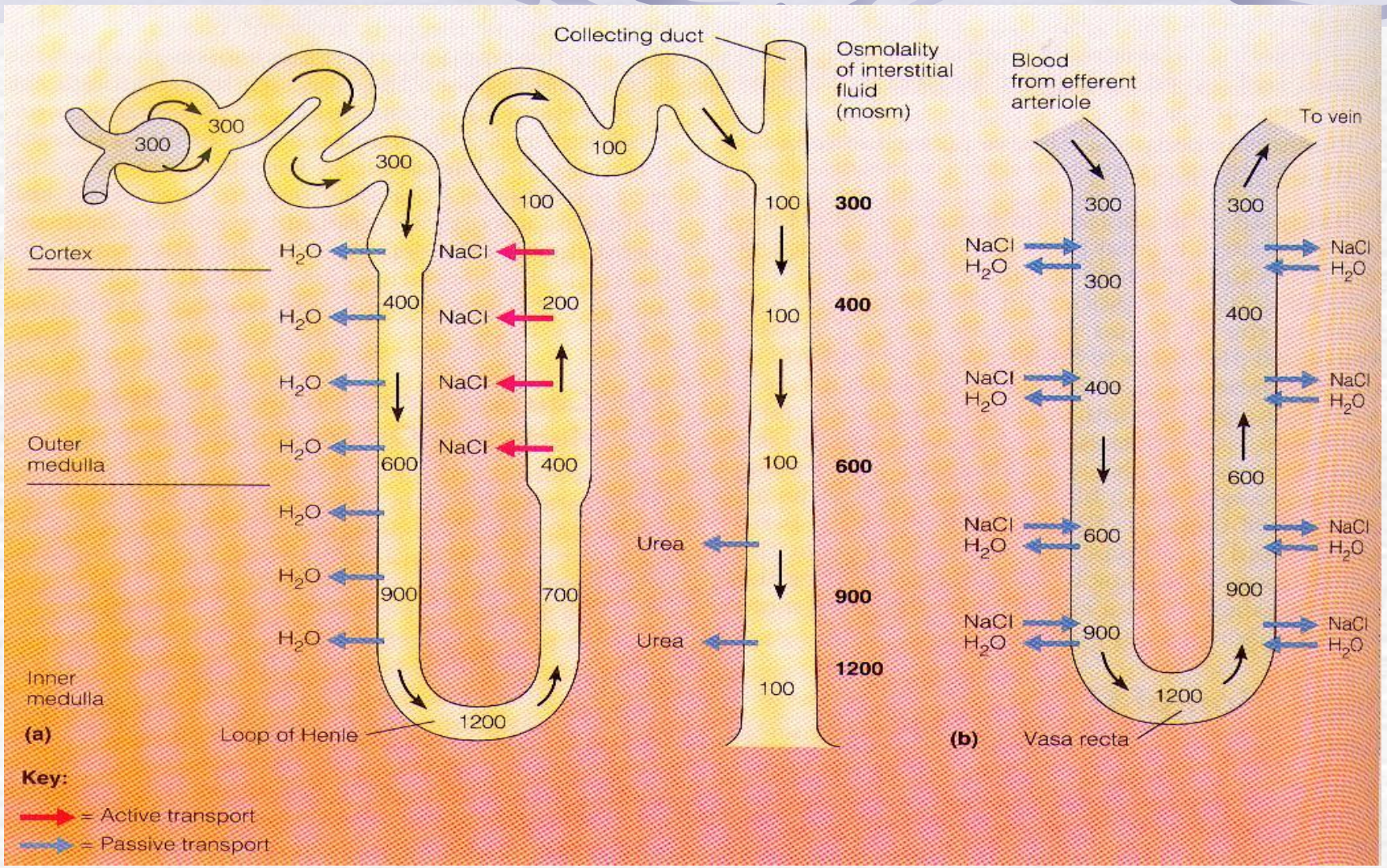
- The ascending limb is impermeable to water (because of a lack of aquaporin, a common transporter protein for water channels in all cells except the walls of the ascending limb of the loop of Henle) but permeable to solutes, but here Na^+, Cl^-, and K^+ are actively transported into the medullary space, making the filtrate hypotonic (with a higher water potential). This constitutes the *single effect* of the countercurrent multiplication process.
- Active transport of these ions from the thick ascending limb creates an osmotic pressure drawing water from the descending limb into the hyperosmolar medullary space, making the filtrate hypertonic (with a lower water potential).
- The countercurrent flow within the descending and ascending limb thus increases, or *multiplies* the osmotic gradient between tubular fluid and interstitial space.

- **Counter-Current Exchanger**

At any level the solute concentration in the descending limb will be less than in the ascending limb! But, because both limbs are freely permeable, **sodium chloride will diffuse from the ascending into the descending**while **water will diffuse from the descending to the ascending**…see *block arrows*. When equilibrium is reached both limbs will, once again, have the same concentration of water and solutes. Water is exchanged for sodium chloride...the counter-current exchange mechanism.


Proximal Tubule
H_2O Na^+Cl^-
Glomerulus
Iso
H_2O
Hypo
descending limb
ascending limb
Na^+Cl^-
Hyper
Loop of Henle


CORTEX
300 mOsm/l
Renal corpuscle
300
300
PCT
nutrient
electrolyte
DCT
100
300
300
300
300
325
600
600
600
descending limb
Loop of Henle
ascending limb
1000
1000
1200
1200
1200
vasa recta
collecting duct
1000
1200
urea
MEDULLA


Collecting duct
Osmolality of interstitial fluid (mosm)
Blood from efferent arteriole
To vein
300
300
300
100
100
100
300
Cortex
H_2O
NaCl
400
200
400
100
H_2O
NaCl
H_2O
NaCl
Outer medulla
H_2O
NaCl
600
400
600
100
H_2O
Urea
H_2O
900
700
900
100
H_2O
Urea
Inner medulla
1200
100
1200
(a)
Loop of Henle
(b)
Vasa recta
Key:
= Active transport
= Passive transport

MEDULLARY GRADIENT(GRADUAL INCREASE IN THE OSMOLARITY OF THE MEDULLARY INTERSTITIAL FLUID)

- The osmolarity of the interstitial fluid in the renal cortex,Adrenal medulla near the cortex is similar to that of plasma and it is 300mOsm/L.
- The osmolarity of the interstitisl fluid gradually increases and reaches the maximum at the inner most part of medulla near the sinus.Here it is1200mOsm/L.

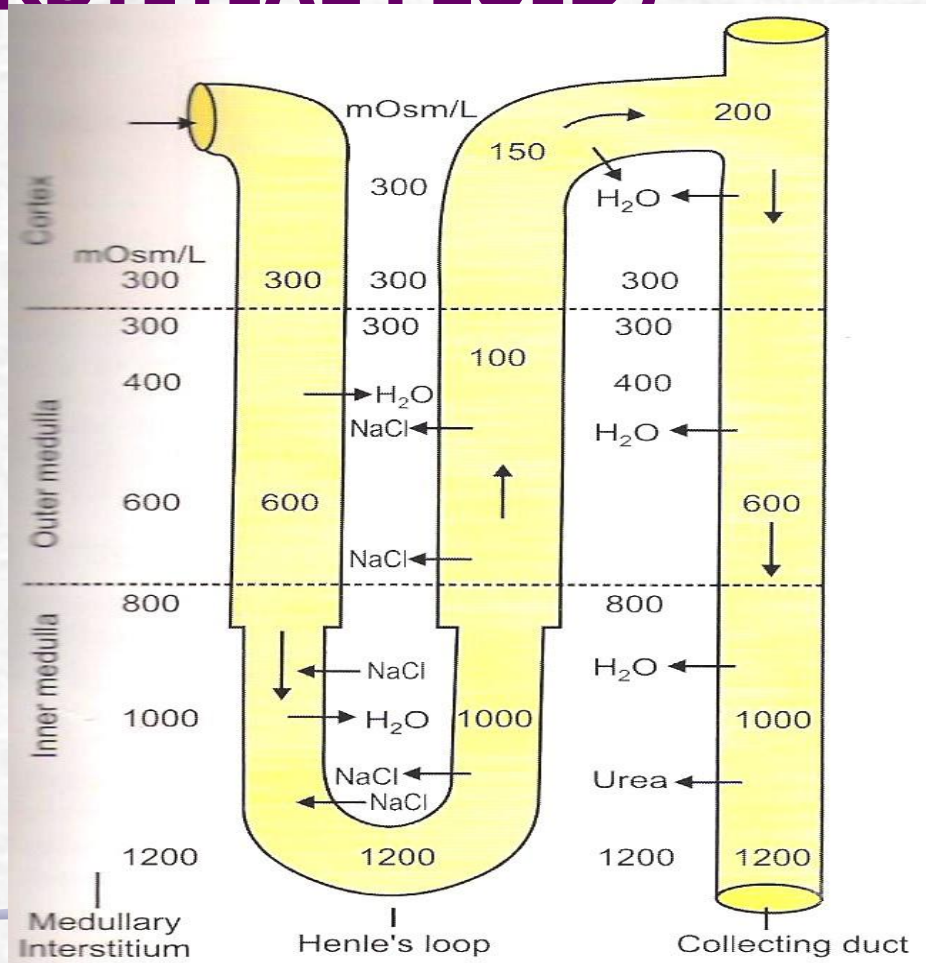
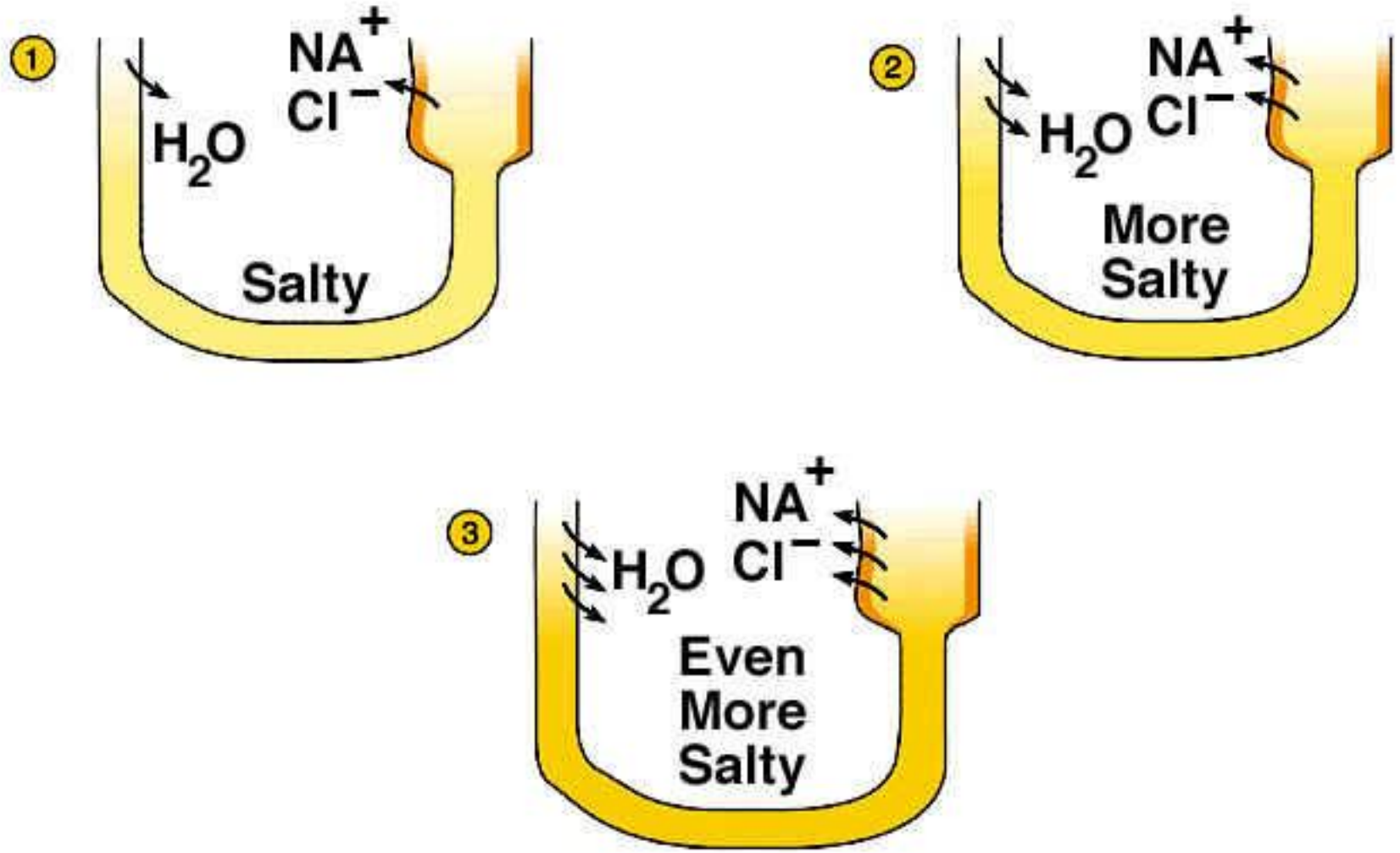


FIGURE 53-1: Countercurrent multiplier. Numerical indicate osmolarity (mOsm/L)

Countercurrent Mechanism



COUNTER CURRENT MECHANISM

- Countercurrent system is a system of U SHAPED tubules(tubes)in which, the flow of fluid is in opposite direction in different limbs of the U SHAPED tubules
- In kidneys the structures which form the Counter Current System are:

1. Loop of henle(counter current multiplier)
2. Vasa recta(counter current exchanger)

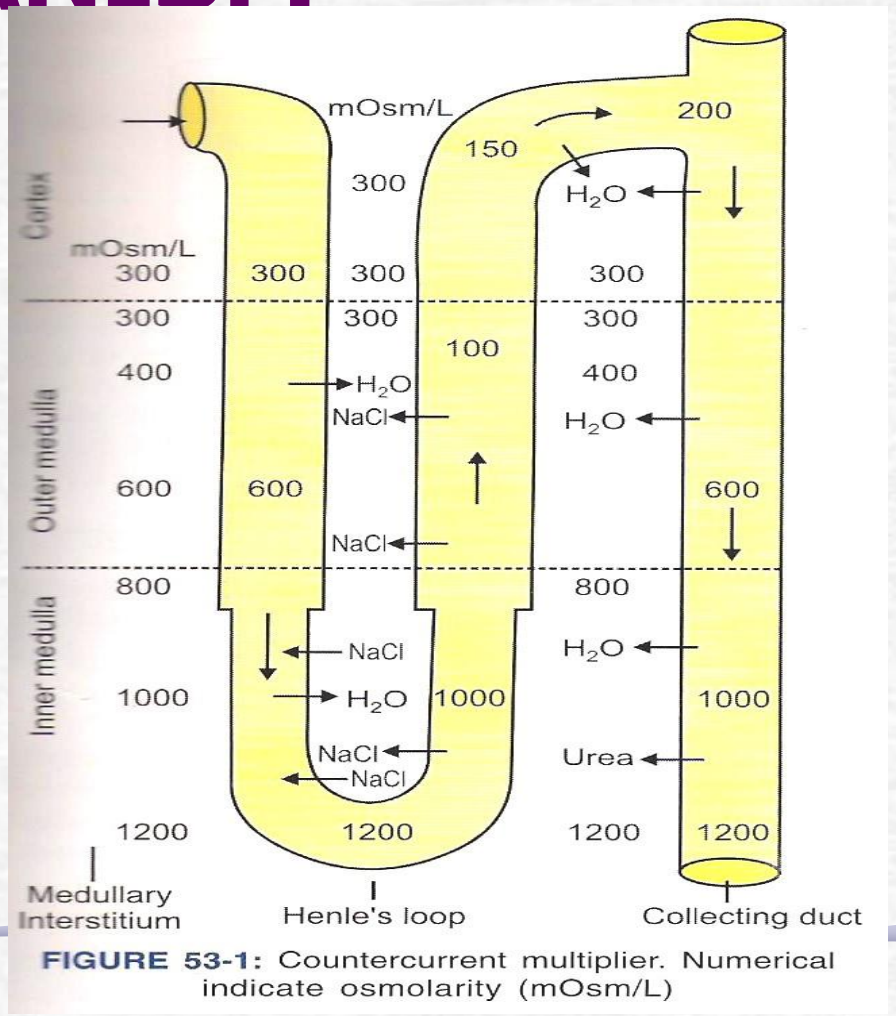


FIGURE 53-1: Countercurrent multiplier. Numerical indicate osmolarity (mOsm/L)

COUNTER CURRENT MULTIPLIER(ROLE OF LOOP OF HENLE IN THE DEVELOPMENT OF MEDULLARY GRADIENT)

- Loop of Henle of Juxtraglomerullary nephrons(long and extends up to the deeper parts of medulla) plays a major role as CC Multiplier rather then that of cortical nephrons.

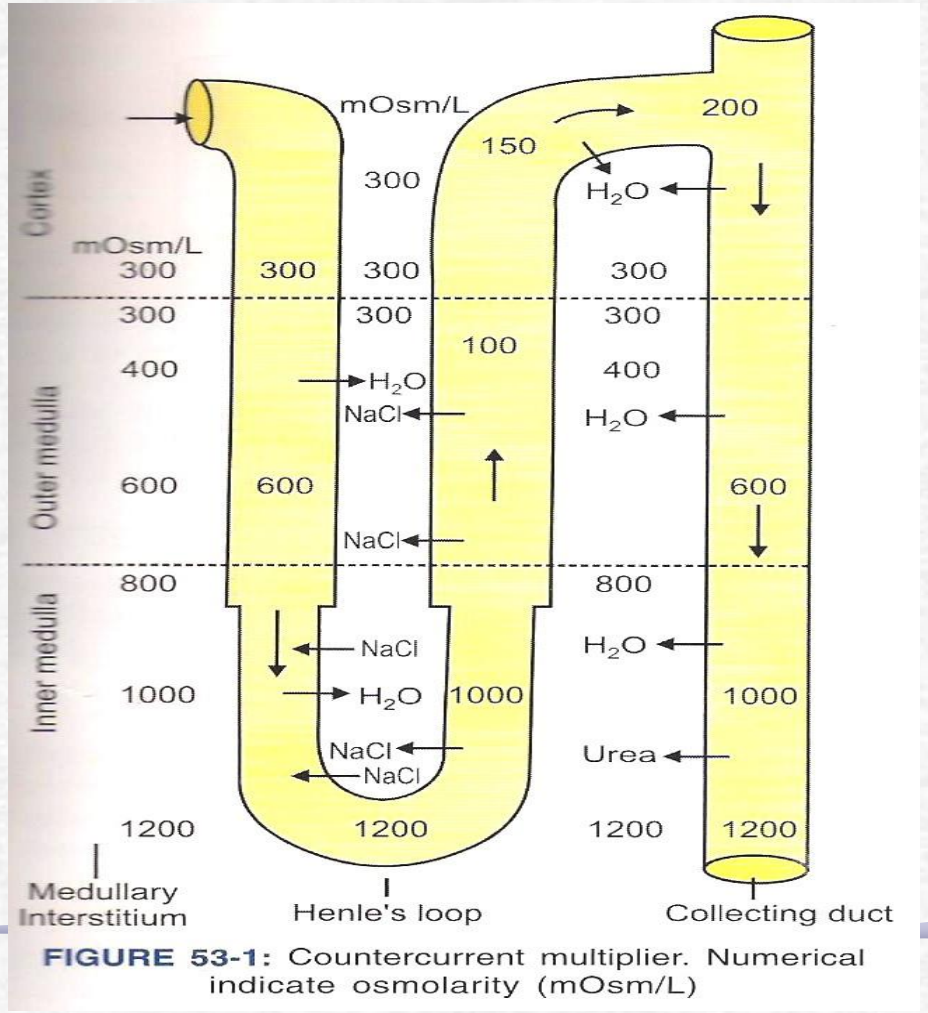


FIGURE 53-1: Countercurrent multiplier. Numerical indicate osmolarity (mOsm/L)

CC MULTIPLIER (ROLE OF LOOP OF HENLE IN DEVELOPMENT OF MEDULLARY GRADIENT

- The major cause for the hyperosmolarity of medullary interstitial fluid is the active reabsorption of Na,Cl and other solutes from ascending limb of Henle loop into the medullary interstitium.These solutes accumulates in the medullary interstitium and increase the osmolarity.

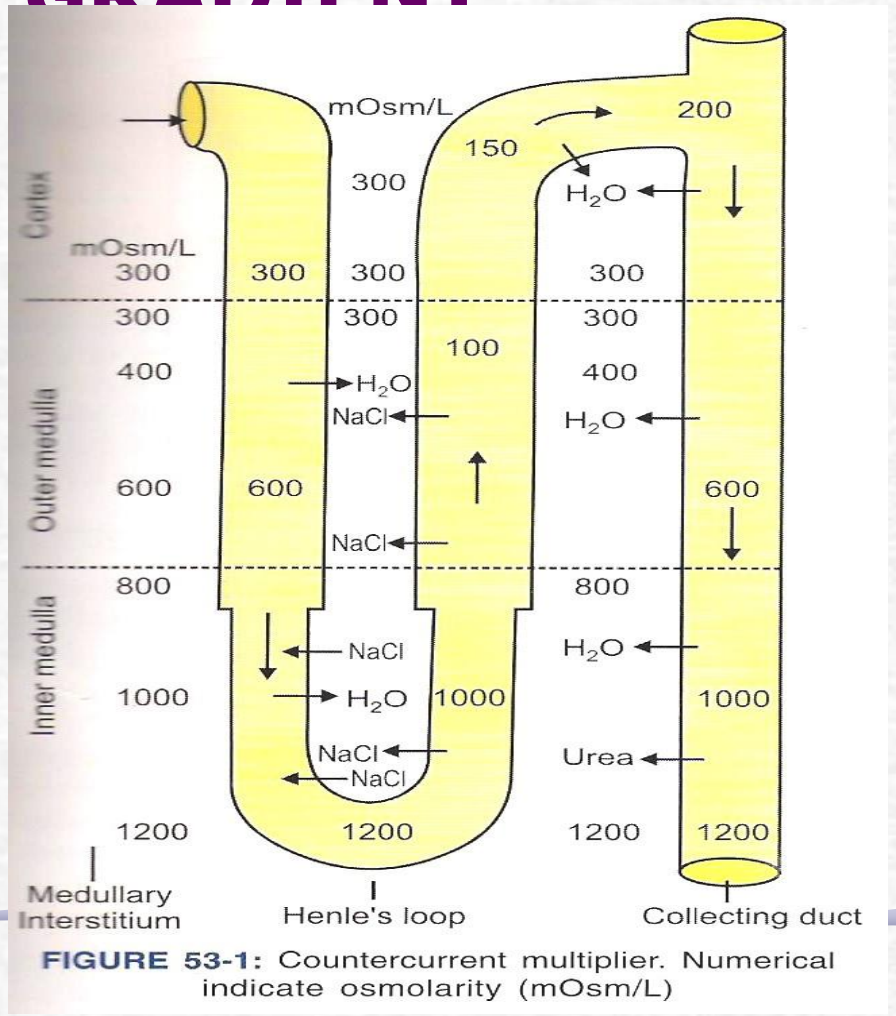
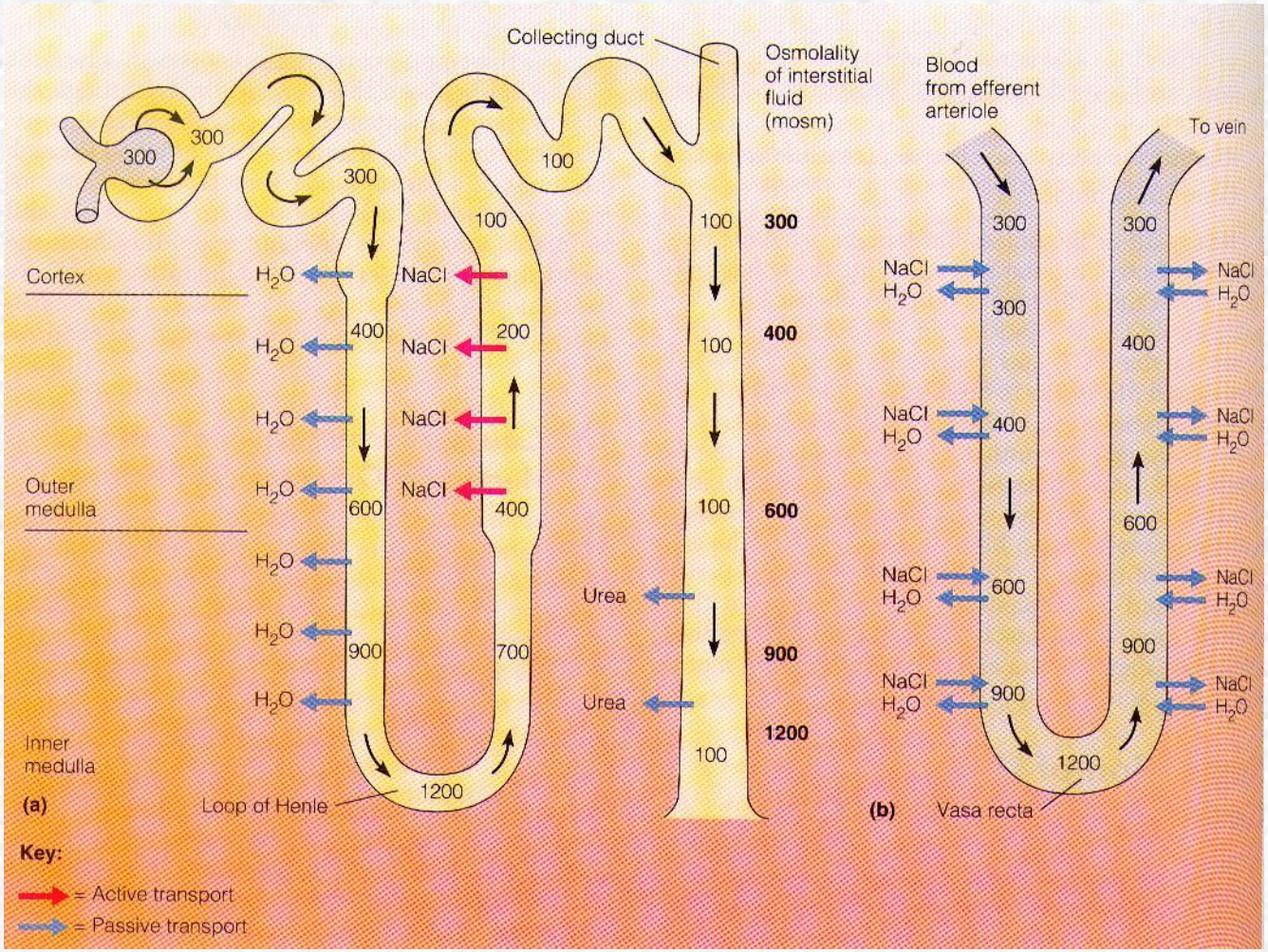


FIGURE 53-1: Countercurrent multiplier. Numerical indicate osmolarity (mOsm/L)


Collecting duct
Osmolality of interstitial fluid (mosm)
Blood from efferent arteriole
To vein
300
300
300
100
100
100
300
Cortex
H_2O
NaCl
400
200
100
400
Outer medulla
600
400
100
600
Urea
900
700
100
900
Urea
1200
100
1200
Inner medulla
(a)
Loop of Henle
(b)
Vasa recta
Key:
= Active transport
= Passive transport

CC MULTIPLIER(ROLE OF LOOP OF HENLE IN THE DEVELOPMENT OF MED GRADIENT

- Due to the concentration gradient,the Na and Cl ions diffuse from medullary interstitium into the descending limb of Henle loop and reach the ascending limb again via the hair pin bend.
- Thus the Na and Cl ions repeatedly recirculated between the descending limb and ascending limb of Henle loop through medullary interstitial fluid leaving a small portion to be excreted in the urine.This helps to increase the osmolarity of the medullary interstitial fluid and development of medullary gradient.

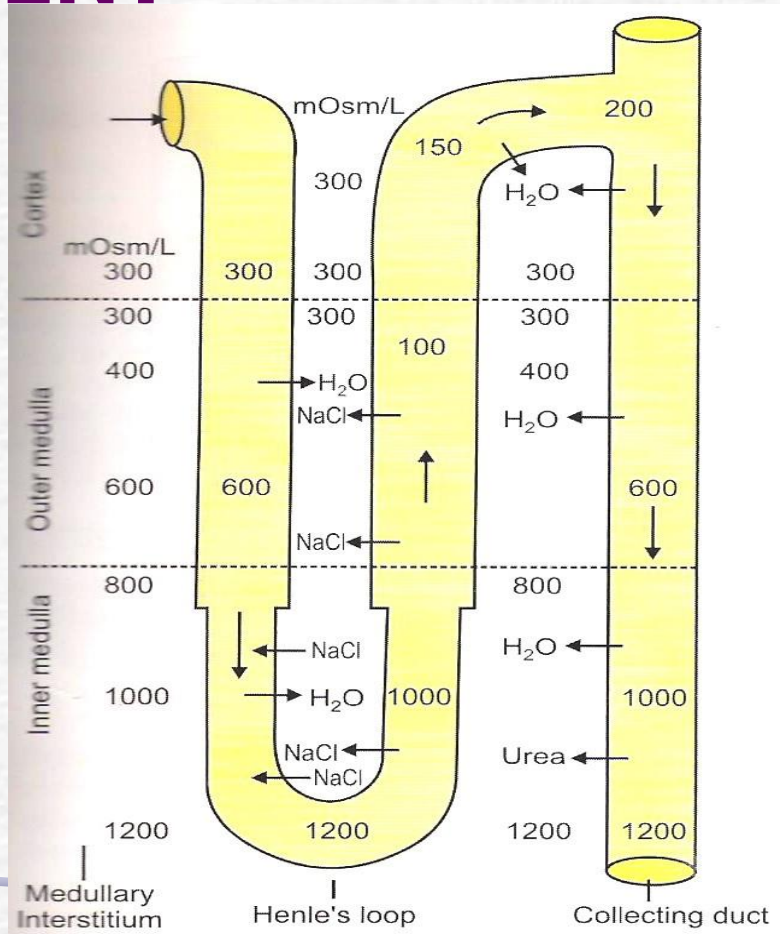


FIGURE 53-1: Countercurrent multiplier. Numerical indicate osmolarity (mOsm/L)

CC MULTIPLIER(ROLE OF LOOP OF HENLE IN DEVELOPMENT OF MEDULLARY GRADIENT)

- Apart from this there is regular addition of more Na and Cl ions by constant filtration process.Henle loop retains these new ions also in the medullary interstitium.Hence It is called counter current multiplier.

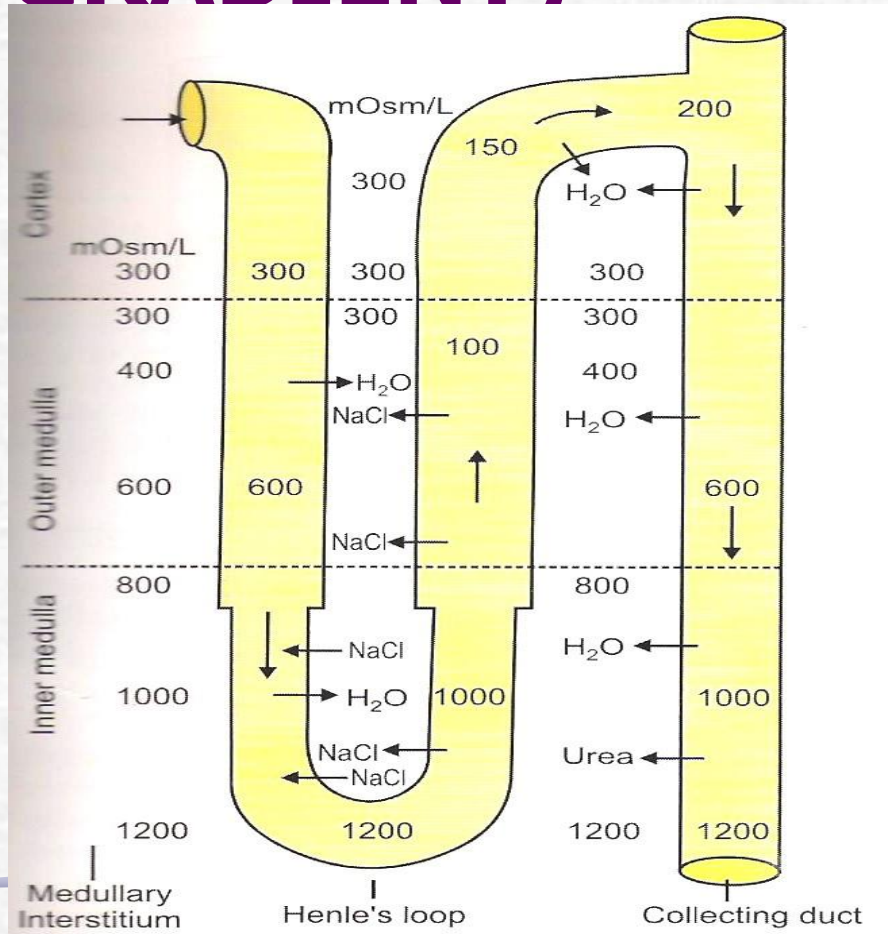


FIGURE 53-1: Countercurrent multiplier. Numerical indicate osmolarity (mOsm/L)

OTHER FACTORS RESPONSIBLE FOR HYPEROSMOLARITY OF MEDULLARY INTERSTITIAL FLUID

- Reabsorption of Na from medullary part of collecting duct into the medullary interstitium which adds to the osmolarity.
- Urea recirculation:urea is completely filtered in the glomeruli.

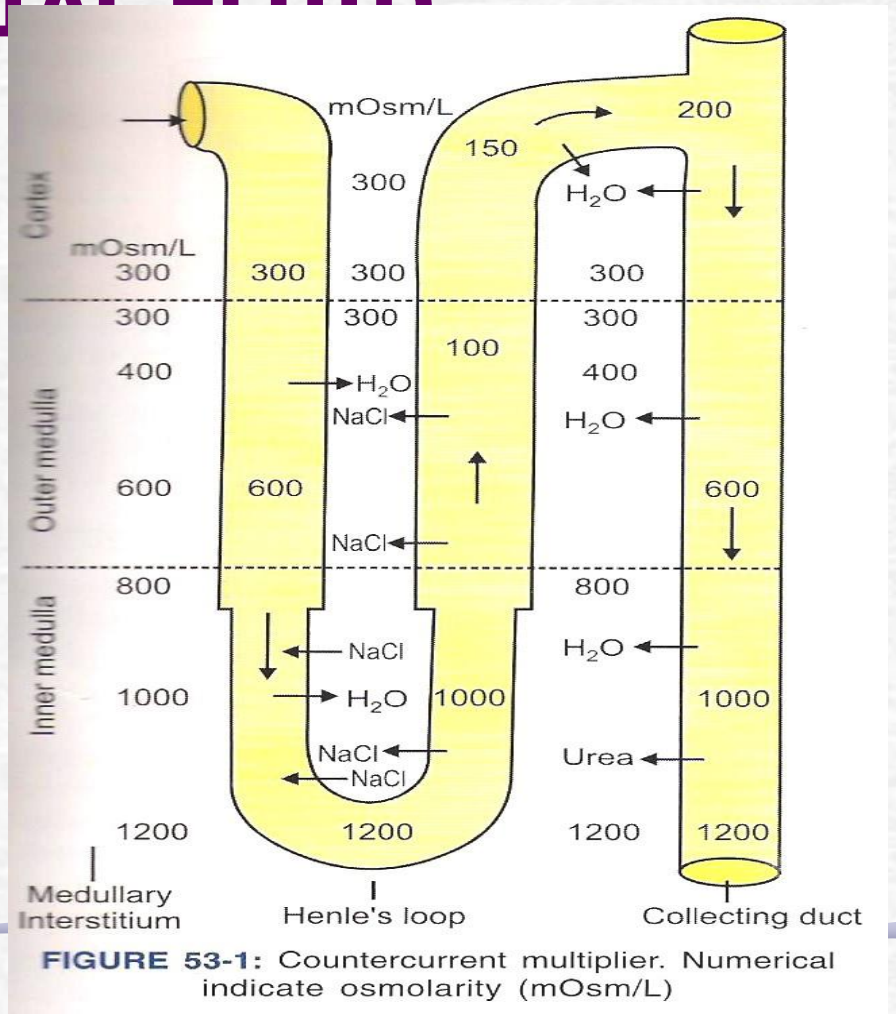


FIGURE 53-1: Countercurrent multiplier. Numerical indicate osmolarity (mOsm/L)

CC MULTIPLIER(ROLE OF LOOP OF HENLE IN THE DEV OF MEDULLARY GRADIENT)

Urea is completely filtered in the glomeruli.But it is not reabsorbed from the renal tubule.So,all the molecules of urea reach the collecting duct and the conc of urea increases in the collecting duct.Now due to conc gradient,ure diffuses from collecing duct into the inner med interstitium.So the osmolalility increases in the inner medulla.

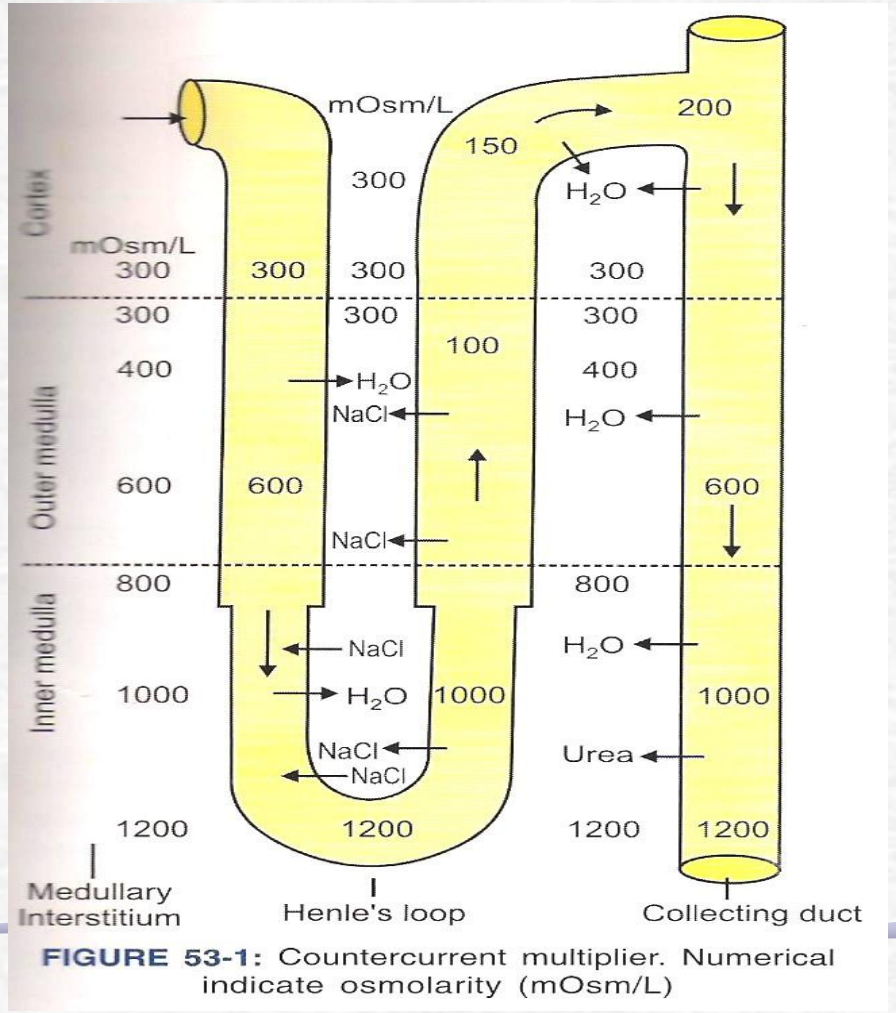


FIGURE 53-1: Countercurrent multiplier. Numerical indicate osmolarity (mOsm/L)

CC MULTIPLIER(ROLE OF LOOP OF HENLE IN THE DEV OF MEDULLARY GRADIENT)

Due to the continuous diffusion, the conc of urea increases in the med interstitium.Again by conc gradient urea enters the ascending limb.From here, it passes through distal convoluted tubule and reaches the collecting duct.From here, urea enters the medullary interstitium and the cycle repeats.By this way urea recirculates, and helps to maintain hyperosmolarity in the inner medullary interstitium.

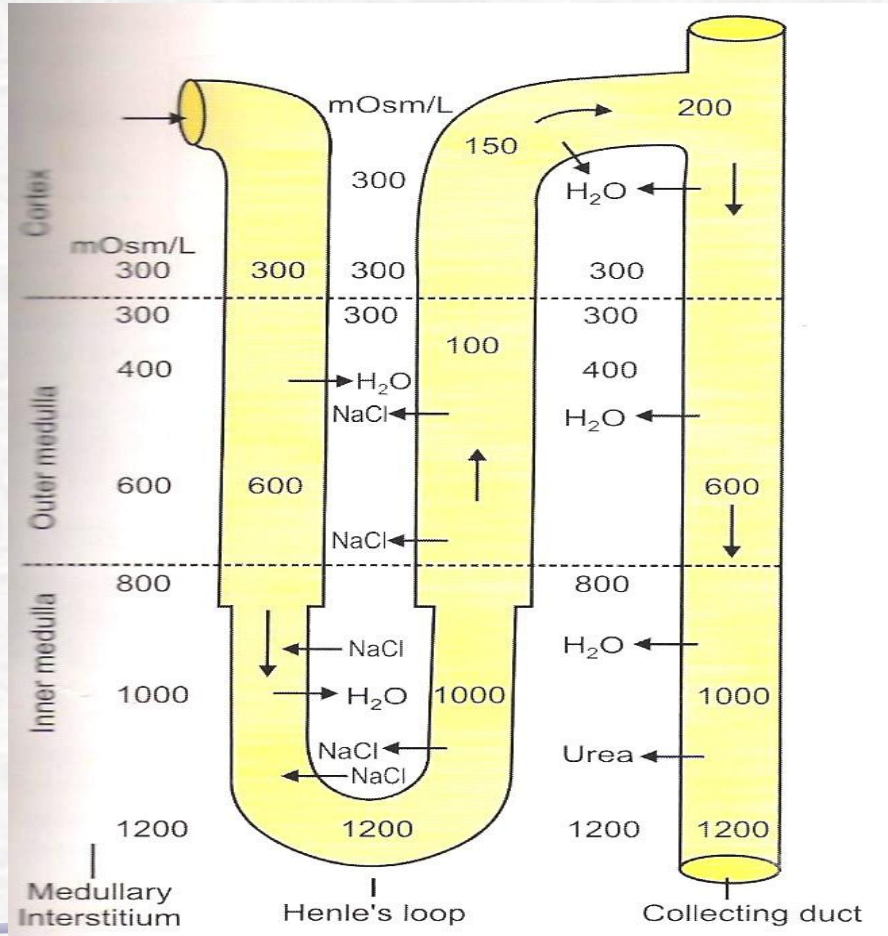
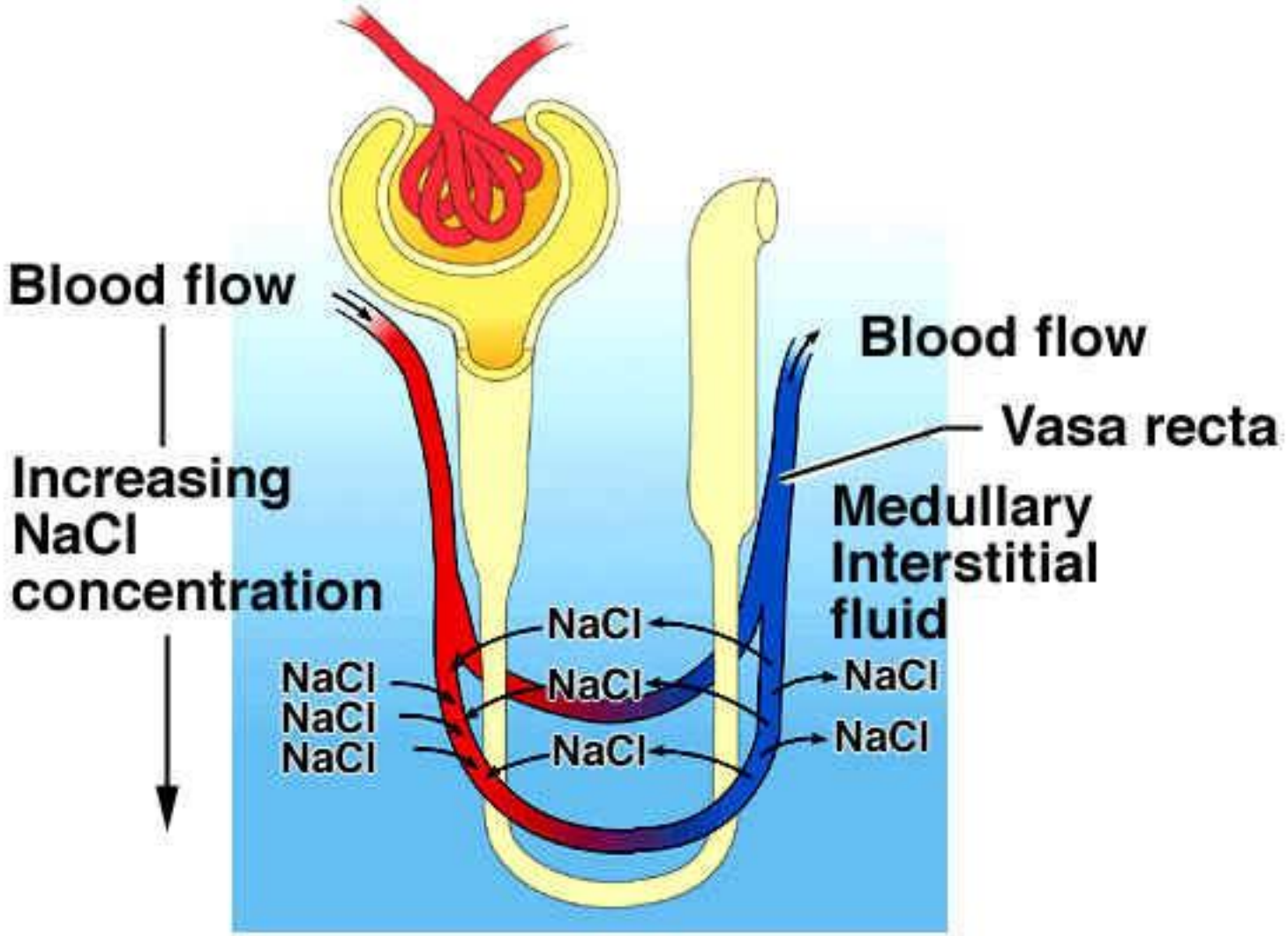


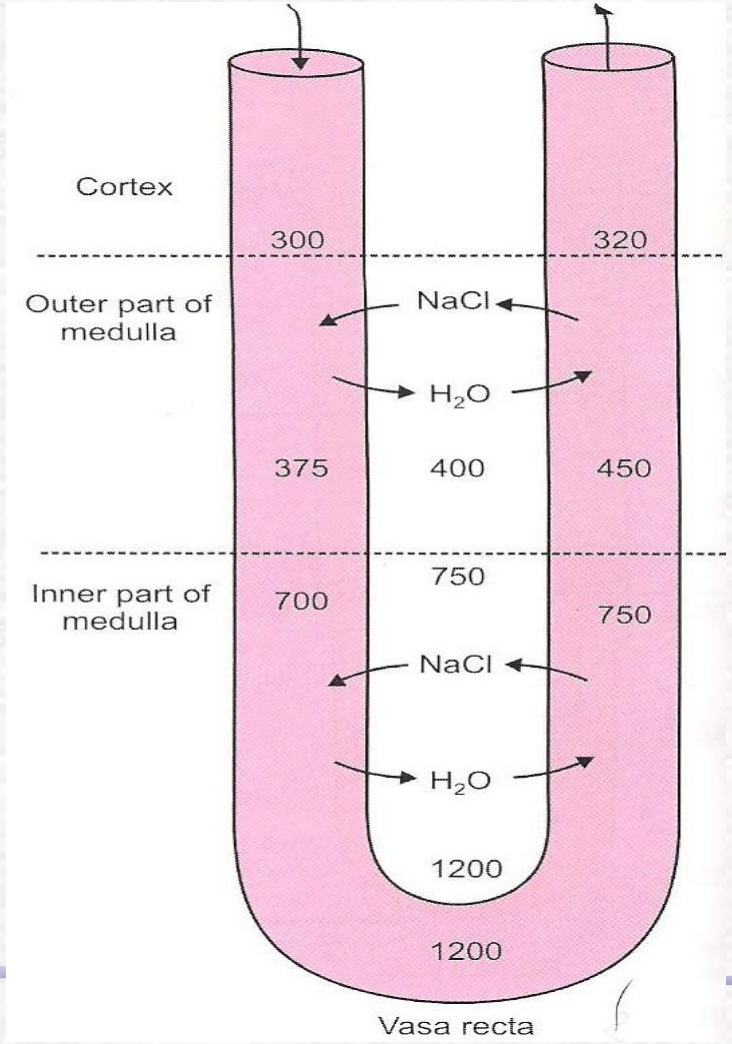
FIGURE 53-1: Countercurrent multiplier. Numerical indicate osmolarity (mOsm/L)

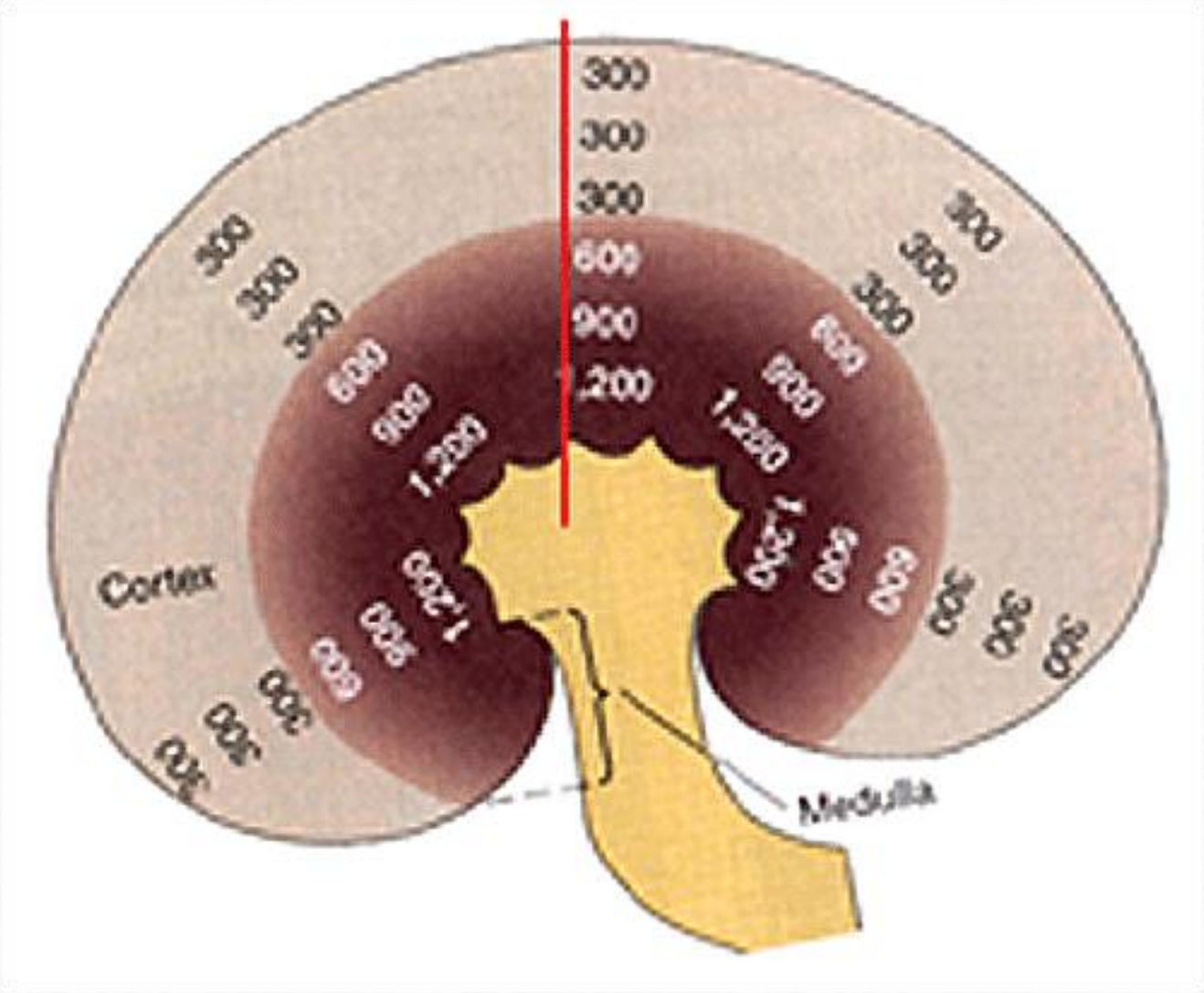
Countercurrent Mechanism—Vasa Recta



COUNTRCURRENT EXCHANGER

- Vasa recta functions as countercurrent exchanger. It is responsible for the **maintenance of the hyperosmolarity** of the medullary interstitial fluid and the **medullary gradient development** by countrcurrent multiplier.



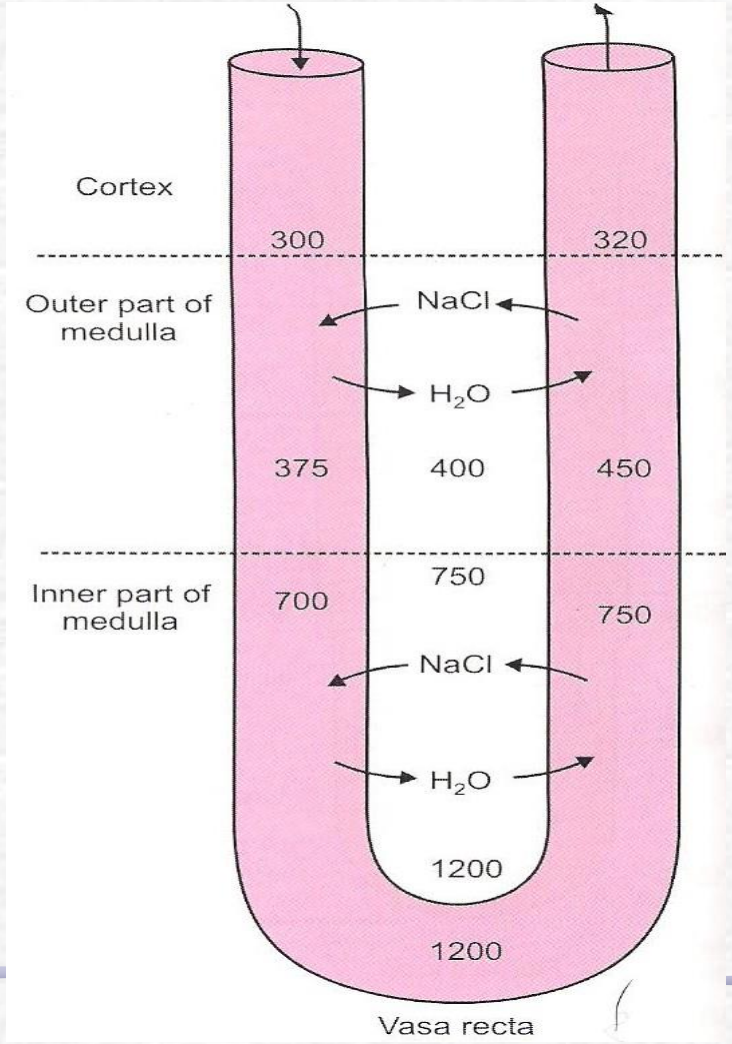

300
300
300
600
900
1,200
Cortex
Medulla

TERMINOLOGY RELATING TO COUNTER CURRENTMULTIPLIER SYSTEM

- **HYPOOSMOTIC** means having total solute concentration less then that of normal extracellular fluid
- **HYPEROSMOTIC** means having total solute concentration more then that of normal extracellular fluid.
- **ISO OSMOTIC** means having the same total solute concentration as extracellular fluid.

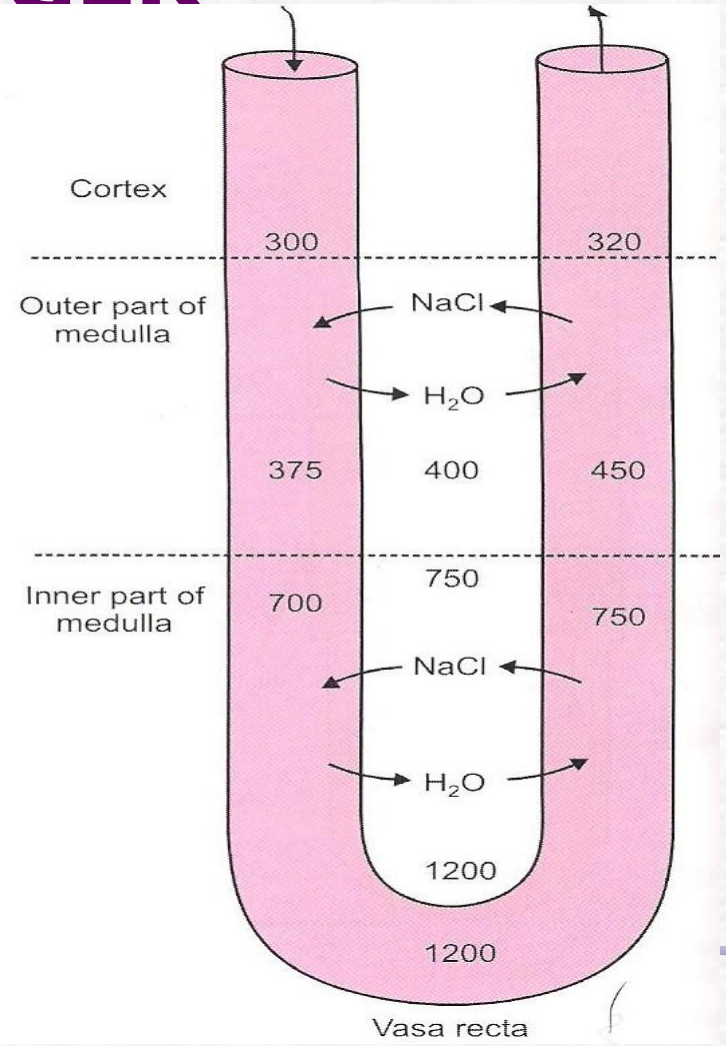
COUNTER CURRENT EXCHANGER

- Vasa recta acts like CC exchanger because of its position.It runs parallel to loop of Henle.Its descending limb runs along the ascending limb of Henle loop and its ascending limb runs along with descending limb of Henle loop.



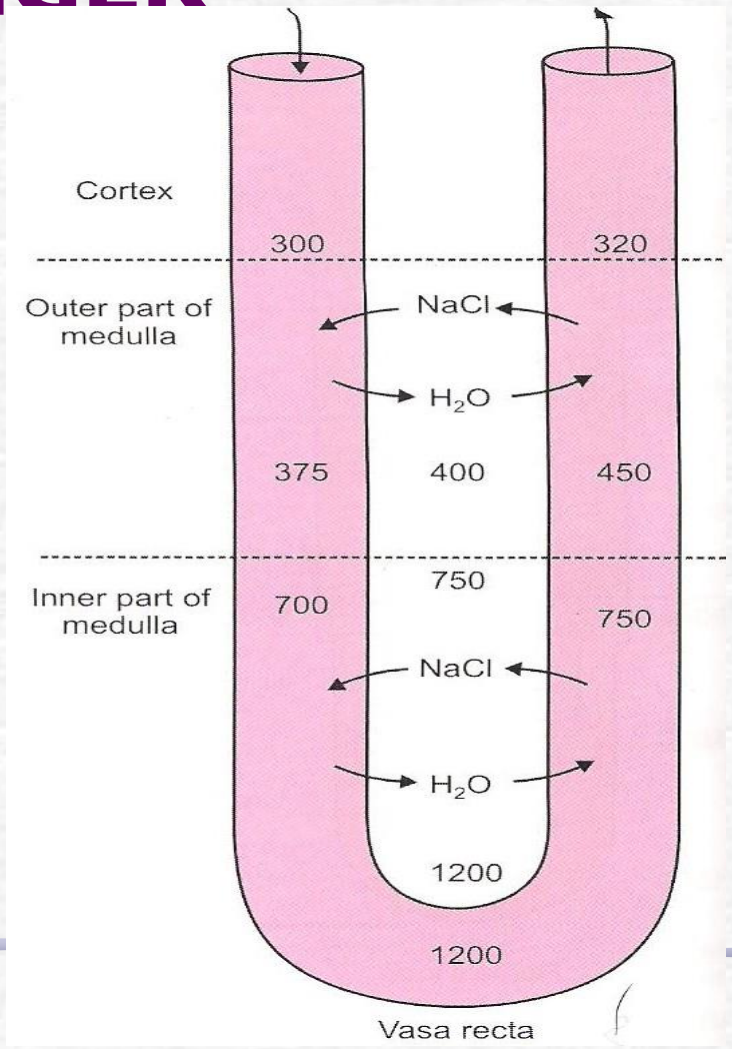
COUNTER CURRENT EXCHANGER

- The Nacl reabsorbed from **ascending limb** of Henle loop enters the **med interstitium**.From here it enters the **descending limb of vasa recta**.Water diffuses from descending limb of vasa recta into medullary interstitium.



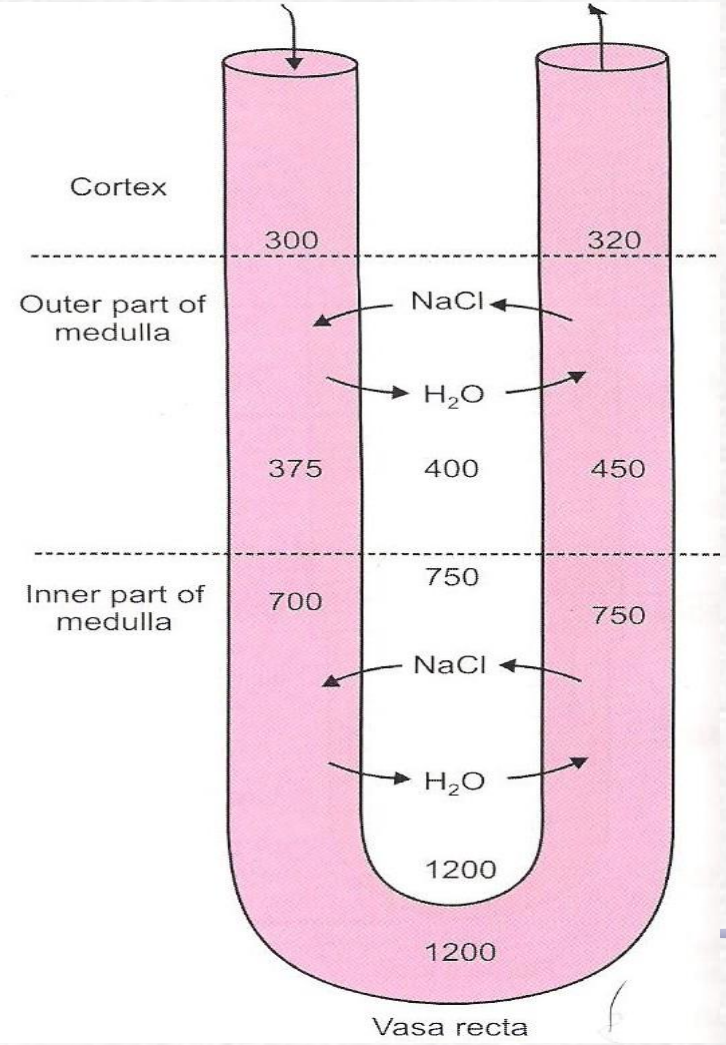
COUNTER CURRENT EXCHANGER

- The blood flows very slowly through vasa recta.So large quantity of Nacl accumulates in the decending limb of vasa recta and flows slowly towards ascending limb.By the time the blood reaches the ascending limb of vasa recta,the concentration of Nacl increases very much.This causes diffusion of Nacl into medullary interstitium.Water from medullary interstitium enters the ascending limb of vasa recta.And the cycle is repeated.



COUNTER CURRENT EXCHANGER

- When the blood passes through the ascending limb of vasa recta,Nacl diffuses out of blood and enters the interstitial fluid of medulla and,water diffuses into the blood.Thus vasa recta retains Nacl in the medullary interstitium and removes water from it.So the hyperosmolarity of the medullary interstitium is maintained.



COUNTERCURRENT EXCHANGER

- Recycling of urea also occurs by vasa recta from medullary interstitium,along with Nacl,urea also enters the descending limb of vasa recta.When blood passes through the ascending limb of vasa recta,urea diffuses back into medullary interstitium along with Nacl.Thus,Nacl and urea are exchanged for water between the ascending and descending limbs of vasarecta,hence the system is called counter current exchanger.

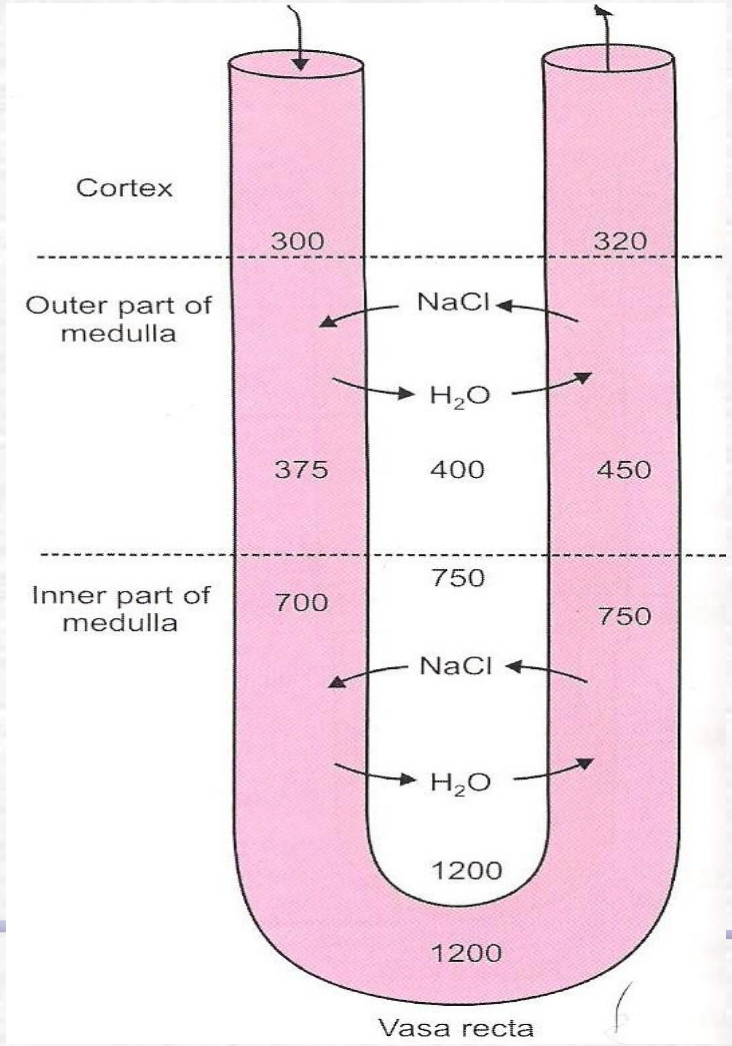
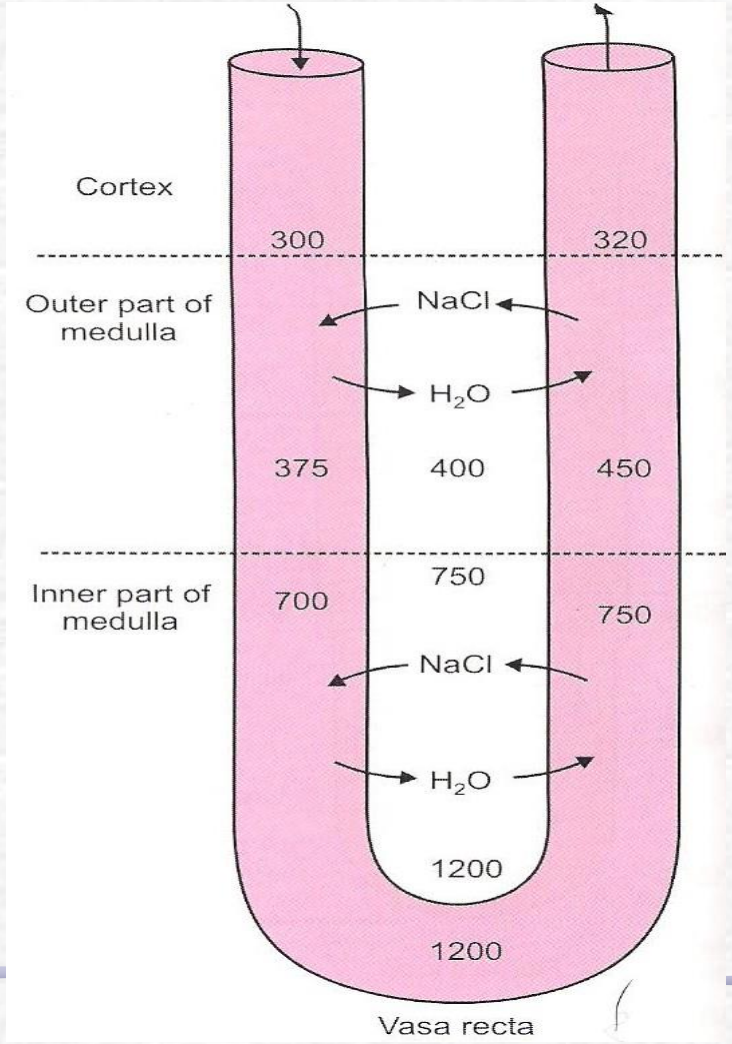


TABLE 20.3 Role of ADH in Regulating Urine Concentration and Volume

1. Concentration of water in the blood decreases.
2. Increase in the osmotic pressure of body fluids stimulates osmoreceptors in the hypothalamus.
3. Hypothalamus signals the posterior pituitary gland to release ADH.
4. Blood carries ADH to the kidneys.
5. ADH causes the distal convoluted tubules and collecting ducts to increase water reabsorption by osmosis.
6. Urine becomes more concentrated, and urine volume decreases.

ROLE OF ADH

- The final conc of urine is achieved by ADH.
- The distal convoluted tubule and the collect duct are not permeable to water.
- In the presence of ADH,distal conv tubule and collecting duct become permeable to water resulting in water reabsorption.



SUMMARY OF URINE CONCENTRATION(BOWMANS CAPSULE)

- The glomerular filtrate collected at the bowmans capsule has the same osmolarity of plasma as it contains all the subatances of plasma except proteins.The osmolarity of the filterate at the bowmans capsule is 300mOSM/L

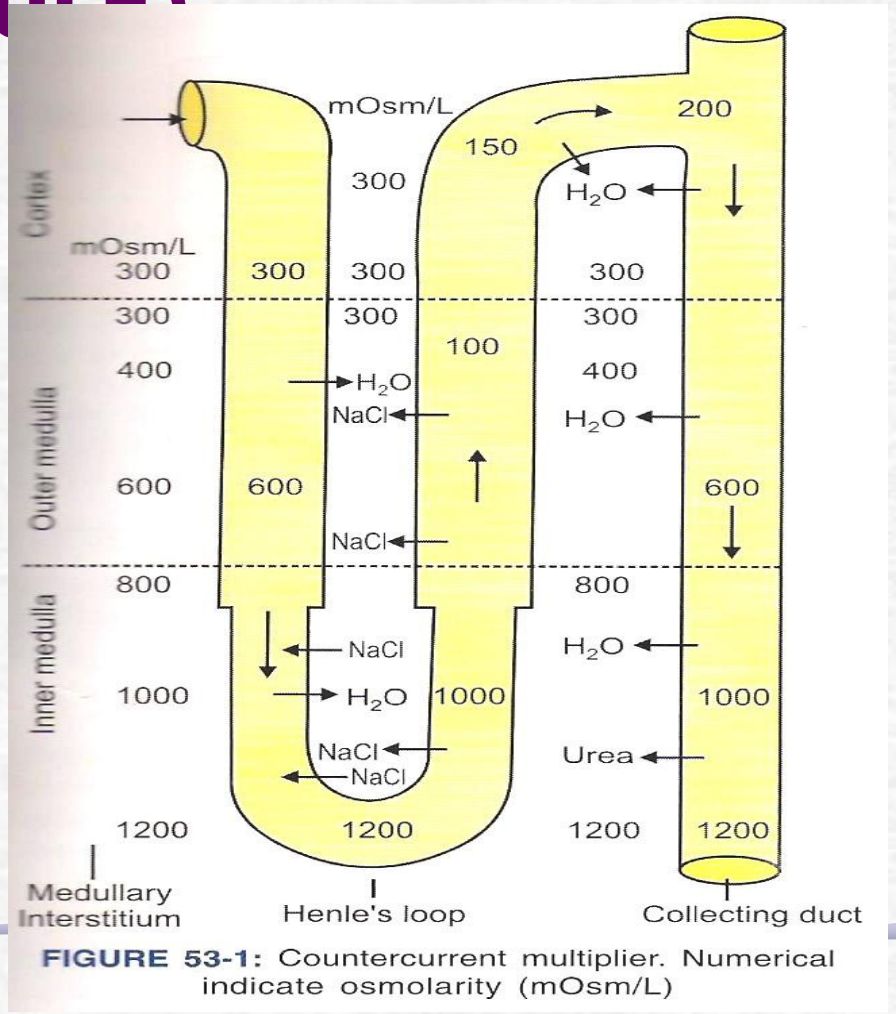


FIGURE 53-1: Countercurrent multiplier. Numerical indicate osmolarity (mOsm/L)

SUMMARY OF URINE CONC(PROXIMAL CONVOLUTED TUBULE)

When the filtrate flows through proximal conv tubule, there is active reabsorption of Na and Cl followed by obligatory reabsorption of H2O.So osmolarity,of the fluid remains the same as in the case of Bowmans capsule I,e 300mOsm/L

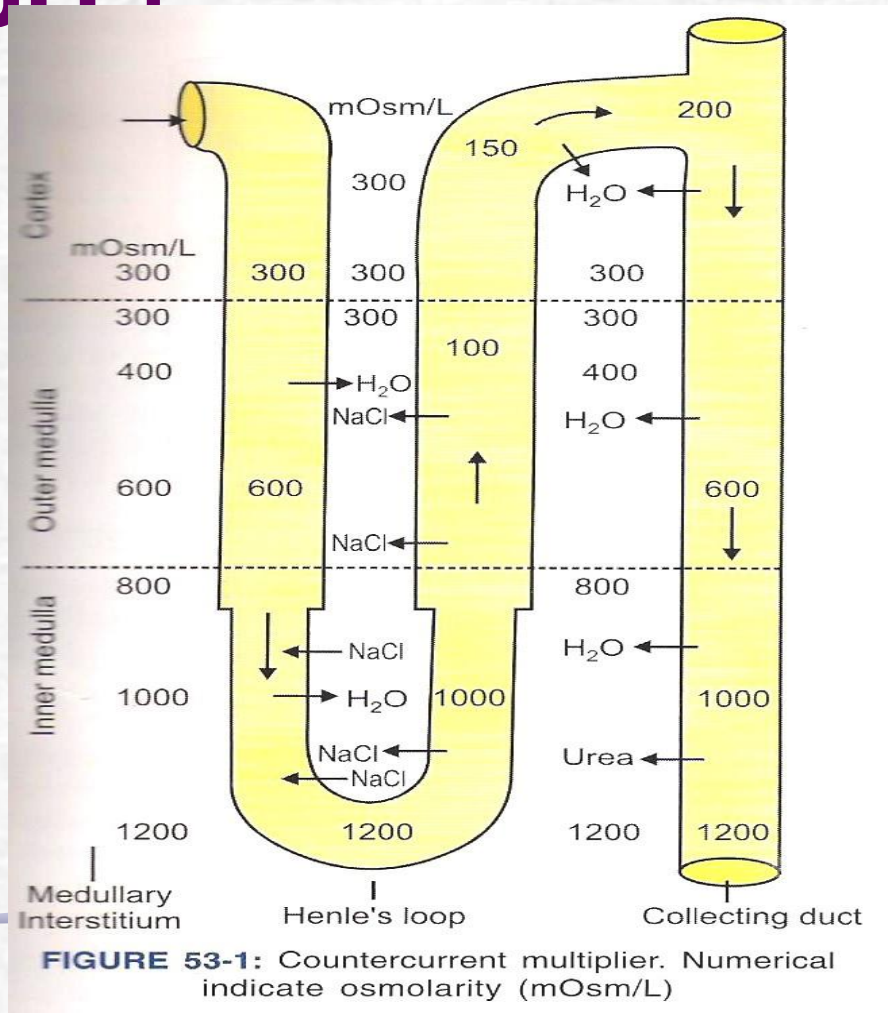


FIGURE 53-1: Countercurrent multiplier. Numerical indicate osmolarity (mOsm/L)

SUMMARY OF URINE CONC(THICK DESCENDING SEGMENT)

1. When the fluid passes through thick descending segment, water is reabsorbed from the tubule into the outer medullary interstitium by means of osmosis.it is due to the increased osmolarity in the medullary interstitium
2. So the **fluid inside this segment become slightly hypertonic and the osmolarity is between 450 and 600mOSM/L.**

SUMMARY OF URINE CONC(THIN DESCENDING SEGMENT OF HENLE LOOP)

- As the thin descending seg of Henle loop passes through the inner medullary interstitium(which is increasingly hypertonic)**more H2O is reabsorbed**.This **segment is highly permeable to water**,and the osmolarity of tubular fluid become equal to that of the surrounding medullary interstitium.
- In the short loops of cortical nephrons, the osmolarity of fluid at the hairpin bend of loop becomes600mOsm/L.
- In the long loops of juxtramedullary nephrons,at the hairpin bend, the osmolarity is 1200mOsm/L.

SUMMARY OF URINE CONC(THIN ASCENDING SEGMENT OF HENLE LOOP)

- When the thin ascending seg of the loop ascends upwards through the medullary region **osmolarity decreases gradually**.
- Due to conc gradient **Nacl diffuses out of tubular fluid** and the osmolarity decreases to 400mOsm/L.

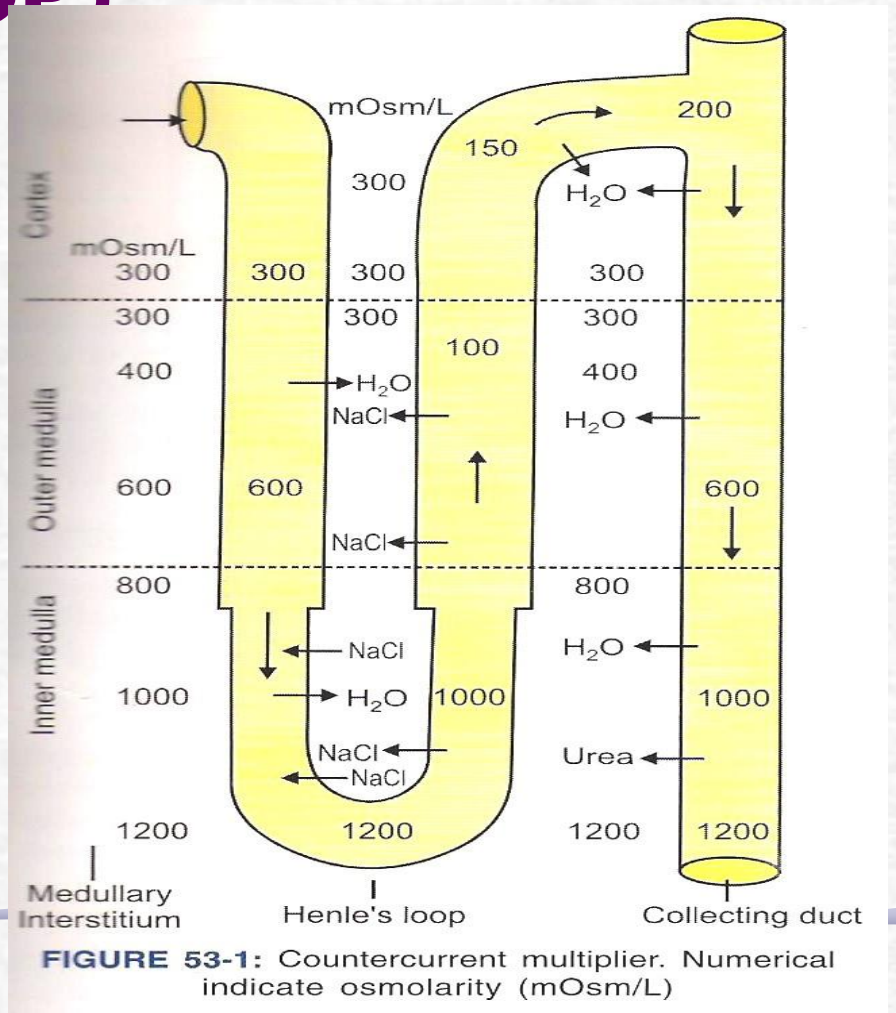


FIGURE 53-1: Countercurrent multiplier. Numerical indicate osmolarity (mOsm/L)

THICK ASCENDING SEGMENT(SUMMARY OF URINE CONCENTRATION)

1. This **segment is impermeable to H2O**.
2. But there is active **reabsorption of Nacl** from this.
3. Reabsorption of Na decreases the osmolarity of tubular fluid to a greater extend.
4. The fluid inside become hypotonic to plasma.The osmolarity decrease to 400mOsm/L

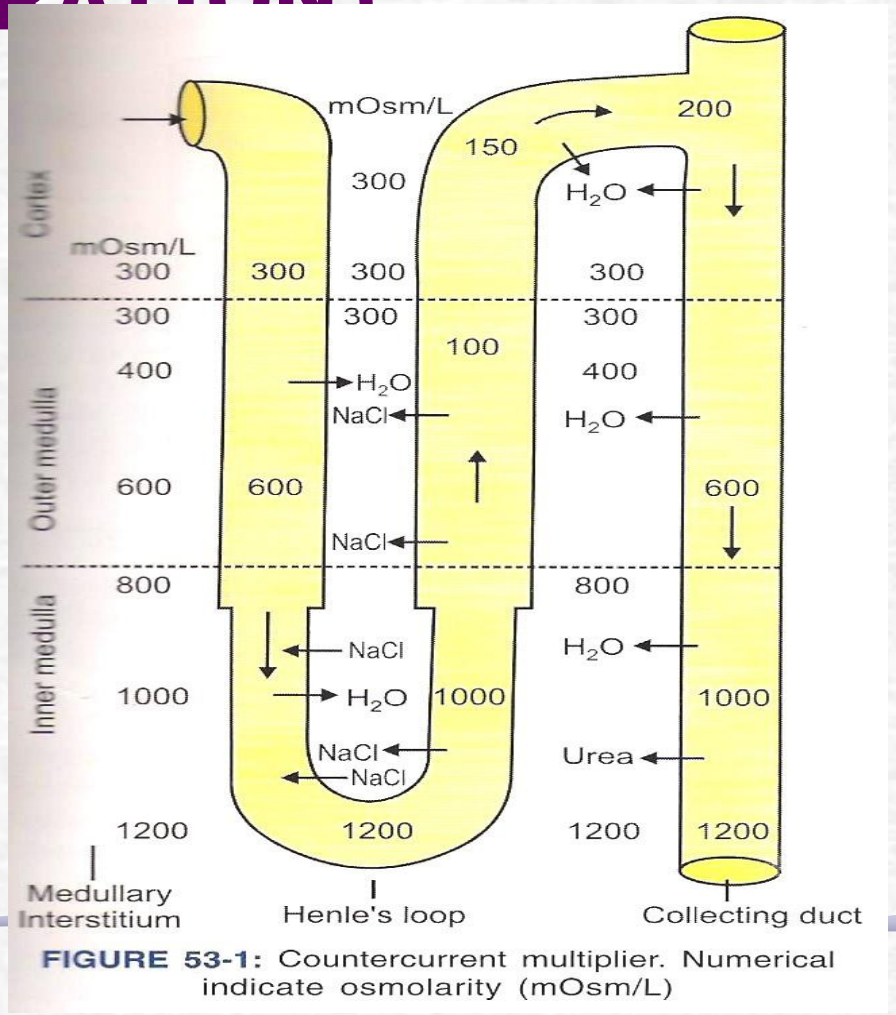


FIGURE 53-1: Countercurrent multiplier. Numerical indicate osmolarity (mOsm/L)

DISTAL CONVOLUTED TUBULE AND COLLECTING DUCT(SUMMARY)

- Two segments are impermeable to water but permeable to solutes.So Na and Cl are reabsorbed.
- Tubular fluid become more hypotonic.At the end of the distal convoluted tubule,the osmolarity is 100mOsm/L.
- The osmolarity of urine leaving collecting duct is as low as 60mOsm/L.In this way dilute urine is formed.
- In the presence of ADH distal convoluted tubule and collecting duct become permeable to H2O resulting in H2O reabsorption and final concentration of urine(urine becomes hypertonic with an osmolarity of 1200mOsm/L.

FORMATION OF DILUTE URINE

- When the water content in the body increases, kidney excretes dilute urine. It is achieved by the inhibition of ADH secretion.
- ADH is secreted by posterior pitutary the stimulus for its secretion

1. decreased body fluid volume
2. Increased Na concentration(hyperosmolarity)

- When the volume of body fluid increases or the osmolarity of the body fluid decreases,ADH secretion stops.
- So water reabsorption from the renal tubules does not takes place.This leads to excretion of large amount of water in urine making the urine dilute.