URINE CONCENTRATION AND REGULATION OF ECF OSMOLARITY
Dilute and concentrated urine

1-Dilute urine: Nephron function continuous reabsorption. Solutes while failing to reabsorb water in distal tubule and coll. duct by reducing ADH secretion → urine excreted with 50 mOsm/L or with high ADH urine osmolarity can reach to 1200-1400 mosm/L.

If large excess of water in the body, kidneys excrete up to 20 L/day.
Figure 28-1  Water diuresis in a human after ingestion of 1 liter of water. Note that after water ingestion, urine volume increases and urine osmolality decreases, causing the excretion of a large volume of dilute urine; however, the total amount of solute excreted by the kidneys remains relatively constant. These responses of the kidneys prevent plasma osmolality from decreasing markedly during excess water ingestion.
Kidneys Excrete Excess Water by Forming Dilute Urine

Fig. 28.2  Formation of dilute urine when ADH levels are very low
ADH (VASOPRESSIN)
Increase osmolarity (Reduce ECF) increase ADH which increase permeability of distal tubules and collecting ducts to water which increase H2O absorption and decrease urine volume and vice versa
• **Proximal tubule**: Reabsorption for water and solutes are equal proportion (Remain isosmotic)

• **Descending**: H₂O reabsorbed by osmosis & fluids reaches equilibrium with surrounding interstitium (Hypertonic).

• **Ascending**: especially thick, water impermeable, solutes heavily reabsorbed → osmolarity about 100 mOsm/L (Hypotonic). No effect of ADH

• **Early distal**: same as above → 50 mOsm/L.

• **Late distal & coll duct**: ADH effect
Filtrate has concentration of 100 mosm/liter as it enters distal and collecting tubules.

In the face of a water excess, collecting tubule permeability to H₂O increased by vasopressin.

Concentration of urine may be as low as 100 mosm/liter as it leaves collecting tubule.

Portions of tubule impermeable to H₂O.
Forming concentrated urine

2-Concentrated urine: Maximum urine concentration 1200 - 1400 mOsmole/L.
Australian hopping mouse 10000 mOsm/L.
For concentrated urine need High ADH level & Hyperosmotic renal medulla

Obligatory urine volume 70 Kgm human excrete 600 mOsm/day → minimal volume of urine = 600 mosm/day = 0.5 L/d
1200 mOsm/L
Figure 29-5. Formation of a concentrated urine when antidiuretic hormone (ADH) levels are high. Note that the fluid leaving the loop of Henle is dilute but becomes concentrated as water is absorbed from the distal tubules and collecting tubules. With high ADH levels, the osmolarity of the urine is about the same as the osmolarity of the renal medullary interstitial fluid in the papilla, which is about 1200 mOsm/L. (Numerical values are in milliosmoles per liter.)
Urine Specific Gravity = Weight of solutes in a given volume, determined by size and numbers of solute molecules.

Urine osmolarity = Determined only by the number of solute molecules in given volume.
Figure 2B-3 Relationship between specific gravity (grams/ml) and osmolality of the urine.
3. **Countercurrent mechanism. C.C. Multipleir**

-Factors contribute in building hyperosmolar medulla:

1. Active transport of Na, and Co-transport of Cl⁻ and K⁺, and other ions in thick L.H
2. Active transport of ions from collecting ducts into medulla
3. Passive diffusion of urea from inner modularly coll. duct
4. Water diffusion far less than solutes
- Repetitive reabsorption of NaCl by thick L.H and inflow new NaCl from proximal tubule [counter current multipleir]

- Urea passively reabsorbed from tubule (inner medullary collecting ducts), then diffuses into thin L.H [urea recirculated and creates 500 mOsm/L].
Medulla

Cortex

All values in milliosmols (mosm)/liter.
Figure 29-4. Countercurrent multiplier system in the loop of Henle for producing a hyperosmotic renal medulla. (Numerical values are in milliosmoles per liter.)
Table 29-1  Summary of Tubule Characteristics—Urine Concentration

<table>
<thead>
<tr>
<th>Tubule</th>
<th>Active NaCl Transport</th>
<th>Permeability</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>H₂O</td>
<td>NaCl</td>
<td>Urea</td>
<td></td>
</tr>
<tr>
<td>Proximal tubule</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Thin descending limb</td>
<td>0</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Thin ascending limb</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Thick ascending limb</td>
<td>++</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Distal tubule</td>
<td>+</td>
<td>+ADH</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Cortical collecting tubule</td>
<td>+</td>
<td>+ADH</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Inner medullary collecting duct</td>
<td>+</td>
<td>+ADH</td>
<td>0</td>
<td>+ADH</td>
<td></td>
</tr>
</tbody>
</table>

ADH, antidiuretic hormone; NaCl, sodium chloride; 0, minimal level of active transport or permeability; +, moderate level of active transport or permeability; ++, high level of active transport or permeability; +ADH, permeability to water or urea is increased by ADH.
Filtrate has concentration of 100 mosm/liter as it enters distal and collecting tubules. In the face of a water deficit, Collecting tubule concentration of urine may be up to 1,200 mosm/liter as it leaves collecting tubule.
ROLE OF DIST TUB & COLL DUCT IN EXCRETE CONCENTRATED URINE

1-In cortical collect tub (ADH) large amount of water absorbed more than in the medulla to preserve the high medullary interstitial fluid osmolarity.

2-In medullary collect duct, still more water absorbed but smaller than cortical & absorbed water carried by vasa recta. With high ADH the fluid in the collecting duct has same osmolarity as interstitial fluid of the renal medulla.
Conserving Water (cont.)

- Role of Distal Tubule and Collecting Ducts in Excreting Concentrated Urine

Fig. 28.5 Formation of a concentrated urine when ADH levels are high.
• Urea contribute to hyperosmotic renal medullary interstitium:
  • 1-Contribute about 40-50%
  • 2-Urea passively absorbed from the tubule
  • 3-Little urea absorbed in ascending limb, distal & cortical collecting tubules (not permeate to urea).
  • 4-In the presence of ADH in cortical coll, water absorbed and then in medullary collecting duct cause ^ concentration of urea.
• 5-Diffuse of urea to medullary interstitium facilitate by specific urea transporter (UT-A1) & (UT-A3) activated by ADH
• 6-Some urea secreted in thin loop from medullary interstitium facilitated by (UT-A2).
• This Recirculation of urea is additional mechanism for forming hyperosmotic renal medulla
Figure 21B-6 Recirculation of urea absorbed from the medullary collecting duct into the interstitial fluid. This urea diffuses into the thin loop of Henle and then passes through the distal tubules, and it finally passes back into the collecting duct. The recirculation of urea helps to trap urea in the renal medulla and contributes to the hyperosmolality of the renal medulla. The heavy tan lines, from the thick ascending loop of Henle to the medullary collecting ducts, indicate that these segments are not very permeable to urea. (Numerical values are in millimoles per liter of urea during antidiuresis, when large amounts of antidiuretic hormone are present. Percentages of the filtered load of urea that remain in the tubules are indicated in the blue boxes.)
• VASA RECTA:
• 1-Less than 5% of renal blood flow
• 2-Countercurrent exchanger ,reduce wash out of solutes from medullary interstitium
• 3-During descending blood becomes concentrated by solutes enter and H2O loss
• 4-In Ascending part vice versa.
• 5-It prevent medullary hyperosmolarity from dissipated.
Fig. 28.7 Countercurrent exchange in the vasa recta
• Role of early distal & coll.: - if there is no ADH this part still impermeable to water.
  - if there is ADH this part is highly permeable to water. Water will leave from cortical and from juxtamedulary nephrones, but majority in cortex, to preserve the high medullary interstitial fluid osmolarity.
B] C.C. exchanger:

- Factors keeping hyperosmolarity:
  a. Medullary blood flow is low 1 to 2% of total renal blood flow.
  b. Vasa recta structure: descending and ascending segment.

U-shape minimizes loss of solute from interstitial but does not prevent the bulk flow of fluid & solutes into blood through (Starling capp. circ.)
Regulation of ECF osmolarity and Na concentration

1-Osmoreceptor (hypothalamus)- ADH feedback system:

H2O deficit- ^ osmolarity- ^ADH- ^H2O permeability in DT and collecting duct- ^H2O reabsorption-decrease H2O excretion.
Fig. 28.9 Osmoreceptor-ADH feedback mechanism for regulating ECF osmolarity in response to a water deficit
• ADH Synthesis in the Hypothalamus and Release from Posterior Pituitary
• CV Reflex stimulation of ADH Secretion:
  • Decrease Blood Volume, Decrease BP
• Other stimuli for ADH secretion: Nausea, nicotine, morphine. But alcohol inhibit ADH secretion and cause diuretic.
Osmoreceptor-ADH Feedback System

- **ADH Synthesis in the Hypothalamus and Release from the Posterior Pituitary**

Fig. 28.10
Regulation of ECF osmolarity and Na concentration

2-Osmolarity and Thirst
Conscious desire for water
Thirst center, Third ventricle area that promote ADH release stimulate thirst center
• Thirst Increase with
  • A-Increase osmolarity (Salt)
  • B-Decrease Blood vol
  • C-Decrease BP
  • D-Increase angiotensin II
  • E-Dryness of mouth
• ADH and thirst mechanism work in parallel to regulate ECF osmolarity and Na concentration more effective.

• Angiotensin II and aldosterone have little effect on Na concentration but not the Na quantity and volume (increase absorption of both water and Na).
• **SALT APPETITE:** Decrease extracellular fluid Na concentration, Decrease Blood Volume and BP
• Neural mechanism for salt appetite is analog to that of thirst mechanism.