Renal Physiology - Lectures

1. ✓ Physiology of Body Fluids – PROBLEM SET, RESEARCH ARTICLE
2. ✓ Structure & Function of the Kidneys
3. ✓ Renal Clearance & Glomerular Filtration – PROBLEM SET
4. ✓ Regulation of Renal Blood Flow - REVIEW ARTICLE
5. ✓ Transport of Sodium & Chloride – TUTORIAL A & B
6. ✓ Transport of Urea, Glucose, Phosphate, Calcium & Organic Solutes
7. ✓ Regulation of Potassium Balance
8. Regulation of Water Balance
9. Transport of Acids & Bases
10. Integration of Salt & Water Balance
11. Clinical Correlation – Dr. Credo
12. **PROBLEM SET REVIEW – May 9, 2011 at 9 am**
13. **EXAM REVIEW – May 9, 2011 at 10 am**
14. **EXAM IV – May 12, 2011**

Renal Physiology Lecture 8

Urine Concentration & Dilution

Chapter 5 Koeppen & Stanton Renal Physiology

1. Water Balance
2. Free Water Clearance
3. Antidiuretic Hormone = Arginine Vasopressin (ADH = AVP)
   - Site of secretion
   - Mechanism of action
   - Stimuli for release
4. Countercurrent System
   - Countercurrent multiplication Countercurrent exchange

'Magical Kidneys'

The kidneys have a critical ability to <u>vary relative proportions</u> of *solutes* and *water* excreted in the urine, as needed, to achieve solute and water **balance**.

Terminology

<u>Diuresis</u> - urine flow above usual levels

<u>Water Diuresis</u> - ⇑ urine flow - decreased reabsorption "free" water (i.e. water w/o solute)

<u>Antidiuresis</u> - low rate water excretion (<0.5 ml/min) as *hyper-osmotic* urine

INput = OUTput H_2O – Table 5-1

INPUT	Amount (ml)	OUTPUT	Amount (ml)
Fluids	1,200	** Urine **	1,500
Food	1,000	Feces	200
Aerobic Metabolism	300	Skin/Sweat	450
		Exhaled Air	350
Total	2,500	Total	2,500

OUTput H_2O – Table 5-2

Normal	Amount (ml)	Prolonged Heavy Exercise	Amount (ml)
** Urine **	1,500	** Urine **	⇓ 500
Feces	200	Feces	200
Skin/Sweat	450	Skin/Sweat	⇑ 5,350
Exhaled Air	350	Exhaled Air	⇑ 650
Total	2,500	Total	

* Water Balance Maintained By ⇑ Water Intake *

Kidney Handling of Water - Urine

- Kidneys must excrete ~ 600 mosmol/d
  - 50 – 1,200 mOsm/kg H_2O
- H_2O volumes excreted
  - 0.5 – 18 L/d
- Kidneys control H_2O excretion independently of Na^+, K^+, urea

Renal Physiology Lecture 8

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Free Water Clearance – Estimate Ability to Concentrate or Dilute Urine pg 87

- "Positive" free-water clearance
  - U_{Osm} < P_{Osm} (plasma osmolality)
  - water excreted excess solutes
  - solute - free water = dilute urine
  - **LOW AVP**

Free Water Clearance – Estimate Ability to Conc or Dilute Urine

- "Negative" free-water clearance
  - U_{Osm} > P_{Osm}
  - Solutes excreted excess water = concentrated urine
  - **HIGH AVP**
- Free-water clearance = "Zero"
  - U_{Osm} = P_{Osm}

Renal Physiology Lecture 8

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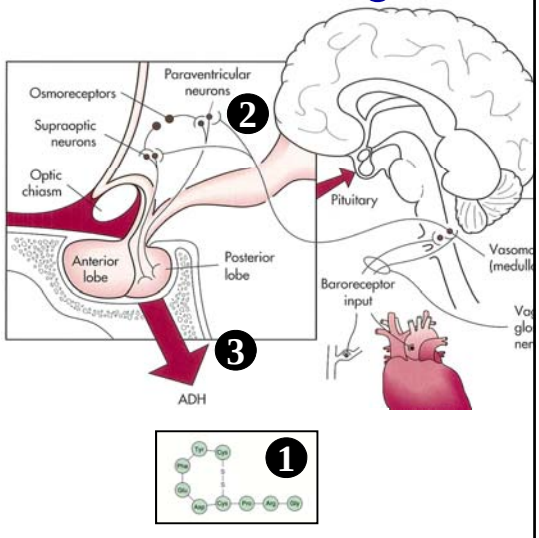
Synthesis & Release of ADH Fig 5-2

1. Peptide hormone (9 aa)
2. Synthesized <u>hypothalamus</u>
3. Stored, released <u>neurohypophysis</u>

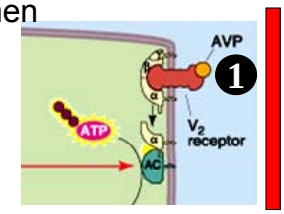


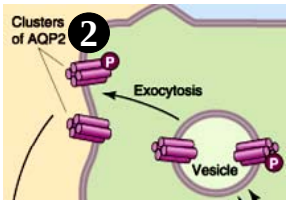
**** Major Stimulus - ⇑ P Osm ****

Tubular Actions of AVP

1. AVP binds $\underline{V_2 \text{ receptor}}$
   - *BL* membrane
2. Insert Aquaporin 2 - AQP2
   - *Apical* membrane

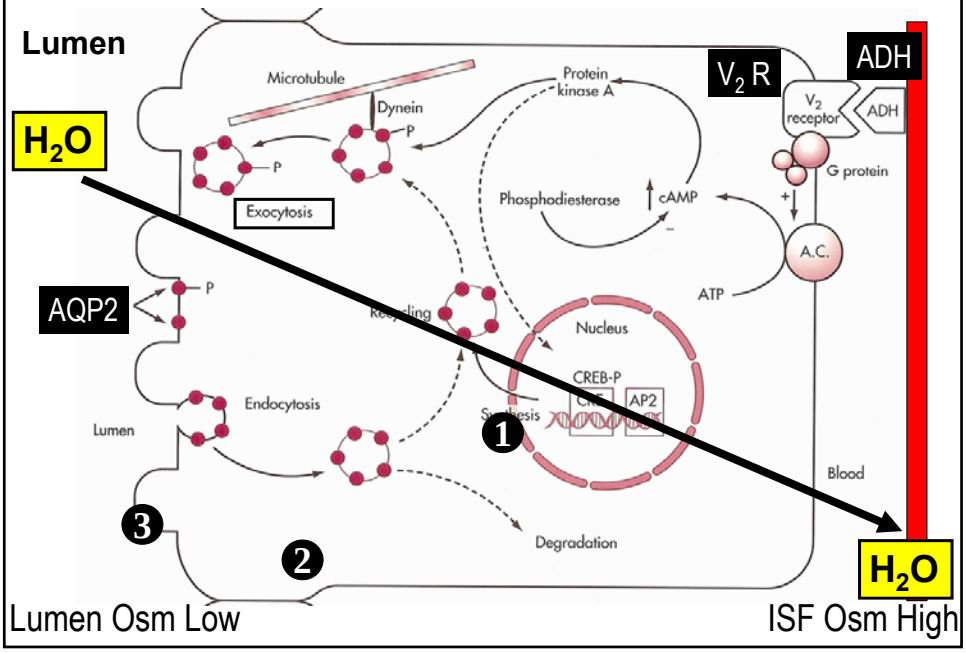
⇑ H_2O *permeability* = ⇑ H_2O reabsorption
   - Minimize dehydration





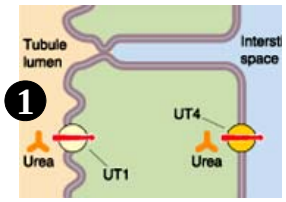
** $\underline{\text{Dissociate}}$ H_2O Reabsorption & Na^+ Reabsorption - Collecting Ducts **

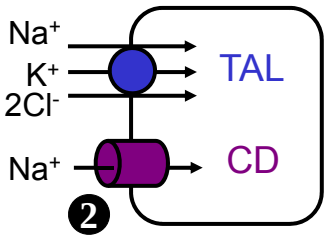
Cellular Mechanisms of AVP - CT & CD Fig 5-5



Tubular Actions of AVP

1. ⇑ apical urea *permeability of MCD*
   - ⇑ urea reabsorption
2. ⇑ NaCl reabsorption TAL, DT, CCD
   - ⇑ H_2O reabsorption
3. ⇑ renal medulla osmolality





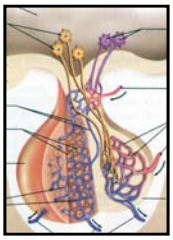
What happens if V2R or AQP2 has lack of function mutation?

Nephrogenic Diabetes Insipidus

- Excessive urination *(polyuria)*
- Increased fluid intake *(polydipsia)*
- Extreme thirst
- Urinary frequency
- Nocturia
- Urine pale, colorless or watery in appearance
- Osmolality or specific gravity low

Stimuli for ADH Release

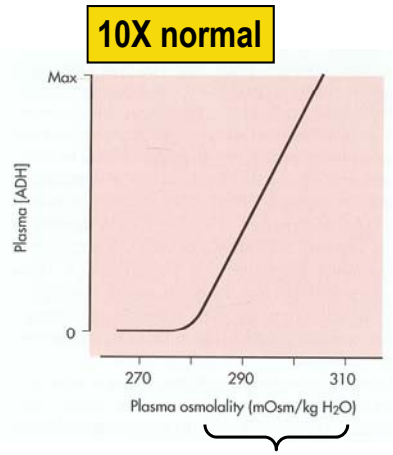
** Osmolality of the Plasma **



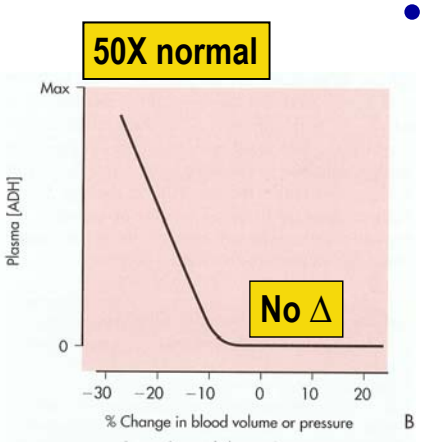
- Osmoreceptors
  - ⇑ P_{Osm} **1%**, ⇑ ADH
- Baroreceptors
  - ⇓ pressure
  - *Low* pressure (LT atrium, large pulmonary
  - *High* pressure (aortic arch, carotid sinus)
  - ⇑ ADH

Regulation of Plasma [ADH] by Osmotic Stimuli Fig 5-3A

- Osmoreceptors
  - Small Δ P_{Osm} = Big Δ ADH release
  - P[ADH] Δ 10-fold
  - **Sensitive** (precise) regulators ADH release



Regulation of Plasma [ADH] by Volume Stimuli Fig 5-3B



- Volume Receptors
  - ⇓ BV ⇑ P[ADH]
  - ⇑ BV NO Δ P[ADH]
  - > **10%** ⇓ BV for Δ P[ADH]
  - P[ADH] ⇑ 50-fold
  - **Powerful**, but not very sensitive, regulators ADH release

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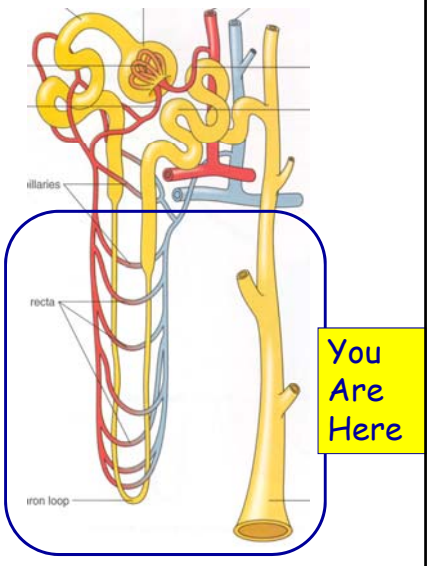
Countercurrent MECHANISM pg 83-85

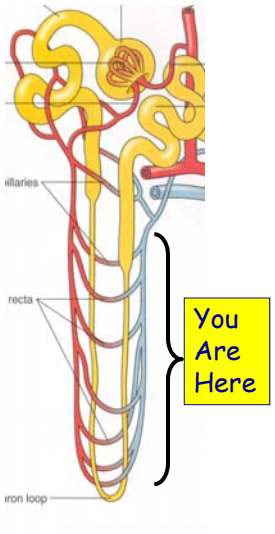
- Mechanism by which urine is *concentrated*
- Dependent upon:
  - unique solute *transport* processes

  AND
  - specific *anatomical* arrangement of loops of Henle & vasa recta



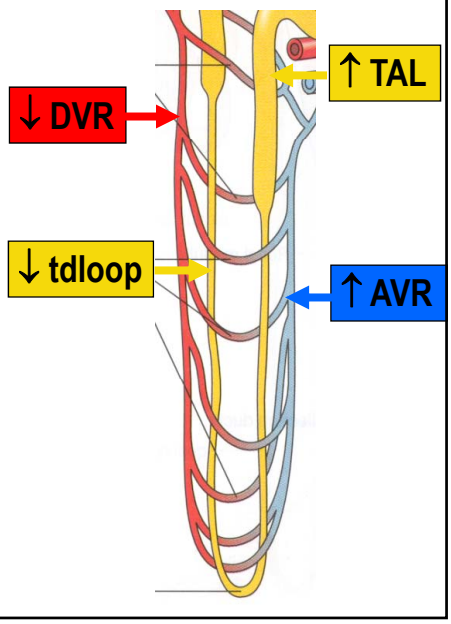
Countercurrent SYSTEM

1. Countercurrent <u>flow</u> – *direction - anatomy*
2. Countercurrent <u>exchange</u> - *vasa recta capillaries*
3. Countercurrent <u>multiplication</u> – *tubule epithelia*



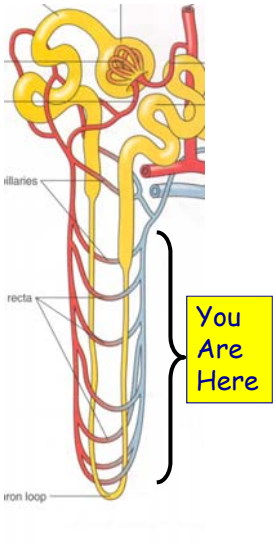
1. Countercurrent FLOW

- **Hairpin** configuration - *anatomical*
  - loops of Henle *(tubules)*
  - vasa recta *(capillaries)*
- Descending limbs close to ascending limbs
- Fluid *flow* in opposite directions

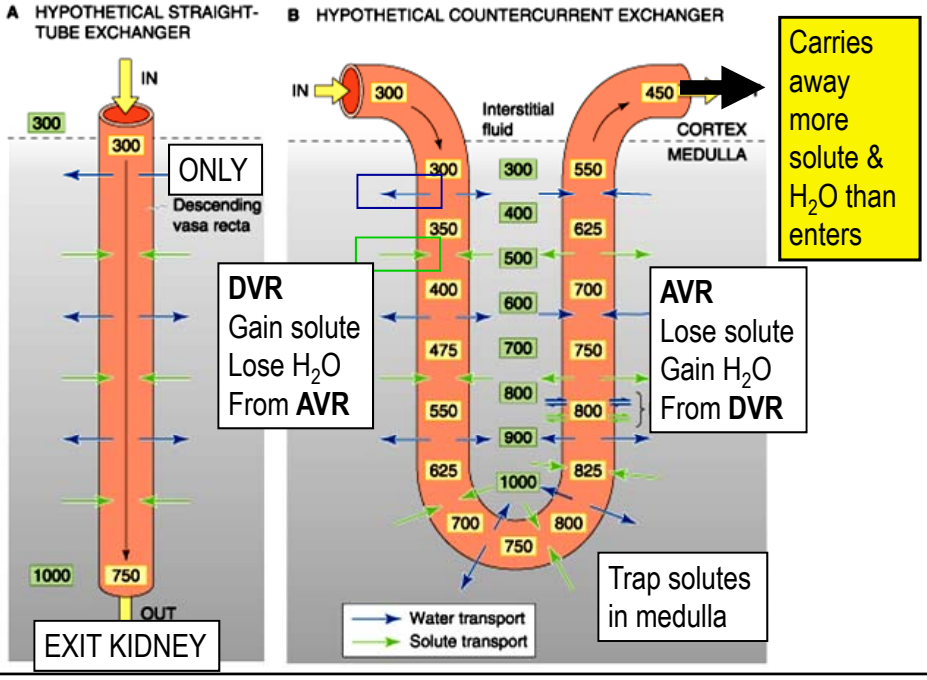


2. Countercurrent EXCHANGER

- Vasa recta (*capillaries*)
  - Countercurrent **exchangers**
    - *Passive* process depends on diffusion solutes & water in both directions across permeable walls vasa recta
    - Restores isotonic plasma
    - Maintains hypertonic medullary interstitium

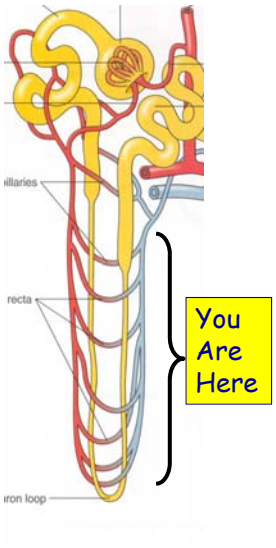


Countercurrent EXCHANGER



3. Countercurrent MULTIPLIER

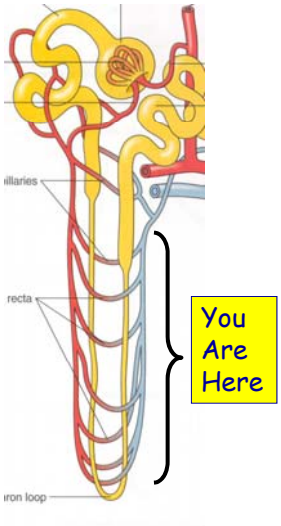
- Loops of Henle (*tubules*)
  - countercurrent **multipliers**
    - *Pumping solute creates large axial gradient*
    - *Small lateral gradient*
    - *Establishes hyperosmotic medullary interstitial fluid*



Countercurrent SYSTEM = 1 + 2 + 3

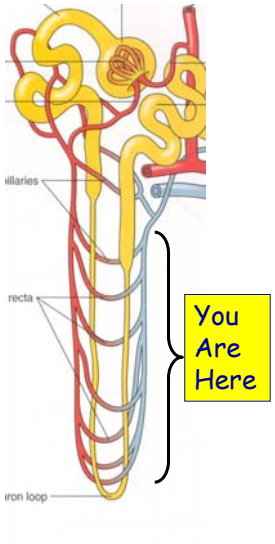
Depends on membrane transport properties

- TAL (tubule)
  - **Active** transport
  - Multiplier
- VR (capillaries)
  - **Passive** transport
  - Exchanger
- Thin descending limb of Henle's loop (tubule)
  - **Passive** structure



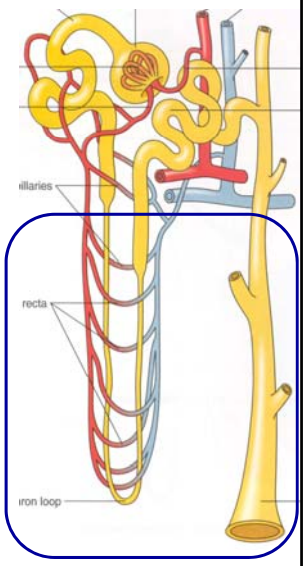
Summary - Countercurrent SYSTEM

- Countercurrent arrangement
  - CD fluid – exposed interstitial <u>hyperosmolality</u>
  - conc urine
  - passive reabsorption H_2O in presence AVP

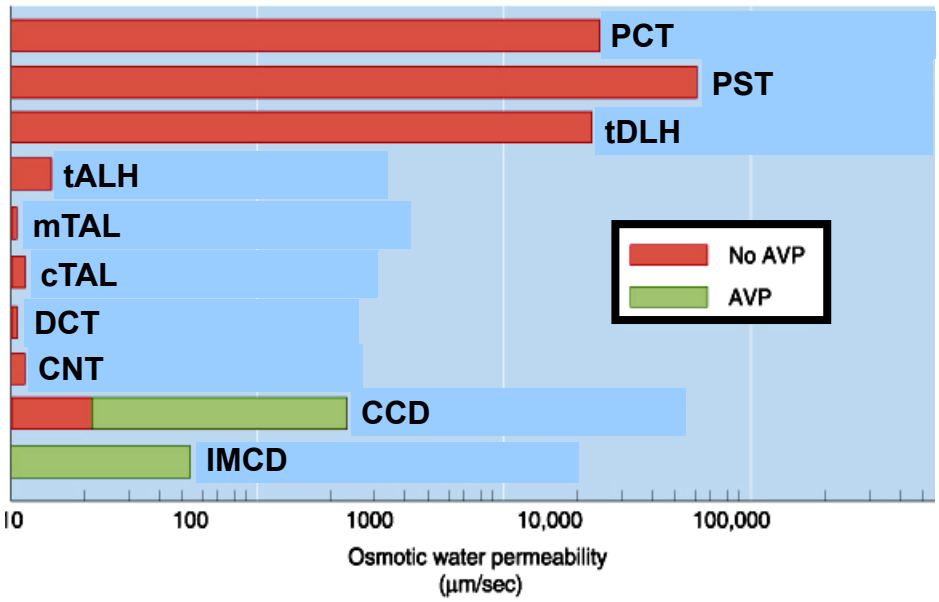


Medullary Interstitium pg 85

- Medullary interstitial fluid osmotic pressure = driving force H_2O reabsorption thin descending limb LOH & CD
- High ADH - ⇑ ⇑ IMCD permeability to urea: medullary ISF osmolality = ½ urea + ½ NaCl
- Urea ineffective osmole for CD; but effective for thin descending limb
- Urine can never be more conc than papillary ISF



H_2O Permeability Characteristics Nephron



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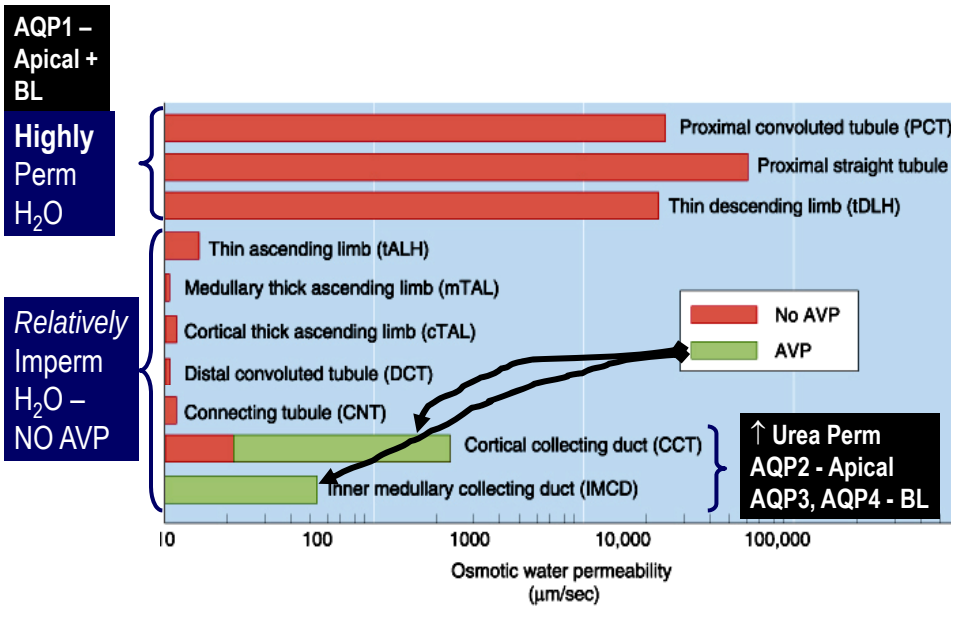
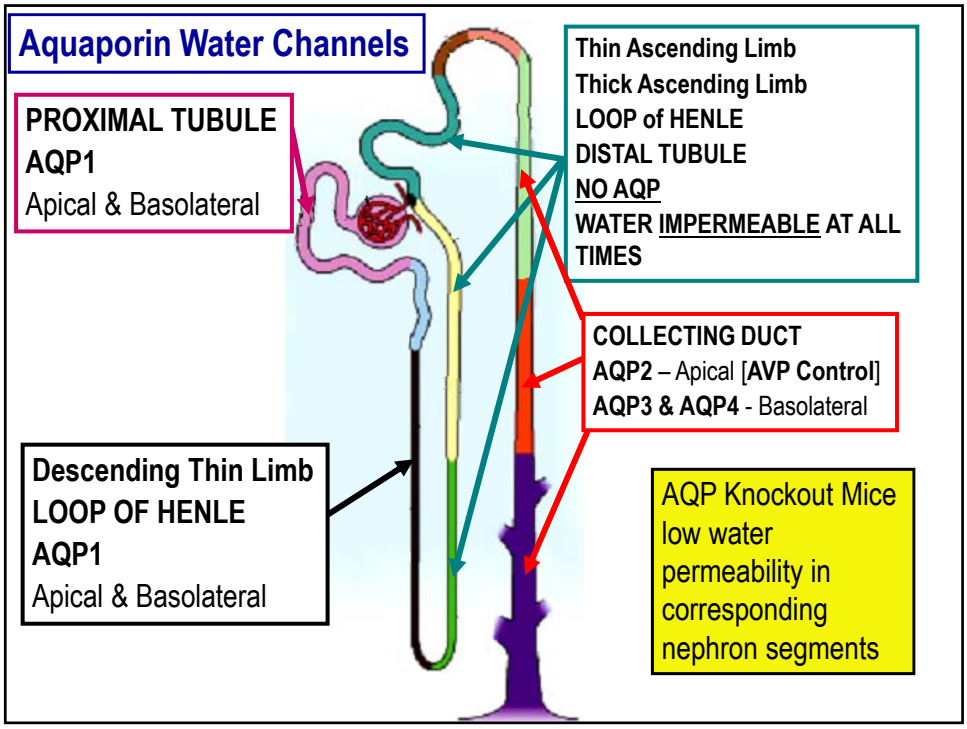
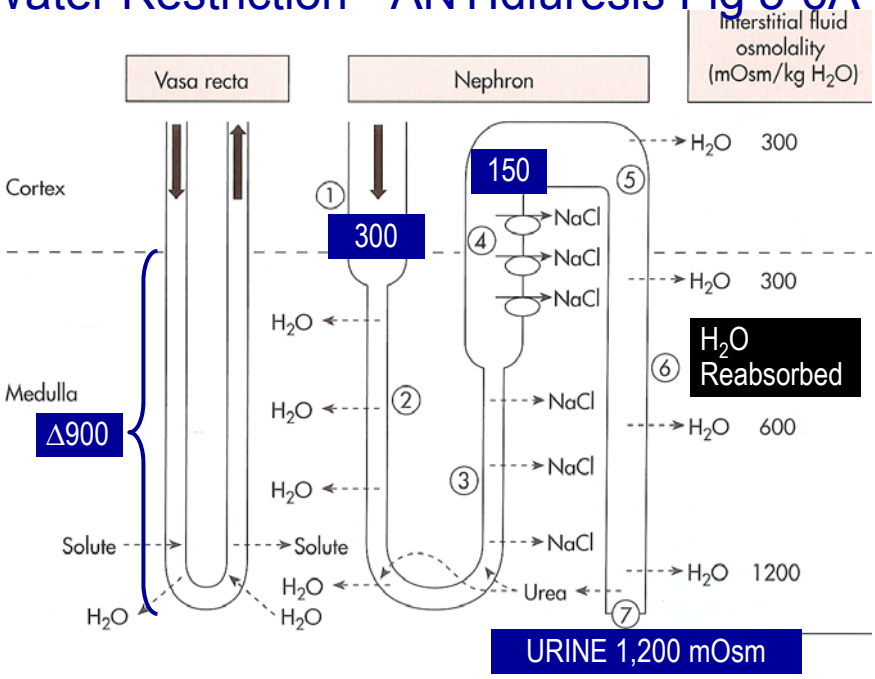




Water Restriction – ANTIdiuresis

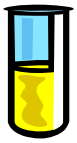
HIGH Plasma [ADH]

Water Restriction - ANTIdiuresis Fig 5-6A



Summary - ANTIdiuresis

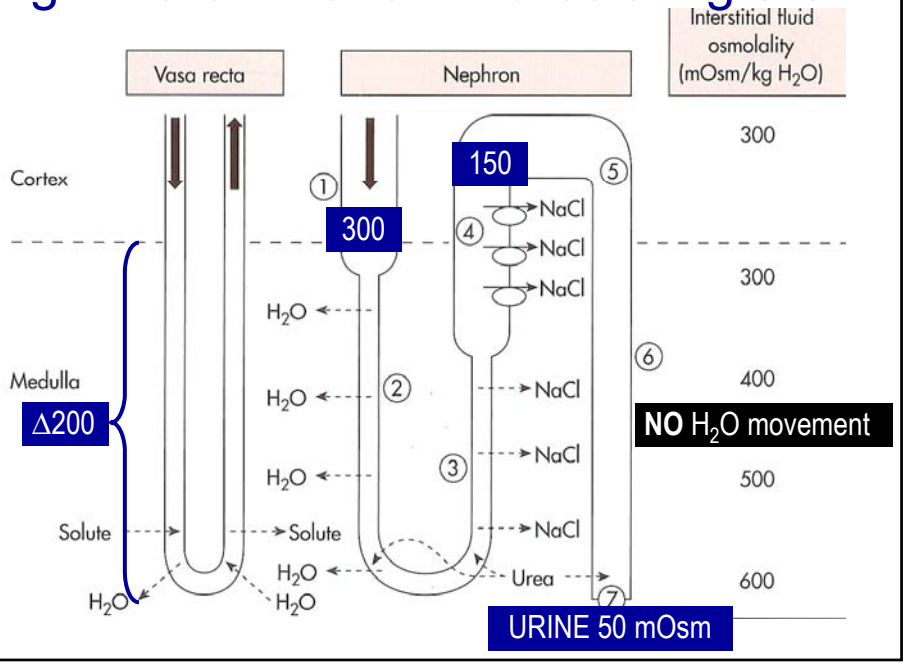
- ⇑ P_{Osm} = ⇑ [ADH]
- Principal cells CT
  - **highly** permeable to water
  - IMCD permeable to urea, passively reabsorbed
  - === Concentrated urine (max 1,200 mOsm/L) w/o major Δ solute excretion



High Water Intake – Diuresis

LOW Plasma [ADH]

High Water Intake - Diuresis Fig 5-6A



Summary - Water Diuresis

- ⇓ P_{Osm} - ⇓ [ADH]
- Papillary Osm ~ ½ of antidiuresis
- Late DT to end nephron
  - relatively **impermeable** to H_2O
- === Dilute Urine (min - 50 mOsm/L)

Important Distinctions Relative to Na^+ & H_2O Balance

- Δ Na^+ balance manifests as Δ ECF **VOLUME**

  (volume depletion or volume expansion)

- Δ H_2O balance manifests as Δ P_{Osm} measured Δ $\mathbf{P_{Na}}$

Important Distinctions Relative to Na^+ & H_2O Balance

Disturbances of H_2O balance:

- Hypernatremia (P_{Na} > 145 mEq/L) – deficit H_20 relative to salt "dehydration"
  - Diabetes Insipidus (Central or Nephrogenic)

Important Distinctions Relative to Na^+ & H_2O Balance

Disturbances of H_2O balance:

- Hyponatremia (P_{Na} < 135 mEq/L) – excess H_20 relative to salt
  - Syndrome of Inappropriate ADH Secretion (SIADH)

What Did We Learn Today?

1. H_2O in = H_2O out
2. Countercurrent mechanism establishes *hyperosmotic* medulla
3. P_{Osm} *major* control AVP release
4. ADH regulates H_2O reabsorption by CD
   - regulate H_2O excretion independent of solute excretion
5. WOW!!! 0.5 to 18 L/day