open.michigan

Author(s): Michael Heung, M.D., 2009

Citation Key

for more information see: http://open.umich.edu/wiki/CitationPolicy

Use + Share + Adapt

{ Content the copyright holder, author, or law permits you to use, share and adapt. }

Public Domain – Government: Works that are produced by the U.S. Government. (17 USC § 105)

Public Domain – Expired: Works that are no longer protected due to an expired copyright term.

Public Domain – Self Dedicated: Works that a copyright holder has dedicated to the public domain.

Creative Commons – Zero Waiver

Creative Commons – Attribution License

Creative Commons – Attribution Share Alike License

Creative Commons – Attribution Noncommercial License

Creative Commons – Attribution Noncommercial Share Alike License

GNU – Free Documentation License

Make Your Own Assessment

{ Content Open.Michigan believes can be used, shared, and adapted because it is ineligible for copyright. }

Public Domain – Ineligible: Works that are ineligible for copyright protection in the U.S. (17 USC § 102(b)) *laws in your jurisdiction may differ

{ Content Open.Michigan has used under a Fair Use determination. }

Fair Use: Use of works that is determined to be Fair consistent with the U.S. Copyright Act. (17 USC § 107) *laws in your jurisdiction may differ

Our determination **DOES NOT** mean that all uses of this 3rd-party content are Fair Uses and we **DO NOT** guarantee that your use of the content is Fair.

To use this content you should **do your own independent analysis** to determine whether or not your use will be Fair.

Physiology of Water Metabolism

Michael Heung, M.D.

M2 Renal Sequence

Fall 2008

University of Michigan
Medical School

Objectives

- Distinguish between solute and free water clearance
- Understand the differential transport of water and electrolytes in the renal tubules
- Understand countercurrent multiplication and its role in urinary concentration
- Know the regulation of ADH release and its effects on water reabsorption
- Be familiar with the aquaporin family of proteins
- Understand the role of thirst in maintaining water balance

Volume vs Osmoregulation

	Osmoregulation	**Volume regulation**
Signal	Plasma osmolality	“Effective” circulating volume
Sensors	Hypothalamic osmoreceptors	Carotid sinus, large vein, atrial, and intrarenal receptors
Effectors	ADH, thirst	Renin/angiotensin, aldosterone, sympathetic nerves, ANP, ADH
Observed responses	Urine osmolality, water intake	Urinary sodium excretion

Typical Daily Water Balance

Source	Water intake (ml/day)	Source	Water output (ml/day)
Ingested water	1400	Urine	1500
Water content of food	850	Skin	500
Water of oxidation	350	Respiratory tract Stool	400 200
Total:	2600	Total:	2600

Daily Renal Resorptive Workload

Substance	Filtered	Excreted	Reabsorbed	% net reabsorbed
Water (L)	180	1.5	178.5	>99
Sodium (mEq)	25,200	150	25,050	>99
Chloride (mEq)	18,000	150	17,850	>99
Bicarbonate (mEq)	4320	2	4318	>99
Potassium (mEq)	720	100	620	>85
Calcium (mEq)	540	10	530	>98
Urea (g)	56	28	28	50
Glucose (mmol)	800	0	800	100

Solute vs. Water Clearance

	Patient 1	Patient 2	Patient 3
P_{Osm}	300 mOsm/ kg water	300 mOsm/ kg water	300 mOsm/ kg water
U_{Osm}	300 mOsm/ kg water	150 mOsm/ kg water	600 mOsm/ kg water
Urine flow (ml/min)	2 mL/min	4 mL/min	1 mL/min

- What is each patient's solute clearance?
- What is each patient's water balance?

Free Water Clearance

- $\text{Clearance}_{osm} = (U_{osm} \times V) / P_{osm}$

  <u>Patient 1:</u> $C_{Osm} = (300 \text{ X } 2)/300 = 2$ mL/min
  Urine flow 2mL/min → ***Even water balance***

  <u>Patient 2:</u> $C_{Osm} = (150 \text{ X } 4)/300 = 2$ mL/min
  Urine flow 4mL/min → ***Free water excretion***

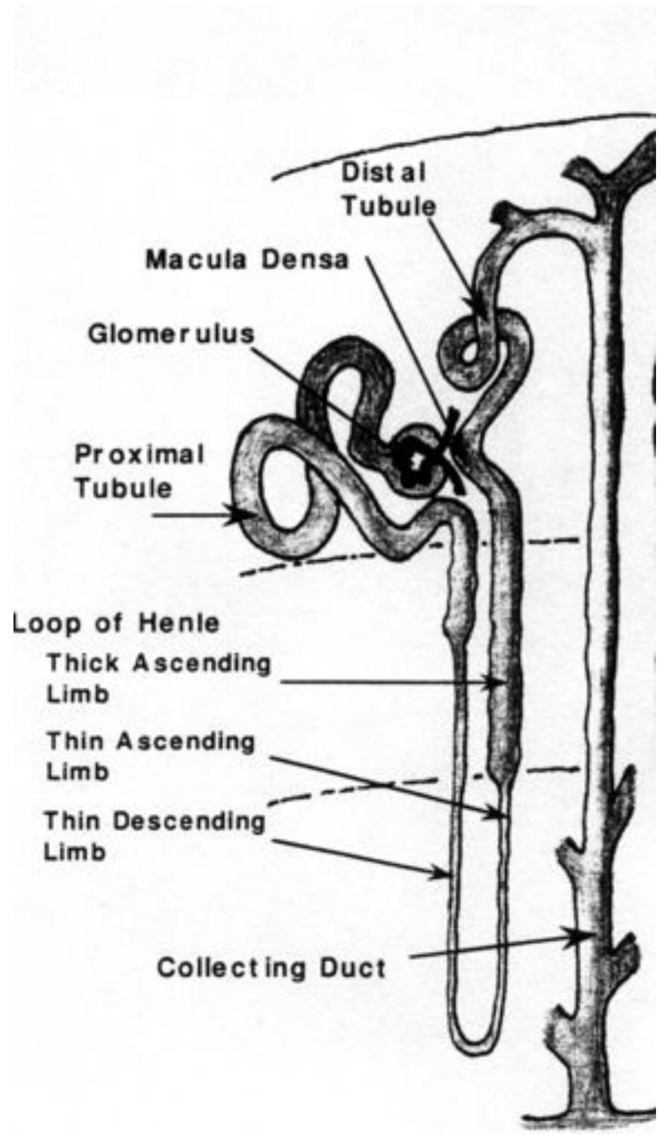
  <u>Patient 3:</u> $C_{Osm} = (600 \text{ X } 1)/300 = 2$ mL/min
  Urine flow 1mL/min → ***Free water retention***

- *Solute clearance is identical, but water clearance is divergent*

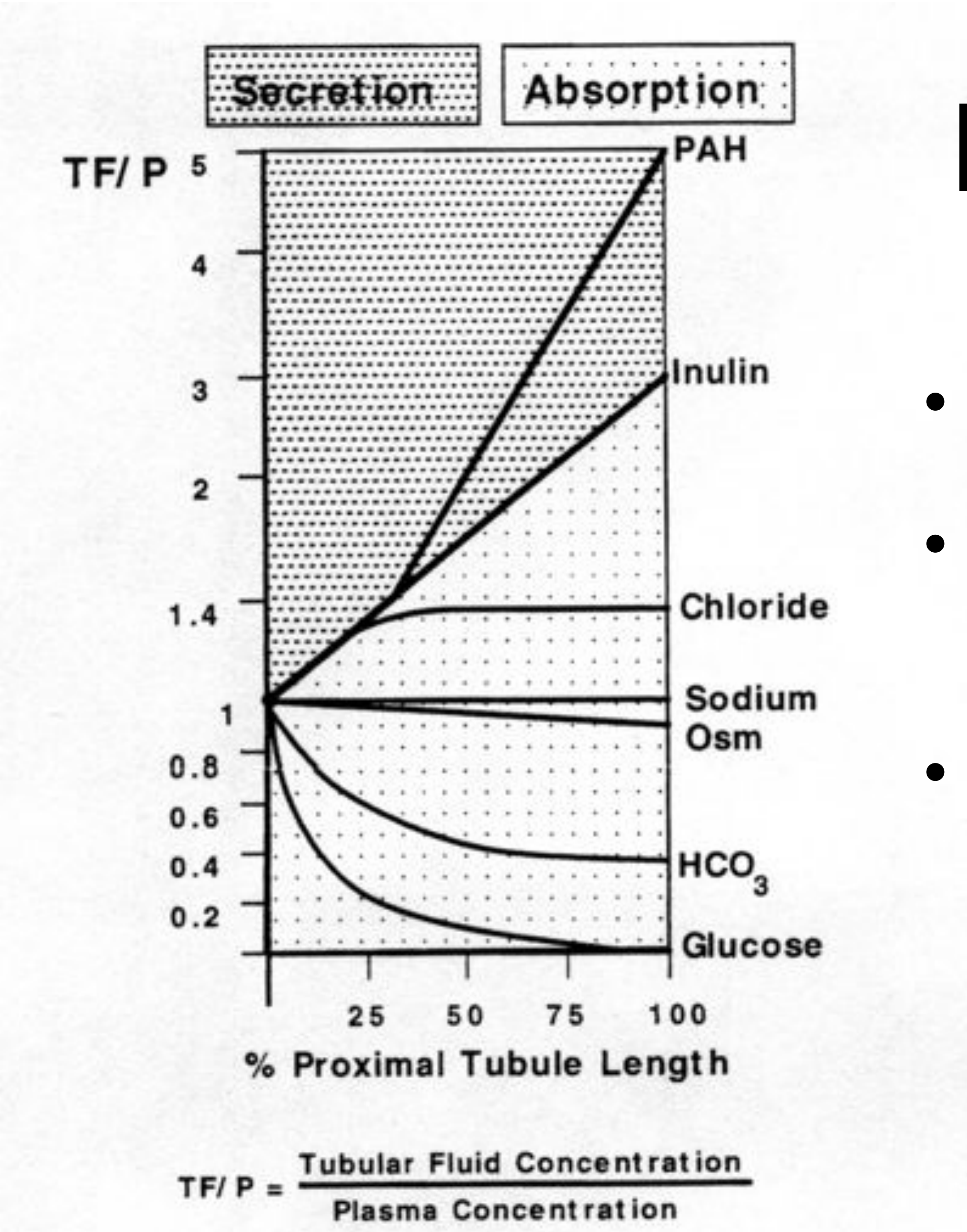
Renal Water Handling

- For renal excretion to vary between filtered substances, there must be differential transport within the tubular epithelium

- Although there is overlap, water and sodium handling are independently regulated



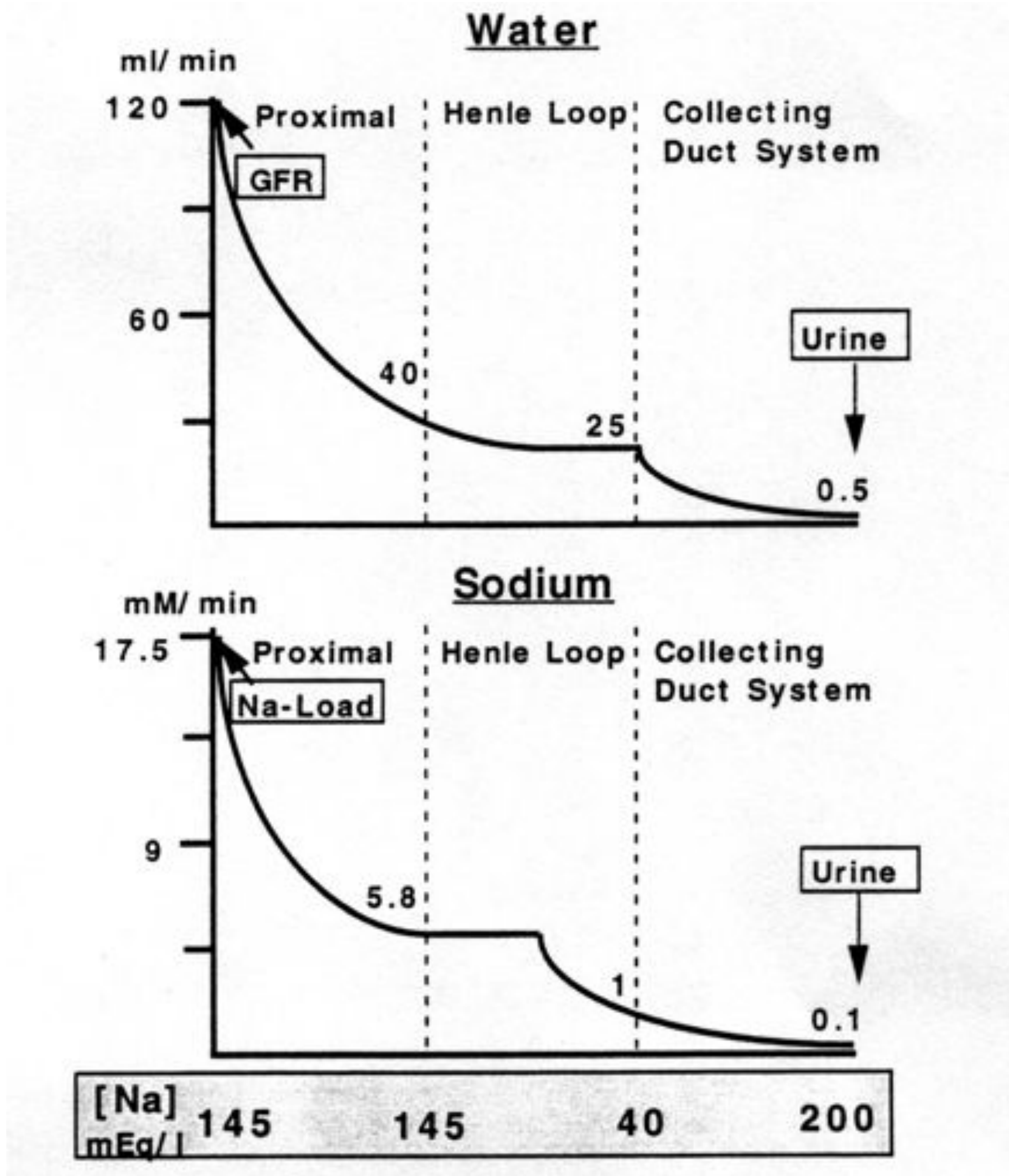
Proximal Tubule



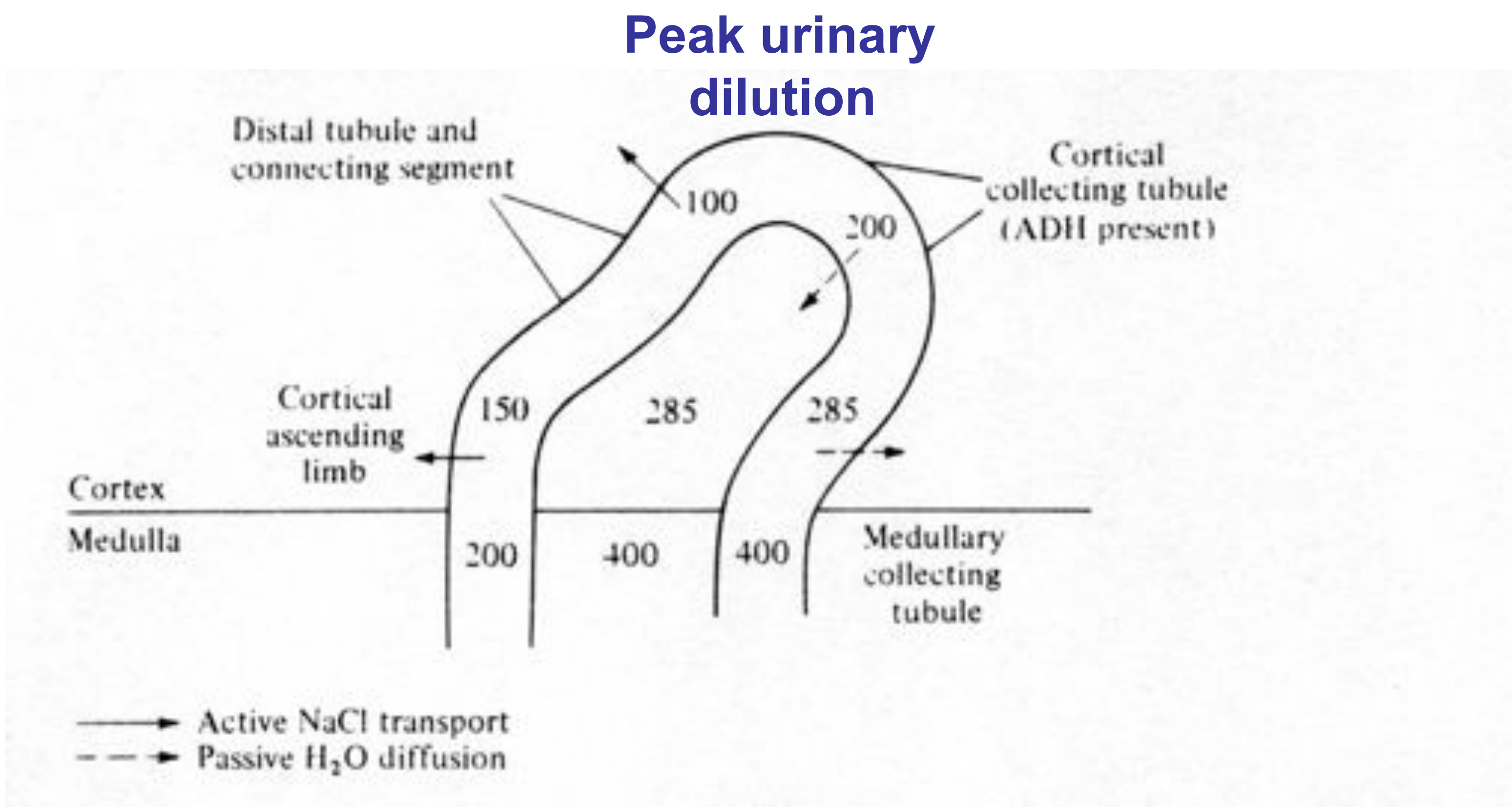
- 67% of filtered load
- Sodium and water are absorbed iso-osmotically
- Water flow is passive and follows the osmotic gradient established by Na reabsorption

Loop of Henle

- Descending thin limb
  - 15% of filtered load
  - Passive reabsorption
- Thick ascending limb
  - Impermeable to water
  - Diluting segment

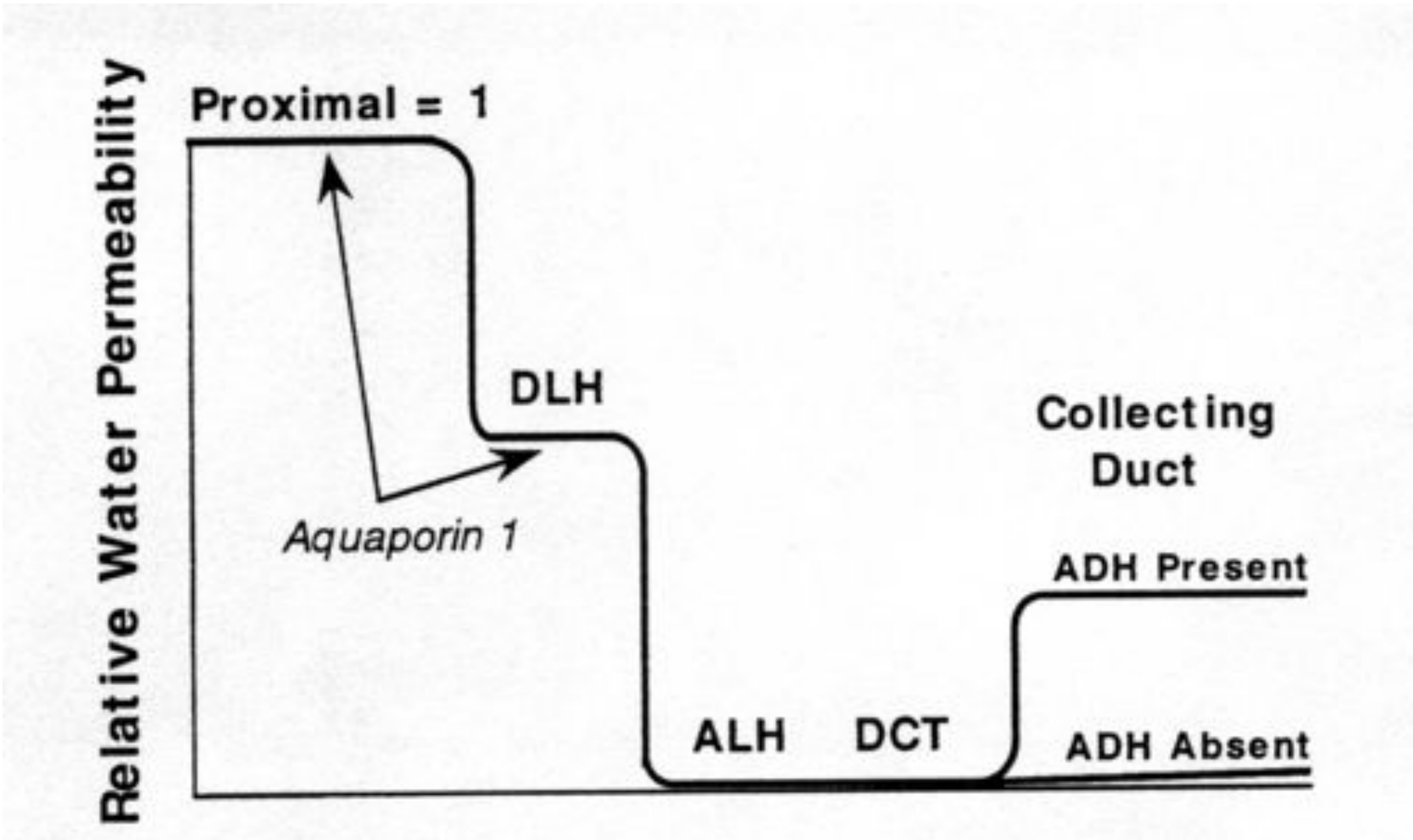


Distal Tubule and Collecting Duct



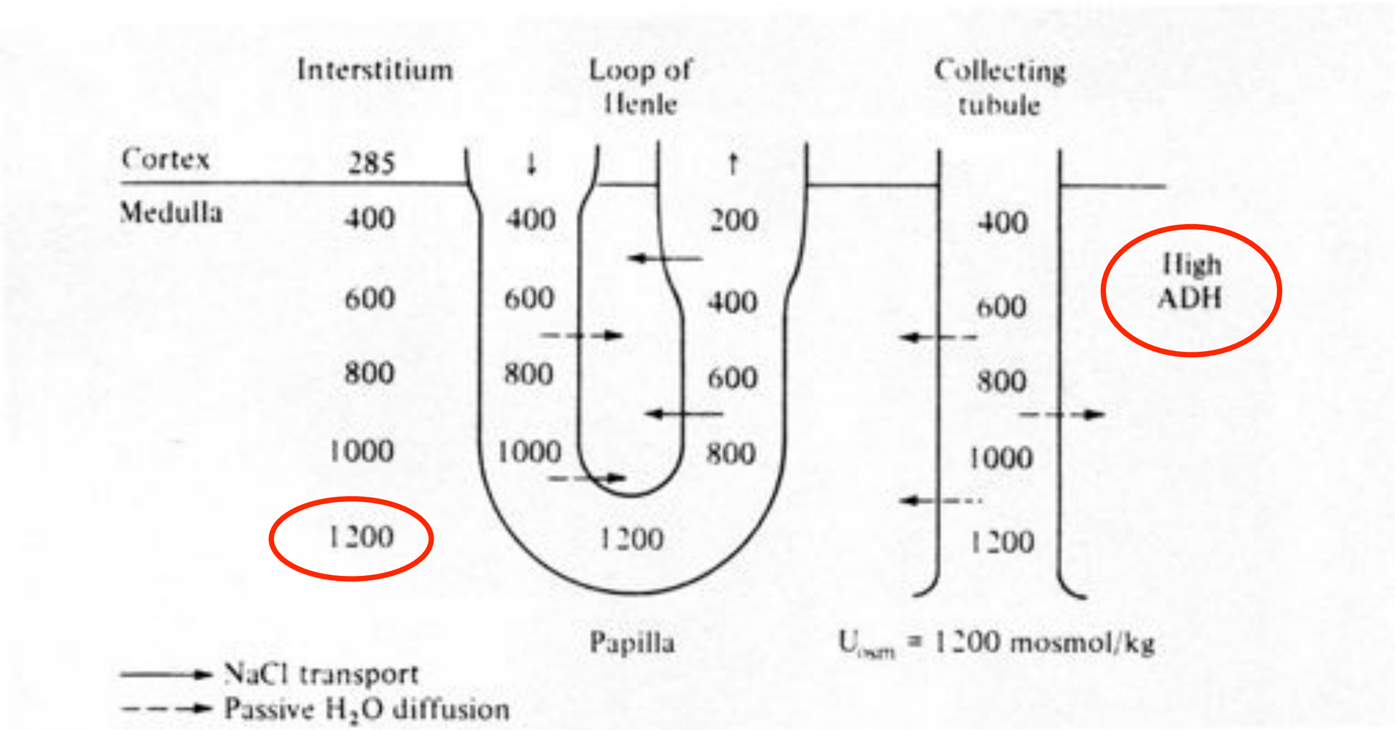
- Early DT is water impermeable: further urinary dilution
- Late DT and CD account for 8-17% of filtered load
  - Permeability is ADH dependent

Summary: Tubular Water Permeability



*** ADH is the most important regulator of water balance*

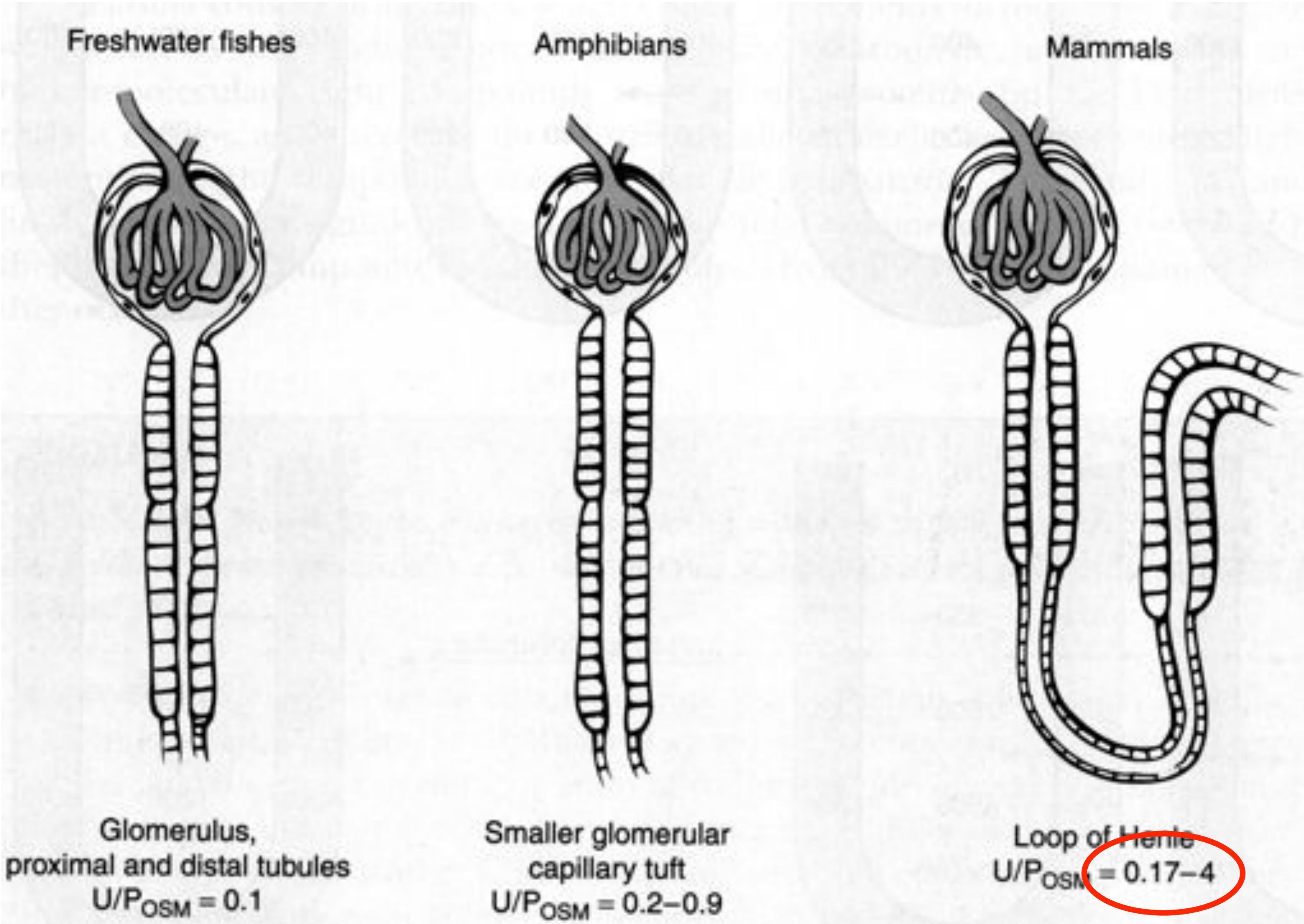
Final Urinary Concentration



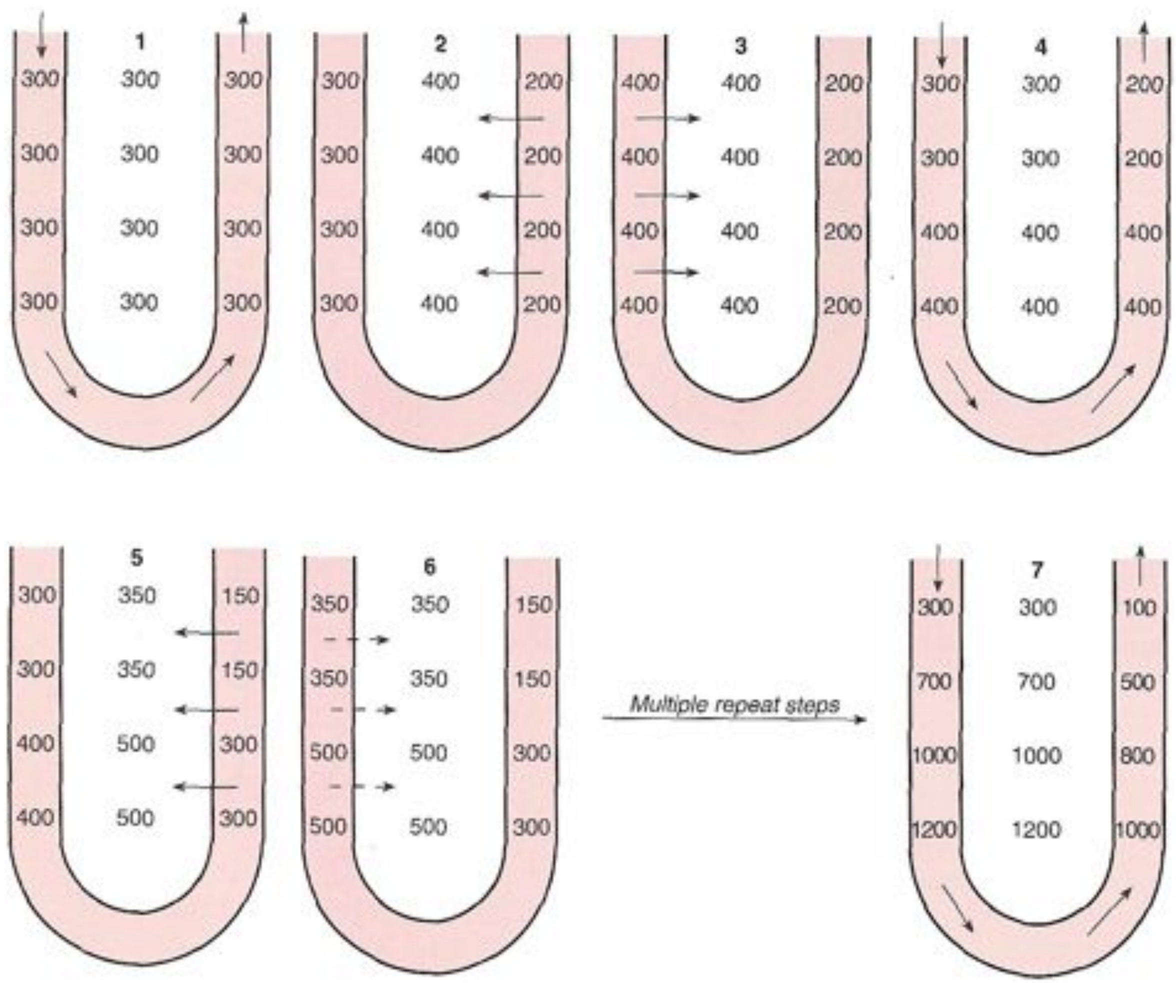
- Concentration is dependent on: 1. Interstitial gradient
  2. ADH effect

- Maximal concentration ~**1200** mOsm/kg water
- Minimal concentration ~**50** mOsm/kg water

Why Do Our Nephrons Have Loops?



Countercurrent Multiplication: Establishing An Osmotic Gradient



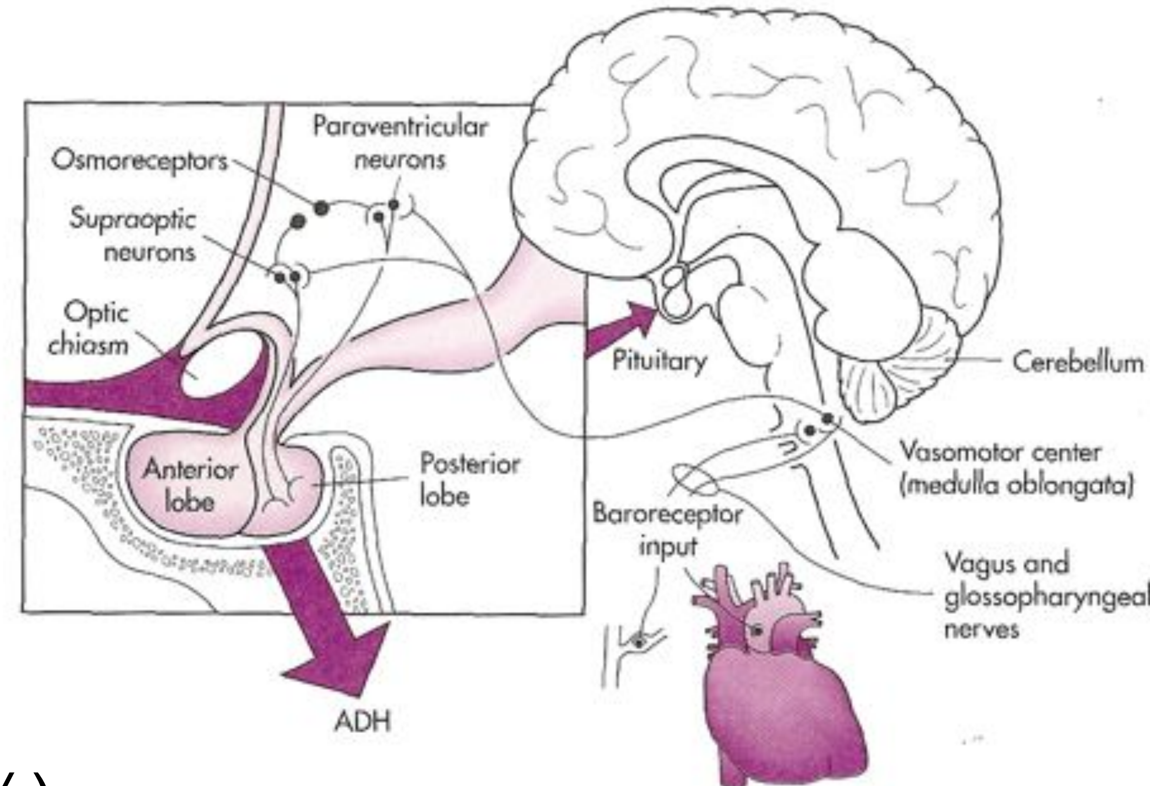
- Active Na transport in ascending limb

- Passive water reabsorption in descending limb

ADH Regulation

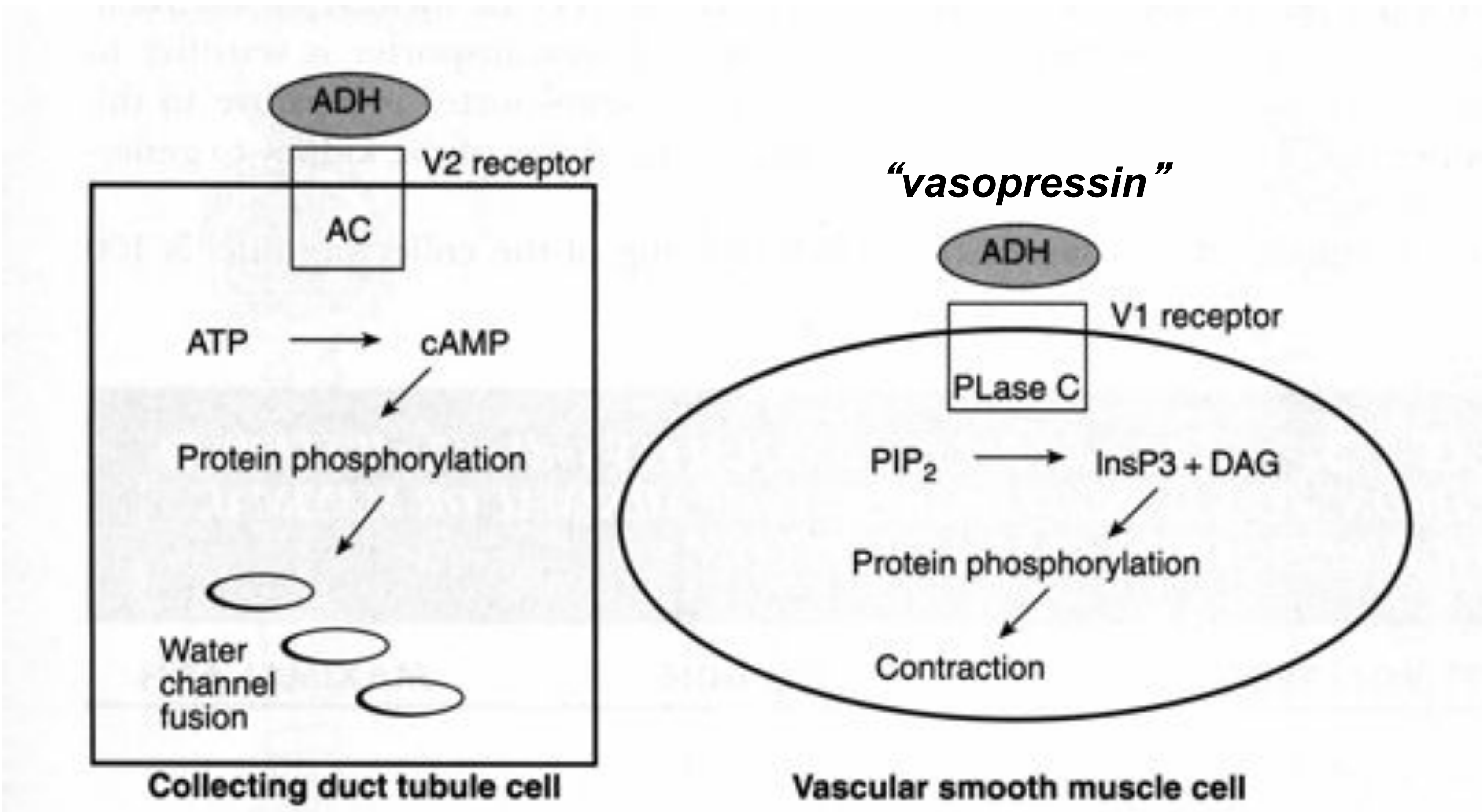
Primary stimuli:

1. Osmolality
   - Hypothalamic osmoreceptors
   - Sensitive (1%)
   - Setpoint
2. Hemodynamic
   - Baroreceptors
   - Insensitive (5-10%) but overriding

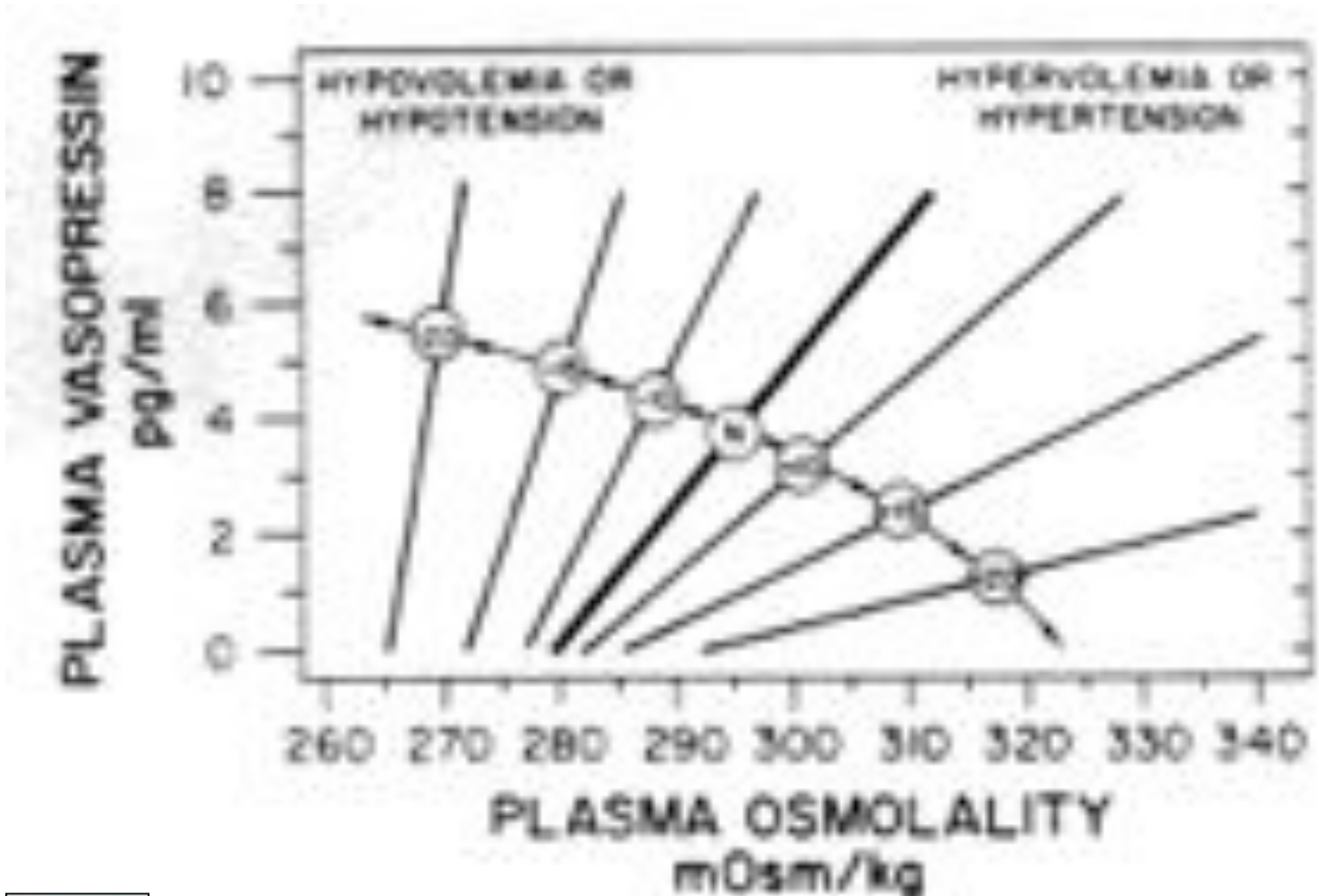


ADH Actions

- 2 main stimuli, 2 different receptors (and 2 names!)



ADH Set Point: Variation with Volume/Pressure



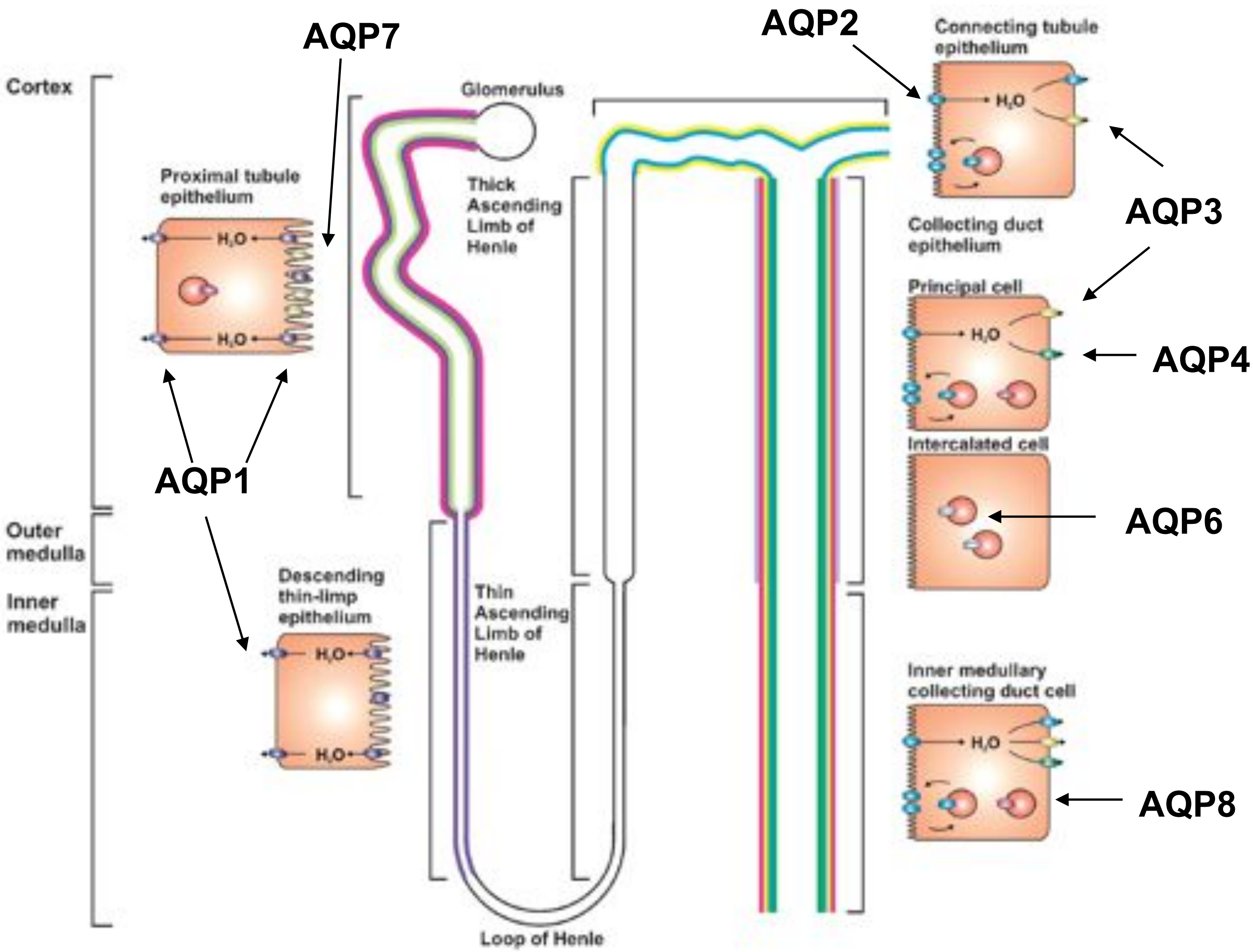
- Can also be altered in pregnancy, cancer, psychosis

Effect of ADH on Tubular Fluid Osmolality

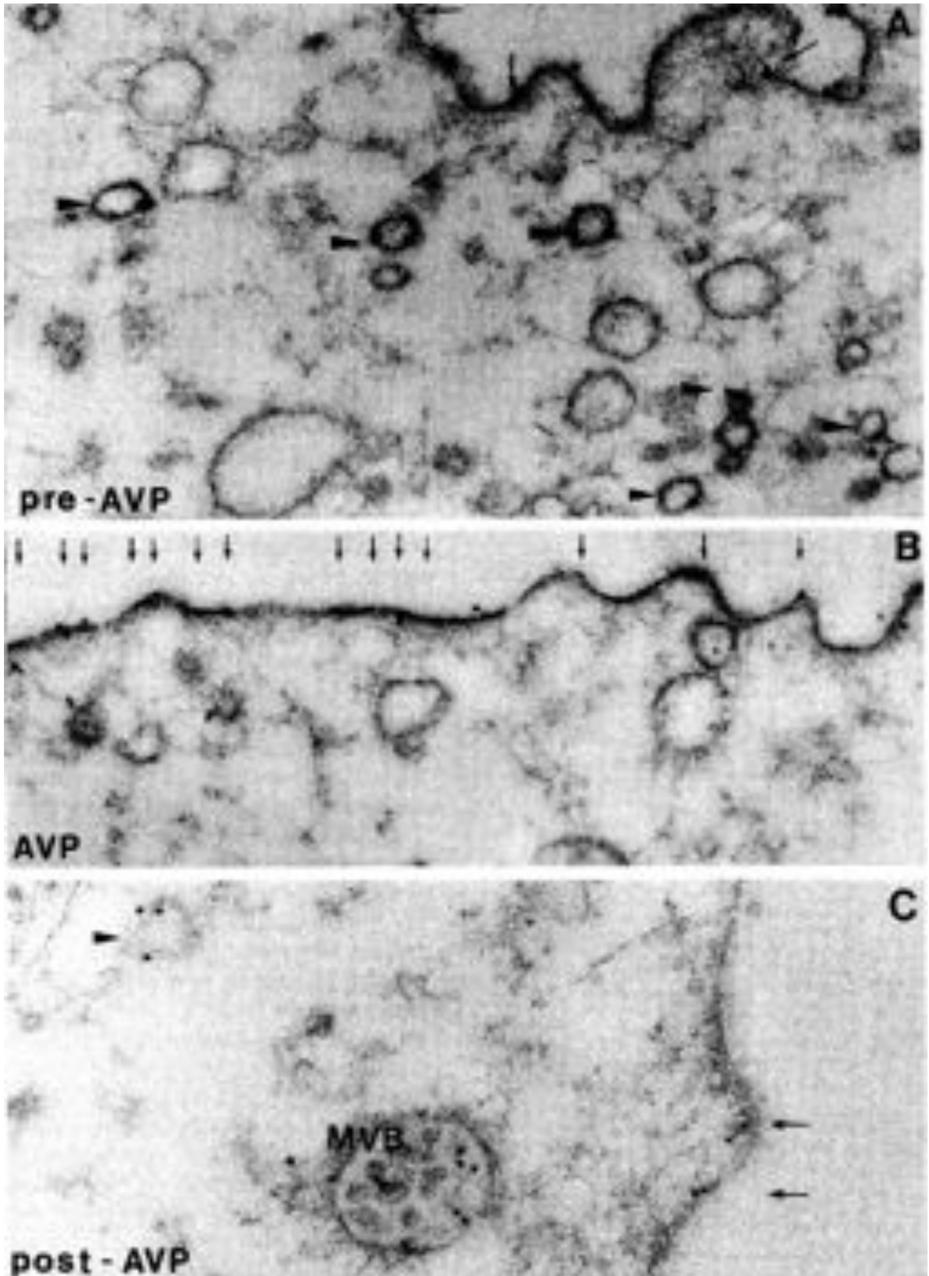
Nephron segment	No ADH	Max ADH
Proximal tubule	300	300
Start of descending thin limb	300	300
Start of ascending thin limb	1200	1200
End of TAL	100	100
End of cortical collecting duct	50-100	300
Final urine	50	1200

*The most important measure of ADH effect is **urine osmolality**.*

The Aquaporin Family

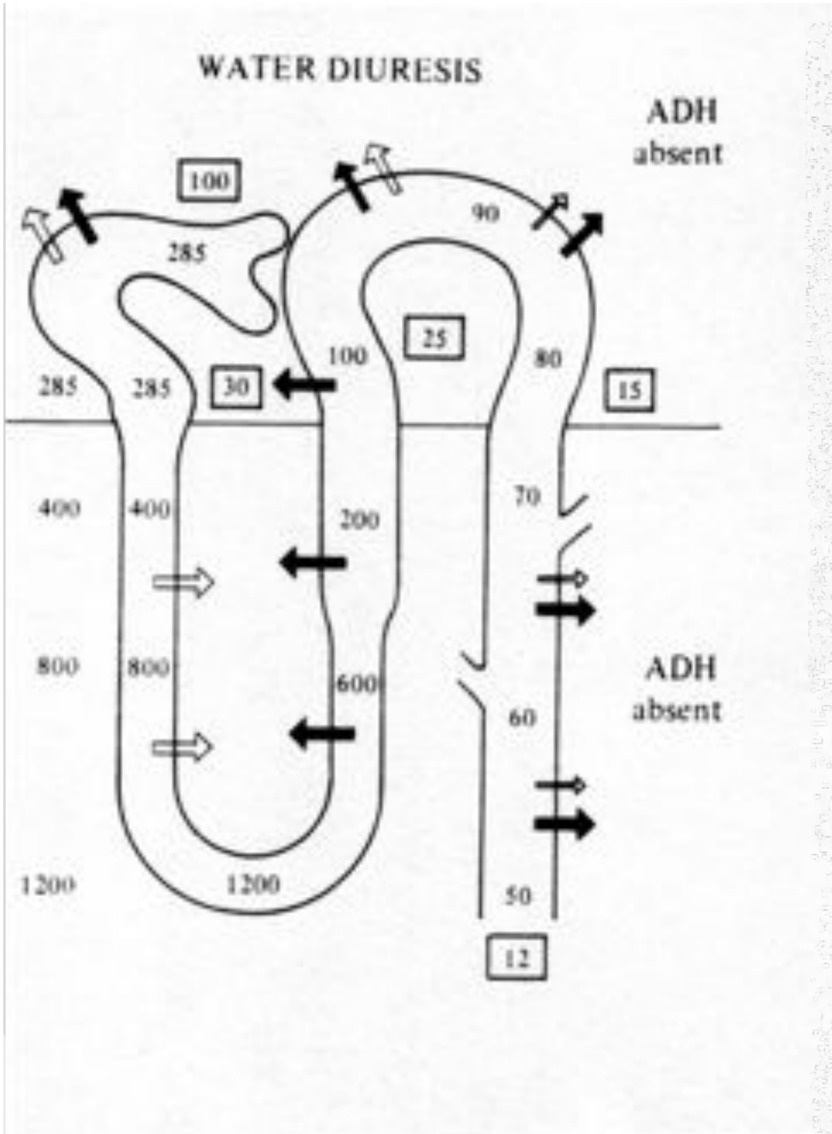


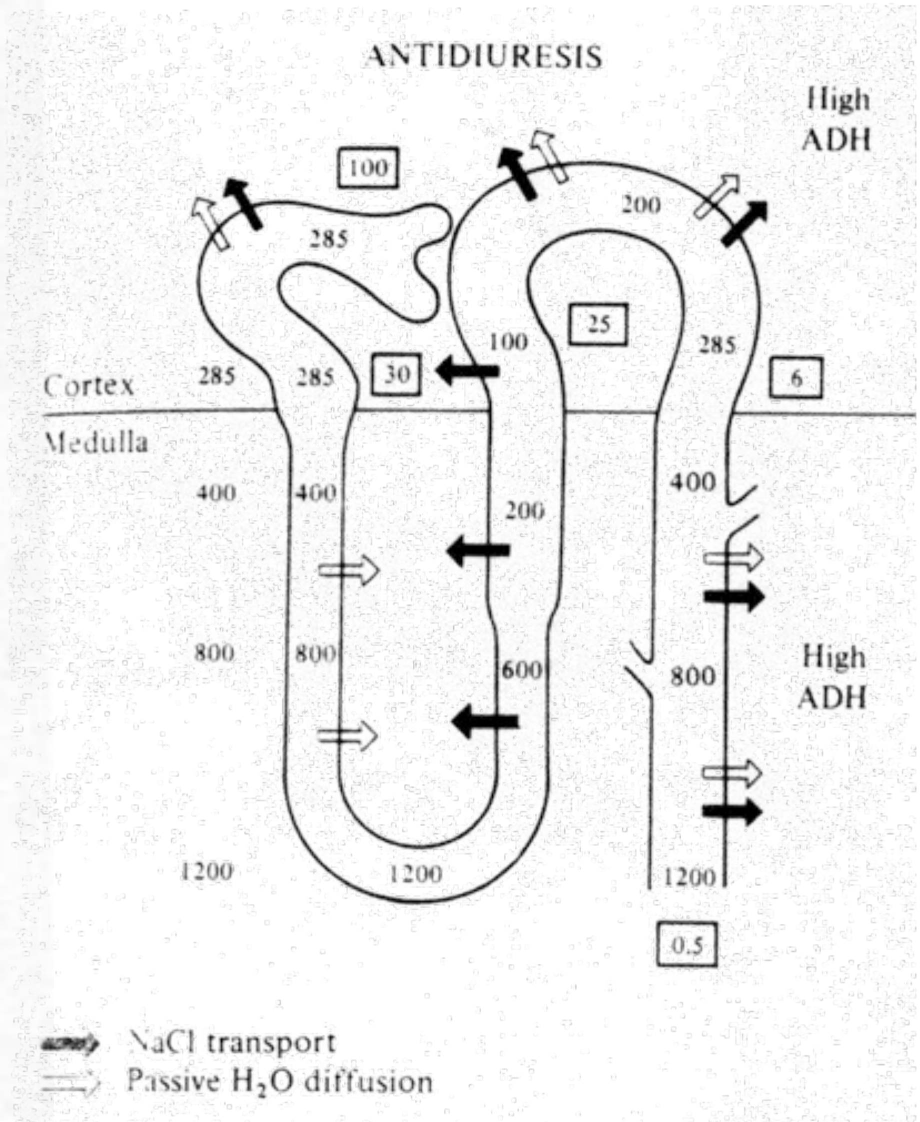
Aquaporin 2



- Stored in intracellular vesicles in collecting duct epithelium
- Through cAMP-mediated signaling, vesicles move to apical membrane
- In absence of ADH, water channels are re-internalized

Summary: Water Transport During Diuresis and Anti-Diuresis





Defining Oliguria

Oliguria: the minimal required urine output to excrete the daily obligate solute load (eg. Na ingestion, protein metabolism)

An average obligate waste solute load is 600 mosm/day. The kidneys' maximal urinary concentration is 1200 mosm/kg H_2O.

Excretion = urine volume x [waste]

- What is the minimal amount of water clearance (i.e. urine output) to excrete the daily waste load?

  600mosm/day / 1200mosm/kg H_2O = 0.5kg H_2O/day
  = 500mL/day

- What would be the minimal amount of urine output if we could only concentrate our urine to 300mosm/kg H_2O?

  600mosm/day / 300mosm/kg H_2O = 2000mL/day!

Is there a *maximal* urine output?

Rule: You can't pee pure water!

An average obligate waste solute load is 600 mosm/day. The kidneys' maximal urinary dilution is 50 mosm/kg H_2O.

Excretion = urine volume x [waste]

What is the maximal amount of urine that can be produced?

600mosm/day / 50mosm/kg H_2O = 12kg H_2O/day

= 12L/day urine output

What happens if you drink more than 12L of water in a day?

Water intoxication → hyponatremia

Regulating Water Ingestion

- Excess water ingestion is managed by increased renal free water excretion
- Free water depletion is managed by both increased renal water reabsorption and water ingestion
- *An intact thirst mechanism alone can prevent the development of significant free water depletion*
- Thirst mechanism: 1. Thirst sensation
  2. Access to water

Thirst

- Regulated by hypothalamic receptors:
  - Subfornical organ
  - Organum vasculosum
- Signals: 1. Osmolality

  2. Hemodynamic sensing
  - Independent from (but synergistic with) ADH secretion
  - Also stimulated by angiotensin II
- Receptors in oropharynx and upper GI tract sense water intake
  - Relief even before correction of osmolality

Questions?

Additional Source Information

for more information see: http://open.umich.edu/wiki/CitationPolicy

Slide 5: Michael Heung
Slide 6. Michael Heung
Slide 7: Michael Heung
Slide 8: Michael Heung
Slide 10: Source Undetermined
Slide 11: Source Undetermined
Slide 12: Source Undetermined
Slide 13: Source Undetermined
Slide 14: Source Undetermined
Slide 15: source Undetermined
Slide 16: Source Undetermined
Slide 17: source Undetermined
Slide 18: Source Undetermined
Slide 19: source Undetermined
Slide 20: Source Undetermined
Slide 21: Michael Heung
Slide 22: Source Undetermined
Slide 23: Source Undetermined
Slide 24: Source Undetermined (Both Images)
Slide 28: Bottled Water by greggoconnell, http://www.flickr.com/photos/greggoconnell/65346703/