NEPHROLOGY

PHRAMONGKUTKLAO HOSPITAL

POLYURIA

Krit Tipchaichatta

OUTLINE

Introduction

NEPHROLOGY
PHRAMONGKUTKLAO HOSPITAL

- Water metabolism
- Urine concentration and dilution
- Polyuria definition
- Diagnosis and approach
- Treatment

Physiology of Water balance

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- In the steady state : Water intake = Water loss
- Need to maintain a physiologic serum osmolality of 285 to 290 mOsm/kg H_2O
- Typical solute load 900 to 1200 mOsm/day (Thai 600-900)
- To dilute (minimal Uosm 60 mOsm/kg H_2O) and To concentrate (maximal Uosm 1,200 mOsm/kg H_2O) the urine allows wide flexibility in urine flow
  - maximal urine volume = 15-20 L/day
  - minimal urine volume = 0.75-1 L/day

***Urine volume = Total daily solute (mOsm) / Urine Osm (mOsm/kgH_20)

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Body fluid compartment

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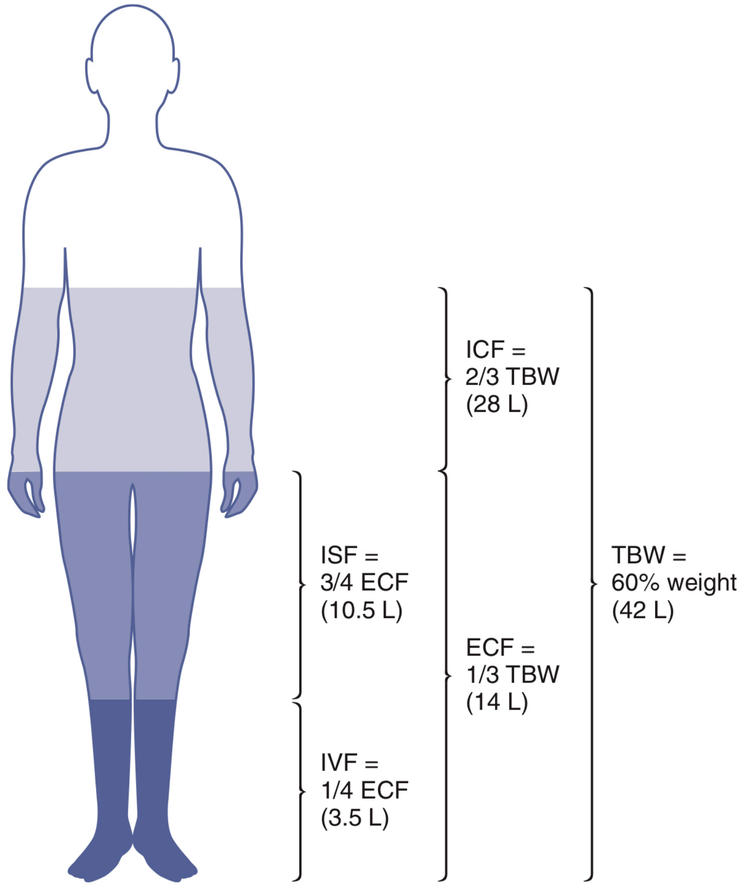

- **TBW = 60% of BW**
  - **2/3 = ICF**
  - **1/3 = ECF** (ISF [3/4] **+ IVF** [1/4])

Extracellular water (1/3)		Intracellular water (2/3)	
Interstitial (2/3)	Blood (1/3)		
140		25	Na^+
4.5		150	K^+
1.2		15	Mg
2.4		0.01	Ca^{2+}
100		2	Cl
25		6	HCO_3^-
1.2		50	Phos

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Water balance

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- Water metabolism is responsible for the **balance between the intake and excretion of water**
  - **Intake**
    - **Unregulated :** ingested foods, consumption of beverages
    - **Regulated :** fluids consumed in response to thirst
  - **Excretion**
    - **Unregulated :** insensible water losses (e.g., sweating, exhaled air, GI loss) {8 to 10 ml/kg upto 20 ml/kg depend on BT and physical activity}
    - **Regulated :** renal excretion

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Quantitation of renal water excretion

- Urine volume(V) =Osmolar clearance (C_{osm}) + Free water clearance (C_{water})
- $V = C_{osm} + C_{water}$

$C_{water} = V - C_{osm}$; $C_{osm} = U_{osm} \times V/P_{osm}$

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

$= V\{1-(U_{osm}/P_{osm})\}$

*$P_{osm}=P_{Na}$
** $U_{osm}=U_{Na}+U_K$

- $C_{water} = V\{1-(U_{osm}/P_{osm})\}$

$= V\{1-(U_{Na}+U_K/P_{Na})\}$

-In hypotonic urine ($U_{osm} < P_{osm}$), C_{water} is postive
-In isotonic urine ($U_{osm} = P_{osm}$), C_{water} is zero
-In hypertonic urine ($U_{osm} > P_{osm}$), C_{water} is negative

-If ($U_{Na}+U_K < P_{Na}$), C_{water} is postive -> Hypernatremia
-If ($U_{Na}+U_K > P_{Na}$), C_{water} is negative -> Hyponatremia

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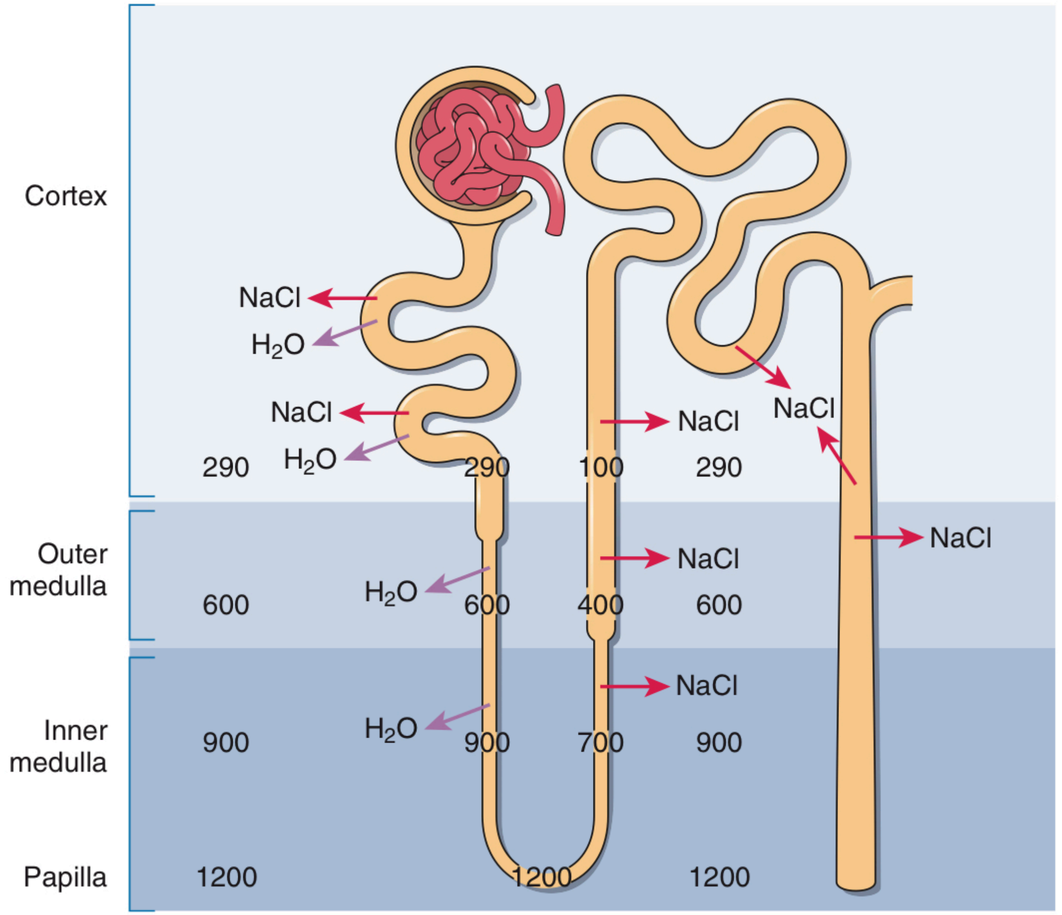
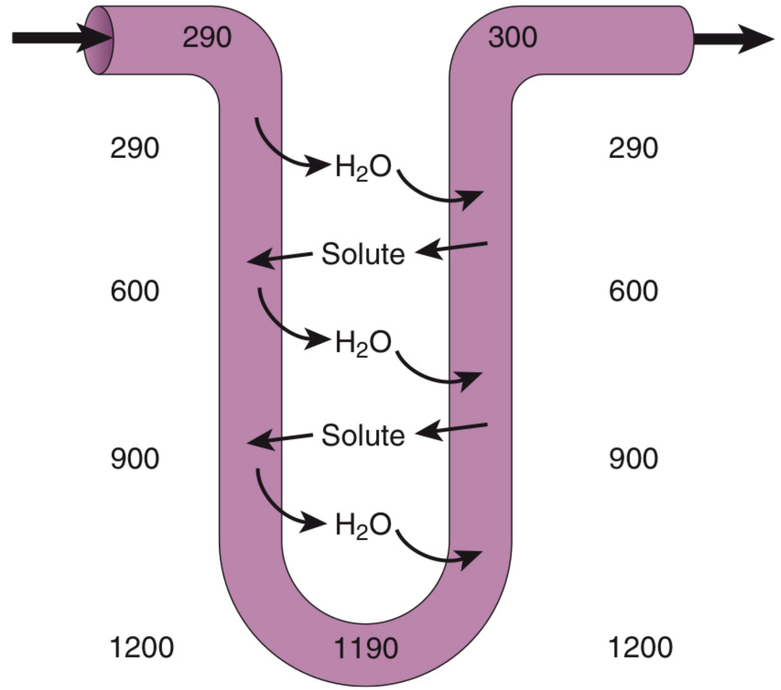
Countercurrent system

Countercurrent Multiplication



Countercurrent Exchange



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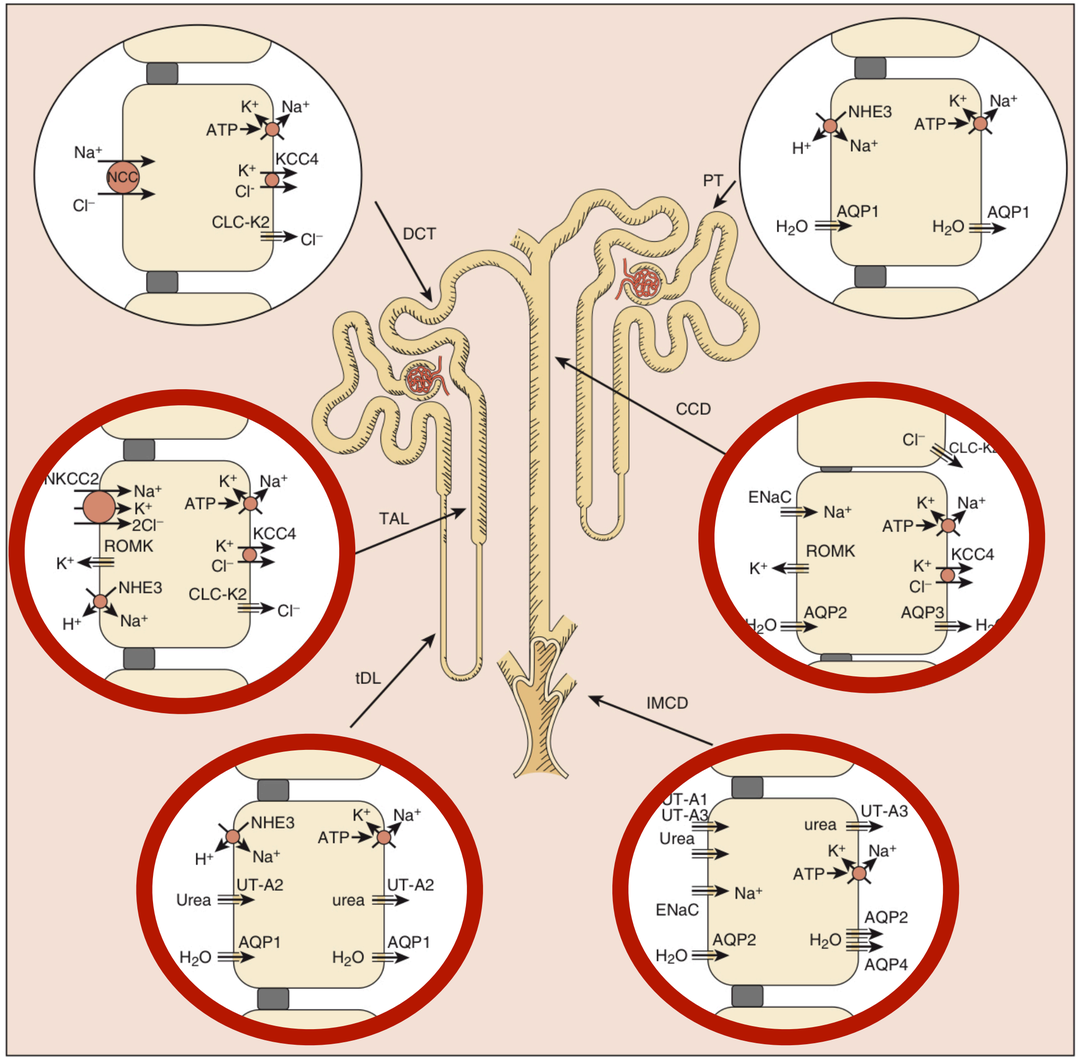
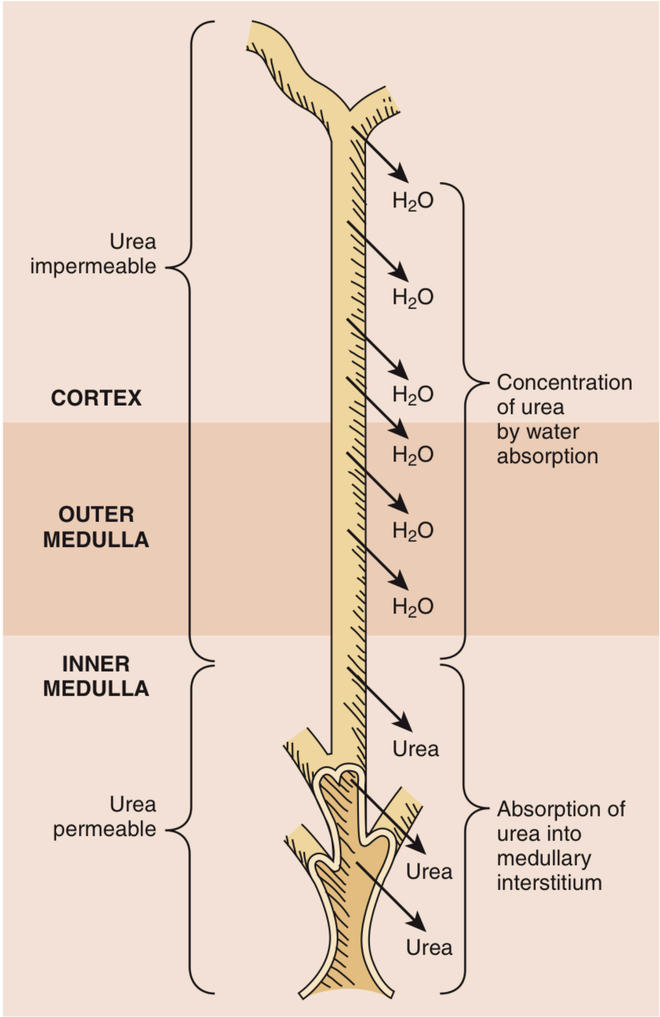
Countercurrent system





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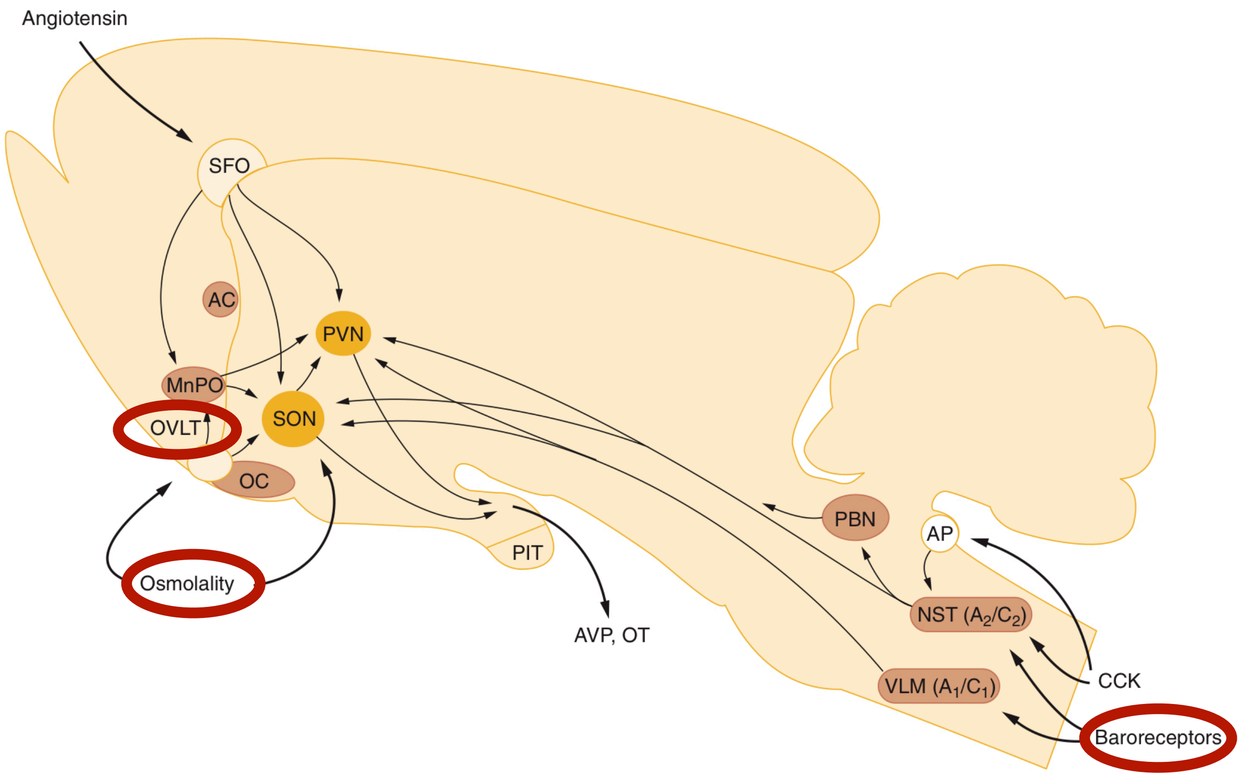
Arginine vasopressin



- AVP : anitidiuretic hormone (ADH)
- 9-amino acid peptide synthesized by hypothalamus
- Lysine substitue arginine at position 8 -> vasopressin
- Isoleucine substitue phenylalanine at position 3 and leucine for arginine at position 8 -> oxytocin (OT) (weak antidiuretic activity)

SFO : subfornic organ
MnPO : median pre optic nucleus
OVLT : vascular organ of the lamina terminals
SON : supraoptic nucleus
PVN : paraventricular nucleus
NST : nucleus of the solitary tract
PBN : parabrachial nucleus
VLM : ventrolateral medulla

} magnocellular

<— CN IX, X <— Baroreceptors (cardiac atria, aorta, carotid sinus)

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Arginine vasopressin

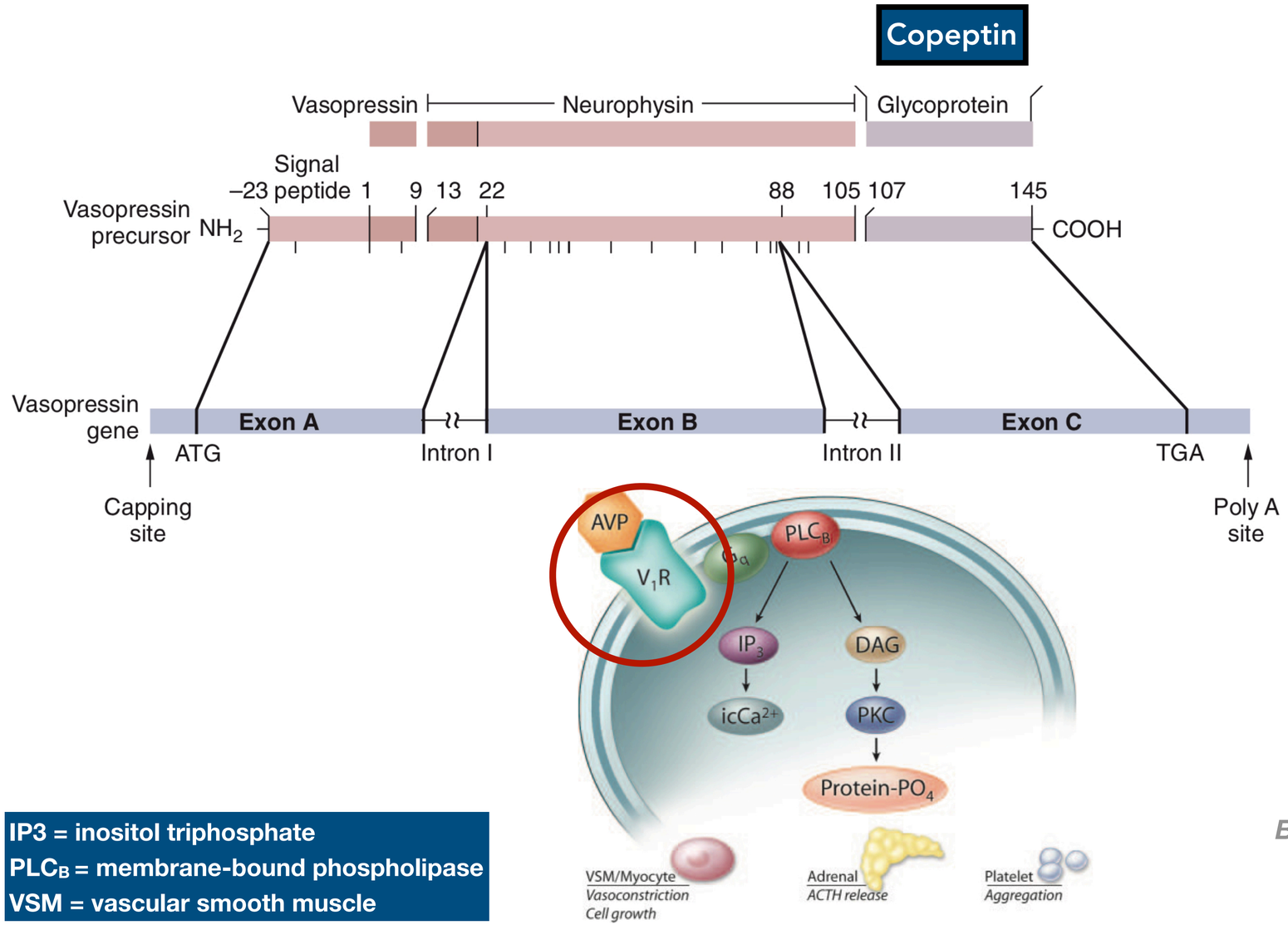

Table 1 | Vasopressin receptor location and functions

Receptor	Localization	Functions
V1a	Vascular smooth muscle	Vasoconstriction, myocardial hypertrophy
	Platelets	Platelet aggregation
	Hepatocytes	Glycogenolysis
	Myometrium	Uterine contraction
V1b[a]	Anterior pituitary	ACTH release
V2	Basolateral membrane collecting tubule	Insertion of AQP2 water channels into apical membrane, induction of AQP2 synthesis
	Vascular endothelium	vWF and factor 8 release
	Vascular smooth muscle	Vasodilatation

ACTH, adrenocorticotropin hormone; AQP2, aquaporin-2.
[a]Termed V3 in some classification schemes.

IP3 = inositol triphosphate
PLC_B = membrane-bound phospholipase
VSM = vascular smooth muscle

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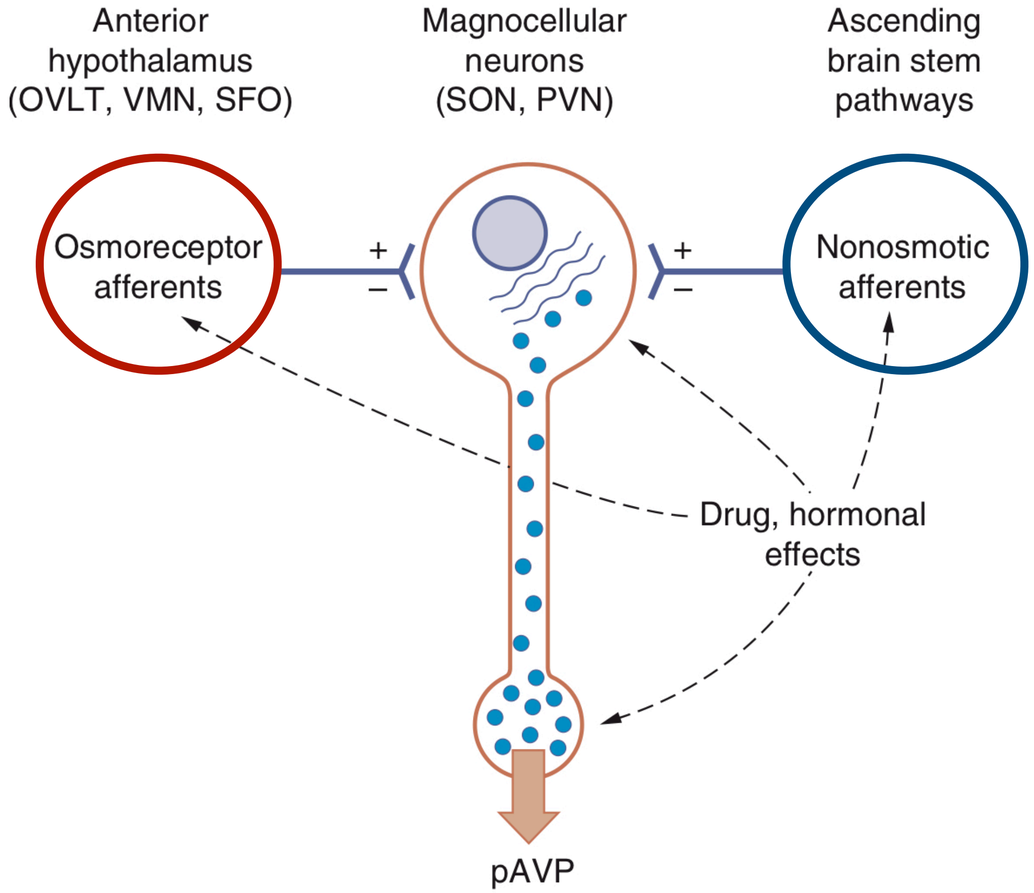
Kidney Int. 2006 Jun;69(12) : 2124-30
Circulation. 2008 Jul 22; 118(4):410-21.

AVP secretion



- **Osmotic regulation**
- Nonosmotic regulation
  - Hemodynamic stimuli
  - Drinking
  - Nausea
  - Hypoglycemia
  - Renin-Angiotensin-Aldosterone system
  - Stress
  - Hypoxia / Hypercapnia
  - Drugs

SFO : subfornic organ
MnPO : median pre optic nucleus
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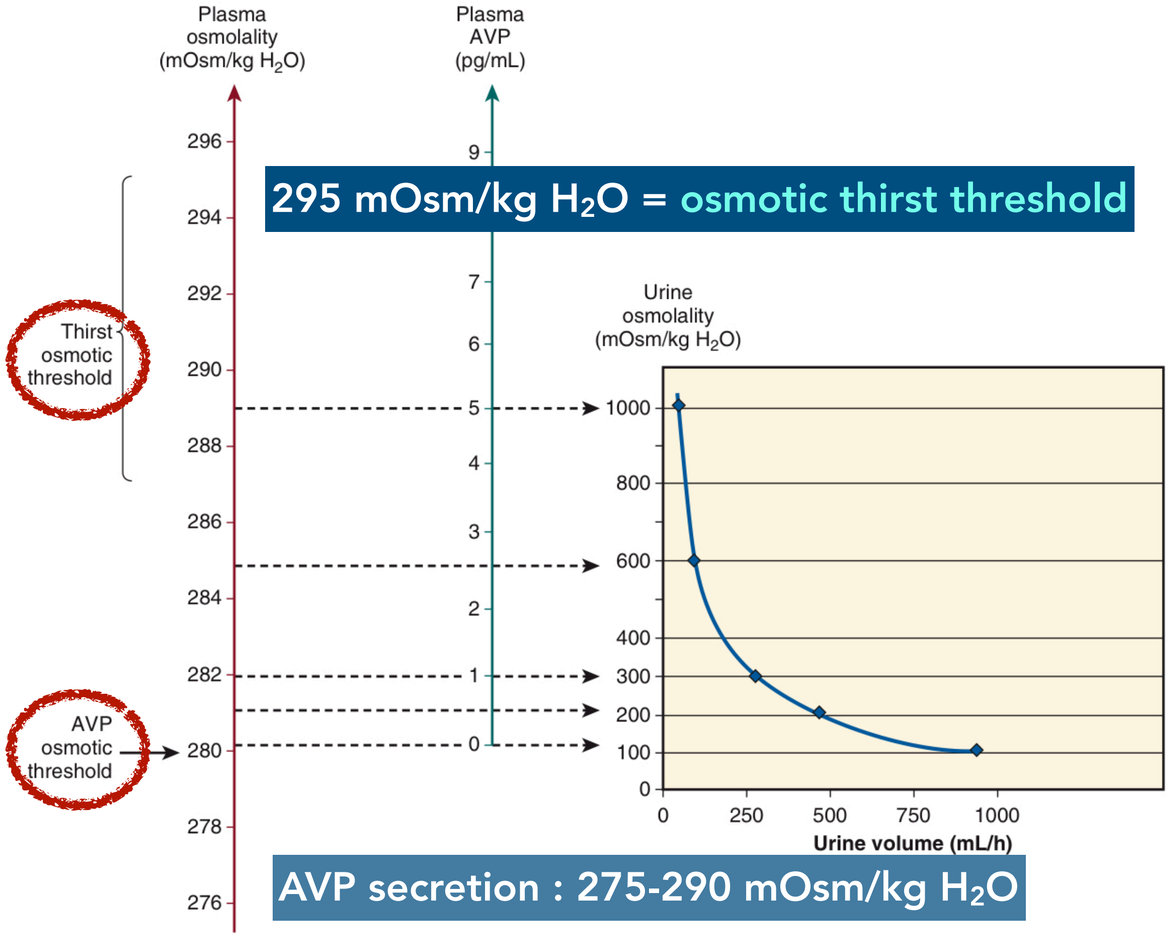
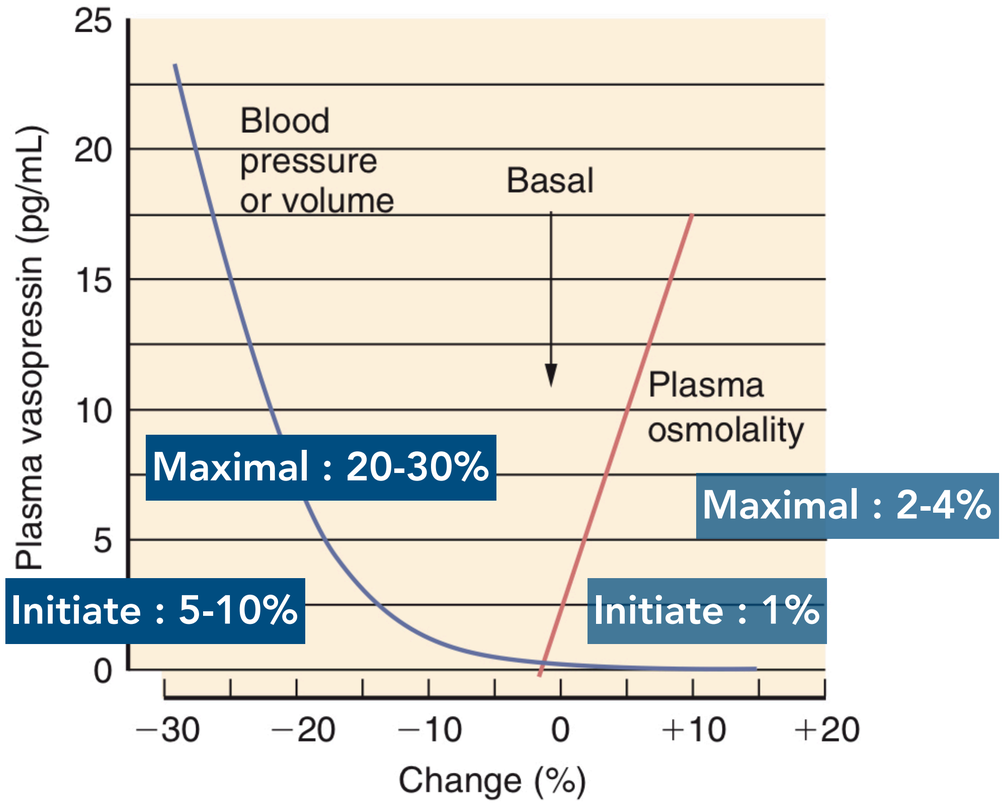
AVP secretion



295 mOsm/kg H_2O = osmotic thirst threshold

AVP secretion : 275-290 mOsm/kg H_2O



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AVP secretion

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- Osmotic regulation
- Nonosmotic regulation
  - Hemodynamic stimuli
  - Drinking
  - Nausea — AVP increased upto 200 - 400 pg/mL
  - Hypoglycemia — Decreased glucose level 20% -> AVP secretion, transient
  - Renin-Angiotensin-Aldosterone system — Ang II via SFO -> SON and PVN
  - Stress — Endotoxin-induced Fever via IL-1 and IL-6
  - Hypoxia / Hypercapnia
  - Drugs

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AVP secretion

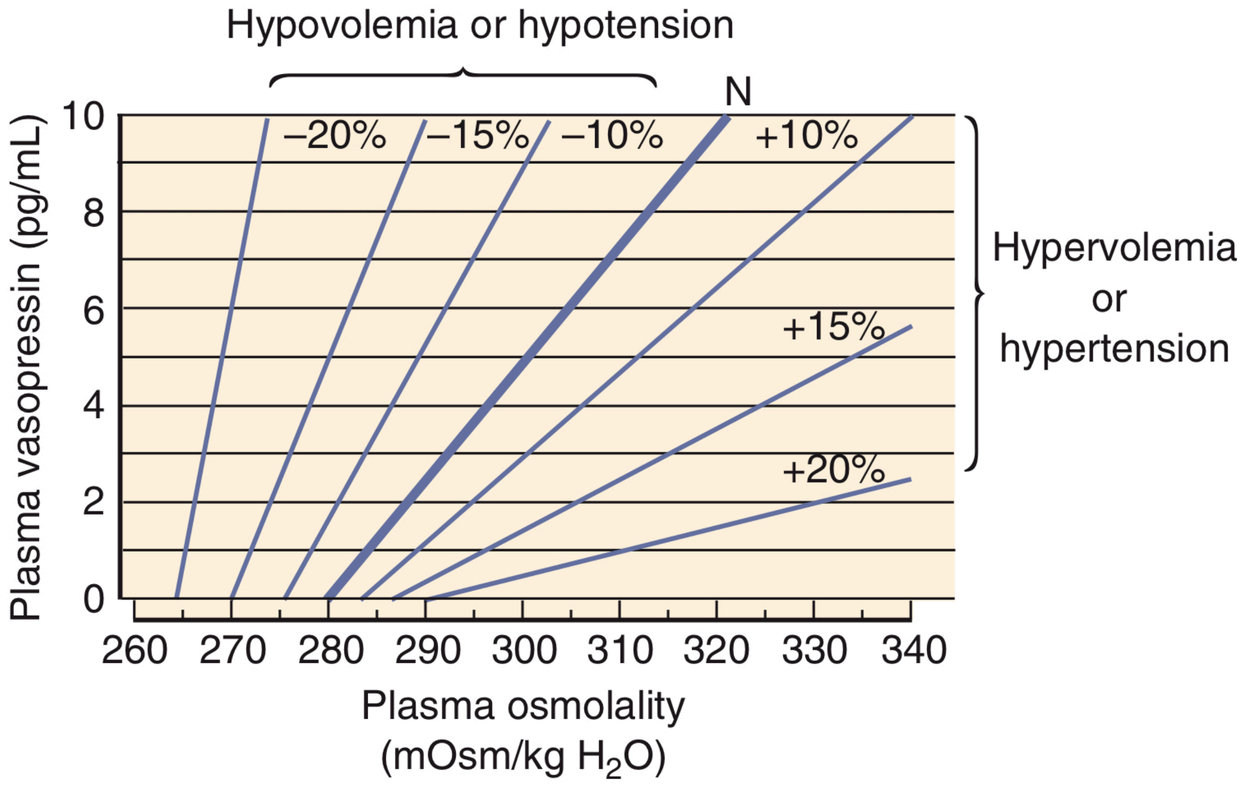

Table 15.1 Drugs and Hormones That Affect Vasopressin Secretion

Stimulatory	Inhibitory
Acetylcholine	Norepinephrine
Nicotine	Fluphenazine
Apomorphine	Haloperidol
Morphine (high doses)	Promethazine
Epinephrine	Oxilorphan
Isoproterenol	Butorphanol
Histamine	Opioid agonists
Bradykinin	Morphine (low doses)
Prostaglandin	Ethanol
β-Endorphin	Carbamazepine
Cyclophosphamide IV	Glucocorticoids
Vincristine	Clonidine
Insulin	Muscimol
2-Deoxyglucose	Phencyclidine
Angiotensin II	Phenytoin
Lithium	
Corticotropin-releasing factor	
Naloxone	
Cholecystokinin	

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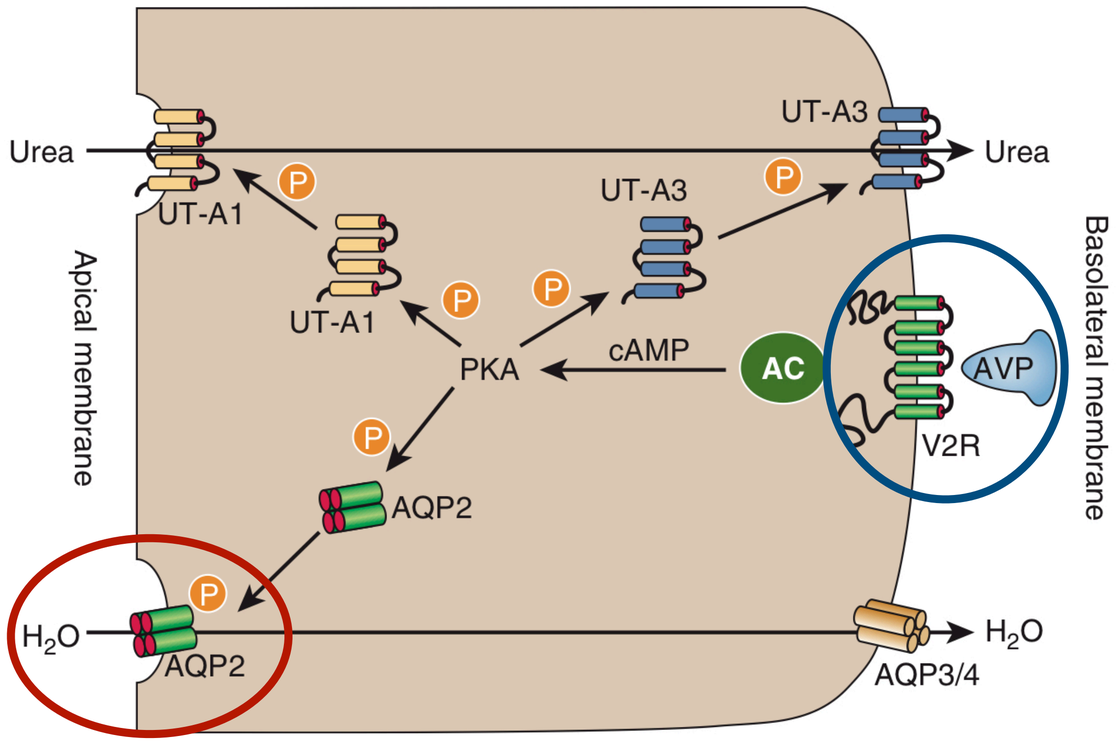
AVP secretion



- AQP1 @ apical and basolateral membrane of Proximal tubule and Descending limb of loop of Henle
- AQP2 @ apical membrane and intracellurlar vesicles of CD principal cells
- AQP3 @ basolateral membrane along CD
- AQP4 @ basolateral membrane only inner medullary CD and hypothalamus (as Osm R)

- **Action via V_2 receptors (basolateral membrane of principal cells in late distal tubule and along CD) -> increased water permeability through AQP2**

- **AVP stimulating Na+ reabsorption in TAL and urea reabsorption via UT-A1 and UT-A3 at inner medullary CD (increase tonicity and driving force for water reabsorption)**

>> Short-term regulation -> rapid and reversible increase in CD water permeability after AVP administration (shuttle hypothesis ; within minutes)

>> Long-term regulation -> increased transcription of gene involves in AQP2 production (≥ 24 hours)

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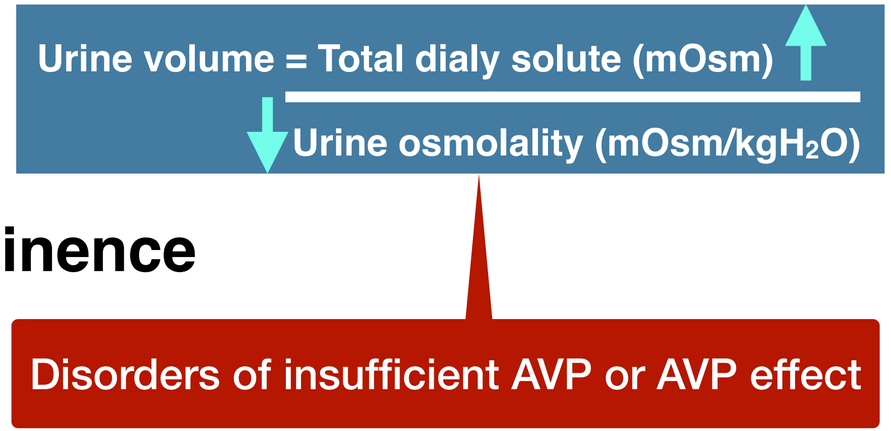
Polyuria

- **Polyuria : passage of excessive quantity of urine**
  - **U volume > 3 L/day (adult)**
  - **U volume > 2,000 ml/m²/day (Children)**
- **Polyuria associate with Polydipsia (water intake > 6L/d)**
- **dDx Frequency of urine**
  - **Frequent passage of small amounts of urine**
  - **Causes : UTI, BPH, UT stones, Urinary incontinence**

** U/O (L)= 100/UCr



- Urine volum flow = C_{osm} + C_{water}
- ↑C_{osm} : loop diuretic, salt wasting, excess salt ingestion, vomiting (bicarbonaturia), alkali or manitol administration
- ↑C_{water} : excess ingestion of water or abnormal renal concentration

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Naowanit Nata. Polyuria. Jul. 2014. PowerPoint Presentation.

Polyuria

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- Types of Polyuria
  - Water diuresis
  - Solute diuresis
  - Mixed water + solute diuresis

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Polyuria

Water diuresis

- Decreased ADH secretion
- Diabetes inspires (DI)
  - >Central DI (CDI)
  - >Nephrogenic DI (NDI)

Mixed water -Solute diuresis

- Combined uncontrolled DM and CKD
- Post relief of obstructive uropathy
- Diuretic phase of ATN

Solute diuresis

- Non-electrolyte
- Electrolyte

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Initial investigation

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- Urine volume
- UA : Urine Sp.Gr., urine glucose
- Serum : BUN, Cr, glucose, electrolyte, Osm
- Urine Osm.
- Total solute excretion in 24 hours
- 24-hour solute clearance (Cosm)
  - Cosm = (Uosm/Posm) x Volume (L)
- Fractional excretion of solute (Cosm/GFR)

Polyuria

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Water diuresis

- Uosm/Posm < 0.9
- 24-hour excretion < 900 mOsm
- 24-hour solute clearance (Cosm) < 3 ml/min
- FE of solute (Cosm/GFR) < 3%

Mixed water -Solute diuresis

- Uosm/Posm < 0.9
- 24-hour excretion > 900 mOsm
- Cosm > 3.3 ml/min
- FE of solute > 3%

Solute diuresis

- Uosm/Posm > 0.9
- 24-hour excretion > 900 mOsm
- Cosm > 3.3 ml/min
- FE of solute > 3%

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Naowanit Nata. Polyuria. Jul. 2014. PowerPoint Presentation.

Water diuresis

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Box 15.1 Causes of Hypotonic Polyuria

Central (Neurogenic) Diabetes Insipidus

Congenital (congenital malformations; autosomal dominant, arginine vasopressin [AVP] neurophysin gene mutations)
Drug- or toxin-induced (ethanol, diphenylhydantoin, snake venom)
Granulomatous (histiocytosis, sarcoidosis)
Neoplastic (craniopharyngioma, germinoma, lymphoma, leukemia, meningioma, pituitary tumor; metastases)
Infectious (meningitis, tuberculosis, encephalitis)
Inflammatory, autoimmune (lymphocytic infundibuloneurohypophysitis)
Traumatic (neurosurgery, deceleration injury)
Vascular (cerebral hemorrhage or infarction, brain death)
Idiopathic

Osmoreceptor Dysfunction

Granulomatous (histiocytosis, sarcoidosis)
Neoplastic (craniopharyngioma, pinealoma, meningioma, metastases)
Vascular (anterior communicating artery aneurysm or ligation, intrahypothalamic hemorrhage)
Other (hydrocephalus, ventricular or suprasellar cyst, trauma, degenerative diseases)
Idiopathic

Increased AVP Metabolism

Pregnancy

Nephrogenic Diabetes Insipidus

Congenital (X-linked recessive, AVP V_2 receptor gene mutations; autosomal recessive or dominant, aquaporin-2 water channel gene mutations)
Drug-induced (demeclocycline, lithium, cisplatin, methoxyflurane)
Hypercalcemia
Hypokalemia
Infiltrating lesions (sarcoidosis, amyloidosis)
Vascular (sickle cell anemia)
Mechanical (polycystic kidney disease, bilateral ureteral obstruction)
Solute diuresis (glucose, mannitol, sodium, radiocontrast dyes)
Idiopathic

Primary Polydipsia

Psychogenic (schizophrenia, obsessive-compulsive behaviors)
Dipsogenic (downward resetting of thirst threshold, idiopathic or similar lesions, as with central DI)

Water diuresis

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- **Central (Neurogenic) Diabetes Insipidus**
- **Osmoreceptor Dysfunction**
- **Increased AVP Metabolism**
- **Nephrogenic Diabetes Insipidus**
- **Primary Polydipsia**

Central (Neurogenic) Diabetes Insipidus

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Traumatic (neurosurgery, deceleration injury)
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Idiopathic

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Central diabetes insipidus

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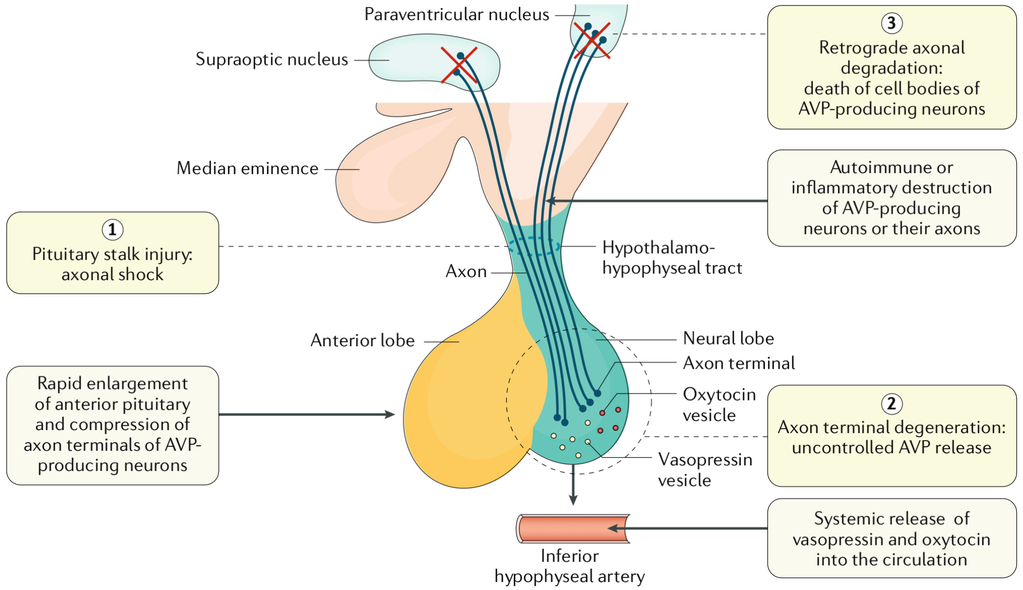
- Caused by inadequate secretion of AVP from the posterior pituitary in response to osmotic stimulation
- Clinical features :
  - Abrupt onset
  - Prefer drink cold water
  - Nocturia
- Severity depend on degree of destruction of the neurohypophysis -> partial or complete CDI



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Nat Rev Dis Primers. 2019 Aug 8; 5(1):54.

Central diabetes insipidus

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Congenital

✓Autosomal dominant
- ✳Mutation of gene encode AVP (copeptin not be effect) -> misfolding of precursor -> cannot release from hypothalamus and pituitary
- ✳Mild polyuria, polydipsia in first year of life

✓Autosomal recessive (Wolfram syndrome)
- ✳DIDMOAD (DI(late manifestration), DM, optic atrophy and deafness)
- ✳Linked to chromosome 4 -> involve abnormality of mDNA

Accquired

✓ Post-traumatic
✓ Iatrogenic (postsurgical)
✓ Tumor (metastatic from breast, craniopharyngioma, pinealoma)
✓ Histiocytosis
✓ Granuloma (Tb, sarcoidosis)
✓ Aneurysm
✓ Meningitis
✓ Encephalitis
✓ GBS
✓ Drugs
✓ Idiopathic

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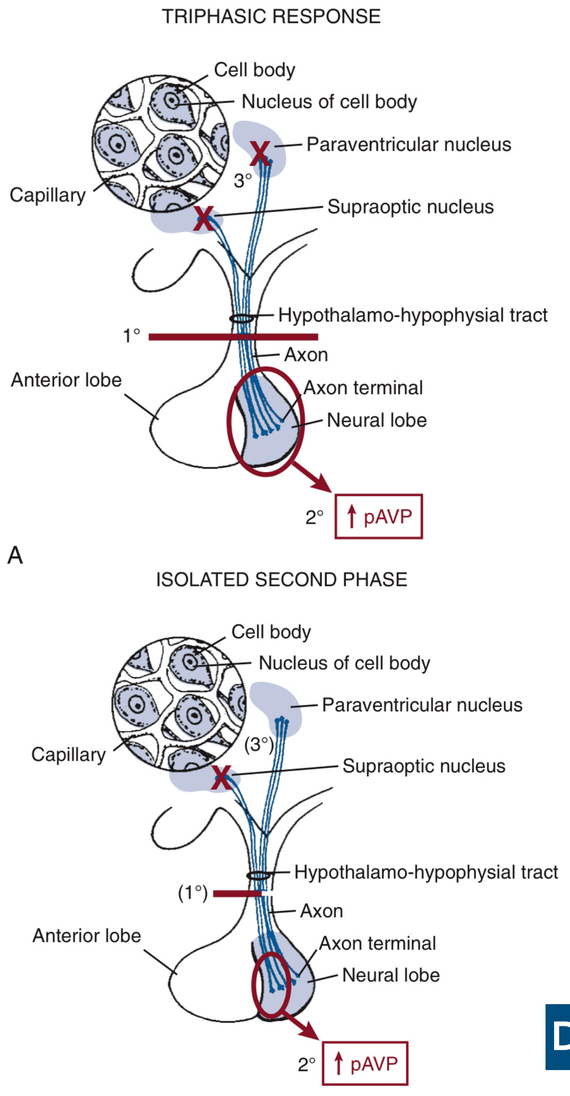
CDI from Traumatic injury or surgery



- Develop after pituitary stalk transection
- Tiphasic Response
  - First phase(Initial DI) : several hours to several days(4-5d), axon shock
  - Second phase(antidiuretic phase) : 2 to 14 days(6-11d), uncontrolled release of AVP from disconnected and degenerating posterior pituitary (SIAD-like)
  - Third phase (Permanent DI) : following after depleted AVP

Depend on level of injury

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Water diuresis

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- Central (Neurogenic) Diabetes Insipidus
- **Osmoreceptor Dysfunction** →
- Increased AVP Metabolism
- Nephrogenic Diabetes Insipidus
- Primary Polydipsia

Osmoreceptor Dysfunction

Granulomatous (histiocytosis, sarcoidosis)
Neoplastic (craniopharyngioma, pinealoma, meningioma, metastases)
Vascular (anterior communicating artery aneurysm or ligation, intrahypothalamic hemorrhage)
Other (hydrocephalus, ventricular or suprasellar cyst, trauma, degenerative diseases)
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Water diuresis

- Central (Neurogenic) Diabetes Insipidus
- Osmoreceptor Dysfunction
- **Increased AVP Metabolism** → **Increased AVP Metabolism**
  Pregnancy
- Nephrogenic Diabetes Insipidus
- Primary Polydipsia

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Gestational DI

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- Increase rate of AVP metabolism by cysteine amino peptidase (oxytocinase or vasopressinase produce by placenta) -> peak in 3rd trimester, undetectable at 2-4 weeks postpartum
- OT and AVP -> similar structure
- Types of Gestational DI
  - 1st : Increased Enzyme activity -> vasopressin-resistant DI of pregnancy (association with preeclampsia, acute fatty liver, HELLP -> decrease metabolism of enzyme by liver, multiple gestations)
  - 2nd : Increased metabolic clearance of vasopressin
- Treatment with desmopressin (resistant to degradation by Enzyme)

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Uptodate, 2022

Water diuresis

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- Central (Neurogenic) Diabetes Insipidus
- Osmoreceptor Dysfunction
- Increased AVP Metabolism
- **Nephrogenic Diabetes Insipidus**
- Primary Polydipsia

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Nephrogenic DI

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- Resistance to action of AVP (defect within kidney)
- Causes
  - ✓Congenital
  - ✓Drug-induced (demeclocycline, Li, cisplatin, methoxyflurance)
  - ✓Hypercalcemia, Hypokalemia
  - ✓Infiltrative lesion (sarcoidosis, amyloidosis)
  - ✓Vascular (sickle cell anemia)
  - ✓Mechanical (polycystic kidney disease, bilateral ureteral obstruction)
  - ✓Solute diuresis (glucose, mannitol, sodium radiocontrast media)
  - ✓Idiopathic

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Nephrogenic DI : Drug

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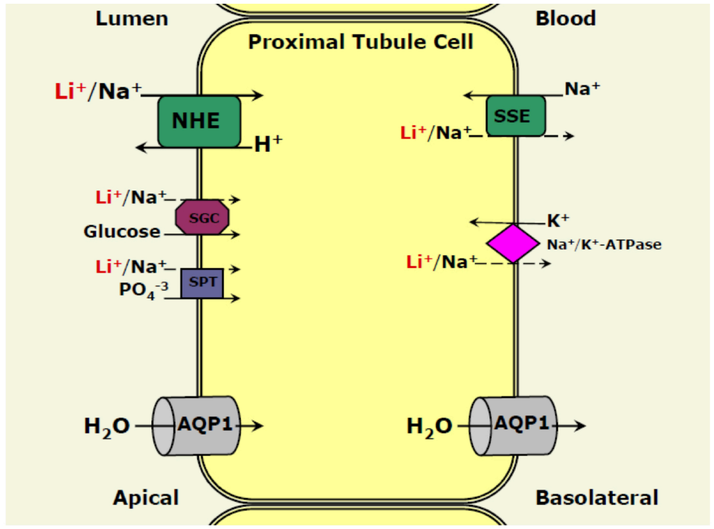

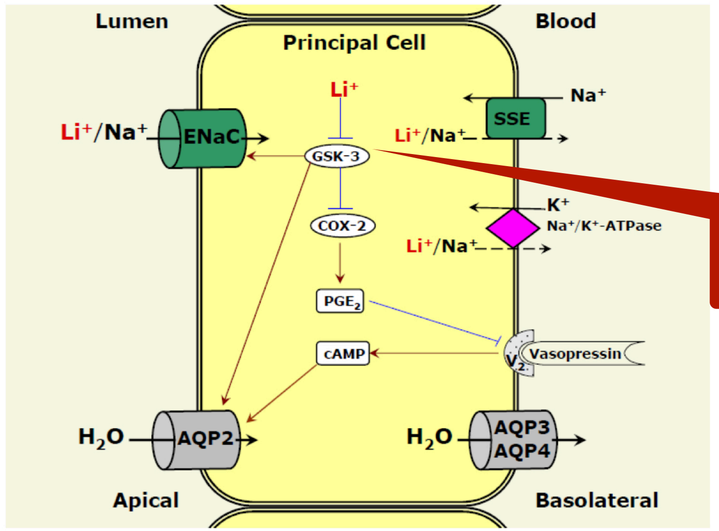

- **Lithium**
  - ✓10-20% of chronic Li therapy -> NDI
  - ✓Entry principal cell by uptake via ENaC
    1. Inh. GSK3 signaling pathway -> Inh. AC -> decrease PKA -> decrease AQP2 insertion
    2. Inh GSK3-B -> increased COX 2 -> increased PGE2 -> endocytosis of AQP2
    3. Reduce AQP2 gene transcription
    4. Reduce Principal cells

Main Mech. Inh. GSK3

Brenner and Rector's The Kidney, 10th Edition., Comprehensive Clinical Nephrology 7th ed(2023), Nat Rev Dis Primers. 2019 Aug 8; 5(1):54., Alla, S. (2015). Lithium-induced Nephrogenic Diabetes Insipidus-A Case Report and Discussion on the pathophysiological mechanism.

Nephrogenic DI : Drug

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TABLE 8.8 Acquired Nephrogenic Diabetes Insipidus: Causes and Mechanisms

Disease State	Defect in Medullary Interstitial Tonicity	Defect in cAMP Generation	Downregulation of Aquaporin 2	Other
Chronic kidney disease	Yes	Yes	Yes	Downregulation of V_2 receptor message
Hypokalemia	Yes	Yes	Yes	—
Hypercalcemia	Yes	Yes	—	—
Sickle cell disease	Yes	—	—	—
Protein malnutrition	Yes	—	Yes	—
Demeclocycline therapy	—	Yes	—	—
Lithium therapy	—	Yes	Yes	—
Pregnancy	—	—	—	Placental secretion of vasopressinase

cAMP, Cyclic adenosine monophosphate.

Nephrogenic DI : Hypercalcemia

NEPHROLOGY
PHRAMONGKUTKLAO HOSPITAL

- Water diuresis
  - Calcium deposit -> secondary tubulointerstitial injury -> impaired osmotic gradient
  - via CaS R at luminal membrane of principal cell -> stimulate Gi-protein -> decreased AC -> decreased cAMP -> decreased PKA stimulation -> decreased insert AQP2
  - via CaS R at luminal membrane of Principal cells -> AQP2 degradation
- Solute diuresis
  - via CaS R at basolateral membrane -> inh NKCC at TAL
  - Increased PGE2 -> inh. NaCl reabsorption at TAL

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Nephrogenic DI : Hypokalemia

NEPHROLOGY
PHRAMONGKUTKLAO HOSPITAL

- Stimulate water intake
- Decreased Na-Cl reabsorption in TAL -> decreased interstitial tonicity
- Decreased cAMP
- Enhanced autophagic AQP2

} Decrease AQP2

- Downregulation Urea transporter

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Water diuresis

- Central (Neurogenic) Diabetes Insipidus
- Osmoreceptor Dysfunction
- Increased AVP Metabolism
- Nephrogenic Diabetes Insipidus
- Primary Polydipsia

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Primary polydipsia

NEPHROLOGY
PHRAMONGKUTKLAO HOSPITAL

- Excessive fluid intake (polydipsia) -> hypotonic polyuria
- Normal pituitary and kidney function
- Clinical as CDI (suppress AVP secretion due to hypoosmolality) and NDI (decreased AQP2 expression due to low level of AVP)
- Associated with mental illness (e.g. schizophrenia, mania, OCD) = "Psychogenic polydipsia"
- Psychogenic polydipsia : symptoms -> fluctuation

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Primary polydipsia

NEPHROLOGY
PHRAMONGKUTKLAO HOSPITAL

- Dipsogenic DI (abnormal osmoregulatory control of thirst): no overt psychiatric illness, idiopathic or secondary to organic structural lesion in hypothalamus as cause of CDI (neurosarcoidosis, TB meningitis, MS, trauma)
- Dipsogenic DI : symptoms -> constant day to day
- Hyponatremia develop when excessive intake > renal water excretion (>20L/day)
  - Transient : Psychosis, intermittent hyponatremia, and polydipsia (PIP) syndrome
  - Combine with SIADH (acute psychosis)-> symptomatic hyponatremia

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Water Deprivation Test

NEPHROLOGY
PHRAMONGKUTKLAO HOSPITAL

Box 15.2 Fluid Deprivation Test for the Diagnosis of Diabetes Insipidus (DI)

Procedure

1. Initiation of the deprivation period depends on the severity of the DI; in routine cases, the patient should be made NPO after dinner, whereas in patients with more severe polyuria and polydipsia, this may be too long a period without fluids, and the water deprivation should be started early on the morning (e.g., 6 AM) of the test.
2. Obtain plasma and urine osmolality and serum electrolyte and plasma AVP or copeptin levels at the start of the test.
3. Measure urine volume and osmolality hourly or with each voided urine.
4. Stop the test when body weight decreases by ≥3%, the patient develops orthostatic blood pressure changes, the urine osmolality reaches a plateau (i.e., <10% change over two or three consecutive measurements), or the serum Na^+ > 145 mmol/L.
5. Obtain plasma and urine osmolality and serum electrolyte and plasma AVP or copeptin levels at the end of the test, when the plasma osmolality is elevated, preferably >300 mOsm/kg H_2O.
6. If serum Na^+ < 146 mmol/L or plasma osmolality < 300 mOsm/kg H_2O when the test is stopped, then consider a short infusion of hypertonic saline (3% NaCl at a rate of 0.1 mL/kg/min for 1 to 2 hours) to reach these end points.
7. If hypertonic saline infusion is not required to achieve hyperosmolality, administer AVP (5 U) or desmopressin (DDAVP; 1 μg) subcutaneously and continue following urine osmolality and volume for an additional 2 hours.

Interpretation

1. An unequivocal urine concentration after AVP or DDAVP (>50% increase) indicates central diabetes insipidus (CDI); an unequivocal absence of urine concentration (<10%) strongly suggests nephrogenic DI (NDI) or primary polydipsia (PP).
2. Differentiating between NDI and PP, as well as cases in which the increase in urine osmolality after AVP or DDAVP administration is more equivocal (e.g., 10%–50%), is best done using the relationship between plasma AVP or copeptin levels and plasma osmolality obtained at the end of the dehydration period and/or hypertonic saline infusion and the relationship between plasma AVP levels and urine osmolality determined under basal conditions (see Figs. 15.12, 15.13, and 15.16).

TABLE 8.6 Interpretation of Water Deprivation Test

Condition	Urinary Osmolality with Water Deprivation (mOsm/kg H_2O)	Serum Vasopressin After Dehydration (pg/ml)	Increase in Urinary Osmolality with Exogenous Vasopressin or Desmopressin
Normal	>800	>2	Little or no increase
Complete central diabetes insipidus	<300	Undetectable	Substantially increased
Partial central diabetes insipidus	300-800	<1.5	Increase of >10% of urinary osmolality after water deprivation
Nephrogenic diabetes insipidus	<300-500	>5	Little or no increase
Primary polydipsia	>500	<5	Little or no increase

Stop!!! Wt. decreased ≥ 3%, orthostatic hypotension, Uosm change < 10% over 2-3 consecutive test, Na > 145

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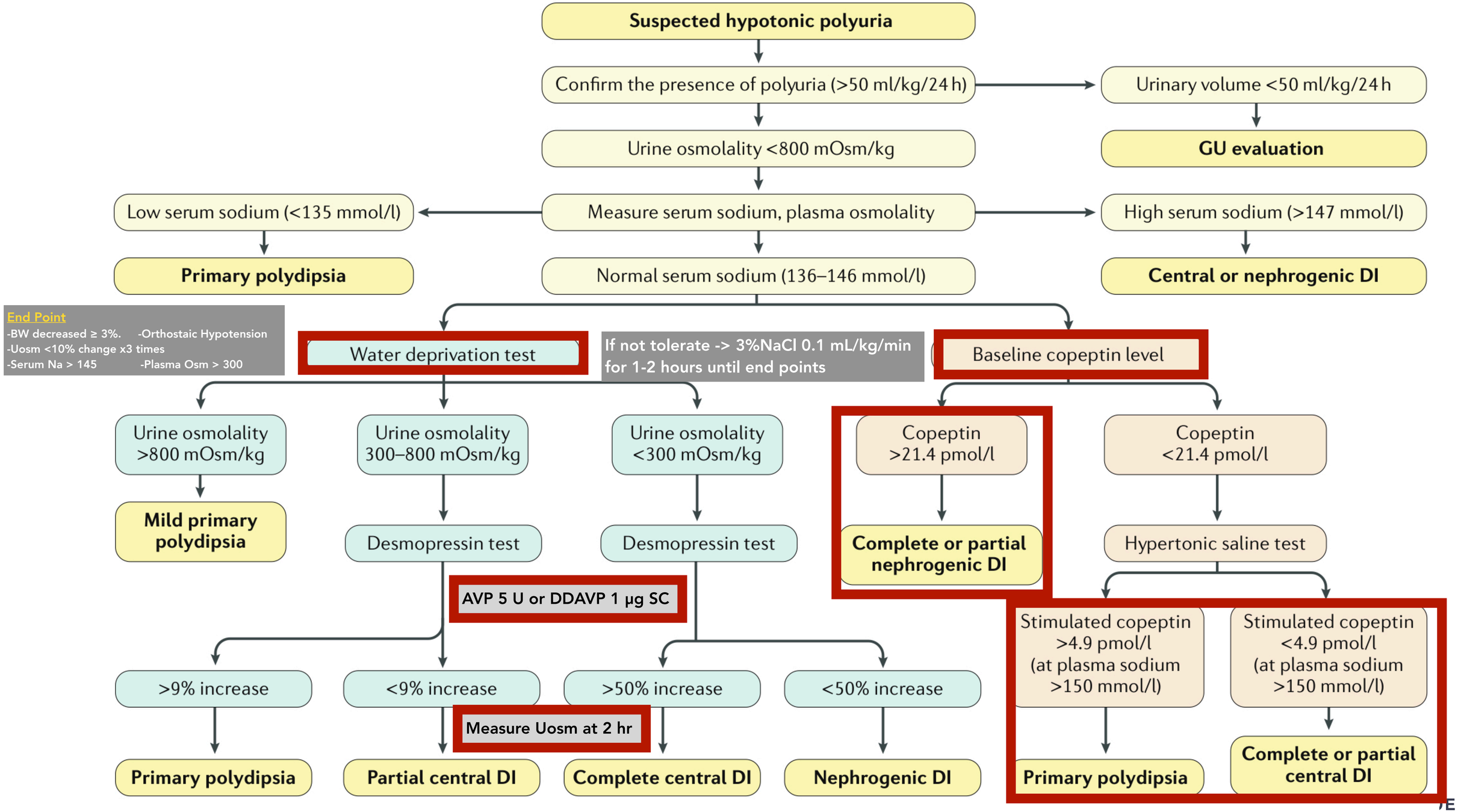

Brenner and Rector's The Kidney, 10th Edition., Nat Rev Dis Primers. 2019 Aug 8; 5(1):54.

Treatment of CDI

NEPHROLOGY
PHRAMONGKUTKLAO HOSPITAL

Free Water deficit

- TBW deficit = 0.6 x premorbid weight x {1-(140/[Na^+])

Arginine Vasopressin (AVP)

- Synthetic AVP
- 20 units/mL
- Half-life : 2 to 4 hours
- Increased BP if IV form
- For acute situation : postoperative DI

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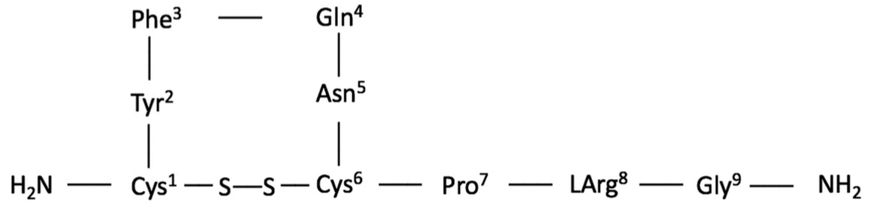
Treatment of CDI

NEPHROLOGY
PHRAMONGKUTKLAO HOSPITAL

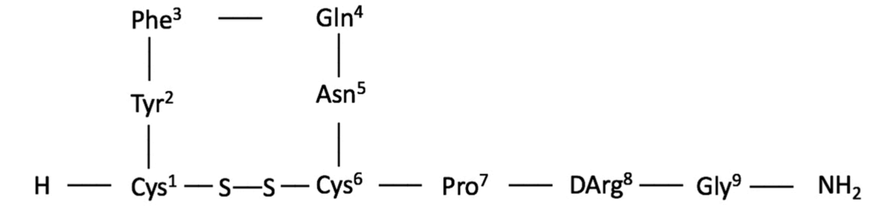
Desmopressin (DDAVP)

- **Agonist of AVP V2 receptor**
- **Longer half-life than AVP : 8 to 20 hours**
- **Drug of choice for acute and chronic situation : CDI**
- **Intranasal (10 *μ*g in 0.1 ml), oral (0.1 or 0.2 mg), Sublingual (60 to 120 *μ*g)**
- **Acute Emergency : solution contain 4 *μ*g/mL -> dose 1 to 2 *μ*g every 8 to 12 hours (IV or SC or IM)**

Arginine Vasopressin



L - Desamino – 8 – D – arginine vasopressin



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Treatment of CDI

NEPHROLOGY
PHRAMONGKUTKLAO HOSPITAL

Chlorpropamide (Diabines)

- Oral hypoglycemic agent (SU) -> hydroosmotic effect of AVP in kidney
- Reduce polyuria by 25 to 75% in CDI
- Action site at renal tubule to potentiate the hydroosmotic action of circulating AVP, also evidence of pituitary effect to increase the release of AVP
- Use in severe CDI and near total AVP deficiency
- Dose : 250 to 500 mg/d -> response in 1 or 2 days and maximum in 4 day
- Not safety in pregnancy and children
- Avoid in patient with risk of hypoglycemia

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Treatment of other type of DI

NEPHROLOGY
PHRAMONGKUTKLAO HOSPITAL

Osmoreceptor Dysfunction

- Replacing the underlying free water deficit
- Long-term : regulate fluid intake by hydration status (daily BW)
- Monitor Serum Na weekly -> every month : keep serum Na normal = target BW

Gestational DI

- Desmopressin (not destroyed by oxytocinase or vasopressinase)
- Only 2 to 5% OT activity of AVP

Primary Polydipsia

- Fluid restriction
- Ice chips or candies to increase salivary flow

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Treatment of CDI

NEPHROLOGY
PHRAMONGKUTKLAO HOSPITAL

- Eliminate cause (avoid Li, treatment hypercalcemia, hypokalemia)
- Restrict sodium intake + thiazide ± PG synthetase inh or amiloride (thiazide and sodium restriction -> volume depletion -> proximal tubular solute reabsorption and decrease solute distal flow, thiazide enhance water reabsorption in IMCD independent of AVP-> increased AQP2)
- Beware use Li with diuretic -> volume contraction -> increased Li intoxication
- Amiloride use for lithium-induced NDI (Block ENaC)
- High dose of DDAVP or AVP can be use in partial NDI
- NSAID : inhibit PG synthesis

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Approach

Polyuria : urine volume > 3L/day

Uosm < 600 mOsm/KgH_2O

Total daily solute excretion < 1,000 mOsm/day

Water diuresis

- Water deprivation test
- Primary polydipsia
- Complete CDI
- Complete NDI
- Partial NDI

Total daily solute excretion > 1,000 mOsm/day

Uosm/Posm < 0.9

Mixed solute / Water diuresis

- Combined uncontrolled DM + CKD
- Post obstructive diuresis
- Diuretic phase of ATN

Uosm/Posm > 0.9

Solute Diuresis

Uosm > 600 mOsm/KgH_2O

Solute Diuresis

$2(U_{Na}+U_K)/Uosm > 0.6$

- <u>Electrolyte diuresis</u>
- IV fluid load
- Salt load
- HCO_3^- load
- Salt wasting

2(UNa+UK)/Uosm < 0.4

- <u>Non-Electrolyte diuresis</u>
- Glucosuria
- Urea
- Mannitol
- Glycerol
- Amino acid

เนาวนิตย์ นาทา./(2563). polyuria/บัญชา สถิรพจน์และคณะ, Pocket Nephrology/(น.2-50).กรุงเทพ:/นำอักษรการพิมพ์.

THANK YOU