POLYURIA

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OUTLINE

- Physiology of water balance
- Definition and pathophysiology
- Type of diuresis
- Investigation
- Treatment

BASIC PRINCIPLE

- Solute= substances dissolved in body water : NaCl, glucose
- Solvent= liquid that solutes dissolved: mostly water
- Osmolality of solute : mOsm/kg of the solvent
- Osmolarity : mOsm/L of the solution

- Steady state : maintain physiologic serum osmolality of 285-290 mOsm/kg

WATER BALANCE

- Intake
  - Regulated : fluids consumed in response to a perceived sensation of thirst
  - Unregulated : intrinsic water content of ingested foods
- Output
  - Regulated : renal excretion of free water, rate of urine solute excretion
  - Unregulated : insensible water losses

DAILY BALANCE OF SOLUTE AND WATER

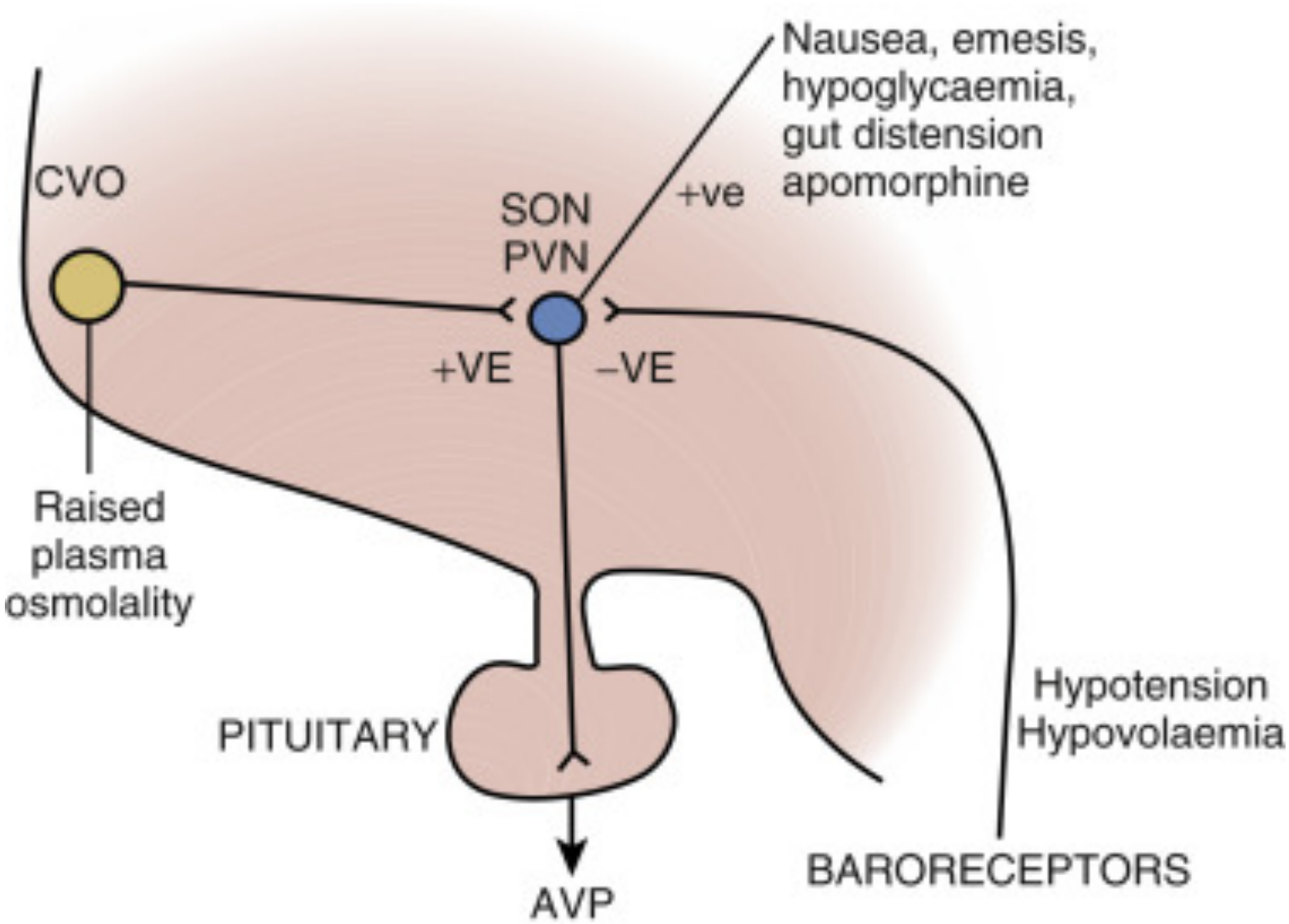
- Body maintain water and solute balance
  - oral intake = excretion
  - solute intake = solute excretion

    (solute load) (adjusted by concentration of the urine)
  - 900-1200 mOsm/day = (600 mOsm/kg H2O)(1.5-2 L/day)

PHYSIOLOGY OF WATER BALANCE

- Arginine vasopressin (AVP) or antidiuretic hormone (ADH)
  - critical role in determining the concentration of urine
  - synthesized and secreted by supraoptic and paraventricular magnocellular nuclei in the hypothalamus
  - half-life : 15-20 mins
  - metabolized in the liver and kidney
- Thirst and water balance : osmotic threshold: 290-295 mOsm/kg H2O
  - stimuli for thirst : hypovolemia, hypotension, angiotensin II

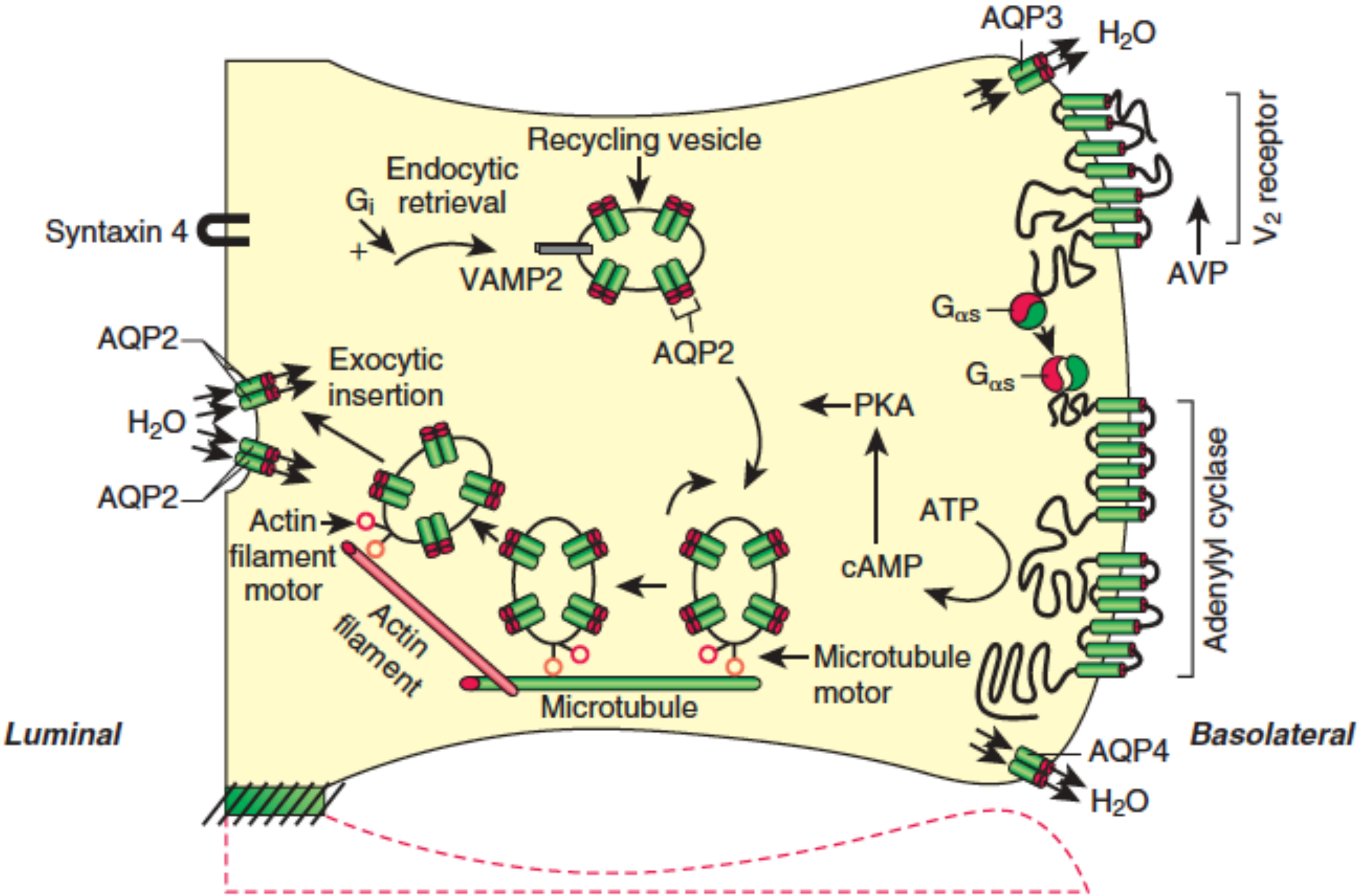
REGULATION OF AVP SECRETION



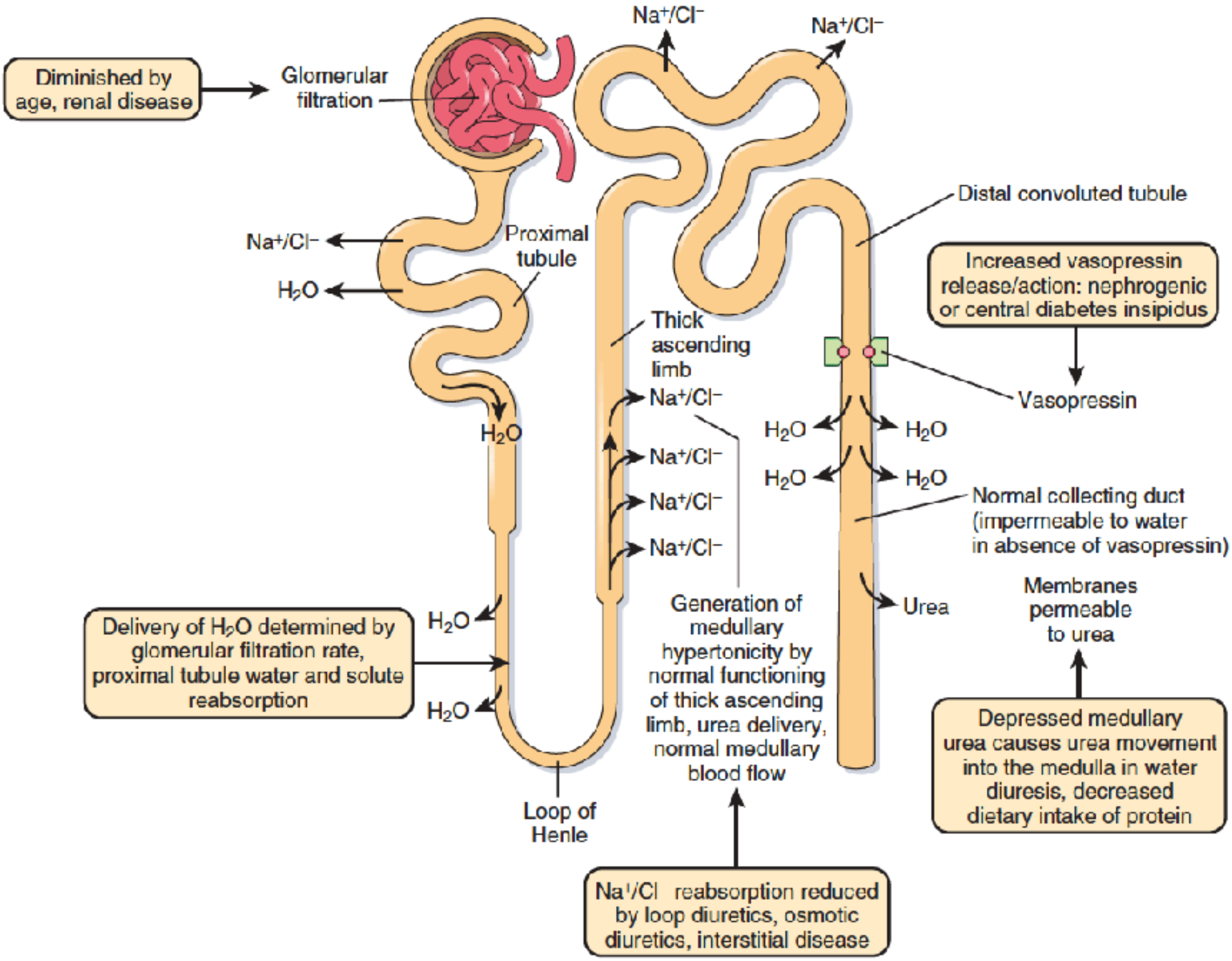
VASOPRESSIN RELEASE

- Osmotic stimuli
  - Osmoreceptor cells: supraoptic nuclei in the hypothalamus
  - Change 1-2% of plasma osmolality : activation of TRPV4 channels : release vasopressin
- Nonosmotic stimuli
  - Decrease effective circulatory volume (>7%)
    - Baroreceptor at carotid sinus → parasympathetic afferent nerves → vasopressin secretion.
  - nausea, postoperative pain, pregnancy, drugs

VASOPRESSIN ACTION AT PRINCIPAL CELL OF THE COLLECTING DUCT



MECHANISM OF URINE CONCENTRATION



RENAL WATER EXCRETION

- $V = C\ Osm + C\ water$
- $C\ water = V - C\ Osm$
- $C\ Osm = \frac{(UOsm \times V)}{P\ Osm}$
- $C\ water = V - \frac{(U\ Osm \times V)}{P\ Osm} = V\left(1 - \frac{U\ osm}{P\ Osm}\right)$
- $C\ water\ (e) = V\left(1 - \frac{U\ Na + U\ K}{P\ Na}\right)$

V= urine volume flow

C Osm= isotonic portion of urine

C water= free water clearance

C water is positive: serum [Na+] will increase

C water is negative : serum [Na+] will decrease

POLYURIA: DEFINITION

- defined as > 3 L UOP per day, > 40ml/kg/day
- Cause of polyuria
  - solute diuresis
  - water diuresis
  - mixed water and solute diuresis
- Polydipsia : water intake more than 100 ml/kg/day

OSMOTIC DIURESIS

- Non-electrolyte diuresis
  - Glucose: DM, glucose infusion
  - Mannitol
  - Urea: recovering AKI, high protein feeds, hyper catabolism (burns, steroids), post-obstructive diuresis
  - Glycerol
  - Amino acid
- Electrolyte diuresis
  - NaCl administration, excess salt ingestion
  - Diuretic use
  - Hypoaldosteronism
  - Impaired tubular reabsorption due to renal problem
    - chronic tubulointerstitial disease
    - diuretic phase of ATN
    - post obstructive diuresis

WATER DIURESIS

- Decrease ADH secretion
  - Excessive intake of hypotonic fluid
  - Psychogenic polydipsia
- Diabetes Insipidus : abnormalities of renal concentrating mechanism
  - Central DI : Lack of AVP production/secretion
    - partial/complete
  - Nephrogenic DI: nonresponse of kidneys to ADH

CENTRAL DI: ETIOLOGY

- Congenital Causes
  - Autosomal dominant
  - Autosomal recessive: Wolfram syndrome
    - DM
    - Optic atrophy
    - Deafness
- Adipsic DI
  - impaired vasopressin recreation and thirst
- Acquired Causes
  - Post-traumatic
  - Iatrogenic (postsurgical)
  - Tumor
    - Histiocytosis
    - Granuloma (TB, sarcoidosis)
    - Aneurysm
    - Meningitis
    - Encephalitis
    - Guillian-Barre syndrome
    - Idiopathic

NEPHROGENIC DI

- Congenital nephrogenic DI : mutation in genes for aquaporin or vasopressin receptor
  - high urine volume, risk for severe hypernatremia
- Acquired nephrogenic DI :
  - urine concentrating mechanism are partially preserved
  - less volume compare to congenital, Central DI or primary polydipsia : less than 3-4 L/day
  - hypokalemia, hypercalcemia, sickle cell anemia, chronic tubulointerstitial disease, cold diuresis, drugs

LITHIUM AND NEPHROGENIC DI

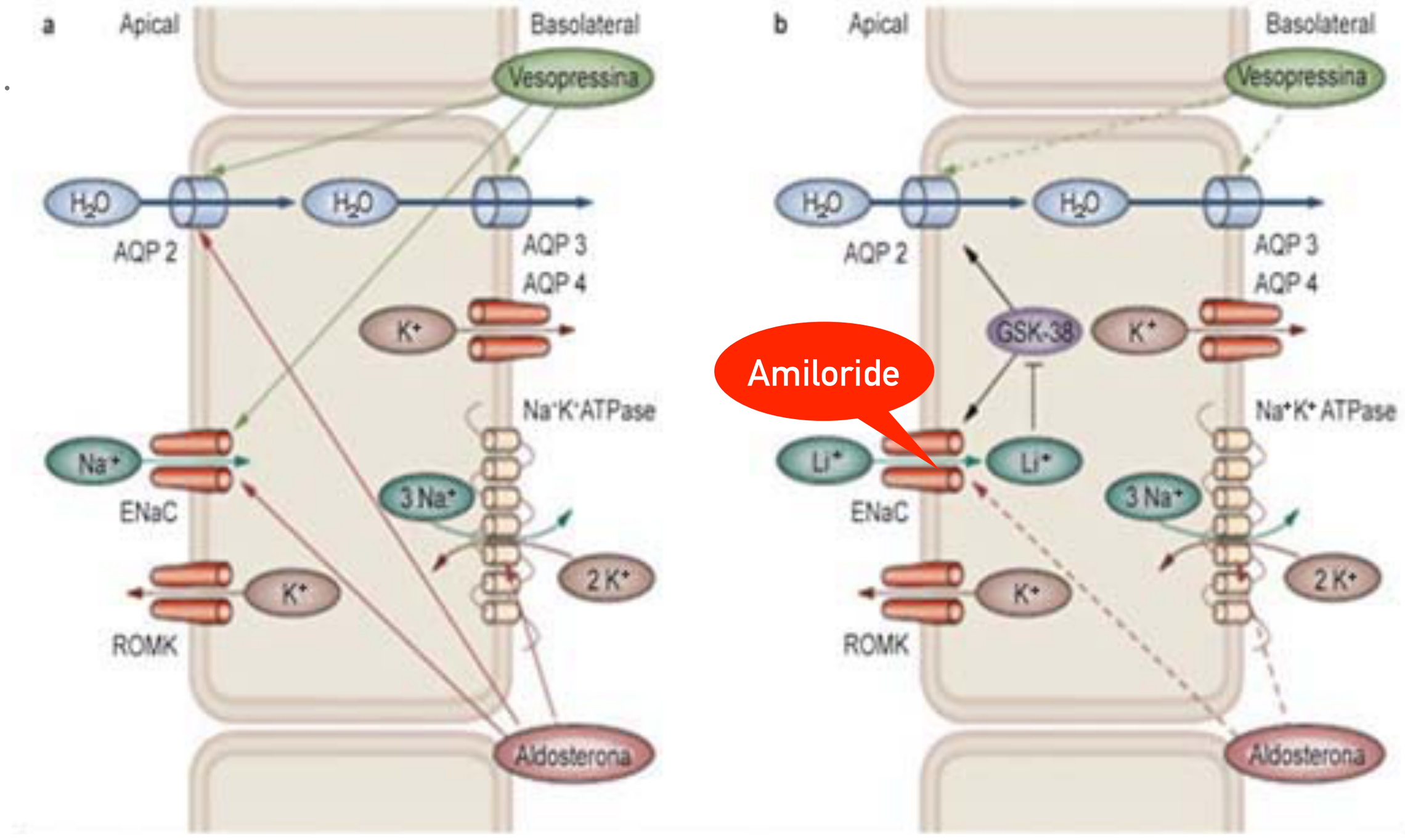


Figure 1 – Transport of water, sodium and potassium in the principal cell of the collecting duct under physiological conditions (a) and in the presence of lithium (b). For further explanation, see text. Source: Grünfeld JP, Rossier BC. Lithium nephrotoxicity revisited. Nat Rev Nephrol 2009; 5: 270-276

Kortenoeven ML, et al. Kidney Int. 2009 Jul;76(1):44-53

ACQUIRED NEPHROGENIC DI : CAUSE AND MECHANISM

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	—	—*amphotericin, foscarnet*
Lithium therapy	—	Yes	Yes	—
Pregnancy	—	—	—	Placental secretion of vasopressinase

MIXED WATER-SOLUTE DIURESIS

- CKD + uncontrolled DM
- Post-obstruction diuresis
- Recovering ATN

CLINICAL FEATURES

- Central DI:
  - abrupt onset
  - very high urine volume (8-10 L/dY)
  - Polydipsia
  - predilection for cold water
  - nocturia
  - Plasma osmolality > 295 mOsm/kg
- Nephrogenic DI:
  - acquired: moderate degree of polyuria (3-4 L/day)
  - Plasma osmolality >295 mOsm/kg
- Polydipsia :
  - vague history of the onset
  - variation in water intake and urine output
  - unusual nocturia
  - Plasma osmolality <270 mOsm/kg

INVESTIGATION

- Timed urine collection (at least 6 hr)and measure Uosm
- 24 hr Osmole secretion rate = 24 hr UOP x UOsm
  - > 1000 mOsm/d : osmotic diuresis, urine Na typically > 20 mmol/L
  - < 800 mOsm/d : water diuresis

CLINICAL HISTORY IN A CASE OF POLYURIA

- Increased urine volume or just increased frequency of urination
- Associated polydipsia
- Weight loss : DM, malignancy
- History of neurosurgery, meningitis, head injury, psychiatric illness or compulsive water drinking
- History of HTN, CKD, hypercalcemia, urinary tract obstruction, polycystic kidney disease
- Drugs: diuretics, lithium, analgesic, vitamin D, calcium supplement, nephrotoxic drugs
- Family history of DM, DI

PHYSICAL EXAMINATION IN A CASE OF POLYURIA

- wasting or cachexia : DM, DI and malignancy
- skin manifestation : cancer, DM
- Clubbind nails : CA of bronchus, CKD nails
- Anemia : CKD and malignancy
- Lymphadenopathy : infiltrative disease, malignancy
- Fundus examination : DM, hypertension

INITIAL INVESTIGATION

- Collect 24 hr urine volume to confirm diagnosis (>3 L/dY)
- Urine analysis
- Serum Osmolality
- Urine Osmolality
- Plasma glucose
- Electrolyte
- BUN, Cr

DETERMINING CAUSE OF POLYURIA

	Water diuresis	Solute diuresis	Mixed water-solute diuresis
UOsm/POsm	<0.9	>0.9	<0.9
24 hr solute excretion	<900 mOsmol	>900 mOsmol	>900 mOsmol

DETERMINING ELECTROLYTE AND NON-ELECTROLYTE DIURESIS

- [2(Urine Na+ Urine K)]/Urine osmol
- >0.6 : Electrolyte diuresis
- < 0.4 : Non-electrolyte diuresis

WATER DIURESIS : INVESTIGATION

- Water deprivation test
  - Start in am
  - check Na, POsm, UOsm, UOP every 1-2 h
  - Adequate dehydration——> stop deprivation
    - Plasma Osmole > ULN (>300 mOsmol/kg), or
    - Plasma Na > ULN (> 150 mEq/L) or
    - BW decrease > 3%
- check Uosm
- Administer aqueous vasopressin (5 unit subq) or dDAVP (10 ug intranasal),
- check Urine volume, Urine sp gr, UOsm every 30 mins at 30,60,120 min

WATER DEPRIVATION TEST

Condition	Urinary Osmolality with Water Deprivation (mOsm/kg H_2O)	Plasma Vasopressin after Dehydration (pg/ml)	Increase in Urinary Osmolality with Exogenous Vasopressin
Normal	>800	>2	Little or no increase
Complete central diabetes insipidus	<300	Undetectable	Substantially increased >50%
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 <10%
Primary polydipsia	>500	<5	Little or no increase

TREATMENT

- primary polydipsia : treat psychiatric illness, check meds, restrict access to free H2O
- Osmotic diuresis : address underlying cause, replace free H2O deficit and ongoing losses
- DI
  - Central DI : desmopressin (dDAVP)
  - Nephrogenic DI : treat underlying cause
    - Na restriction < 2.3 g/day
    - Thiazide
    - Amiloride for lithium-induced DI
    - NSAIDs : Indomethacin
  - Pregnancy-induced DI : due to vasopressinase from placenta : dDAVP

CENTRAL DI: TREATMENT

- Acute setting:
  - Aqueous vasopressin : short duration, less water intoxication, caution in CAD and PVD
- Chronic setting
  - Desmopressin : long half-life
    - Intranasal : 10-20 ug q 12-24 hr
    - Oral : 0.1-0.8 mg q 12 hr
- Partial DI: addition to desmopressin
  - Chlorpropamide 250-500 mg q 24 hr
  - Clofibrate 500 mg q 6-8 hr
  - Carbamazepine 400-600 mg q 24 hr

THANK YOU