Diagnostic Approach to Polyuria and Polydipsia

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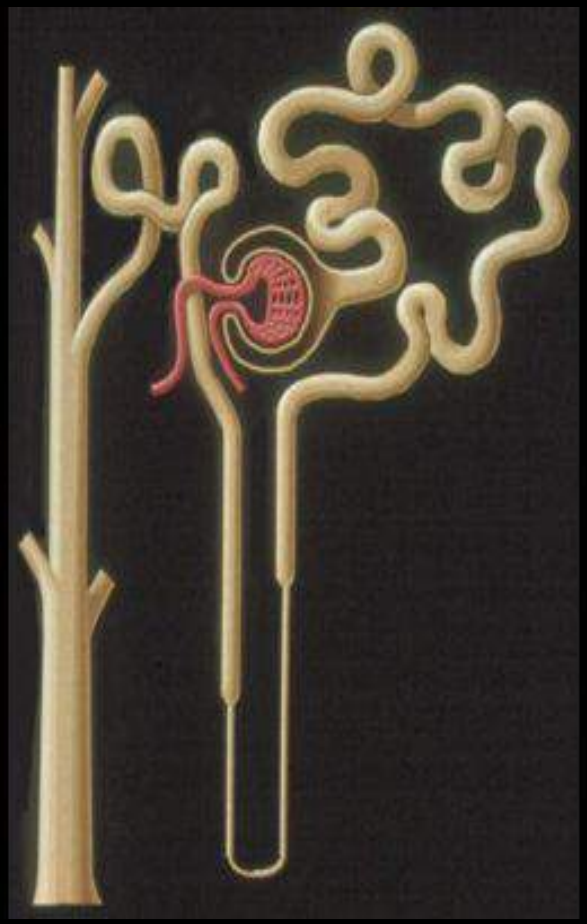
NORMAL WATER HOMEOSTASIS

Fluid Intake and Urine Output

Intact Pituitary – Renal Axis

Antidiuretic Hormone (ADH)

Intact Renal Medullary Interstitium



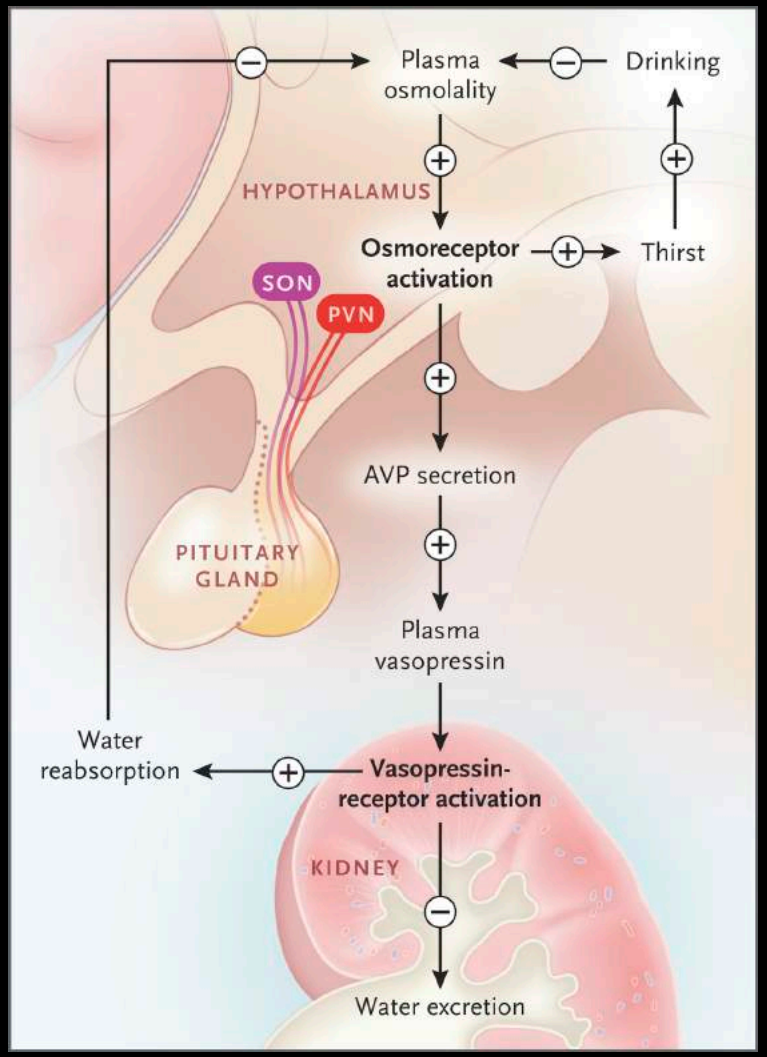
NORMAL WATER HOMEOSTASIS

Fluid Intake and Urine Output

Thirst

Plasma Osmolality
Serum Na concentration

Hypovolemia



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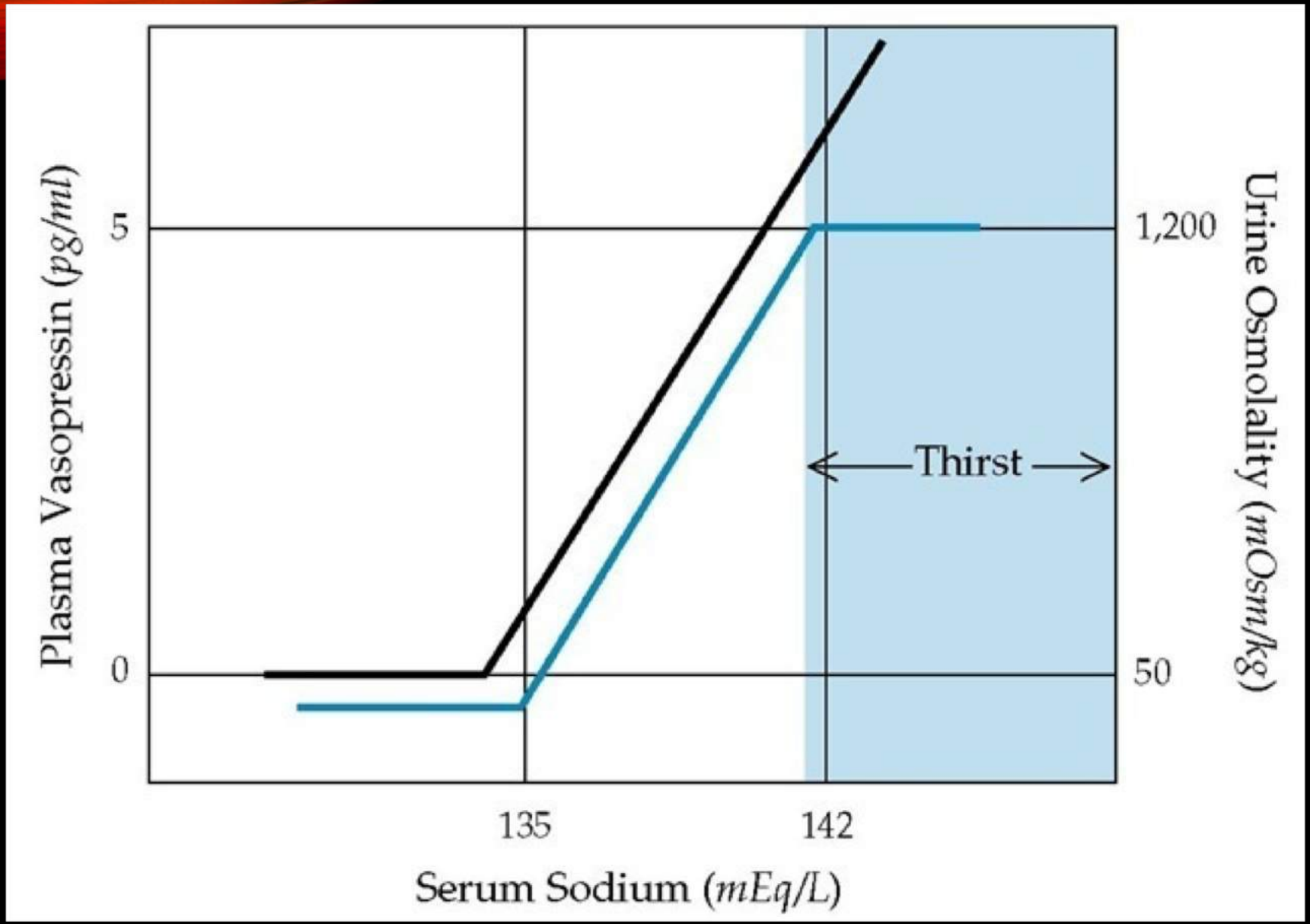
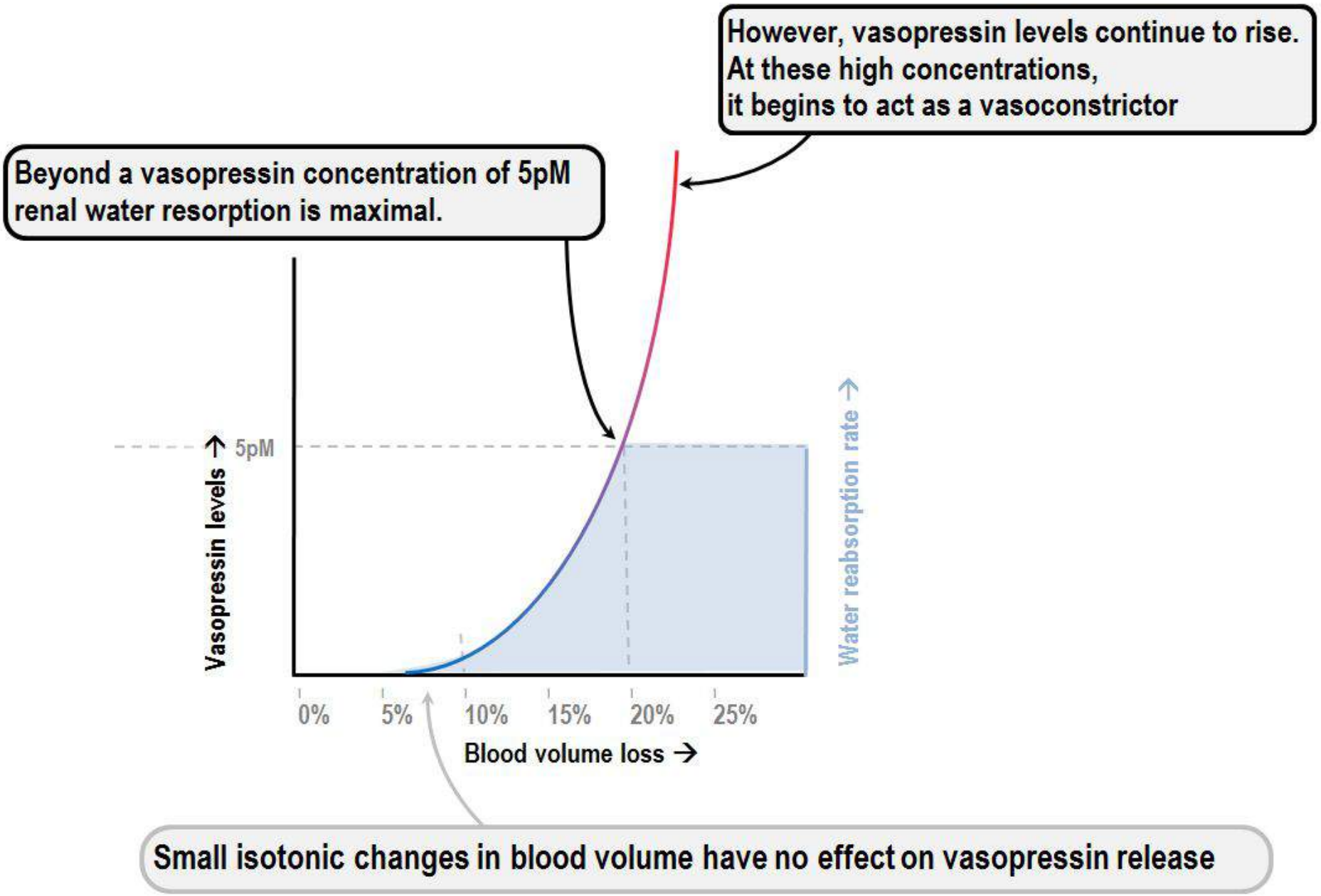
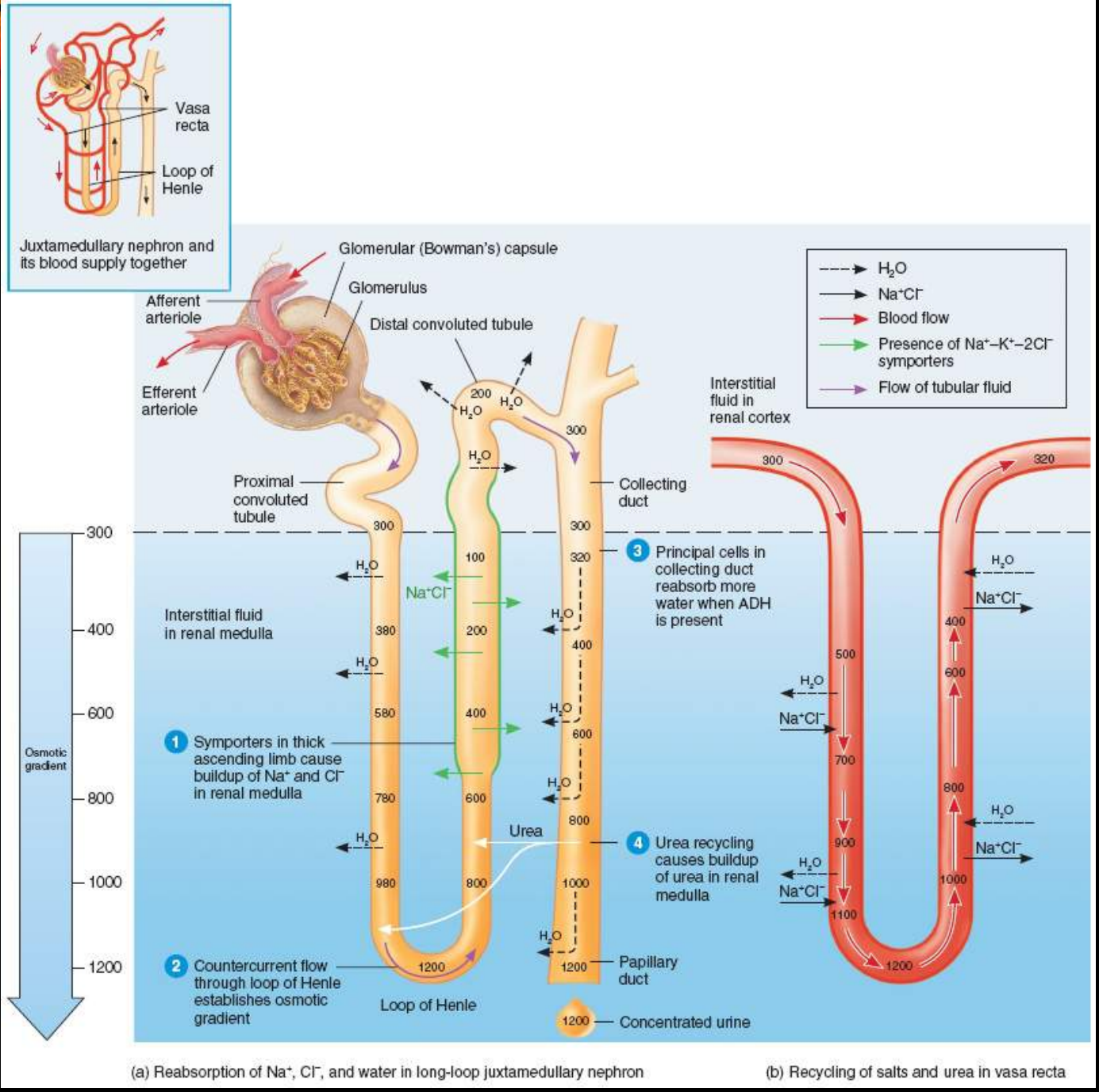
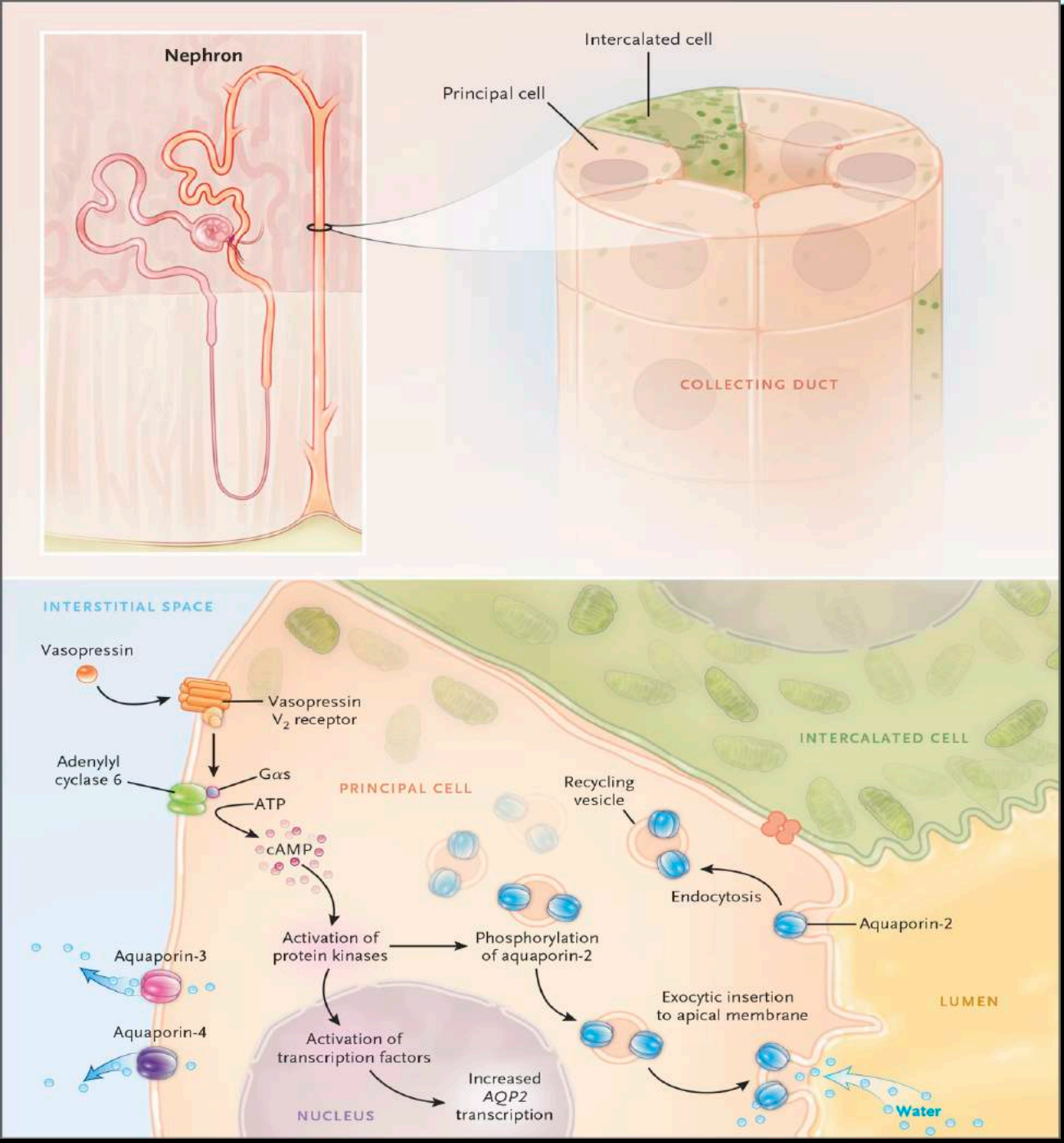

Plasma Vasopressin (pg/ml)
5
0
1,200
50
Urine Osmolality (mOsm/kg)
Thirst
135
142
Serum Sodium (mEq/L)


However, vasopressin levels continue to rise.
At these high concentrations,
it begins to act as a vasoconstrictor
Beyond a vasopressin concentration of 5pM
renal water resorption is maximal.
Vasopressin levels →
5pM
Water reabsorption rate →
0%
5%
10%
15%
20%
25%
Blood volume loss →
Small isotonic changes in blood volume have no effect on vasopressin release


Vasa recta
Loop of Henle
Juxtamedullary nephron and its blood supply together
Glomerular (Bowman's) capsule
Glomerulus
Afferent arteriole
Efferent arteriole
Distal convoluted tubule
Proximal convoluted tubule
Collecting duct
Interstitial fluid in renal cortex
Interstitial fluid in renal medulla
Osmotic gradient
300
400
600
800
1000
1200
H_2O
Na^+Cl^-
Blood flow
Presence of Na^+–K^+–$2Cl^-$ symporters
Flow of tubular fluid
1 Symporters in thick ascending limb cause buildup of Na^+ and Cl^- in renal medulla
2 Countercurrent flow through loop of Henle establishes osmotic gradient
3 Principal cells in collecting duct reabsorb more water when ADH is present
4 Urea recycling causes buildup of urea in renal medulla
Urea
Loop of Henle
Papillary duct
Concentrated urine
(a) Reabsorption of Na^+, Cl^-, and water in long-loop juxtamedullary nephron
(b) Recycling of salts and urea in vasa recta



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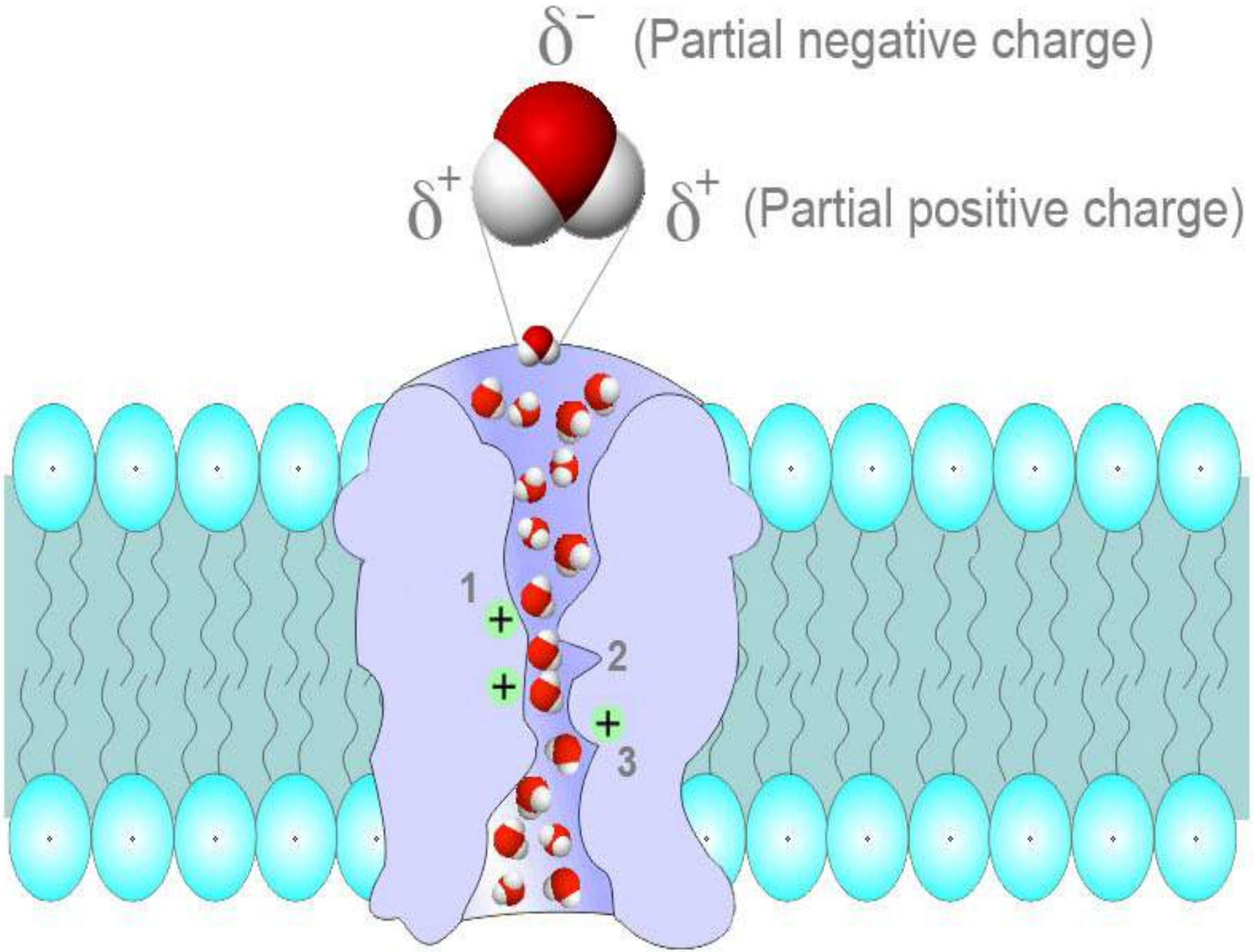
δ⁻ (Partial negative charge)
δ⁺
δ⁺ (Partial positive charge)
1
2
3

Key Proteins Involved in Regulation of Water Balance.

Table 1. Key Proteins Involved in Regulation of Water Balance.

Protein	Gene	Structure or Cell Type Relevant to Water Balance	Manifestation of Loss of Function*	Drugs That Target Protein
Arginine vasopressin	*AVP*	Neurons of supraoptic nucleus and paraventricular nucleus	Central diabetes insipidus	None
Vasopressin receptor				
V_2	*AVPR2*	Renal thick ascending limb of the loop of Henle, distal convoluted tubule, connecting tubule, collecting duct	X-linked nephrogenic diabetes insipidus	Desmopressin acetate (agonist), tolvaptan (antagonist)
V_{1a}	*AVPR1A*	Renal medullary vasculature (vasa recta)	None	Conivaptan (nonselective V_{1a} and V_2 antagonist)
Bumetanide-sensitive sodium–potassium–chloride cotransporter	*SLC12A1*	Renal thick ascending limb of the loop of Henle	Type I Bartter's syndrome	Loop diuretics
Thiazide-sensitive sodium–chloride cotransporter	*SLC12A3*	Renal distal convoluted tubule	Gitelman's syndrome	Thiazide diuretics
Aquaporin				
Aquaporin-1	*AQP1*	Renal proximal tubule, thin descending limb of the loop of Henle, erythrocyte	Colton blood group–null	None
Aquaporin-2	*AQP2*	Renal connecting tubule, collecting duct	Autosomal nephrogenic diabetes insipidus	None
Aquaporin-3	*AQP3*	Renal connecting tubule, collecting duct, erythrocyte	GIL blood group–null	None
Aquaporin-4	*AQP4*	Renal connecting tubule, collecting duct	None	None
Vasopressin-regulated urea channel	*SLC14A2*	Renal inner medullary collecting duct, thin descending limb of the loop of Henle	None	None
Epithelial sodium channel				
Beta subunit	*SCNN1B*	Renal connecting tubule, collecting duct	Type I pseudohypoaldosteronism	Amiloride
Gamma subunit	*SCNN1G*	Renal connecting tubule, collecting duct	Type I pseudohypoaldosteronism	Amiloride

* Data are from the Online Mendelian Inheritance in Man database.

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POLYURIA AND POLYDIPSIA

Physiologic vs pathologic

- Ambient temperature/humidity
- Activity level
- Dietary factors
- Medications

POLYURIA AND POLYDIPSIA

Polyuria vs Pollakiuria

Lower urinary tract disease

- Diagnostic approach
  - UA's, urine culture and sensitivity
  - Imaging : radiographs, US, contrast studies

POLYURIA AND POLYDIPSIA

Owner Assessment

- Subjective
- Water consumption at home

Hospitalization

- Measurement of water consumption and urine output

POLYURIA AND POLYDIPSIA

Normal Water Consumption

40 – 60 mls/kg day

Laboratory animals

Abnormal Water Consumption

> 100 mls/kg/day

POLYURIA AND POLYDIPSIA

- Diagnostic Approach
  - Documentation of pu/pd
  - Physical examination
  - Urinalysis
    - Sp gravity
    - Sediment and dip stick exam
    - Culture and sensitivity
  - CBC, serum chemistries

DIFFERENTIAL DIAGNOSIS

- Renal Disease
- Diabetes Mellitus
- Liver Disease
- Hyperthyroidism
- Hyperadrenocorticism
- Diabetes Insipidus
  - CDI
  - NDI
- Hypercalcemia
- Hypoadrenocorticism
- Pyometra
- Hypokalemia
- Polycythemia
- Medications
- Psychogenic

DIFFERENTIAL DIAGNOSIS

Renal Disease

Pyelonephritis	>	Endotoxins
CRF	>	Loss of nephrons
Fanconi's	>	Glycosuria
Post-obstructive diuresis	>	Osmotic diuresis

DIFFERENTIAL DIAGNOSIS

Diabetes Mellitus

Hyperglycemia

Glycosuria and/or ketonuria

Osmotic diuresis

DIFFERENTIAL DIAGNOSIS

Liver Disease

Medullary washout

Decreased urea production

Low BUN

Altered release of ADH

Altered GABA and dopaminergic tone

Increased secretion of cortisol

DIFFERENTIAL DIAGNOSIS

Hyperthyroidism

- Increased GFR
- Increased renal blood flow
- Psychogenic

DIFFERENTIAL DIAGNOSIS

Hypercalcemia

- Renal tubular mineralization
- Alteration in renal blood flow
  - Renal artery vasoconstriction
- Altered release of ADH
- Tubular resistance to ADH

DIFFERENTIAL DIAGNOSIS

Hyperadrenocorticism

Altered release of ADH

Tubular resistance to ADH

Concurrent UTI's

Pyelonephritis

85 % of patients will be pu/pd

DIFFERENTIAL DIAGNOSIS

Hypoadrenocorticism

Mechanism unknown

Renal Na loss

Osmotic diuresis

20-25 % of patients will be pu/pd

DIFFERENTIAL DIAGNOSIS

Pyometra

Concurrent pyelonephritis

E. coli endotoxins

Tubular resistance to ADH

DIFFERENTIAL DIAGNOSIS

Hypokalemia

- Tubular vacuolization
- Tubular resistance to ADH
- Usually in conjunction with other causes of pu/pd

DIFFERENTIAL DIAGNOSIS

Polycythemia (PCV > 65 %)

- Altered CNS blood flow
  - Altered release of ADH
- Altered renal blood flow
  - Tubular resistance to ADH

DIFFERENTIAL DIAGNOSIS

Medications

- Steroids
- Anticonvulsants
- Diuretics
- Salts
  - Na or K bromide

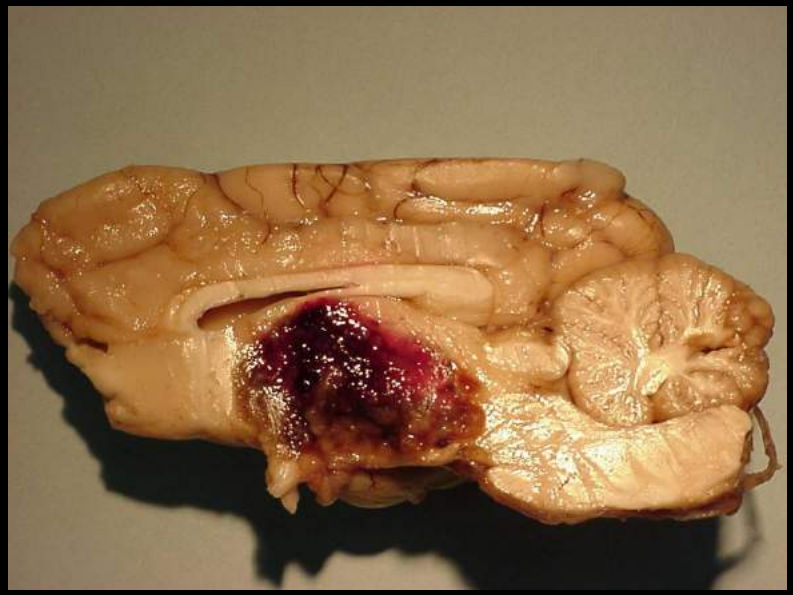
DIFFERENTIAL DIAGNOSIS

Central Diabetes Insipidus

Failure to manufacture, store or secrete ADH

Congenital

Acquired



DIFFERENTIAL DIAGNOSIS

Nephrogenic Diabetes Insipidus

Congenital lack of tubular receptors for ADH

Extremely rare in veterinary medicine

DIAGNOSTIC APPROACH

Completion of Initial Data Base

- Normal physical examination
- Normal laboratory work

Differential Diagnosis

Hyperadrenocorticism, diabetes insipidus, portosystemic shunt (young animals), psychogenic

WATER DEPRIVATION/ADH RESPONSE TESTING

Other differentials have been eliminated

No signs of azotemia/dehydration

Close owner monitoring

Gradual water restriction

ADH administration

WATER DEPRIVATION/ADH RESPONSE TESTING

Gradual water restriction at home for

2 - 3 days

Re-establishment of medullary gradient

Failure to perform gradual water restriction will result in poor response to ADH

WATER DEPRIVATION/ADH RESPONSE TESTING

DDAVP

1-2 drops into the conjunctival sac
once to twice a day

2 to 5 mcg SQ q12h–q24h

Oral 0.1 to 0.2 mg PO once to twice a day

WATER DEPRIVATION/ADH RESPONSE TESTING

Interpretation

Central Diabetes Insipidus

No response to water restriction

Marked increase in urine sp gravity

with DDAVP

WATER DEPRIVATION/ADH RESPONSE TESTING

Interpretation

Nephrogenic Diabetes Insipidus

No response to water restriction

No increase in urine sp gravity

with DDAVP

TREATMENT OF CENTRAL DIABETES INSIPIDUS

Constant access to free water

DDAVP

1-2 drops into the conjunctival sac once to twice a day

2 to 5 mcg SQ q12h–q24h

Oral 0.1 to 0.2 mg once to twice a day

Expense

TREATMENT OF NEPHROGENIC DIABETES INSIPIDUS

Constant access to free water

Salt restriction

Thiazide diuretics

- Hydrochlorthiazide 2 - 4 mg/kg BID
- Loop diuretics such as furosemide will not be effective

PROGNOSIS FOR CENTRAL DIABETES INSIPIDUS

Congenital form

- Other pituitary abnormalities
  - TSH, ACTH, GH, FSH, LH

Adult-onset form

- High incidence of pituitary/hypothalamic neoplasia

PROGNOSIS FOR NEPHROGENIC DIABETES INSIPIDUS

Monitor renal function

May progress to chronic renal failure

Only mild to moderate reductions in pu/pd

with medical management