Clinical Aspects of Hyponatremia & Hypernatremia

Case Presentation: History

62 y/o male is admitted to the hospital with a 3 month history of excessive urination (polyuria) and excess water intake up to a gallon per day. His wife noted that he had lost weight, became forgetful and irascible.

Case Presentation: Physical Examination

Emaciated, somnolent 62 y/o man in no acute distress. Multiple signs of dehydration were evident including low blood pressure upon standing (orthostatic hypotension), loss of normal skin reslience, sunken eyeballs, and low intravascular volume. In addition he was confused, disoriented and had reduced level of consciousness.

Case Presentation: Laboratory I

Blood Tests:

Sodium 150 mEq/L (Nl 138-142)

Chloride 106 mEq/L (nl 95-100)

Kidney Function Decreased 50%

Calcium 16.5 mg/dl (Nl 8-10)

Urine Tests:

Specific gravity 1.008 (Nl for dehydration 1.025-1.035),

Urine sodium Na 15 mEq/L (low), Osm 280 mOsm (low for dehydration)

Case Presentation: Laboratory II

- Serum protein electrophoresis: Abnormal amount of pure (monoclonal) immunoglobulin
- Bone Marrow Biopsy: Multiple Myeloma- a malignant tumor of plasma (immune system) cells that causes
  - Monoclonal immunoglobulin excess
  - high blood calcium by break down of the skeleton.

Signs of Polyuria due to Renal Concentrating Defect

- Orthostatic Hypotension
- Low urine osmolality
- Hypernatremia
  - Excess free water loss
  - Insufficient free water intake

Polyuria: Differential Diagnosis

- Volume Depletion
  - Diabetes Insipidus
    - Central
    - Nephrogenic
  - Diuretics
    - Osmotic
    - Drugs

- Normal Volume
  - Primary Polydipsia

Systemic Consequences of Chronic Hypercalcemia (High Blood Calcium Concentration)

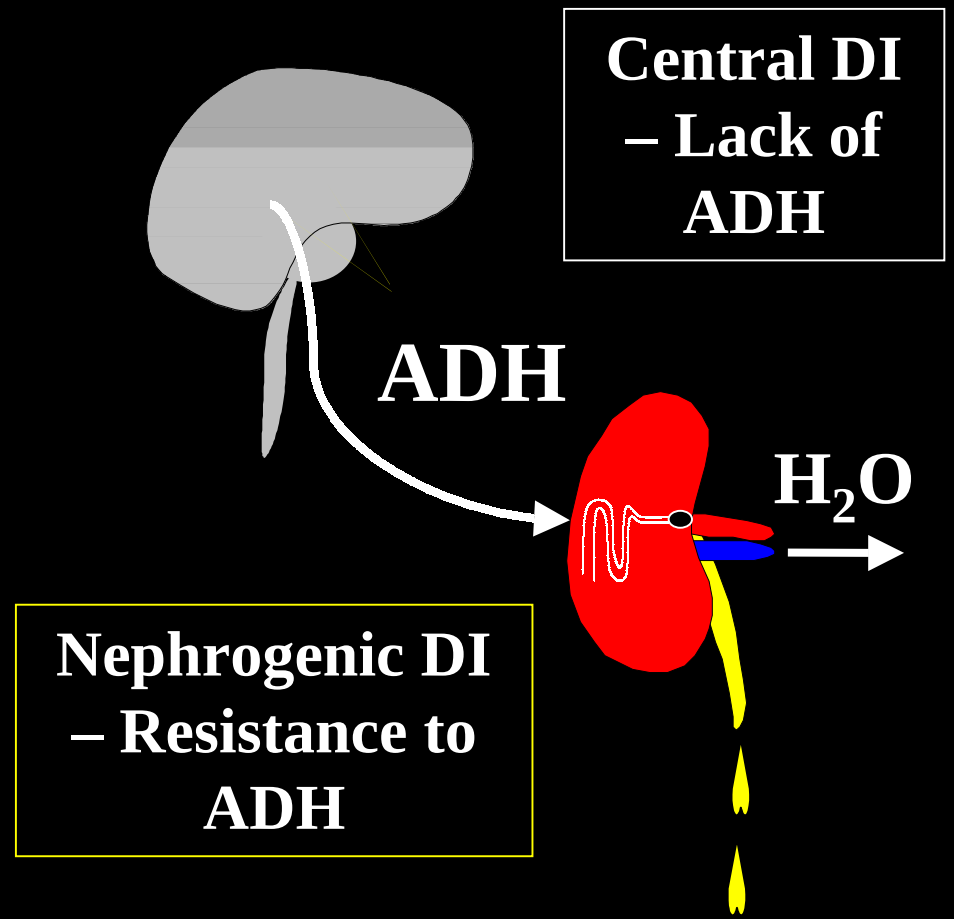
- Neuro: Altered Mental Status, Muscle Weakness
- GI: Anorexia, nausea and vomiting
- Renal Concentrating Defect
  - Polyuria, polydipsia
  - Hypernatremia (coupled with decreased intake of water from loss of appetite and altered mental status)

Consequences of Hypercalcemia: Renal, Fluid and Electrolyte

- Volume Depletion
  - Decreased intake due to anorexia, nausea and vomiting
  - Nephrogenic diabetes insipidus (NDI) causing free water loss
- Hypernatremia from Nephrogenic Diabetes Insipidus
- Renal Insufficiency
  - Decreased blood flow to kidney
  - Calcification of the kidney itself

Diabetes Insipidus (DI)

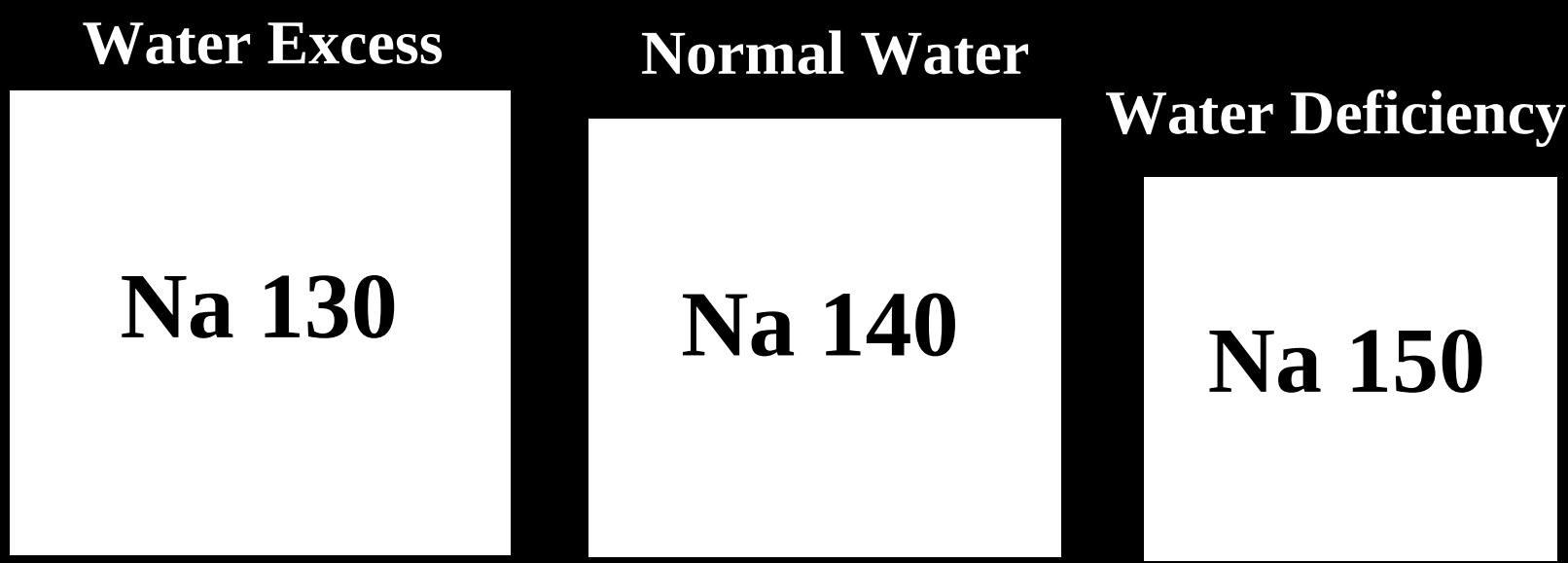
- Excessive water loss by the kidney
- Inability of kidney to concentrate the urine
  - Deficiency of Antidiuretic Hormone (ADH)–Central DI
  - Renal resistance to ADH



Nephrogenic Diabetes Insipidus: Common Causes

- Many chronic renal diseases
- Electrolyte disorders
  - High Blood Calcium Hypercalcemia
  - Low Blood Potassium Hypokalemia
- Drugs
  - including Lithium, AMP-B, Demeclocycline, Gentamicin, cisplatin, others
- Dietary abnormalities, e.g. decreased NaCl or protein intake

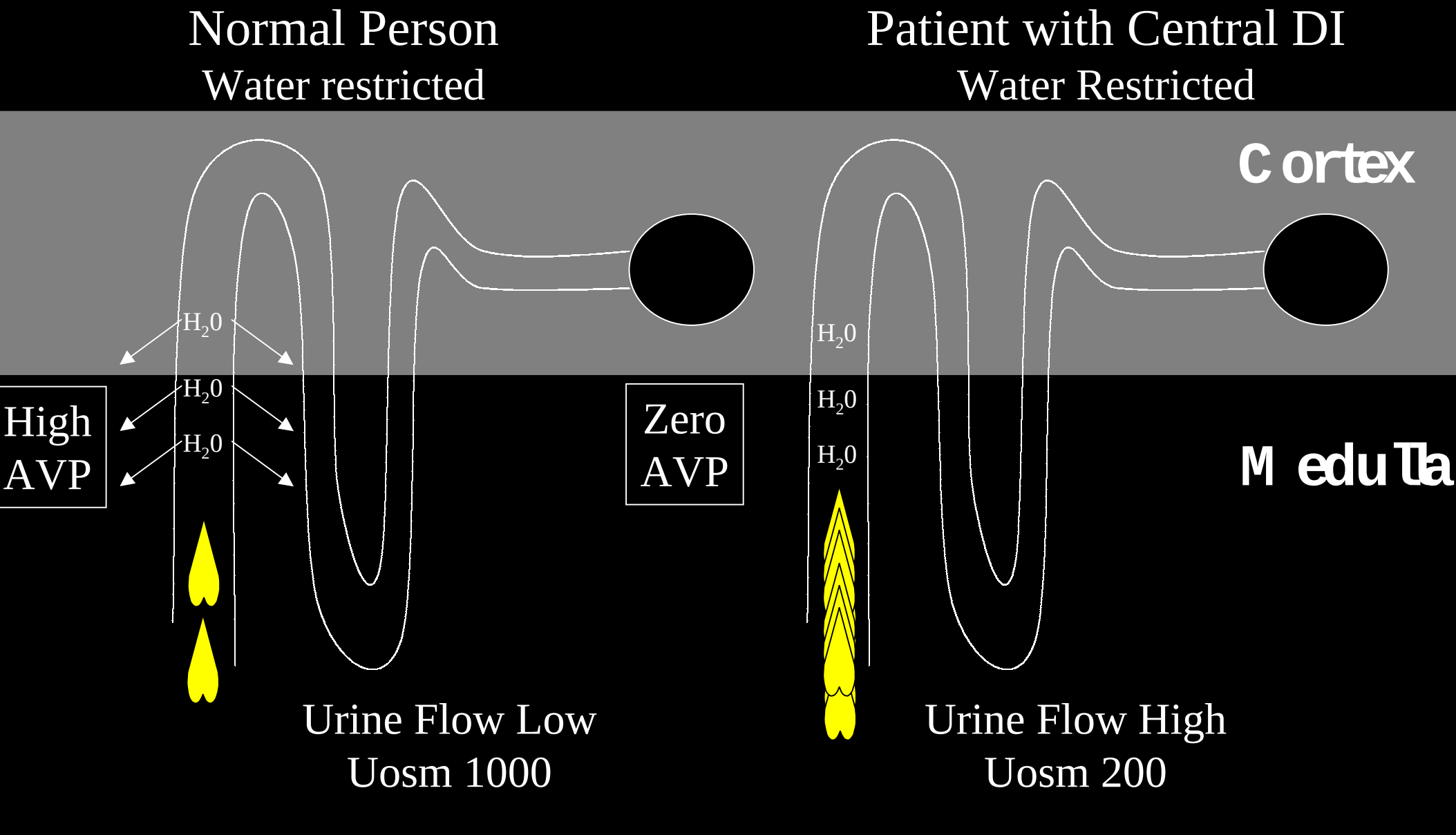
Hyper (High) natremia and Hypo (Low) natremia: Water deficiency and water excess



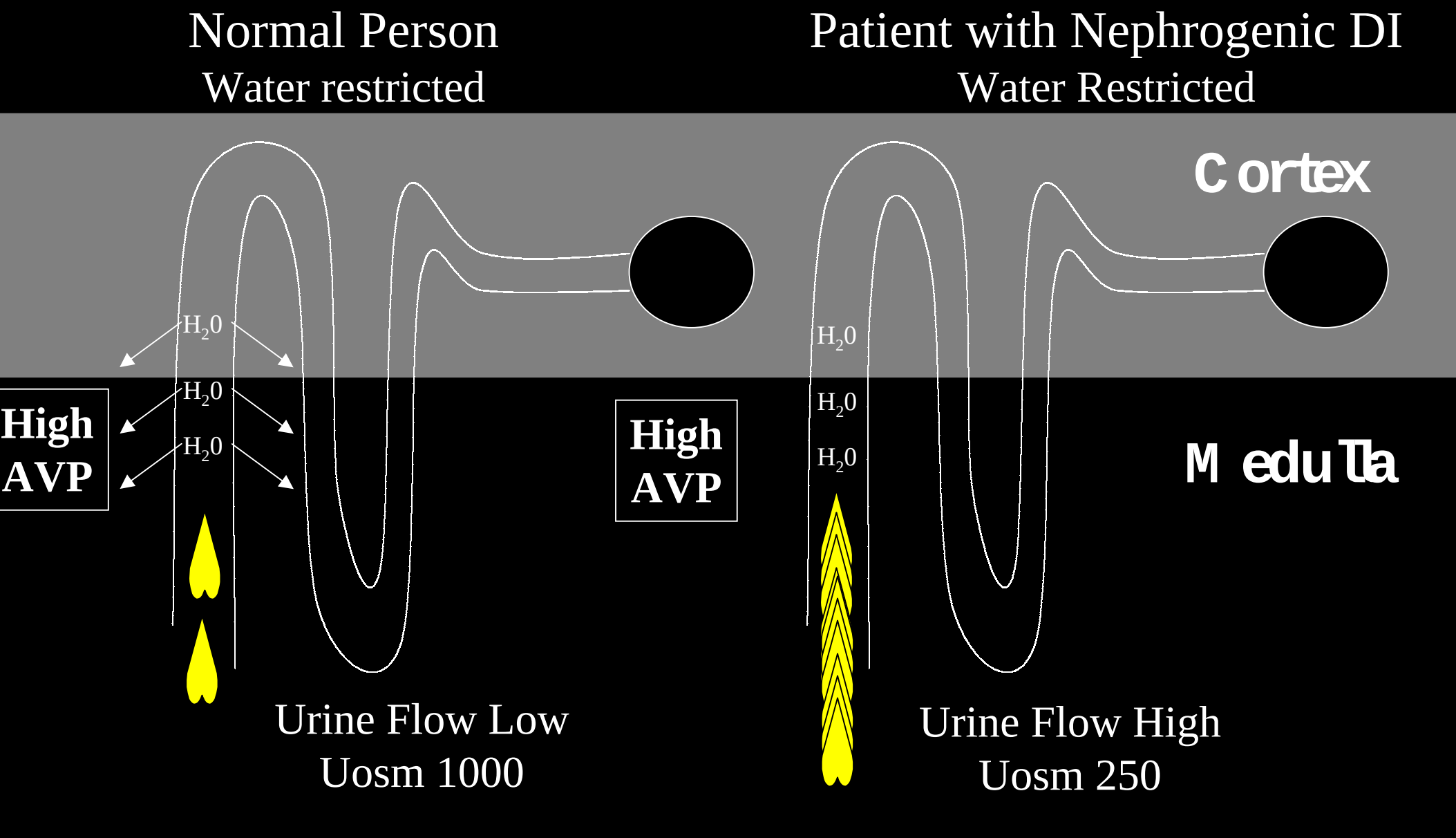
Pathogenetic Mechanisms of Hypernatremia

Condition	Serum Sodium	Example
Pure Water Loss	$\frac{\text{Na}}{\downarrow \text{TBW}}$	Diabetes Insipidus
Sodium and Water Loss	$\frac{\downarrow \text{Na}}{\downarrow\downarrow \text{TBW}}$	Osmotic Diuresis
Sodium Gain	$\frac{\uparrow \text{Na}}{\text{TBW}}$	Hypertonic $NaHCO_3$

Central Diabetes Insipidus



Nephrogenic Diabetes Insipidus



Hypercalcemia as a Cause of Nephrogenic Diabetes Insipidus

- Any chronic hypercalemic state
- Common cause of NDI in Adults
- Mild hypernatremia (145-150) typical
- Decreased renal function common
- Reversible with correction of hypercalcemia
  (unless severe nephrocalcinosis)

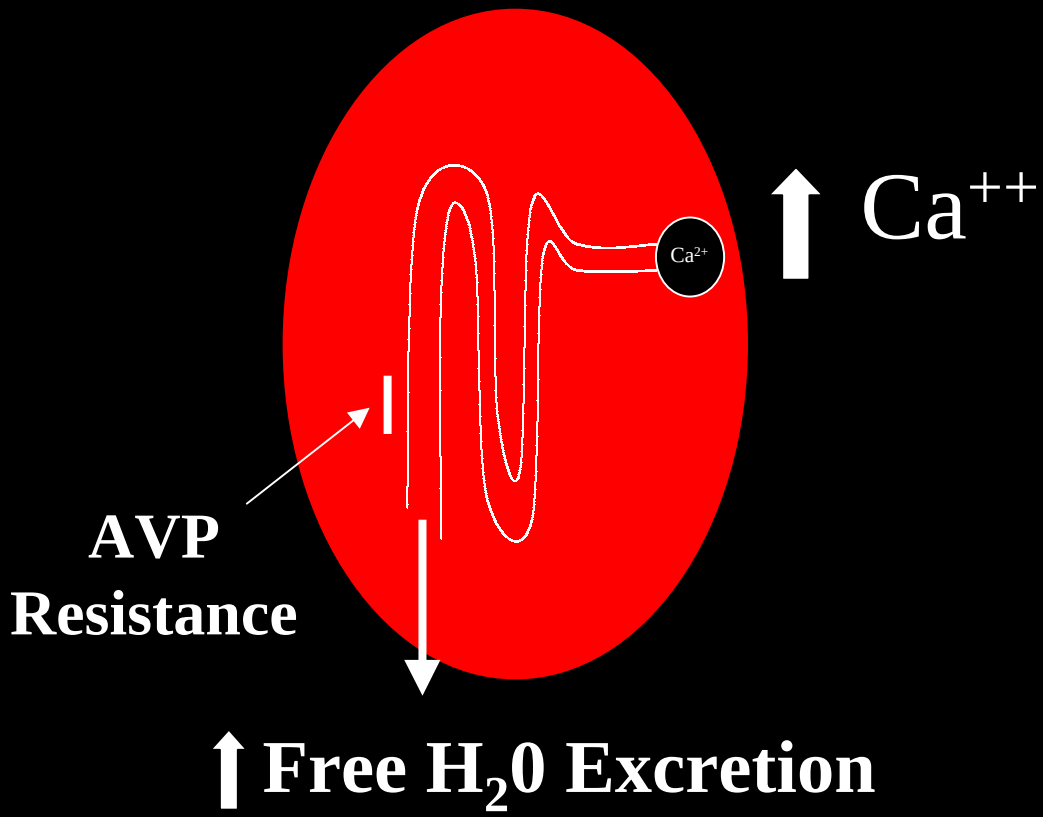
Hypercalcemia and Nephrogenic Diabetes Insipidus

- Hypercalcemia Causes Polyuria
- Vasopressin Resistant Concentrating Defect
- Direct Effect of Calcium on
  Renal Water Handling
- Independent of GFR, PTH, Vitamin D, Calcitonin

How does Hypercalcemia cause Nephrogenic Diabetes Insipidus?

- Decreased delivery of solute to the loop of Henle (reduced GFR)
- Inhibition of NaCl transport in the thick ascending limb
- Inhibition of vasopressin-mediated water permeability in the terminal collecting duct

Hypercalcemia and Nephrogenic Diabetes Insipidus



- Direct Effect of Calcium on Renal water Handling
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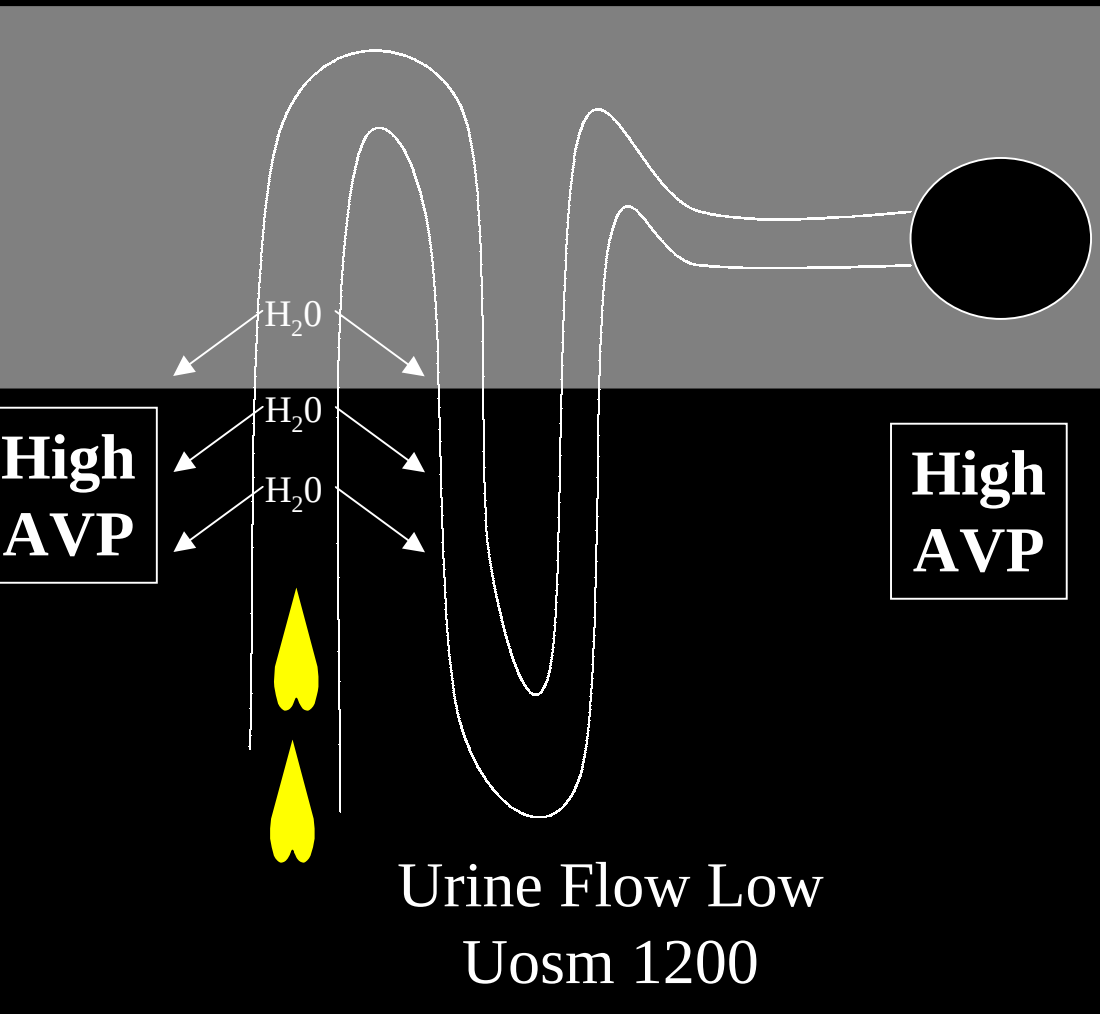
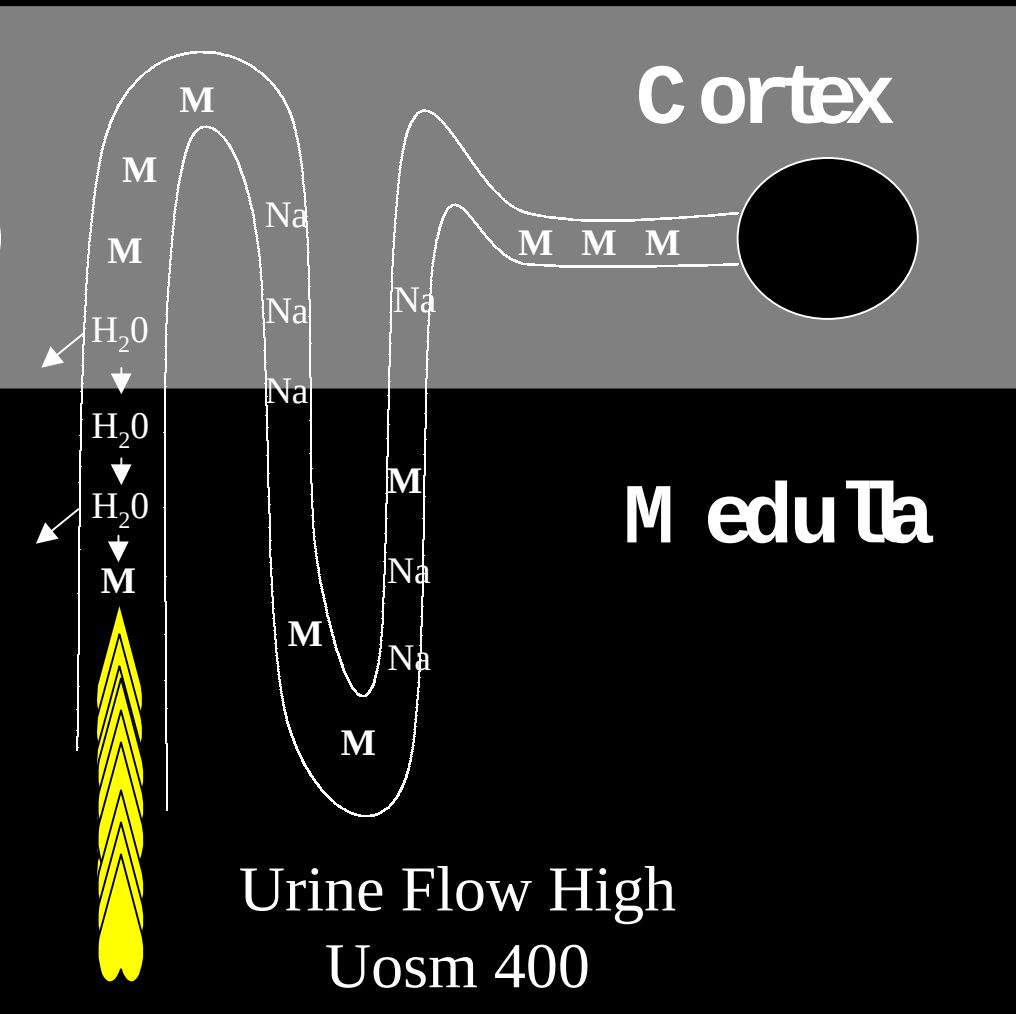
Osmotic Diuresis

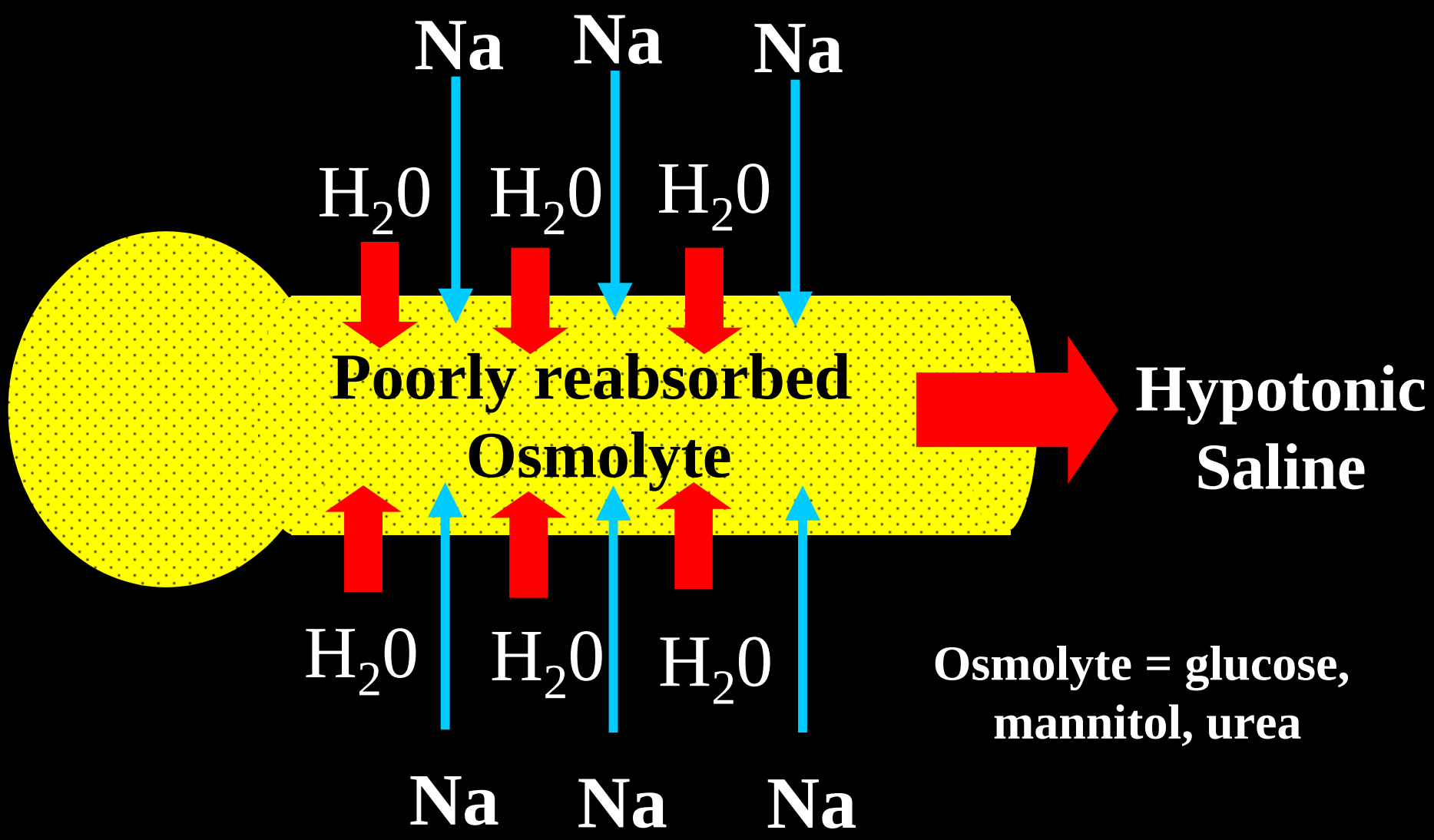
Normal Person
Water restricted



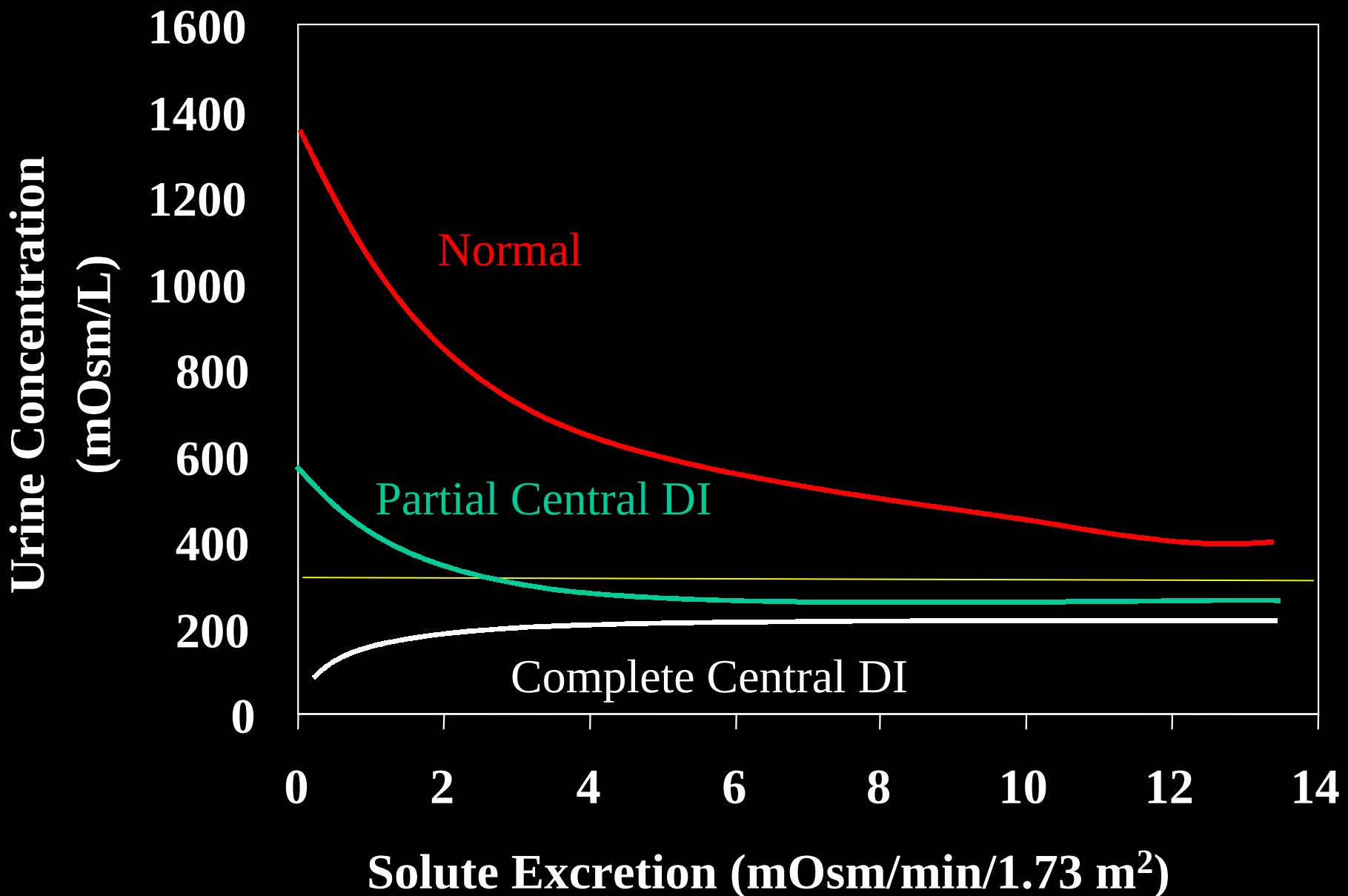
Normal person Mannitol Infusion
Water Restricted



Osmotic Diuresis



Effect of Osmotic Diuresis on Uosm



How to determine the cause of polyuric states: Water Deprivation and ADH responsiveness

- Step 1: Water deprivation
- Step 2: Measure Urine Osmolality
- Step 3: Administer exogenous dose of ADH
- Step 4: Repeat Urine Osmolality Measurement to evaluate response to ADH

Differentiating Polyuric States : Dehydration and AVP Stimulation Tests

Condition	Uosm Max dehydration	Uosm Max after AVP	% Change	Uosm Increase
Normal	1068 ± 69	979 ± 79	-9 ± 3	< 9%
Psychogenic Polydipsia	738 ± 53	780 ± 73	5 ± 2	< 9%
Partial Central DI	438 ± 34	549 ± 28	28 ± 5	> 9% < 50%
Complete Central DI	168 ± 13	445 ± 52	183 ± 41	>50%
Nephrogenic DI	124	174	42	< 50%

Miller et al. Ann. In. Med 73:721, 1970

Calculating Water Deficit in Hypernatremia Due to Pure Water Loss

- Serum Na 150, Normal Na 140, 70 kg man
- Total Body Water Deficit =

$$\text{BW in kg} \times 0.6 \times \frac{[150 - 140]}{140}$$

$$70 \times 0.6 \times [0.06] = 2.8 \text{ L}$$

TBW factor:
Use 0.6 male
0.5 female
0.45 elderly