Brigham and Women's Hospital
Founding Member, Mass General Brigham

Sodium Disorders

David Bruce Mount MD, FRCPC
Associate/Clinical Chief,
Renal Division BWH
Assistant Professor HMS

David B. Mount, MD, FRCPC

University of Toronto Medical School
Medicine Residency @Toronto General Hospital, Toronto, Canada
Renal Fellowship @ Brigham and Women's Hospital (BWH)
Associate/Clinical Chief, Renal BWH
Co-Director, Glomerular Diseases Clinic BWH
Director of Dialysis Services, BWH
Physician, Renal Division VABHS

Research Focus: Urate transport
Clinical Focus: Glomerulonephritis, Electrolyte disorders, Gout, Consultative Nephrology

Financial Disclosures

Author, peer reviewer – UpToDate, McGraw Hill
Consultant/advisory boards
– Gout: Allena Pharmaceuticals, Horizon Pharma/Amgen, Alnylam Pharmaceuticals, ANI Pharmaceuticals, Shanton Pharma
– ANCA-associated vasculitis: Amgen

OVERVIEW

Hyponatremia

- Pathophysiology
- Diagnostic approach
- Clinical sequelae
  - Acute hyponatremia
  - Chronic hyponatremia
- Management

Hypernatremia/polyuria

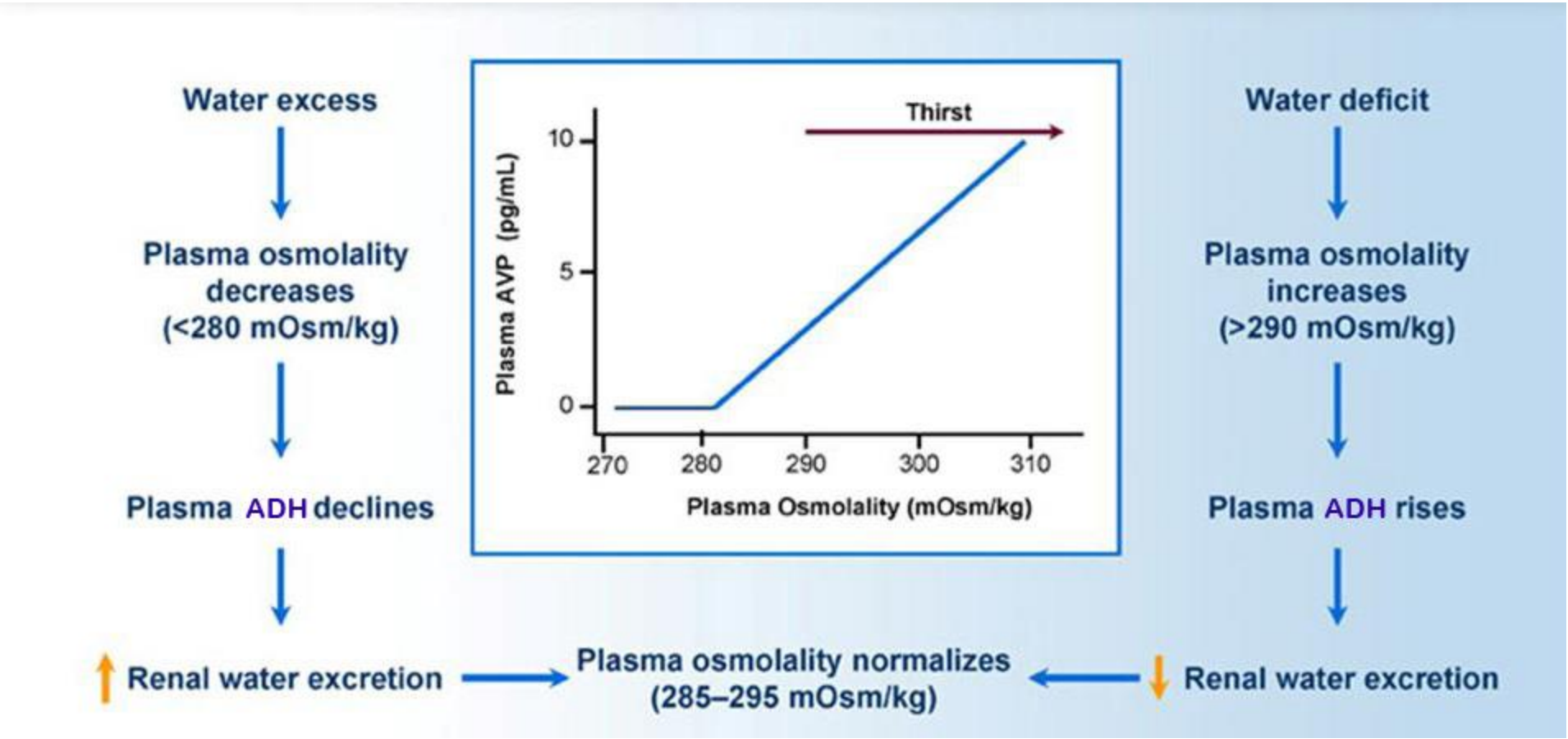
- DD_x and diagnostic approach
- Management

Precious Bodily Fluids

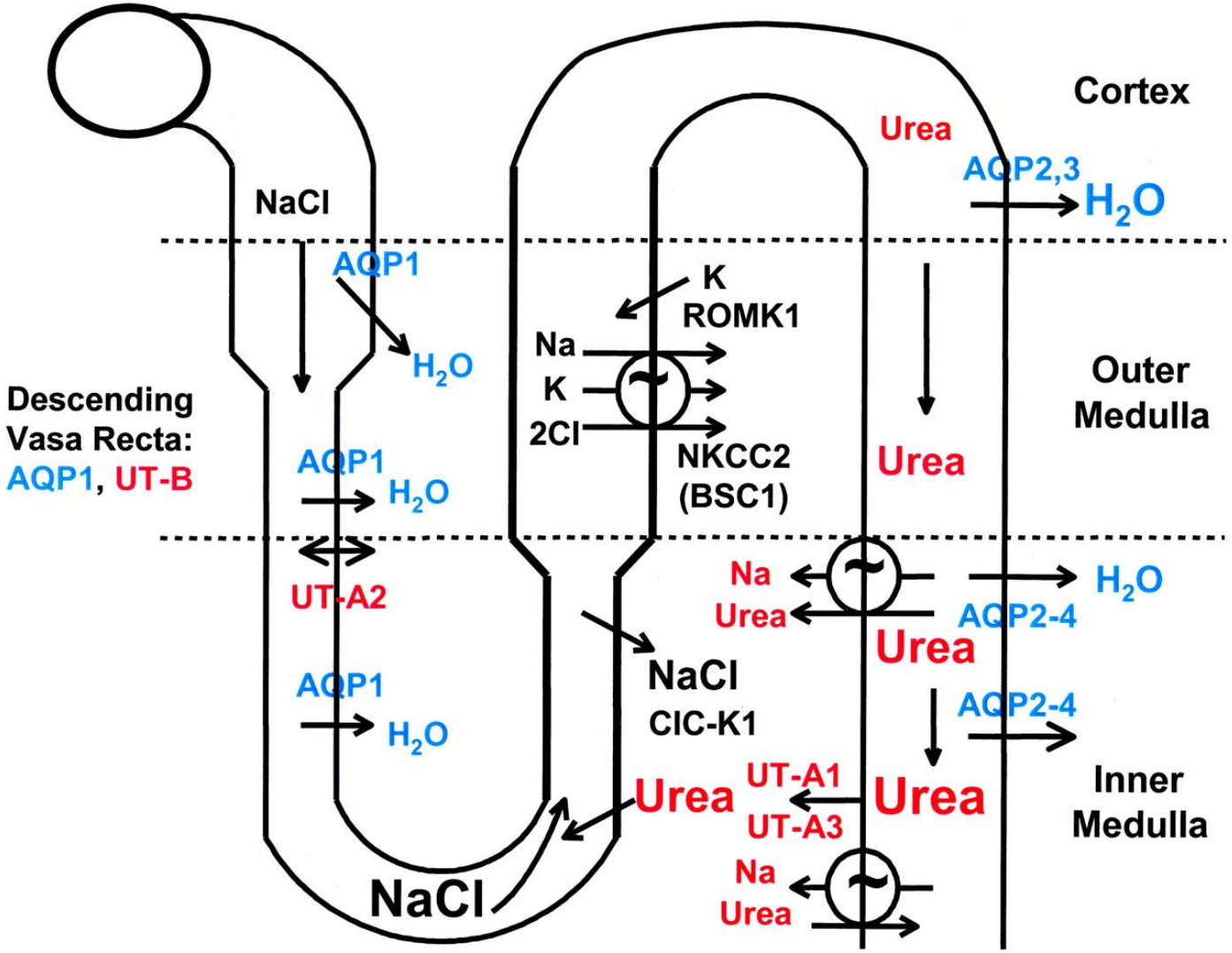
“Water is the source of all life. Seven-tenths of this earth's surface is water. Why, do you realize that seventy percent of you is water?
And as human beings, you and I need fresh, pure water to replenish our precious bodily fluids.”

Colonel Jack D. Ripper
“Dr. Strangelove”, Stanley Kubrick, 1964

Vasopressin (AVP, ADH) Regulates Water Homeostasis and Osmolality

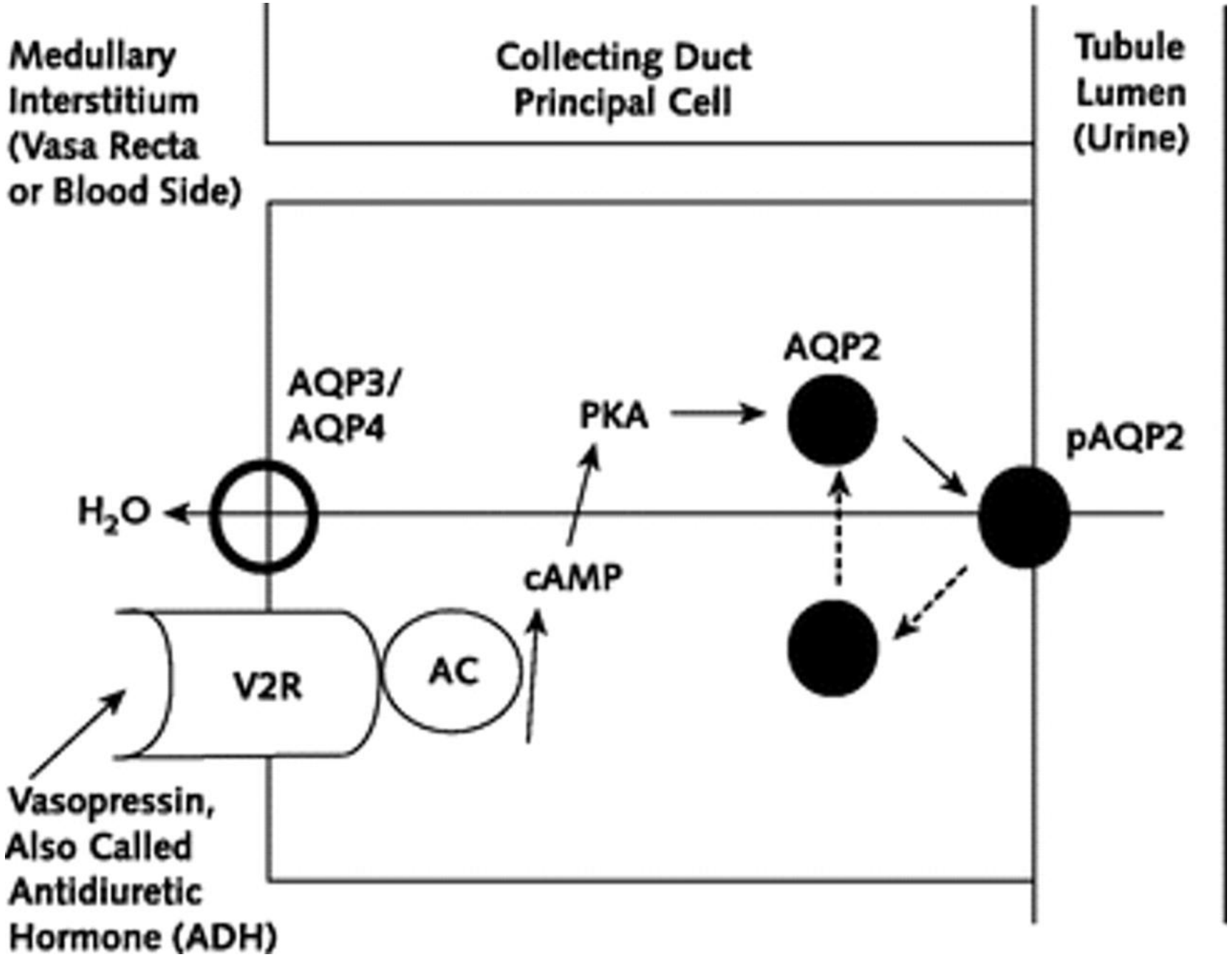


The Renal Concentrating Mechanism in the 21st Century!

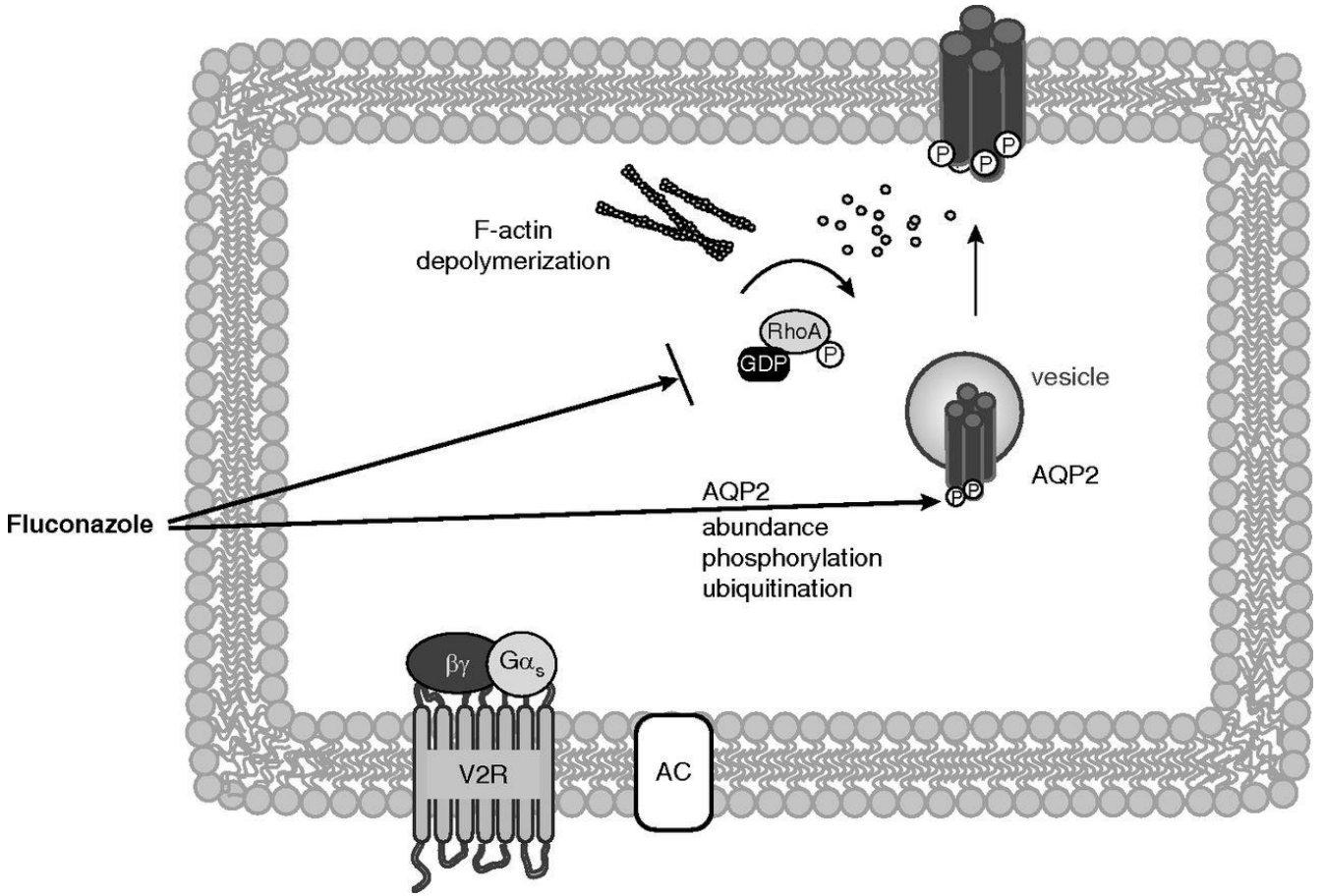


Aqp: aquaporin
UT: urea transporter

Sands, *J Am Soc Nephrol*, 2002


Medullary Interstitium (Vasa Recta or Blood Side)
Collecting Duct Principal Cell
Tubule Lumen (Urine)
AQP3/ AQP4
AQP2
PKA
pAQP2
H_2O
cAMP
V2R
AC
Vasopressin, Also Called Antidiuretic Hormone (ADH)

Novel Therapies Where You Yeast Expect Them: Fluconazole for Nephrogenic DI



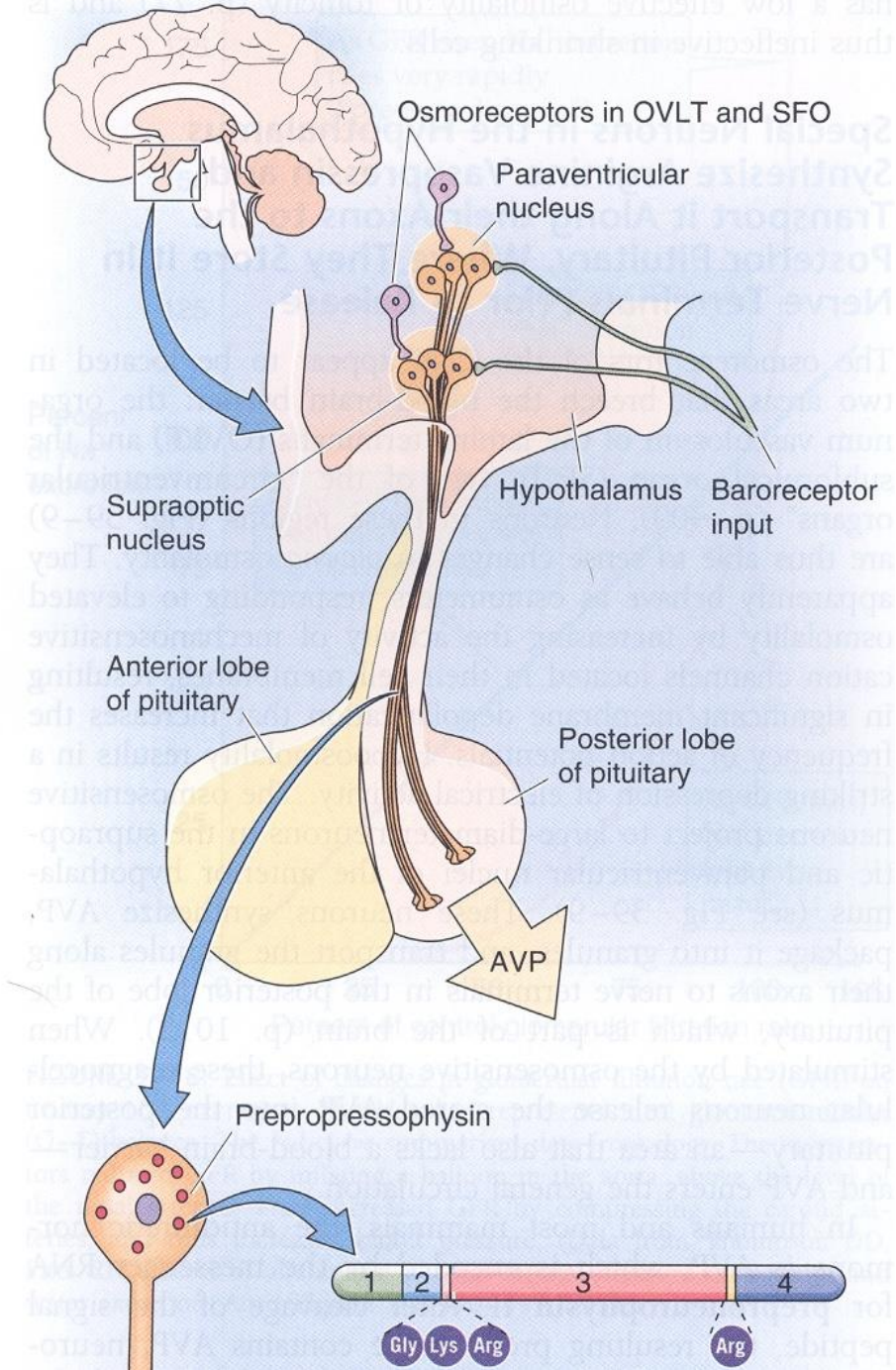
J Am Soc Nephrol. 2019 May;30(5):795-810

Osmoregulation versus Extracellular Volume Regulation

	Osmoregulation	*Volume regulation*
What is being sensed	Plasma osmolality	Arterial perfusion pressure
Sensors	Hypothalamic osmoreceptors	Carotid sinus Afferent arteriole Atria
Effectors	ADH/Vasopressin Thirst	Sympathetic nervous system Renin-angiotensin-aldosterone system ANP/BNP **VASOPRESSIN**
What is affected	Urine osmolality Water intake	Urinary sodium excretion

Black and Rose, *Manual of Clinical Problems in Nephrology*, 1988

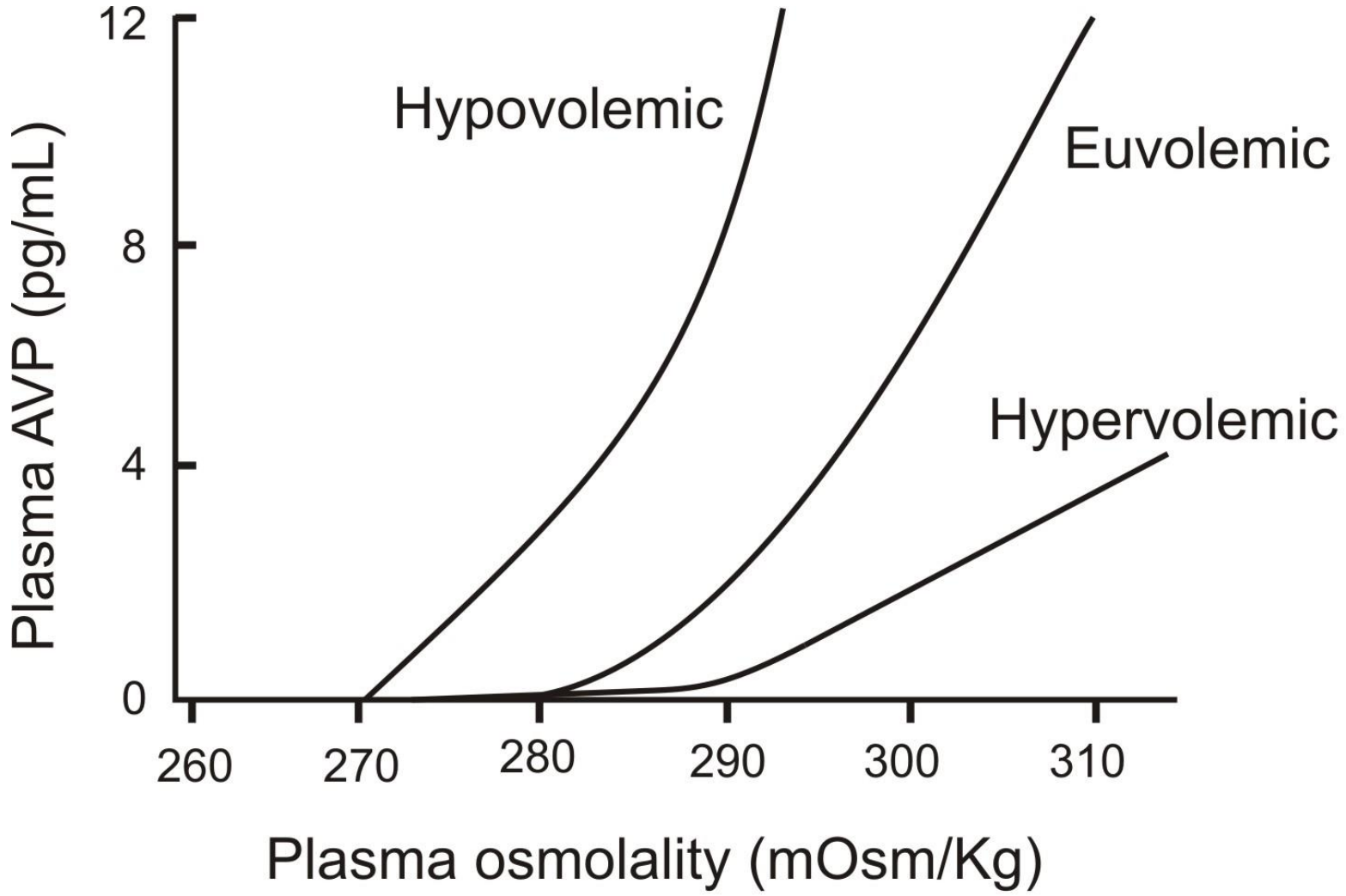
Hypothalamic Control of Vasopressin Secretion



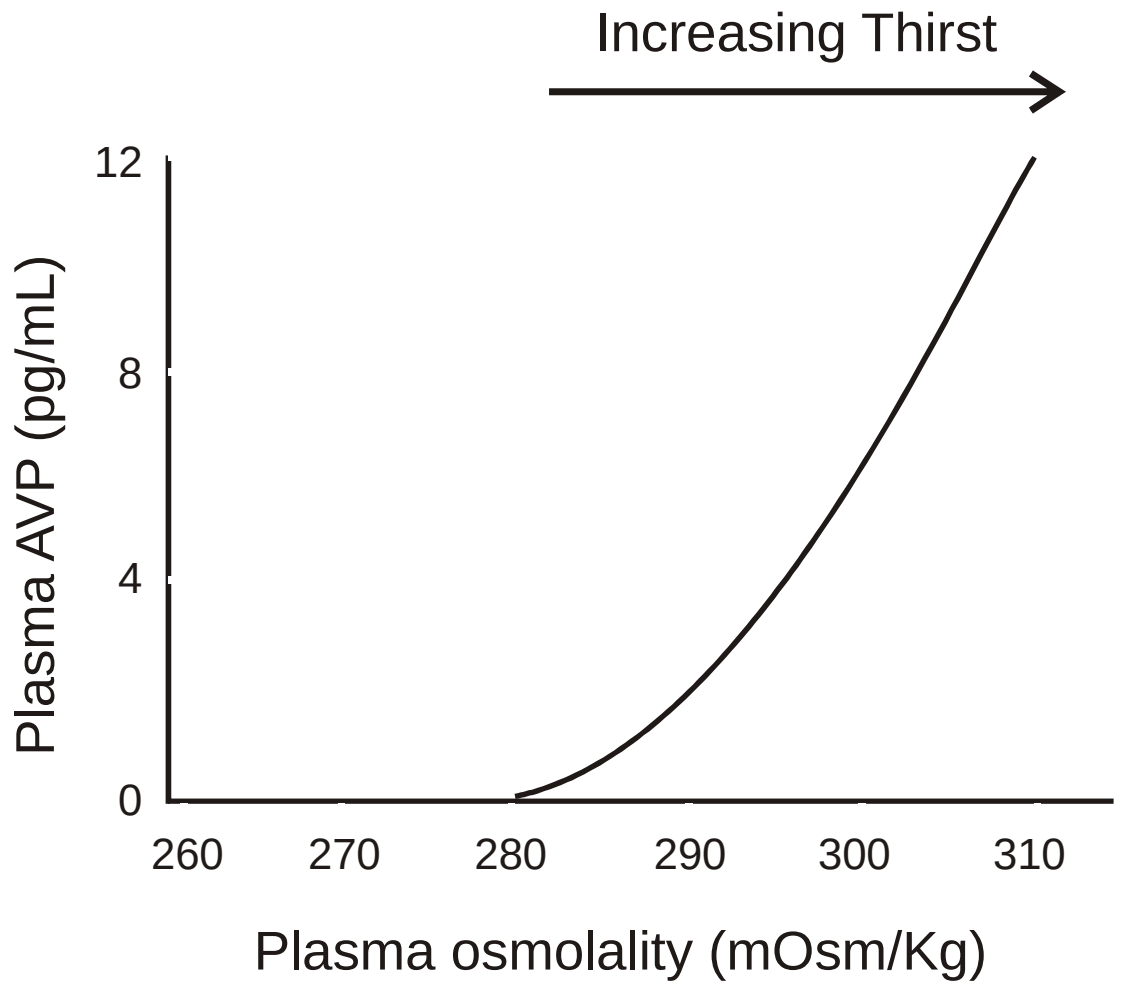
OVLT – organum vasculosum of the lamina terminalis (periventricular, 3rd ventricle)
SFO – subfornical organ

Boron and Boulpaep, *Medical Physiology*, 2004

Volume Status and AVP Release



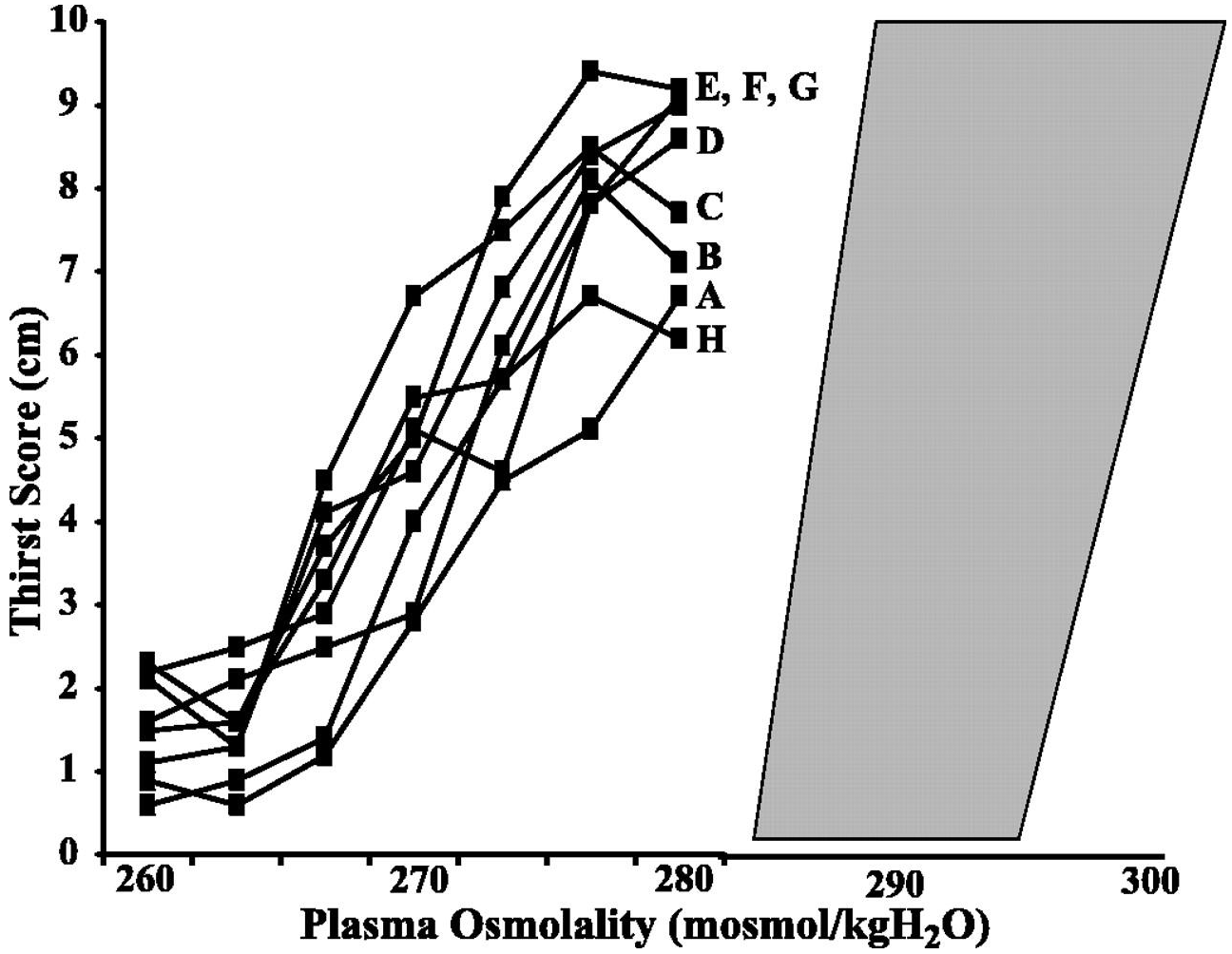
What About Thirst??



Thirst is stimulated over same range of osmolality as AVP, via activation of central osmoreceptors

Typically need intake of H_2O to generate hyponatremia

Leftward Shift of the Thirst Response in SIADH, i.e. Thirst Also Abnormal



A-H: SIADH pts
Grey: Controls

Smith et al, *AJP Endocrinol*, 2004

Initial Evaluation of Hyponatremia

H&P

- Medications. SSRIs are the most common contemporary cause of SIADH.
- PMH. For example, prior pituitary surgery….
- ROS. Symptoms attributable to acute or chronic hyponatremia.
  Symptoms suggestive of a cause, e.g. profuse diarrhea → hypovolemic hyponatremia.
  Chronicity; acute versus chronic (>48 hours).

Exam

- Hypovolemic? Orthostatics, JVP
- Hypervolemic? JVP, edema, chest exam

Initial Lab Evaluation of Hyponatremia

Plasma osmolality
- Low: true hyponatremia
- Normal or elevated: pseudohyponatremia or renal failure

Urine osmolality
- <100 mosmol/kg: primary polydipsia
- >100 mOsmol/kg: reduced H_2O excretion

Urine Na^+ concentration
- <20 mEqu/L: **effective** volume depletion
- >20 mEqul/L: “euvolemic” causes or renal Na^+ wasting

Question #1

63 yo male relapsed alcoholic, >12 beers/day
Patient had been to his PCP two days before, was found to have serum Na of 115 and told to return to the ED.
On exam he is barely rousable but responds to commands slowly. Supine BP 124/67 HR 80; standing BP 170/71 HR 114, then 105/84 HR 105 after 5 minutes
Na <110, K 4.8, Cl 73, HCO3 27, BUN 9, Cr 0.8, Gluc 193, Urine Osm 227, Urine Na <20, Serum Osm 236.

Which of the following is the most likely cause of this presentation?

A. Beer potomania
B. Pure hypovolemic hyponatremia
C. SIADH
D. Polydipsia

Low Solute Hyponatremia?

Patient hx of ETOH dependence with suspicion of recent drinking.
Low Urine Osmoles
Rapid initial correction with IV NS soln.
Exam appears euvolemic (orthostatics confusing). But management would be similar for hypovolemic hyponatremia (avoid rapid saline/solute intake).

Beer Potomania

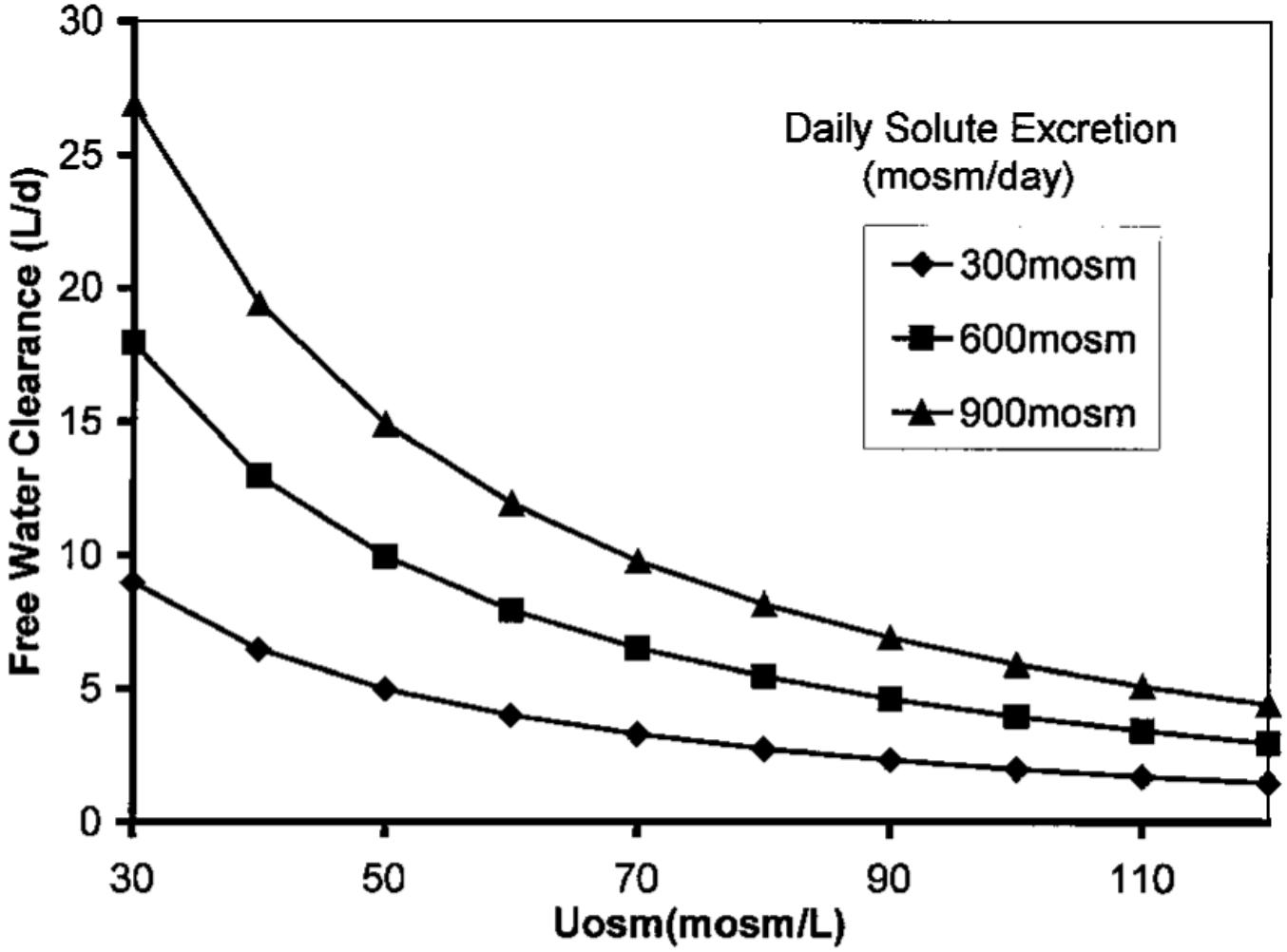
Vasopressin-independent cause of hyponatremia.
Free water excretion in the urine requires a minimum amount of solute.
Beer provides carbohydrates that can sustain, but with no salt or protein it generates minimal urinary solute excretion.
Combined with high free water intake from beer, patients become hyponatremic.
Classically low urine Na/Osm but can be generous.

Lab Data in Beer Potomania

			Presentation Laboratory Results							
Author (year)	Patients no.	Neurological Symptoms on Presentation	Na (mEq/L)	K (mEq/L)	BUN (mg/dL)	U osm (mosm/L)	U Na (mos m/L)	Treatment	Serum Na Change	Outcome
Demanet (71)	1	Unconscious, seizure	107	2.6	12	N/A	N/A	N/A	N/A	N/A
	2	Weakness	105	1.3	15	N/A	N/A	N/A	N/A	Death - brain autopsy with atrophy of mammillary bodies
	3	Weakness	104	2.6	30	N/A	N/A	N/A	N/A	Death - no brain autopsy
	4	Unconscious	103	2.5	13	N/A	N/A	300 MEQ Na IV d 1 and 2	10 mmol/48 h	N/A
	5	Weakness, "grand mal"	101	1.4	19	N/A	N/A	N/A	N/A	Death - normal brain autopsy
	6	Unconscious, "grand mal"	99	1.8	18	N/A	N/A	N/A	N/A	Death - brain autopsy with CPM
	7	Unconscious, "grand mal"	98	4.4	30	N/A	N/A	N/A	N/A	N/A
Gwinup (72)	8	Weakness	122	5.1	N/A	N/A	N/A	Fluid restriction	20 mmol/72 h	No neurological sequelae reported
Hilden (75)	9	Debility, dizziness, confusion	123	2.7	N/A	N/A	N/A	0.9% NS 2–3 L	12 mmol/48 h	No neurological sequelae reported
	10	Debility, dizziness, confusion	109	2.5	N/A	79	N/A	No IVFs	15 mmol/48 h	No neurological sequelae reported
	11	Debility, dizziness, confusion	108	2.7	N/A	69	N/A	0.9% NS 2–3 L	19 mmol/48 h	No neurological sequelae reported
	12	Debility, dizziness, confusion	127	2.5	N/A	N/A	N/A	No IVFs	2 mmol/48 h	No neurological sequelae reported
	13	Debility, dizziness, confusion	117	3.1	N/A	N/A	N/A	No IVFs	9 mmol/48 h	No neurological sequelae reported
Swenson (76)	14	Weakness	106	3.8	N/A	199	5.6	Fluid restriction	8 mmol/48 h	No apparent neurological sequelae
Evans (85)	15	Confused, restless	118	4.1	2.3	N/A	N/A	1.8% NS × 6 h then 10 DW or 0.9% NS	9 mmol/48 h	Long-term impaired memory, confabulation
Joyce (86)	16	Agitation, confusion, seizures	110	3	N/A	N/A	N/A	3% NS × 30 mL, 0.9% NS @ 300 ml/h	14 mmol/24 h	Discharged d 2, lost to follow-up
Fenves (95)	17	Tremor	121	3.6	4	50	1	0.9% NS @ 100 mL/h	13 mmol/13 h	Not reported
	18	Unconscious, seizures	97	3.6	2	338	12	0.9% NS @ 150 mL/h and 3% NS @ 20 mL/h × 160 Ml	30 mmol/48 h	No apparent neurological sequelae
Kelly (98)	19	Unconscious	109	3.6	16	340	<10	NS 3 L/24 h	20 mmol/48 h	ODS
Lens (01)	20	Confusion/weakness	97	2.1	14	N/A	N/A	0.45 NS + KCl supplements	21 mmol/48 h	ODS
Sanghvi (06)	21	Weakness	100	2.7	4	218	53	NS, later fluid restriction with D5	15 mmol/24 h, 24 mmol/48 h	ODS
	22	Weakness	104	4.3	7	547	10	Fluid restriction	7 mmol/24 h, 14 mmol/48 h	No apparent neurological sequelae

Sanghvi et al AJKD 2007:50(4) 673-680

Free Water Clearance and Solute Excretion

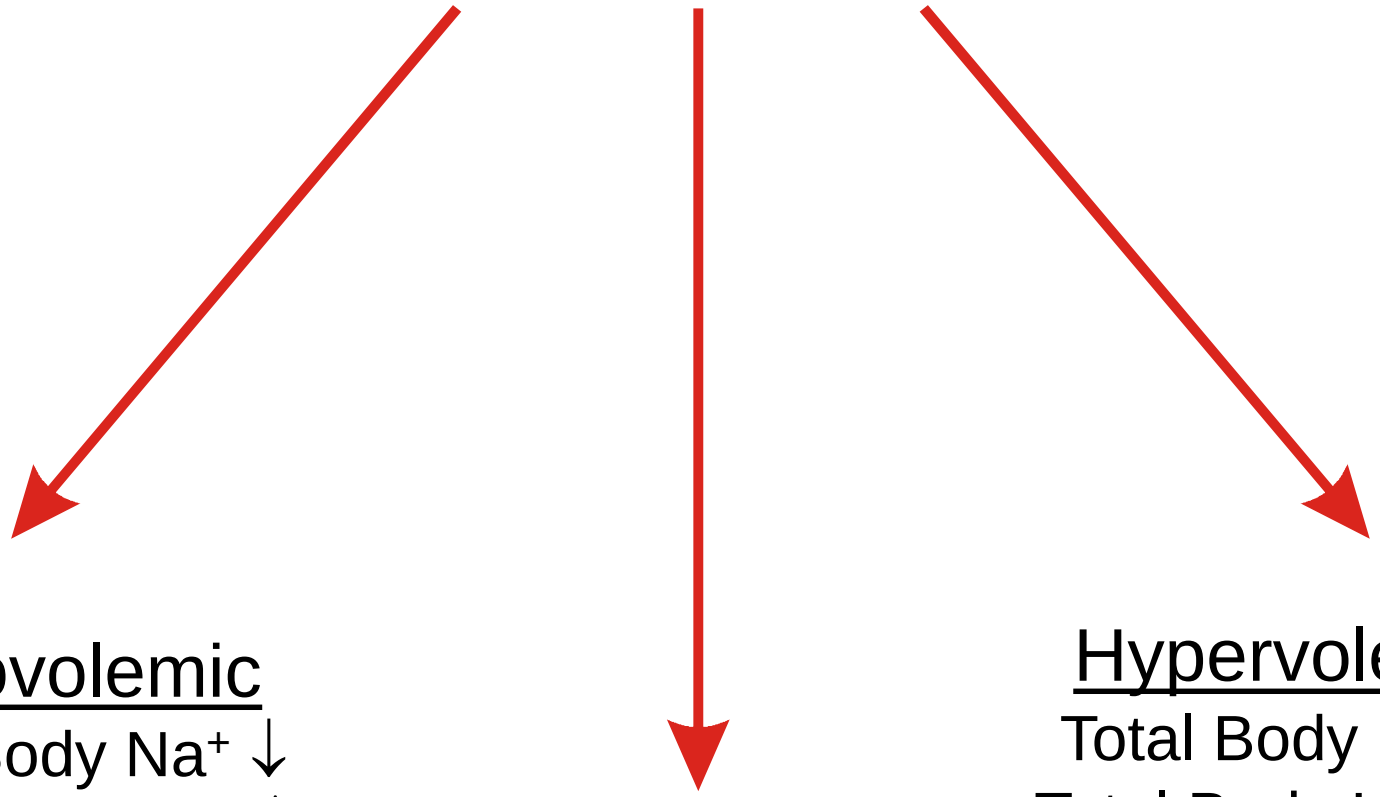


Thaler et al, Am J Kidney Dis 1998;31(6):1028-1031

Further Testing in Hyponatremia

TSH – rule out hypothyroidism
Random cortisol – primary or secondary adrenal failure. Check other indices of pituitary function if hypopit likely
Cosyntrophin stimulation test – if primary adrenal failure likely
CXR; if negative and high likelihood of small cell CA → chest CT
Head CT – look also at sinuses and nasal cavity (squmous cell CA, olfactory neuroblastoma)

Approach to the Hyponatremic Patient with U_{osm} > 100 mOsm/kg

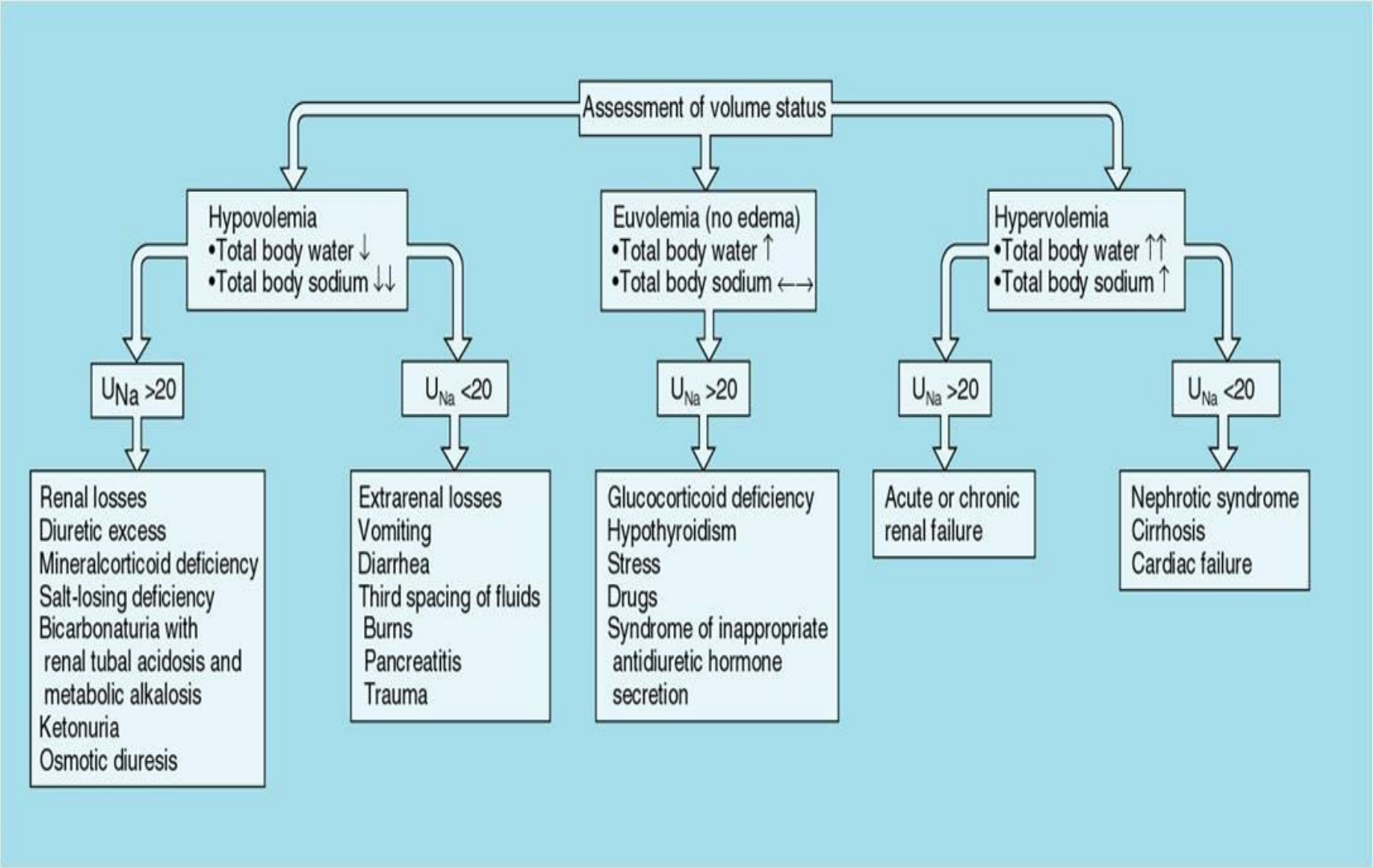


Hypovolemic
Total Body Na^+ ↓
Total Body H_2O ↑

Euvolemic
Total Body Na^+ ~ euvolemic
Total Body H_2O ↑

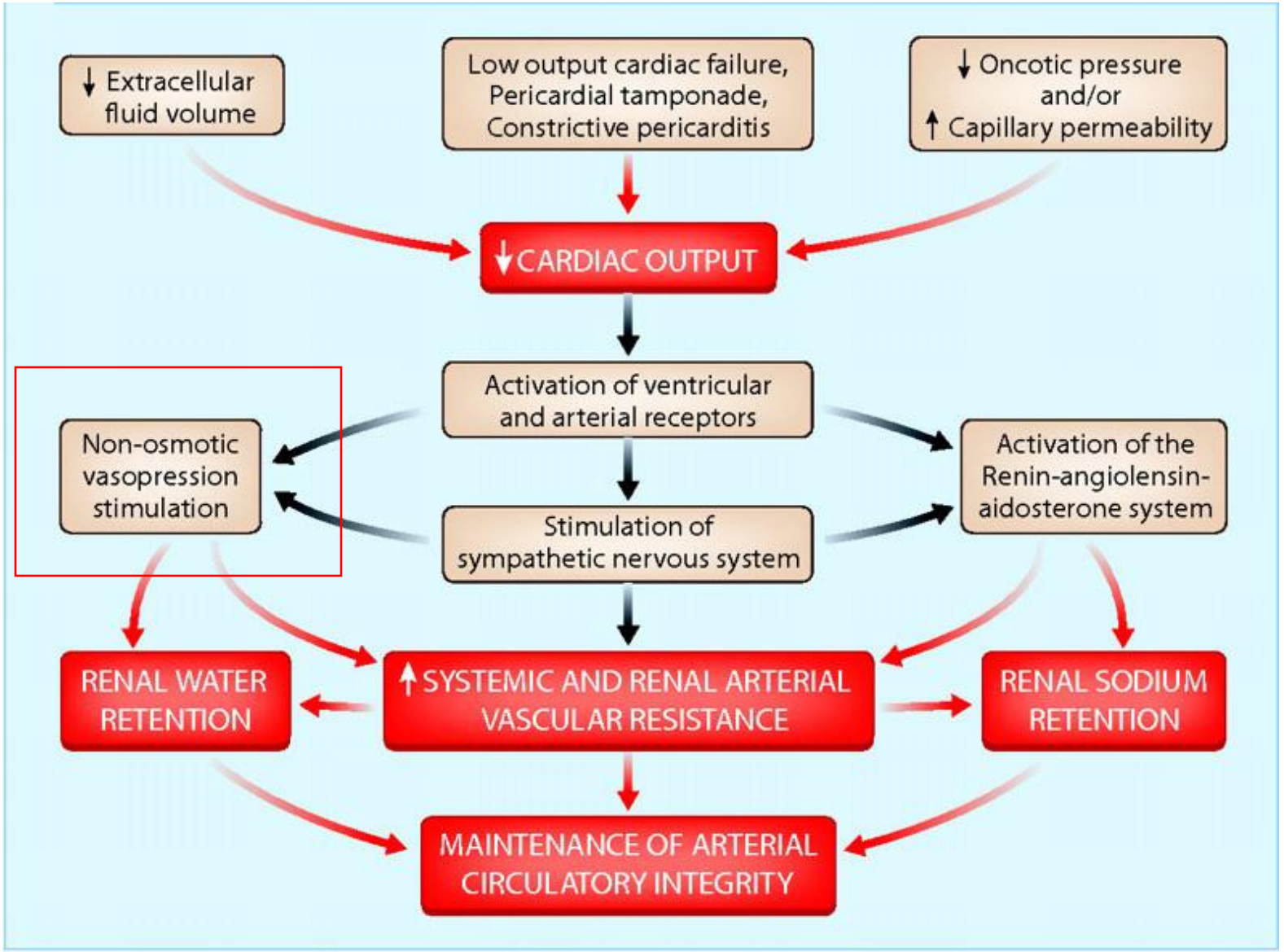
Hypervolemic
Total Body Na^+ ↑
Total Body H_2O ↑↑

Diagnostic Algorithm



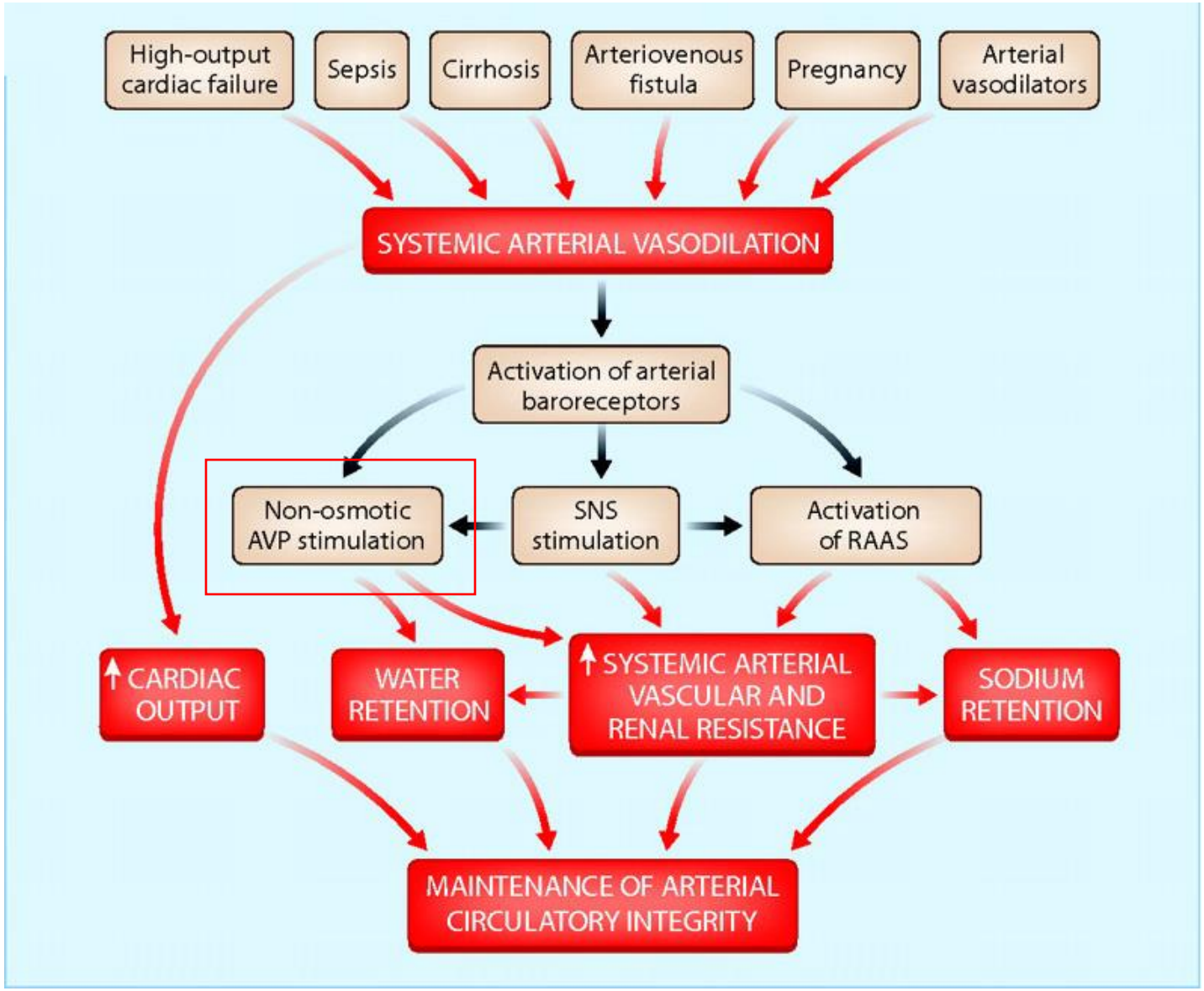
Kumar and Berl, Atlas of Diseases of the Kidney, 1999

Defense of Circulatory Integrity in ↓ Cardiac Output



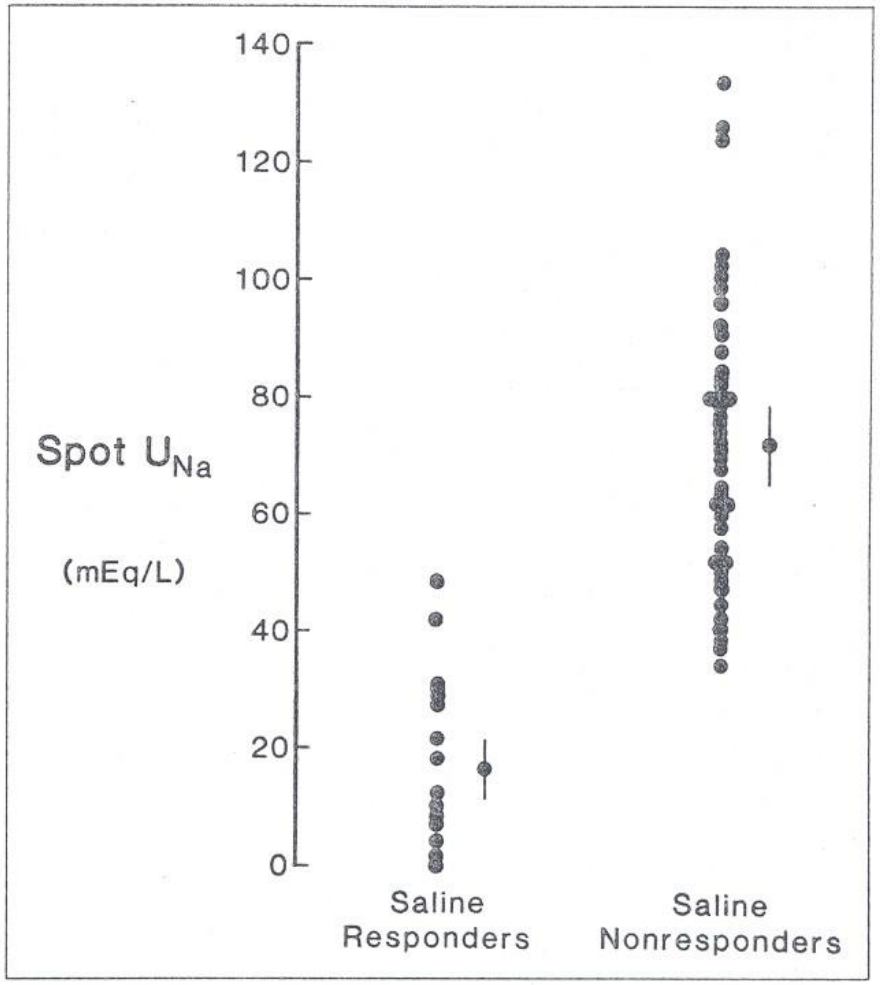
Schrier, JASN, 2007

Defense of Circulatory Integrity in Vasodilatory States



Schrier, JASN, 2007

Spot Urinary Na^+ and the D_x of Hypovolemic Hyponatremia

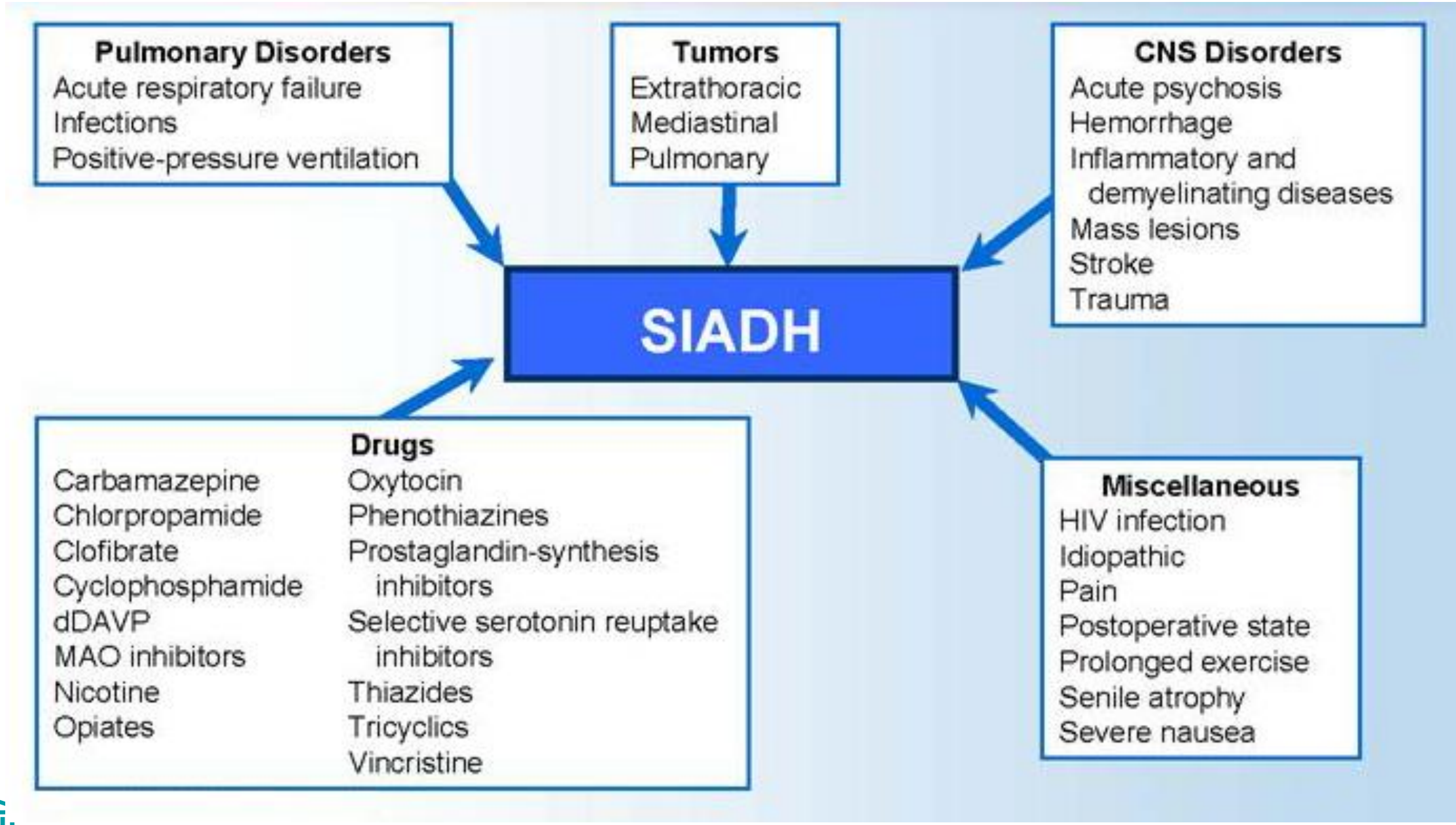


Urine Na^+ in "non-edematous" patients with hyponatremia, who do or do not respond to saline infusion with ↑ serum Na^+

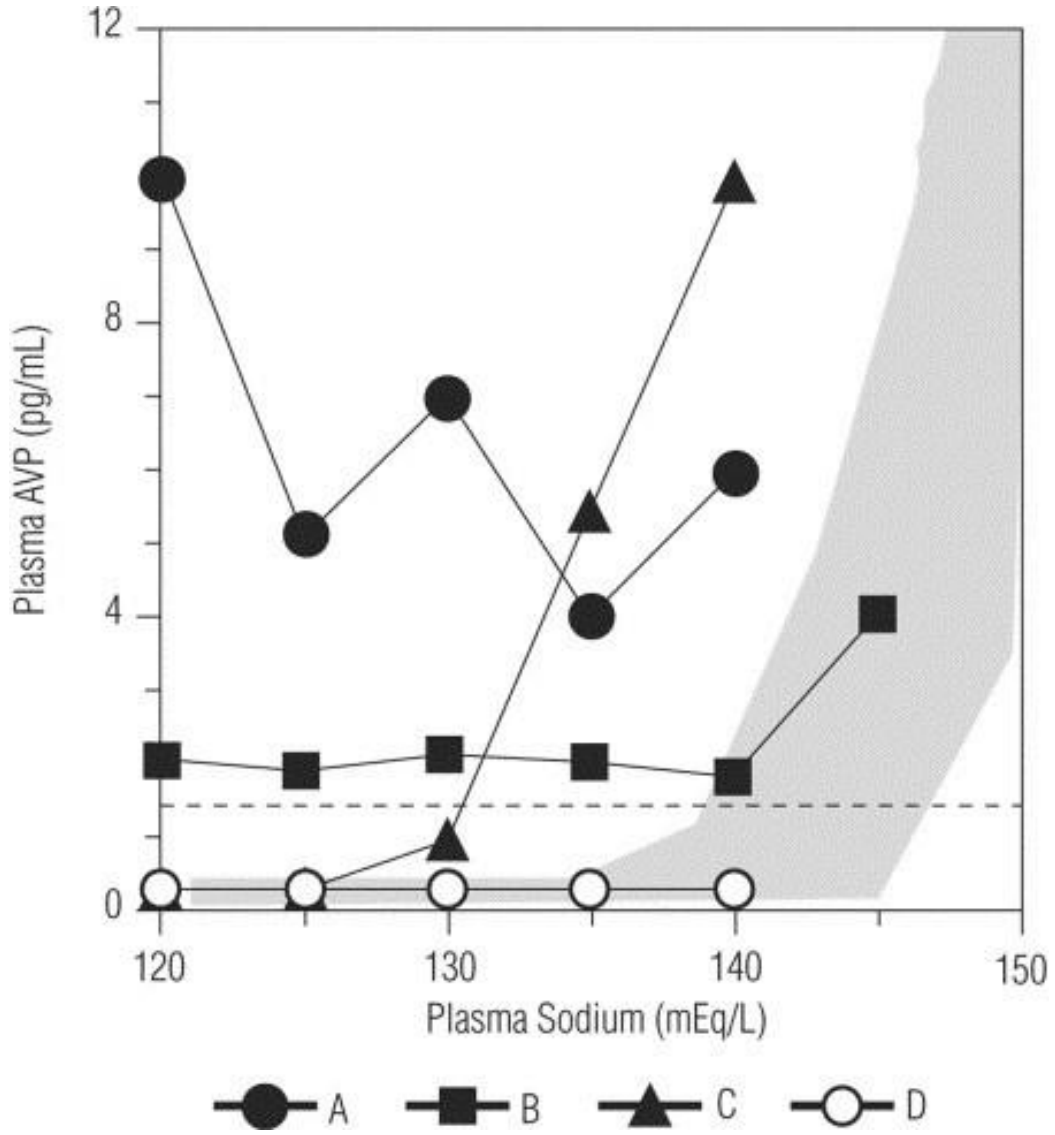
.

Na^+-avid patients have ↑ vasopressin due to hypovolemia → suppressed by normal saline infusion.

Am J Med 83: 905-908, 1987


Pulmonary Disorders
Acute respiratory failure
Infections
Positive-pressure ventilation
Tumors
Extrathoracic
Mediastinal
Pulmonary
CNS Disorders
Acute psychosis
Hemorrhage
Inflammatory and demyelinating diseases
Mass lesions
Stroke
Trauma
SIADH
Drugs
Carbamazepine
Chlorpropamide
Clofibrate
Cyclophosphamide
dDAVP
MAO inhibitors
Nicotine
Opiates
Oxytocin
Phenothiazines
Prostaglandin-synthesis inhibitors
Selective serotonin reuptake inhibitors
Thiazides
Tricyclics
Vincristine
Miscellaneous
HIV infection
Idiopathic
Pain
Postoperative state
Prolonged exercise
Senile atrophy
Severe nausea

Patterns of AVP Release in SIADH



A) Unregulated, erratic
B) Baseline increase, normal osmotic response
C) "Reset osmostat"
D) Suppressed AVP

Robertson, Am J Med. 2006;119(7 Suppl 1):S36-42

Question #2

A 19 yo woman is brought to the emergency department with altered mental status. She had been at a “rave” the night before. She became drowsy at ~2 AM, and vomited several times. At 4 AM she had a generalized seizure that lasted ~15 seconds. On exam, she is unresponsive, ventilated HR 84, bp 145/85. Heart sounds normal, inspiratory crackles on chest exam. Head & neck WNL, no evidence of trauma.

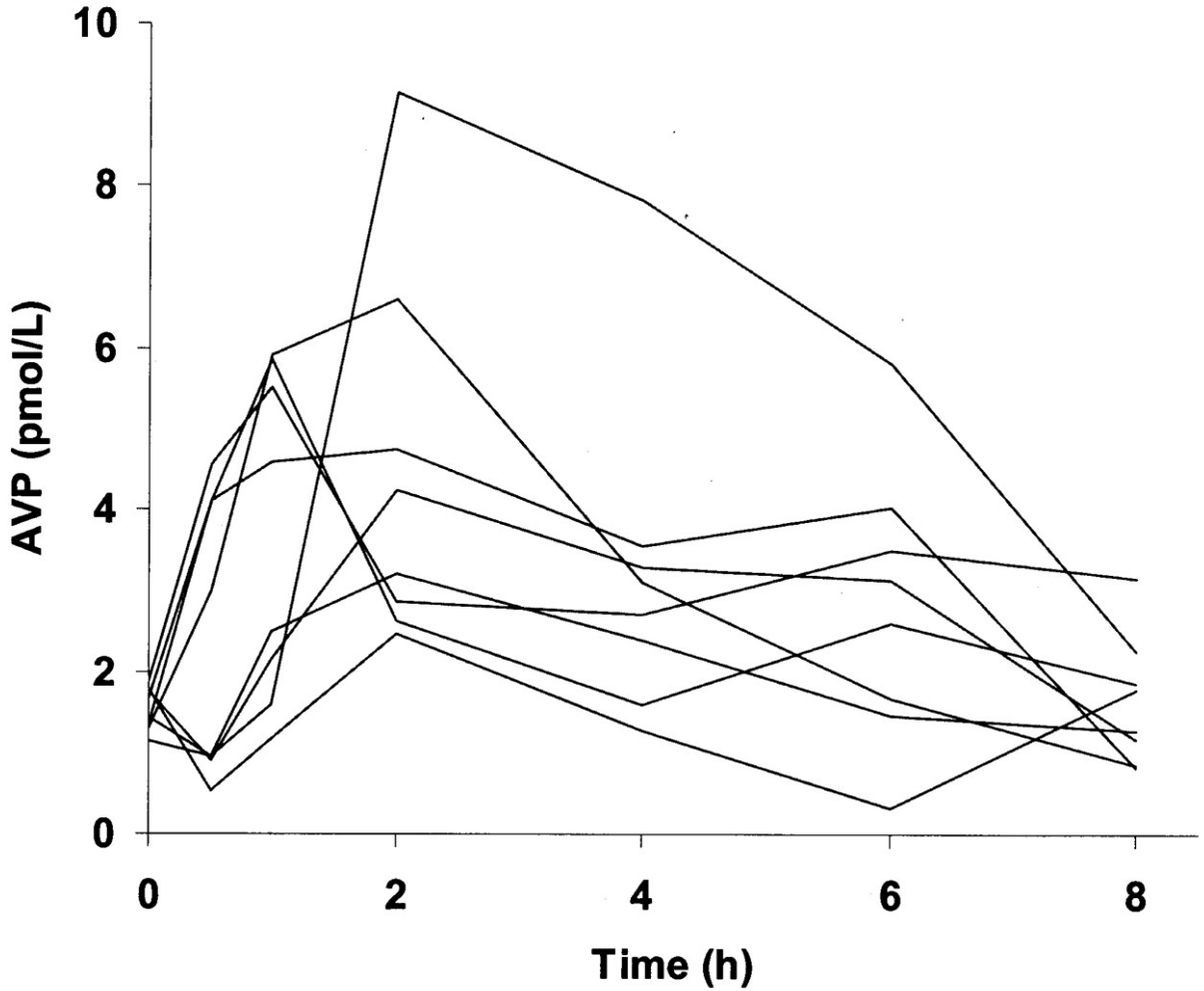
Laboratory Studies:

Na^+	121	Creat	0.5
K^+	3.6	uric acid	3.7
Cl^-	90	Osm	242

Which of the following is the most likely cause of this syndrome?

A. Ecstasy-induced hyponatremia
B. Hyponatremia secondary to seizure
C. Exercise-associated hyponatremia
D. Acute intracerebral bleed
E. Compulsive drinking

MDMA (Ecstasy) Ingestion Causes SIADH In Healthy Volunteers



Fallon et al, *Ann. N.Y. Acad. Sci.*, 2002

Ecstasy and Hyponatremia

Due to a combination of factors:

- Acute, massive increase in AVP – serotonin activates central osmoreceptors → ↑ AVP release from posterior pituitary
- Acute stimulation of thirst – serotonin activates central osmoreceptors
- Deliberate water intake – recommendations have been to increase water intake at raves, given exertion and possible hyperthermia

Causes of Acute Hyponatremia

Iatrogenic
- Postoperative – premenopausal women
- Hypotonic fluids with cause of ↑ vasopressin
- Glycine irrigant – TURP, uterine surgery
- Colonoscopy preparation
- Recent institution of thiazides

Polydipsia

Ecstasy ingestion

Exercise induced

Multifactorial, e.g. thiazide and polydipsia

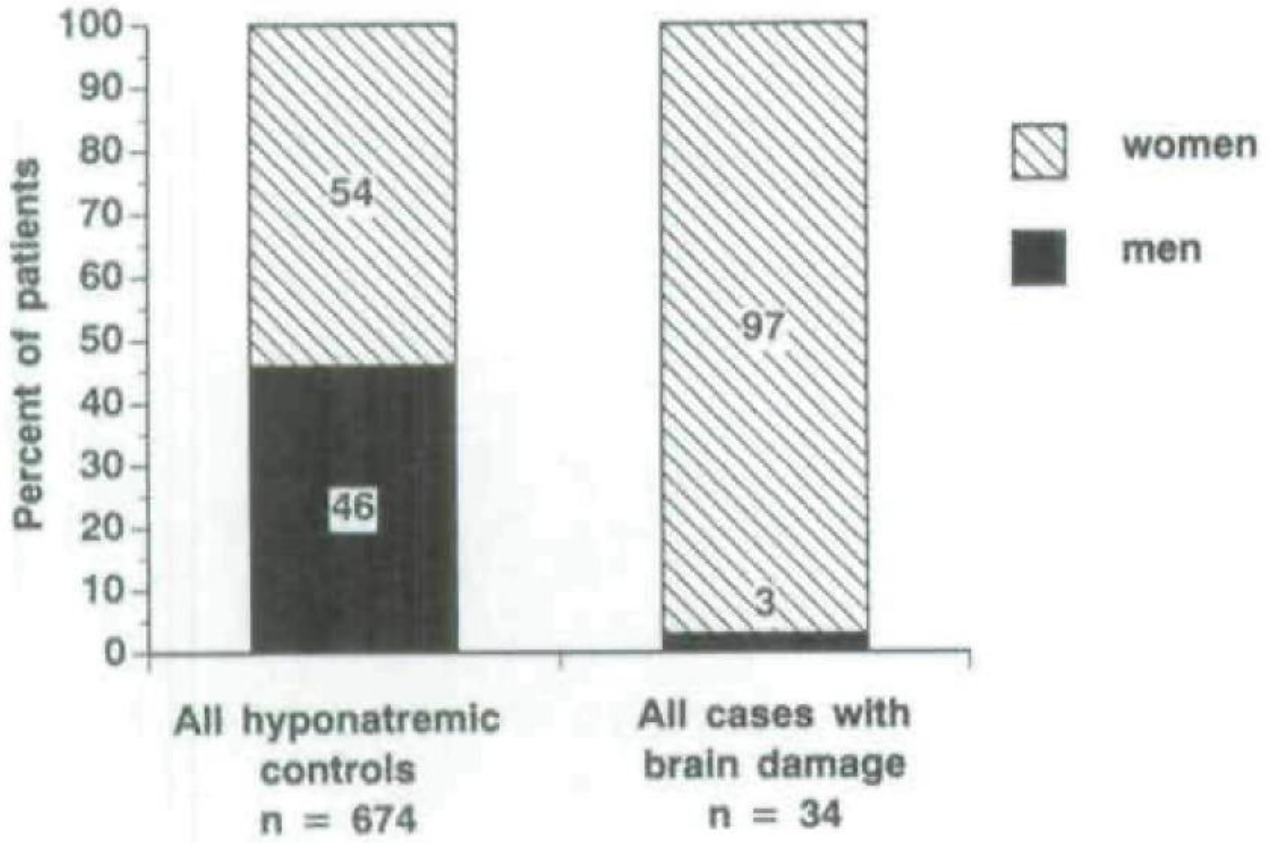
Symptoms/Signs of Acute Hyponatremic Encephalopathy

Early: headache, nausea, vomiting

Advanced: ↓ response to verbal or painful stimuli, inappropriate behavior, asterixis, obtundation, incontinence

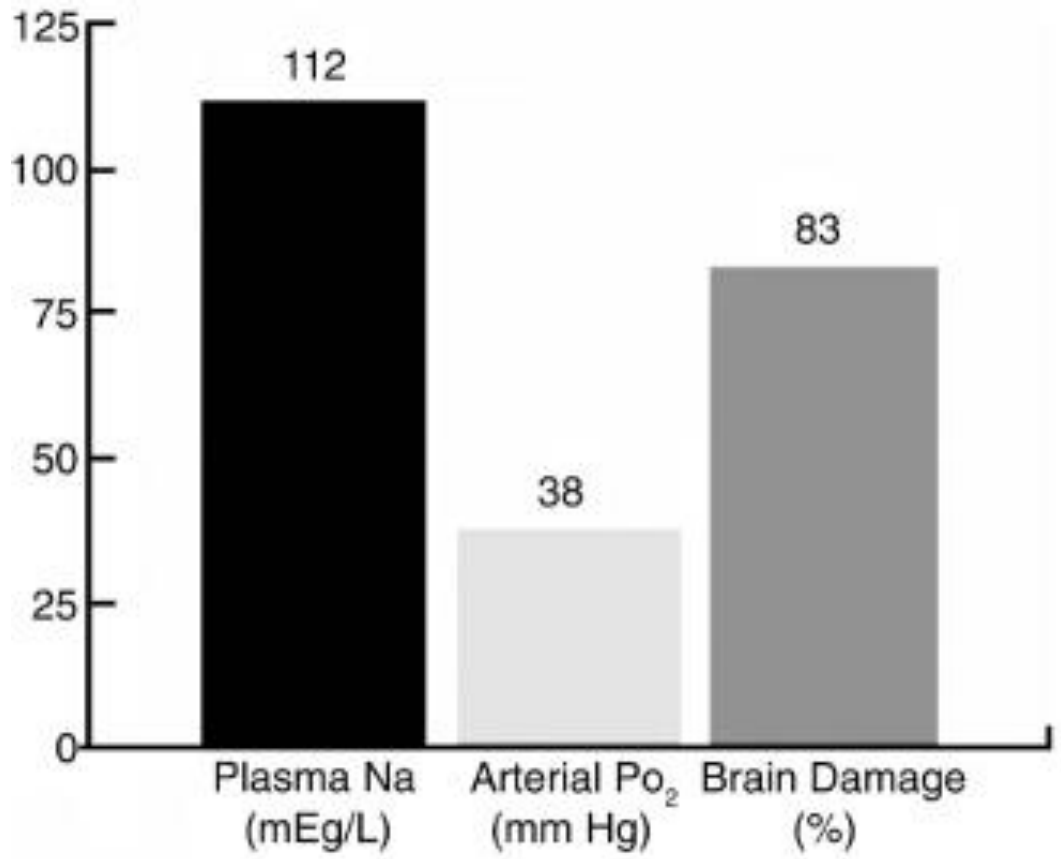
Far advanced: decorticate and/or decerebrate posturing, hyper/hypotension, dilated pupils, **seizures**, **respiratory arrest**, polyuria (central DI), hyperglycemia

The Marked Female Preponderance in Hyponatremic Brain Injury



Ayus et al, *Ann Int Med*, 1992

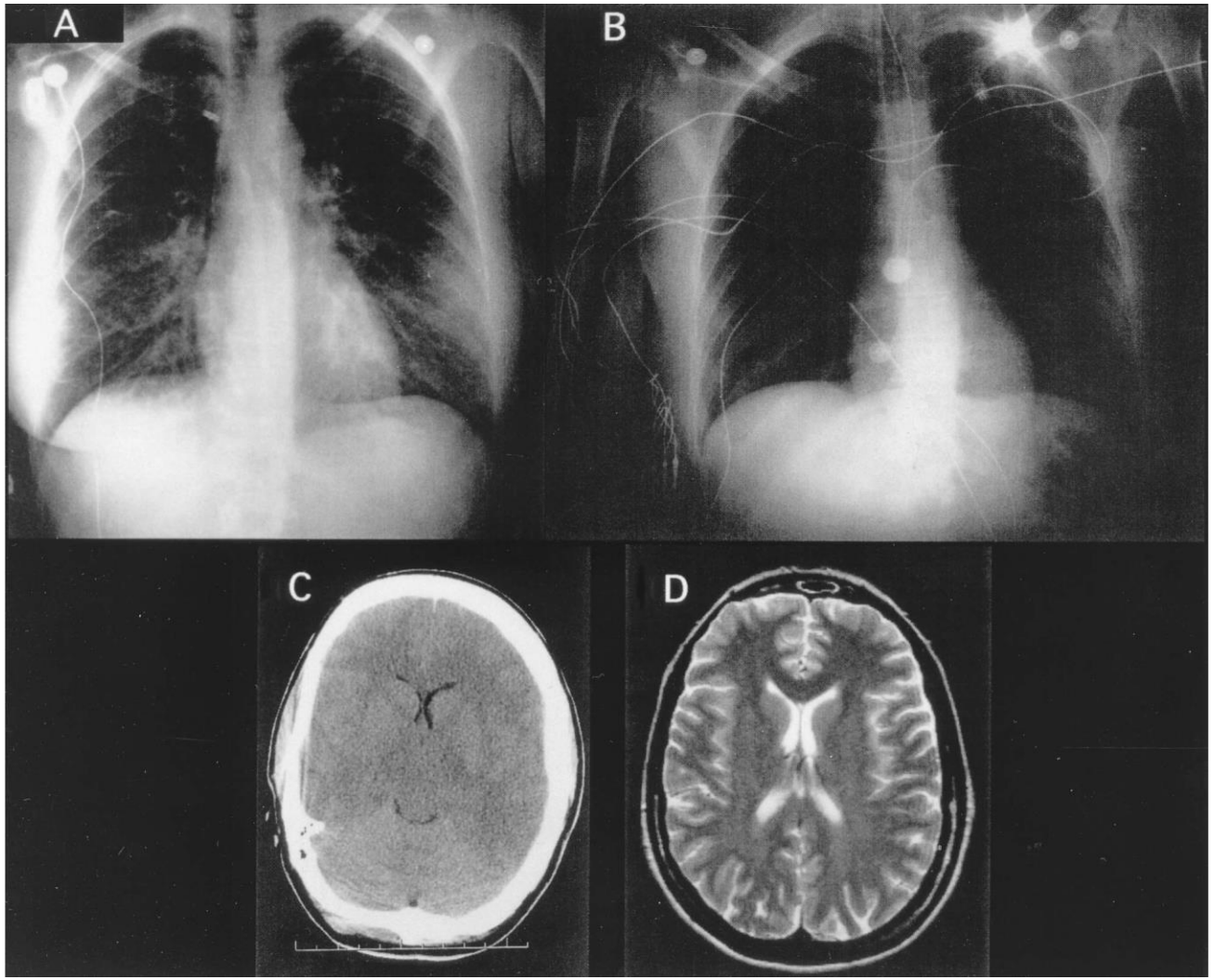
Hyponatremic Encephalopathy And Hypoxia



Hypoxia in 144 patients with hyponatremic encephalopathy

Arieff, *Am J Med*, 2006

Cerebral Edema and Non-Cardiogenic Pulmonary Edema in Acute Hyponatremia



CT head

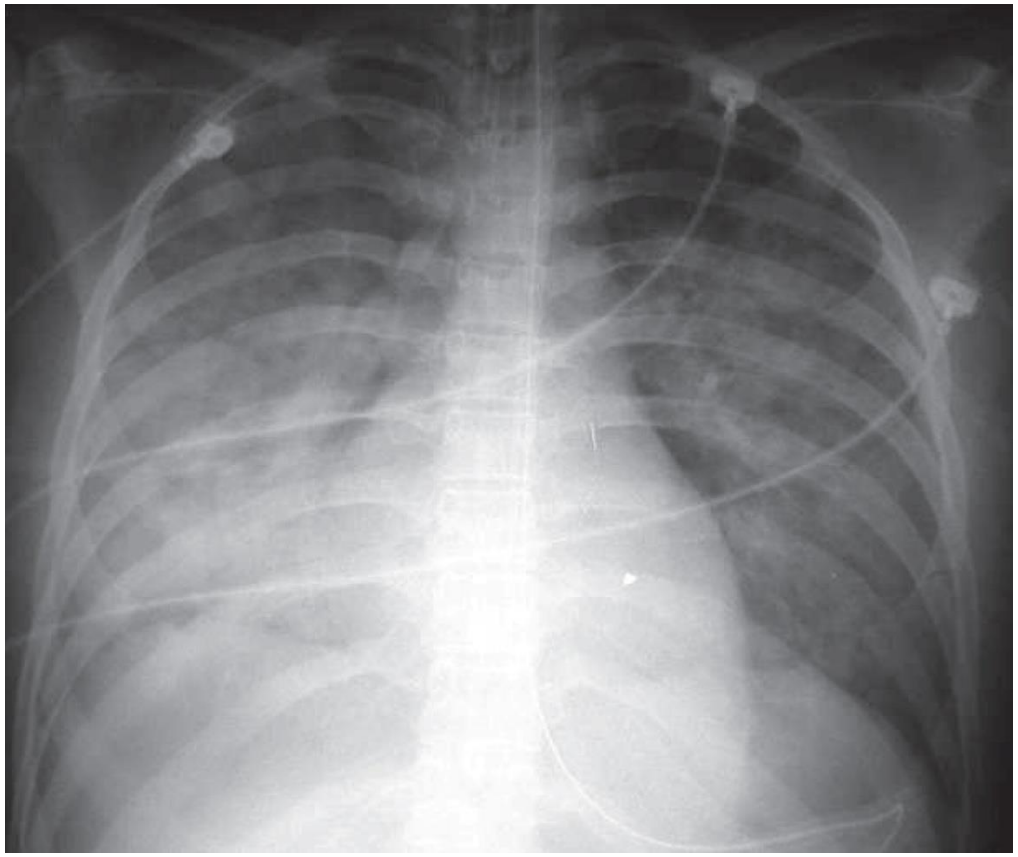
MRI

A&C – @ ER
B&D – after 24 hrs

44 yo female
marathon runner

Ayus et al,
Ann Int Med, 2000

Pulmonary Edema After Ecstasy Ingestion



20 year-old female college student

$[Na^+]$ 117 mM

Nguyen et al, Nature Clin Prac Nephrology, 2006

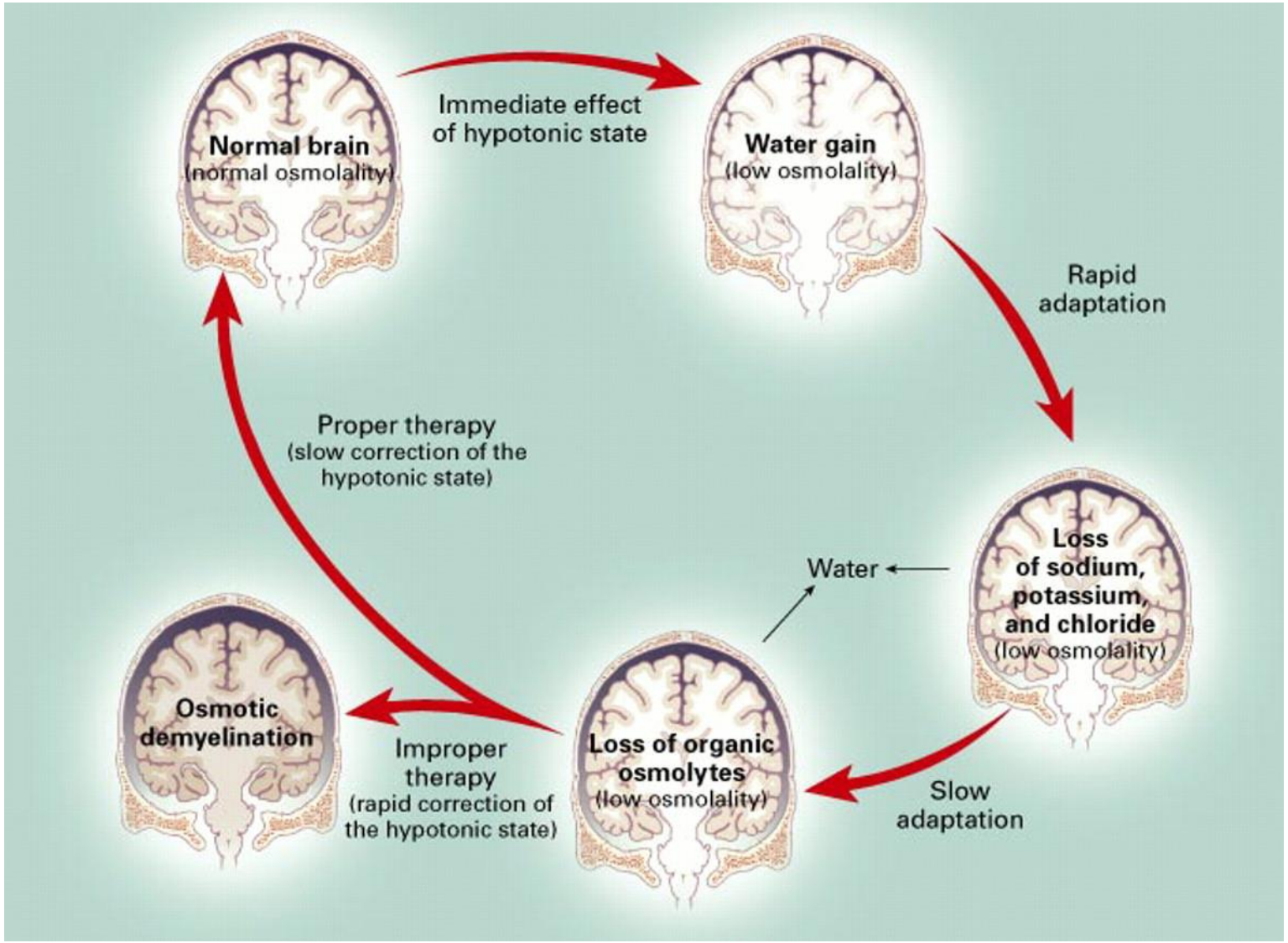
Chronic Hyponatremia

> 48 hours or of unknown duration
CNS response to hyponatremia induces sensitivity to correction rate, wrt osmotic demyelination syndrome (ODS)

Symptoms classically taught as “absent” but may include:

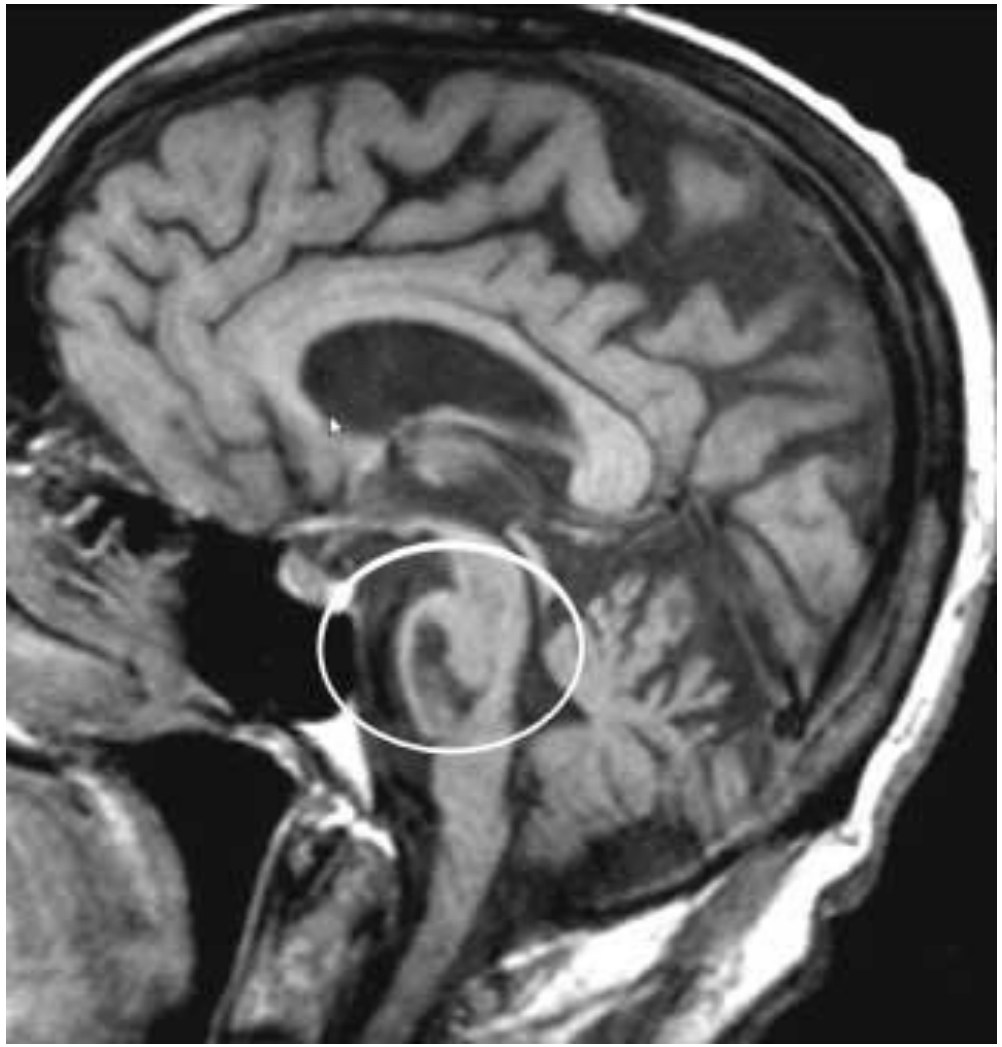
- Nausea and vomiting
- Muscle cramps and weakness
- Ataxia
- Confusion, change in mental status
- Seizures (if Na^+ ↓↓↓)

The CNS Response to Hyponatremia



Adrogue and Madias, *NEJM*, 2000

Central Pontine Myelinolysis (CPM) From Osmotic Demyelination Syndrome (ODS)



Flaccid quadriparesis, Δ corticospinal tract
Dysphagia, from corticobulbar tract
Locked-in syndrome
Symptoms from extra-pontine pathology are variable, depending on region involved

Risk Factors for Osmotic Demyelination

Rate of correction (although CPM/ODS can occur at accepted rates….)
Hypokalemia
Alcoholism
Malnutrition, e.g. with anorexia/bulimia
Liver failure, liver transplantation

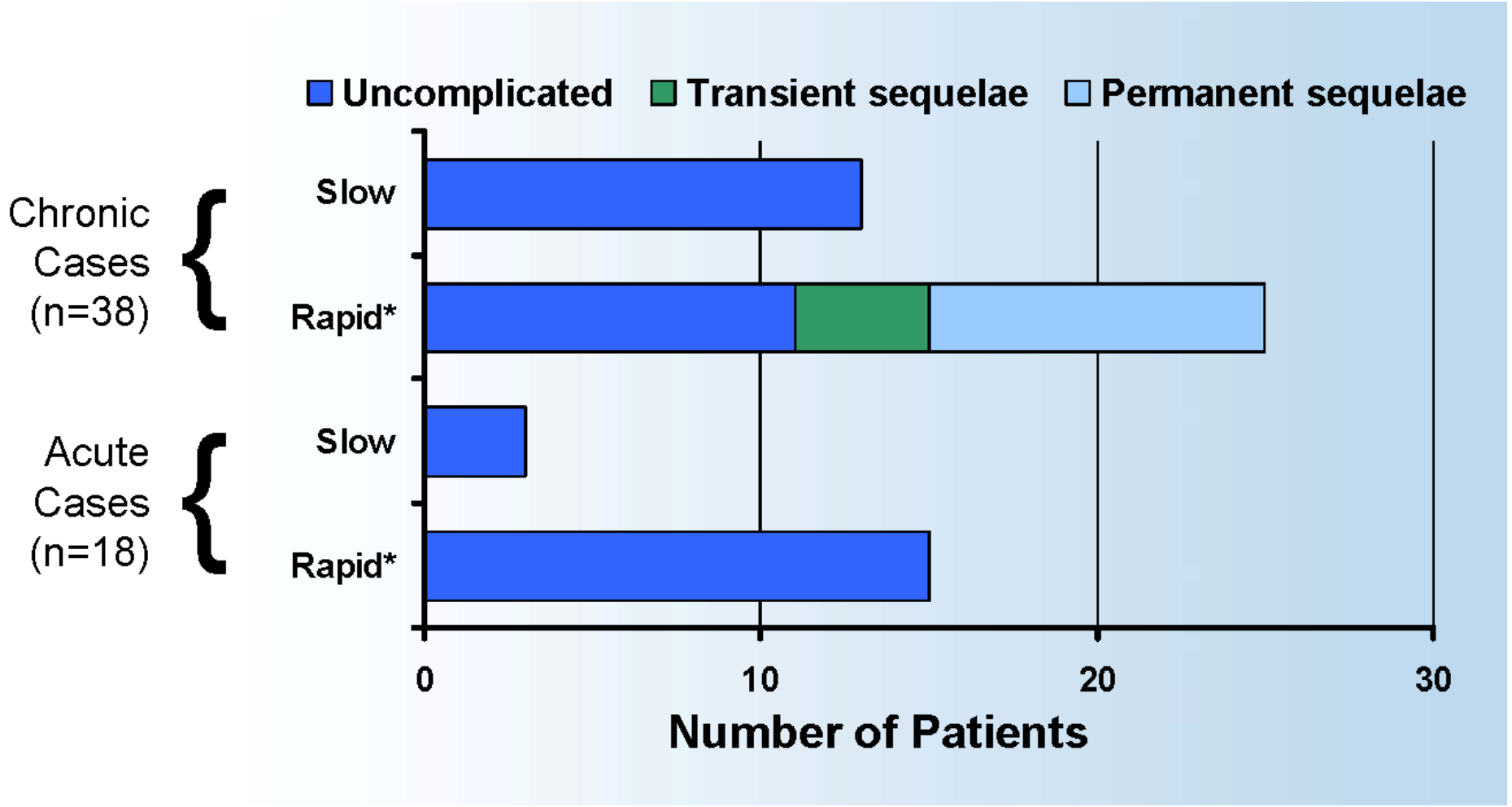
- Similar changes in cerebral osmolytes in liver failure

Pathogenesis of Osmotic Demyelination

Disruption of the blood-brain barrier – leakage of Ig's, complement, cytokines into perivascular brain.
Delayed induction of osmolyte transporters after correction of hyponatremia → ↓ osmoregulatory capacity and cell swelling/death.
Apoptotic or excitotoxic (glutamate-dependent) cell death after correction of hyponatremia.
Defective glial proteostasis – unfolded protein response and ER stress induced by correction*

* J Am Soc Nephrol. 2017 Jun;28(6):1802-1813

Rate of Correction from [Na^+] ≤ 105 mEqu/L and Neurological Outcome



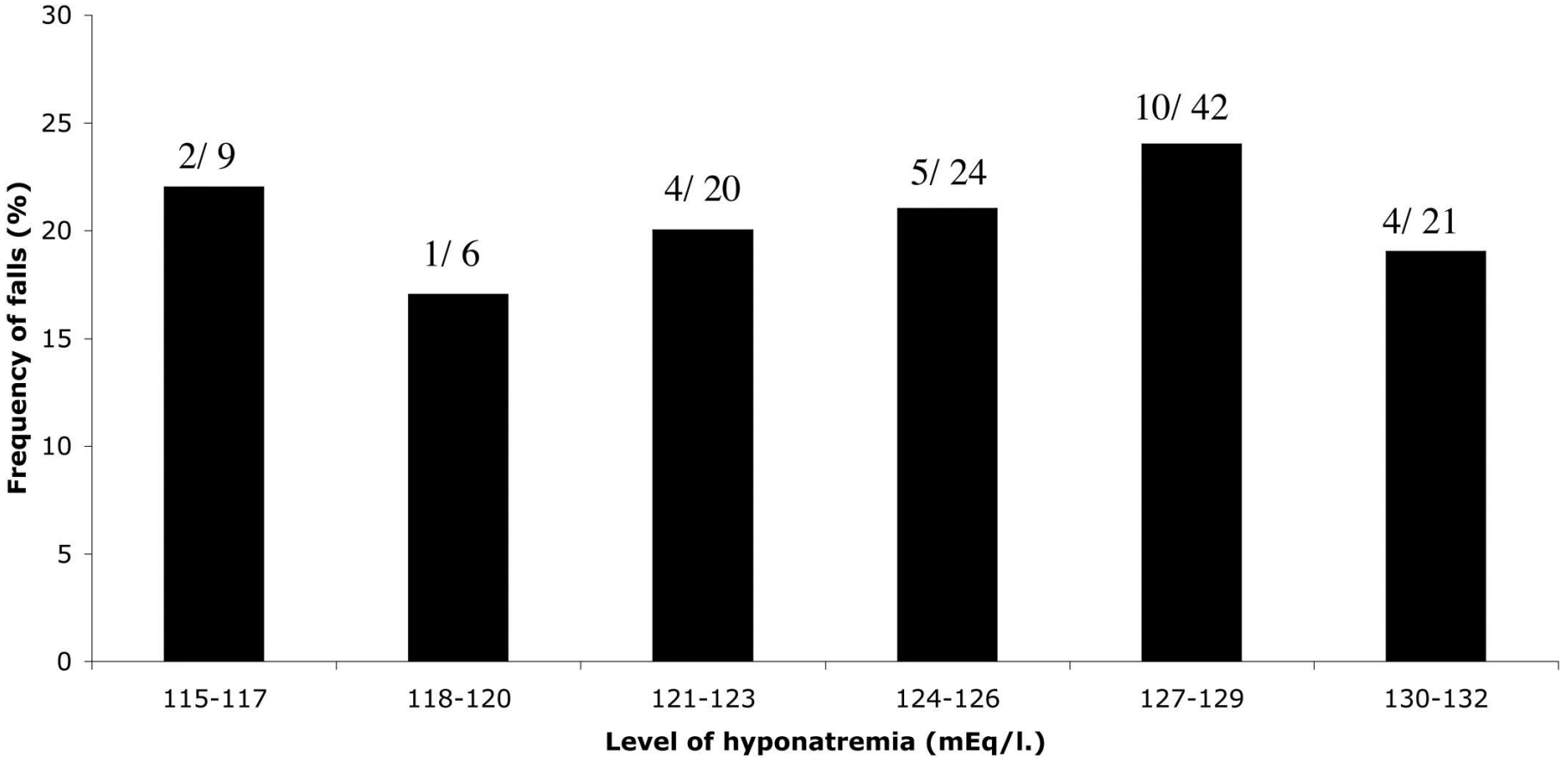
Sterns et al, *JASN*, 1994

Is Chronic Hyponatremia Really That Asymptomatic?

Case-control series of 122 consecutive asymptomatic hyponatremia patients.
Na ranged from 115-135
Prevalence of falls was 21.3% versus 5.4 % in case controls ($p < 0.001$).
Fall was often reason for admission.
Subtle gait and attention defects in a separate cohort of hypoNa patients.

Renneboog, et al, *Am J Med*, 2006

Falls and the Magnitude of Hyponatremia: Occurrence at All Levels



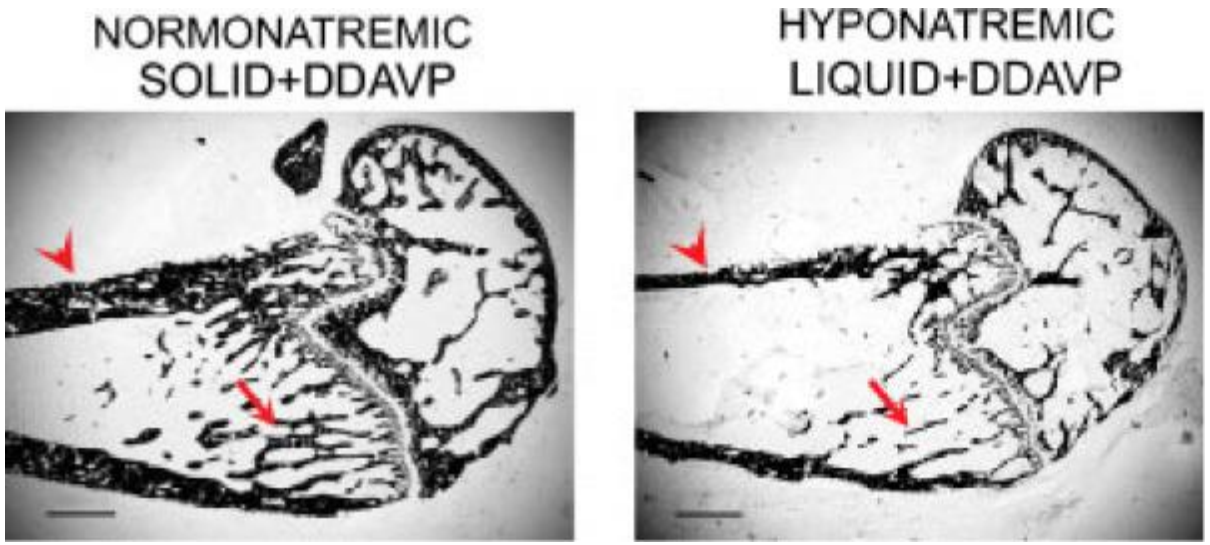
Renneboog, et al, *Am J Med*, 2006

JBMR

Hyponatremia-Induced Osteoporosis

Joseph G Verbalis,[1] Julianna Barsony,[1] Yoshihisa Sugimura,[1,2] Ying Tian,[1,3] Douglas J Adams,[4] Elizabeth A Carter,[5] and Helaine E Resnick[5,6]

[1]Division of Endocrinology and Metabolism, Georgetown University, Washington, DC, USA
[2]Presently: Department of Endocrinology and Diabetes, Nagoya University Graduate School of Medicine, Nagoya, Japan
[3]Presently: Geriatrics and Clinical Gerontology Program, National Institute on Aging, National Institutes of Health, Bethesda, MD, USA
[4]Department of Orthopaedic Surgery, New England Musculoskeletal Institute, University of Connecticut Health Center, Farmington, CT, USA
[5]Department of Epidemiology and Statistics, MedStar Research Institute, Hyattsville, MD, USA
[6]Presently: American Association of Homes and Services for the Aging, Washington, DC, USA



J Bone Miner Res. 2010 Mar;25(3):554-63.

Treatment of Hyponatremia

Management of acute, symptomatic hyponatremia

Management of chronic hyponatremia

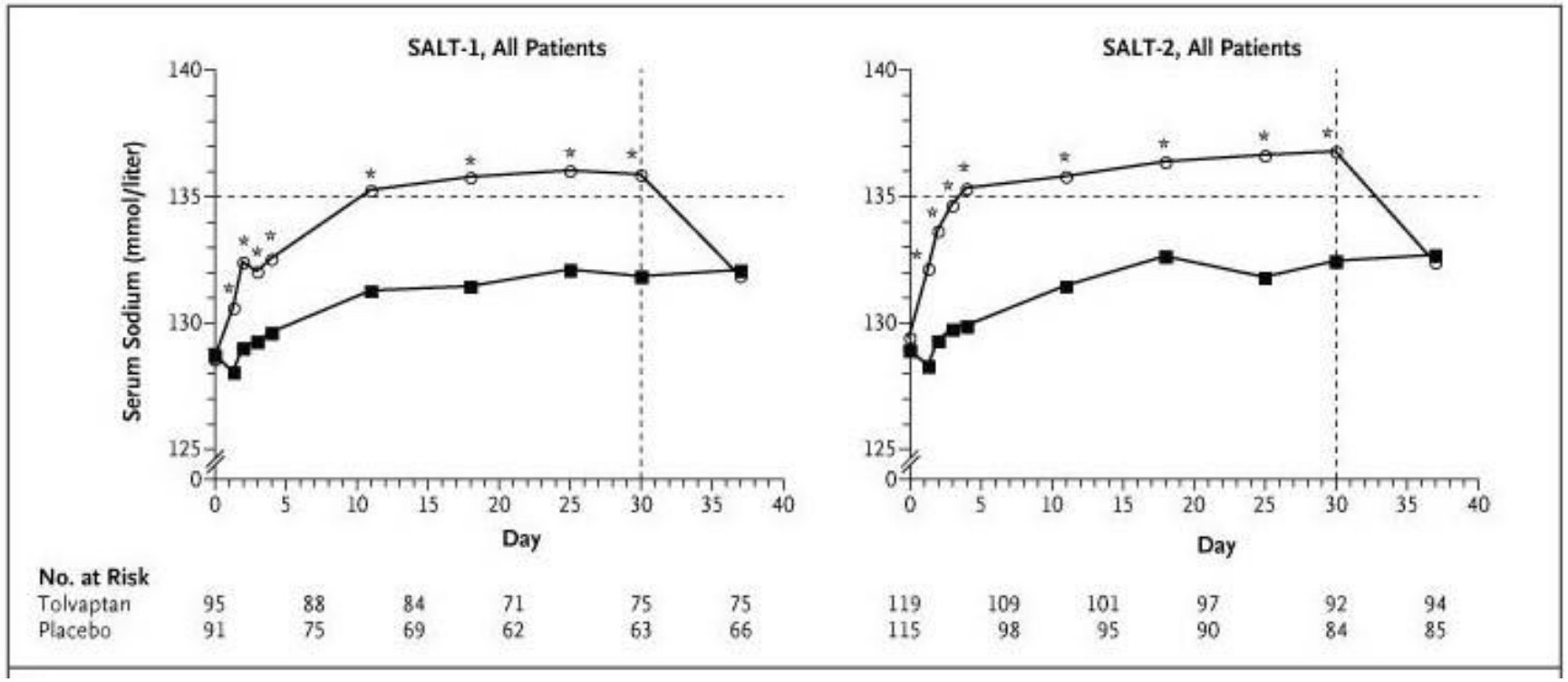
- Fluid restriction
- Furosemide and salt tabs - ↓ countercurrent mechanism and repletion of excreted NaCl
- Demeclocycline - ↓ V_2R response
- Oral urea – "Ure-na"™ – palatable form of oral urea, now available in the U.S.
- Vasopressin antagonists

Vasopressin Antagonists

Drug	*Antagonism*	*Route*	*Dose*
Conivaptan	V1A/V2	IV	20-40 mg/day
Tolvaptan*	V2	PO	15-60 mg/day
Lixivaptan	V2	PO	100-200 mg/day
Satavaptan	V2	PO	12.5-50 mg/day

* FDA advisory, 2013 –>2.5 ↑ in LFTs is more common in patients given Tolvaptan versus placebo in the TEMPO PKD trial. Therefore, do not use in liver disease or for >30 days.

Tolvaptan in Hyponatremia: The SALT Trials

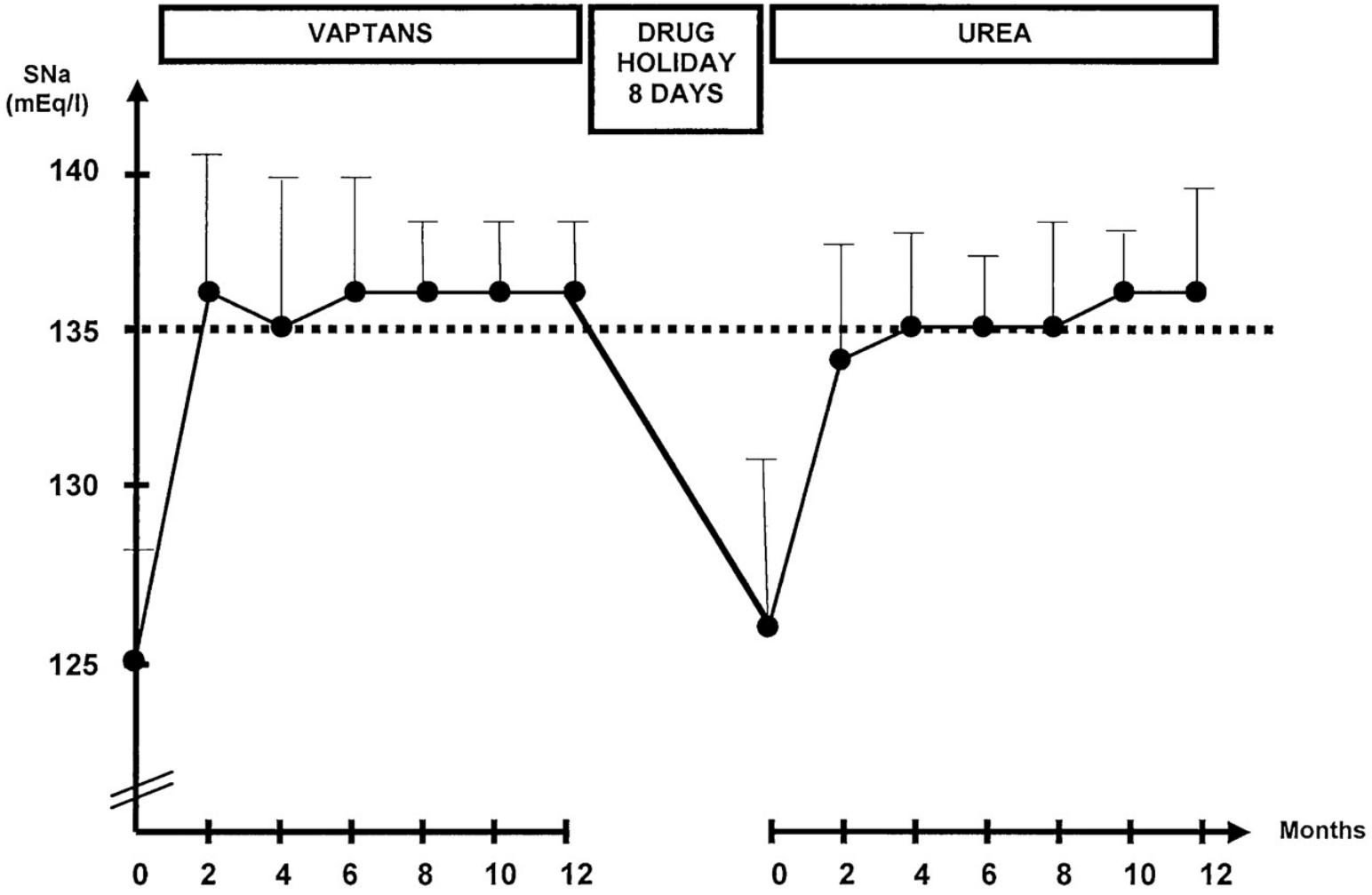


Schrier et al, *NEJM*, 2006

Pros and Cons of the Vaptans

What are the indications in clinical practice?
Significant expense
Risk of overcorrection – minimize by frequent monitoring of serum Na during the first 48 hours and > 2 liters/day water intake
****FDA advisory regarding liver toxicity of tolvaptan****

Oral Urea for SIADH



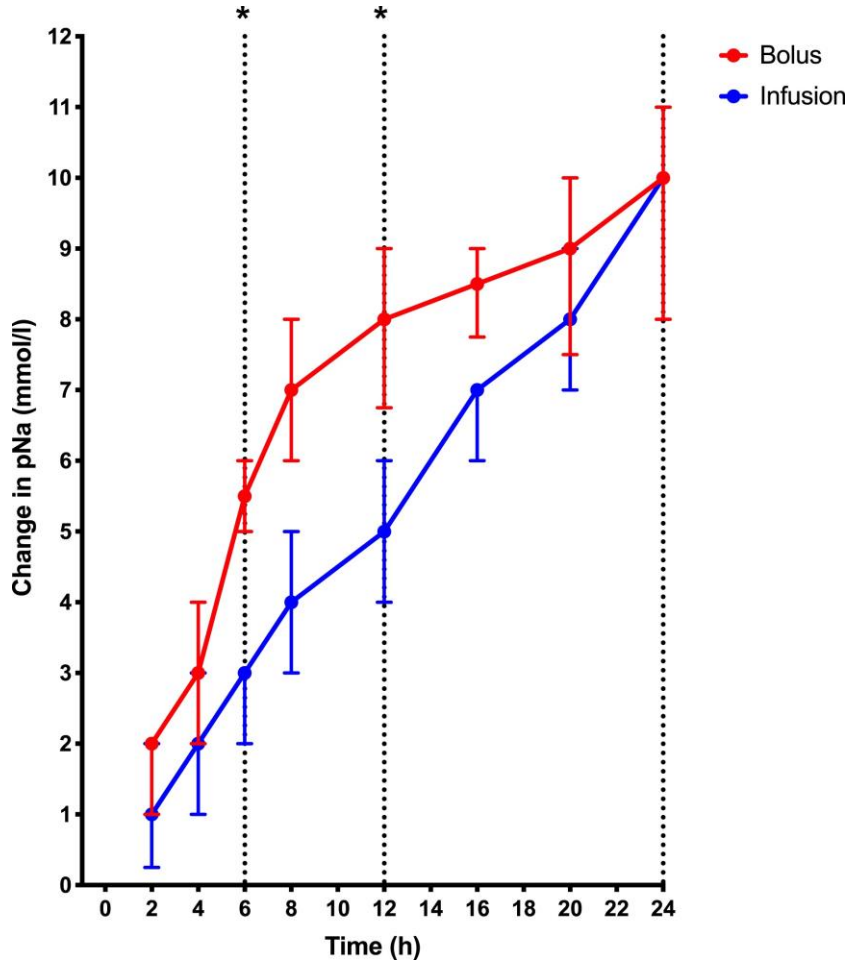
Clin J Am Soc Nephrol 7: 742–747, 2012

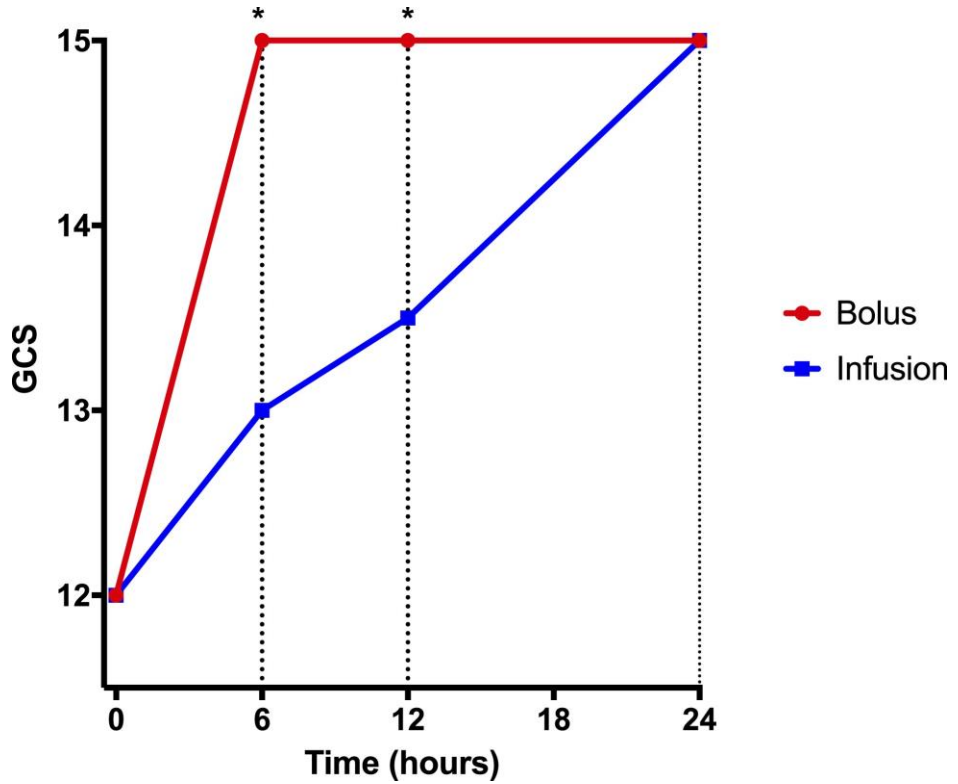
We Hopefully Agree……

Treatment of acute, symptomatic hyponatremia can be life-saving
Management should include:

- hypertonic saline
- ABG, CXR, and CNS imaging (if available – but do **NOT** delay therapy)
- supplemental O_2 prn
- loop diuretic (R_x of pulmonary edema and ↓ countercurrent mechanism)

Bolus Hypertonic Versus Infusion





J Clin Endo & Metabolism, Volume 104, 2019, Pages 3595–3602

Rate of Correction

Acute (< 48 hr) symptomatic hyponatremia

- 1-2 mEq/l per hour, correcting by 4-6 mEqu/L and/or until correction of severe symptoms, then chronic criteria
- hypertonic saline, plus furosemide (particularly if in pulmonary edema)
- Close attention to oxygenation

Chronic hyponatremia (> 48 hr)

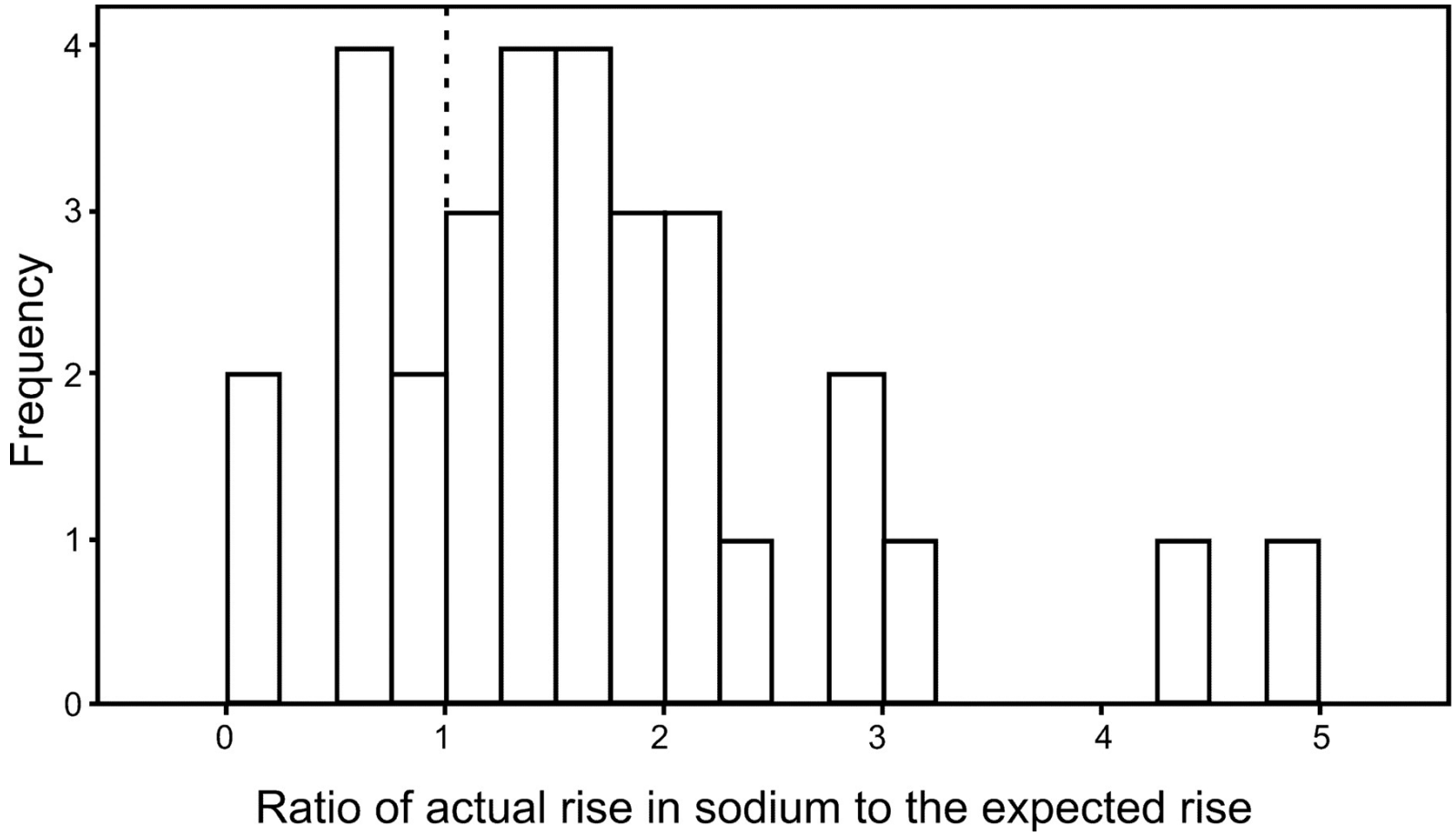
- 0.5 mEq/l per hour, ≤ 10 mEqu/first 24 hours, and ≤ 18/first 48 hours
- Some advocate even more conservative approach in patients at ↑↑ risk of ODS

Formulas For Calculating Initial Saline Infusion Rates

Source	Step 1	Step 2	Example of Rate (ml/hr)
Traditional[1]	$\text{Na required} = \text{TBW} \times ([\text{Na}]_2 - [\text{Na}]_1)$	$\text{Volume (liter)} = \frac{\text{Na required (mmol)}}{513\ \text{mmol/liter}}$	82
Adrogué and Madias[1]	$\Delta[\text{Na}]_S\ \text{(with 1 liter)} = \frac{[\text{Na}]_{inf} - [\text{Na}]_1}{\text{TBW} + 1}$	$\text{Volume (liter)} = \frac{\text{Desired } \Delta[\text{Na}]_S}{\Delta[\text{Na}]_S\text{(with 1 liter)}}$	107
Barsoum and Levine[39]	$\Delta[\text{Na}]_S = \frac{(V_{inf})[\text{Na}]_{inf} - (V_u)[\text{E}]_{urine} - (\Delta V)[\text{Na}]_1}{\text{TBW} + \Delta V}$	$\text{Volume (liter)} = \frac{\text{Desired } \Delta[\text{Na}]_S}{\Delta[\text{Na}]_S\ \text{(with 1 liter)}}$	107
Nguyen and Kurtz[40]		$\text{Volume (liter)} = \frac{\text{TBW} \times \left(1 - \frac{[\text{Na}]_1 + 23.8}{[\text{Na}]_2 + 23.8}\right) + V_{input} - \frac{[\text{E}]_{input} \times V_{input}}{[\text{E}]_{urine}}}{\frac{[\text{E}]_{inf}}{[\text{E}]_{urine}} - 1}$	90
Janicic and Verbalis[9]		Rate (ml/hr) is the goal rate of $[\text{Na}]_S$ rise (mmol/liter/hr) per kg of body weight	70

David Ellison and Tom Berl, *NEJM*, 356, 2064-2072, 2007

The Adrogue/Madias Formula Underestimates ΔNa^+ After Hypertonic Saline



Mohmand et al, *CJASN*, 2007

Calculation of “Na^+ Deficit”

$$\text{Deficit (in mmol)} = 0.6 \times BW \left[\text{Target Na} - \text{Na}\right]$$

Hypertonic (3%) saline contains 513 mEq/L Na

$$\text{Volume of 3\% saline required (in L)} \approx \frac{\text{Deficit}}{500}$$

Rule of thumb: Each D of 1 mEq/Lrequires ~ 70 mL hypertonic saline

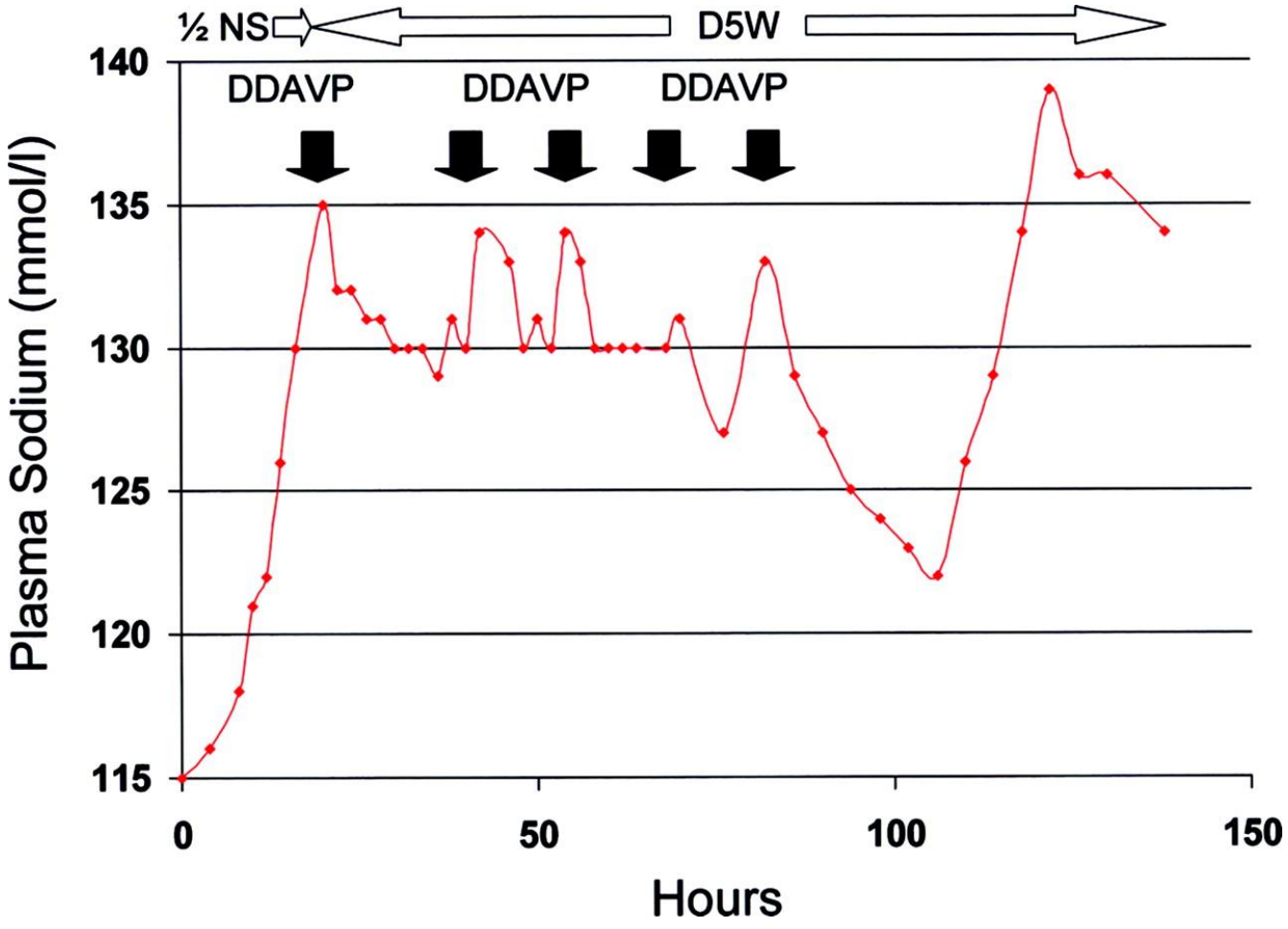
What If You "Over-Correct": Treatment of Osmotic Demyelination

DDAVP and D5W to re-induce hyponatremia – animal and human data

Myo-inositol supplementation during correction – animal data

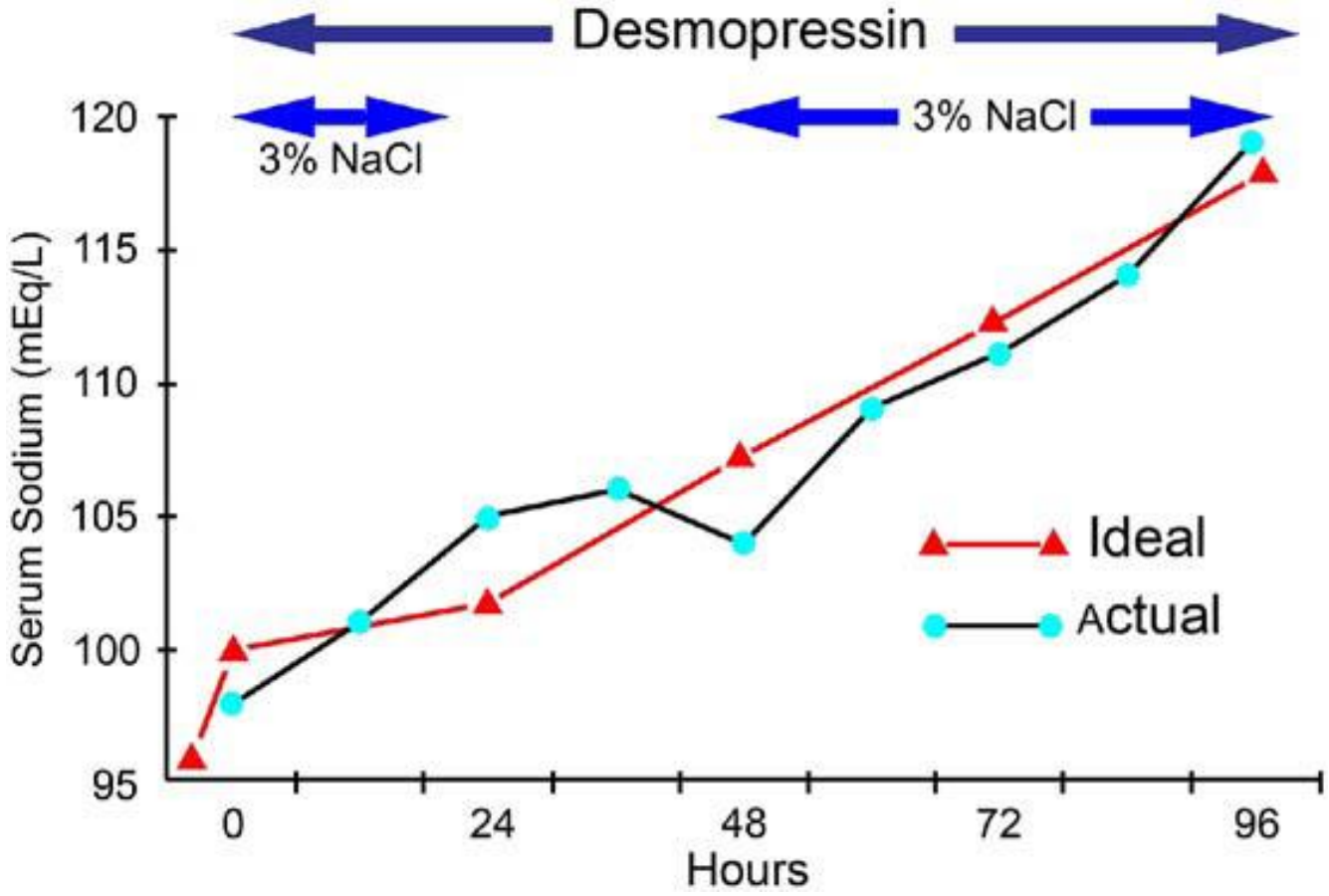
Dexamethasone to restore blood brain barrier function – animal data

Re-Induction of Hyponatremia With DDAVP + Free H_2O



Sterns et al, CJASN, 2008

Alternative Approach: DDAVP "Clamp" with Hypertonic Saline



Am J Kidney Dis 56:774-779, 2010

Question #2

You admit a 40 yo woman with a one-week history of flu-like illness and profuse diarrhea. She has received 1.5 liters of N/S.

On exam, HR is 80 supine, 105 standing, bp 11/70. JVP is seen at 5 cm.

Admission Laboratory Studies:

Na^+	121	K^+	3.6
Urine Na^+	12	Urine Osm	450

Current Labs (6 hours after admission to ER):

Na^+	130	K^+	3.5
Urine Na^+	18	Urine Osm	300

Which of the following therapies is the *most* appropriate?

A. Normal saline at 200 ml/hr
B. Normal saline with 40 mEqu/l at 200 ml/hr
C. Conivaptan 40 mg load then continuous infusion at 20 mg/day
D. D5W at 75 ml/hr
E. D5W at 75 ml/hr, after 1 µg of DDAVP

Hyponatremic Causes Associated With "Overcorrection"

- Hypovolemic hyponatremia, after volume resuscitation with saline and ↓ AVP (half-life of AVP is 10-20 minutes)
- Hypopituitarism with 2º adrenal failure, after treatment with cortisol and and ↓ AVP
- Thiazide-associated hyponatremia, after discontinuation and saline hydration
- Rapid spontaneous resolution of SIADH or of a "non-osmotic" increase in AVP
- Discontinuation of DDAVP
- Beer potomania/low solute intake hyponatremia

TAKE HOME MESSAGES

Central osmoreceptors in hyponatremia.
DDx of acute hyponatremia and hyponatremia prone to overcorrection.
The role of DDAVP+D5W in patients who overcorrect.
DDAVP clamp with hypertonic saline to provide controlled correction.
Use of oral urea in SIADH.
Electrolyte free water clearance in hypernatremia – estimate ongoing loss.

Suggested References:

"Hyponatremia" (Guest editor D.B. Mount), *Seminars in Nephrology*, May 2009;29(3):175-317

- PDF reprint: dmount@bwh.harvard.edu

- Mount D.B., "Fluid and electrolyte disturbances", Harrison's Principles of Internal Medicine, 20th edition, McGraw Hill, 2018, 295-311
- Perianayagam, A, et al : DDAVP is effective in preventing and reversing inadvertent overcorrection of hyponatremia. *CJASN,* 3**:** 331-6, 2008
- Sood et al: Hypertonic saline and desmopressin: a simple strategy for safe correction of severe hyponatremia. *Am J Kidney Dis 61:571-8, 2013*