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Shaken with Salt: Managing Sodium Imbalances in Neurocritical Care

Karen Berger, PharmD, FASHP, FCCM, BCPS, BCCCP

Assistant Professor, Nova Southeastern University

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Disclosure

I do not have a vested interest in or affiliation with any corporate organization offering financial support or grant monies for this continuing education activity, or any affiliation with an organization whose philosophy could potentially bias my presentation (within the last 12 months).

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Pharmacist Presentation Objectives

1. Explain the mechanisms and triggers for each sodium disorder and their impacts on sodium and water balance
2. Analyze serum sodium, urine osmolality, and urine sodium values to distinguish SIADH, DI, and CSW
3. Compare therapeutic options such as hypertonic saline, vasopressin analogs, and fluid management for each condition

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Pharmacy Technician Presentation Objectives

1. Recognize SIADH, DI, and CSW as key conditions affecting sodium balance in critically ill patients
2. Identify therapeutic agents used in the treatment of sodium disorders in critically ill patients

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Special Considerations in Neurocritical Care Patients

- Subarachnoid Hemorrhage (SAH) — Vasospasm, "Triple H"/avoid negative fluid balance
- Hypertonic hyponatremia — Mannitol and hyperglycemia
- Transient hyponatremia with desmopressin (antiplatelet reversal)
- Cerebral edema and elevated ICP — Normonatremia vs hypernatremia goals
- CSW vs SIADH
- Disturbed thirst mechanisms (inadequate water intake)
- Diabetes insipidus

ICP = intracerebral pressure; CSW = cerebral salt wasting; SIADH = syndrome of inappropriate antidiuretic hormone

Murphy-Human, Diringer MN. *J Pharm Pract* 2010;23(5):470-82.

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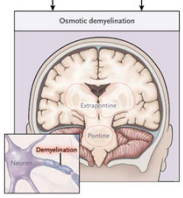
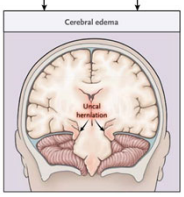
Consequences of Overcorrection

Rapid correction of chronic hyponatremia



Rapid correction of chronic hypernatremia



Sterns RH. *N Engl J Med* 2015;372:55-65.

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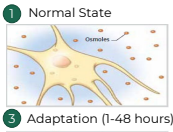
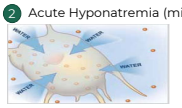
Osmotic Demyelination Syndrome

1. Normal State



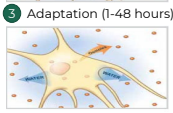
ECF in osmotic equilibrium with ICF
No movement of water across membrane

2. Acute Hyponatremia (minutes)



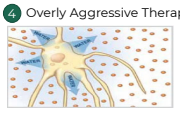
ECF becomes hypotonic
ECF moves into CSF → **cerebral edema**

3. Adaptation (1-48 hours)



Loss of K, Na, & organic solutes from brain cells → ↓ intracell osmolality → **↓ cerebral edema**

4. Overly Aggressive Therapy (rapid ↑ in Na)



ECF osmolality > ICF → excessive H_2O movement out of brain cells → **Osmotic Demyelination Syndrome**

ECF = Extracellular fluid; ICF = Intracellular fluid

Adrogue HJ, et al. *N Engl J Med* 2000;342(21):1584.

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Hyponatremia in Neurocritically Ill

Condition	Incidence	Onset
SAH	40-57%	3-7 days
TBI	13.7-51%	3-14 days
Stroke	12-43%	0-7 days
Cerebral tumor	8.4-35%	Postoperative days 4-10
CNS infections	38.7-73%	Varies
GBS	11.8-48%	8 days

SAH = subarachnoid hemorrhage; TBI = traumatic brain injury; CNS = central nervous system; GBS = Guillain-Barré syndrome

Cui H, et al. *Front Neurol* 2019;13:1170.

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Symptoms of Hyponatremia

Mild	Na 130-135 mEq/L Nausea, vomiting, GI disturbance, malaise
Moderate	Na 125-130 mEq/L Disorientation, confusion, cognitive disturbance, headache
Severe	Na <125 mEq/L Seizure, cerebral edema, coma, permanent brain damage, respiratory arrest, brainstem herniation, death

- Higher risk of falls even at near normal levels
- Many patients asymptomatic (chronic)
- Severity of symptoms depends on the rate and extent of sodium decline

Adrogue HJ, et al. *N Engl J Med* 2000;342(21):1581-9.
Bhat R, et al. *BJA Education* 2022;22(12):466-73.

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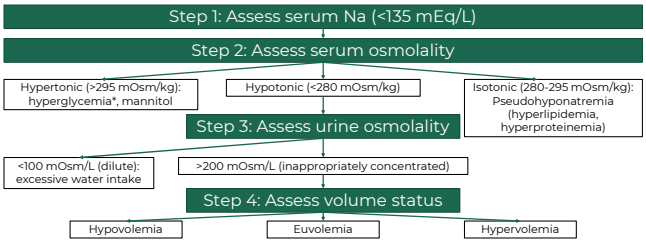
Diagnostic Algorithm for Hyponatremia



Murphy-Human, Diringer MN. *J Pharm Pract* 2010;23(5):470-82.

*Corrected Na = Measured Na + 0.016 (or 0.024) x (serum glucose - 100)

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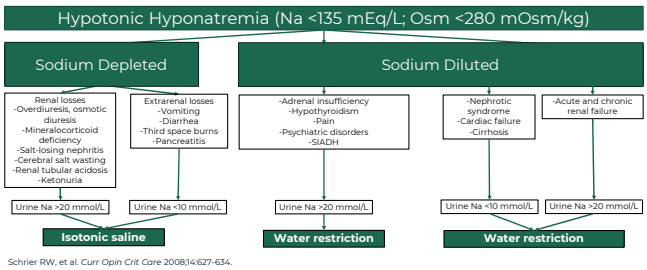
(Hypotonic) Hyponatremia



Schrier RW, et al. *Curr Opin Crit Care* 2008;14:627-634.

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Hyponatremia Diagnosis

- Serum Na <135 mEq/L
- FENa = $\frac{\text{Serum Cr} * \text{Urine Na}}{\text{Serum Na} * \text{Urine Cr}}$
- Free water/sodium deficit
- Serum osmolality
- Glucose
  - For every 100 mg/dL ↑ in glucose over 100 mg/dL → 1.6 mEq/L ↓ Na
- "Get urine lytes"
  - Urine osmolality
  - Urine sodium
  - Urine urea

Adrogue HJ, et al. *N Engl J Med* 2000;342(21):1581-9.
Katz MA. *N Engl J Med* 1973;289(16):843-844.

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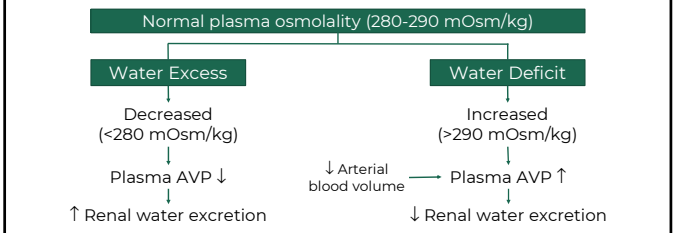
Water Regulation and AVP



AVP = arginine vasopressin

Kumar S, et al. *Lancet* 2008;352:221.
Schrier RW, et al. *Curr Opin Crit Care* 2008;14:627-634.

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Common Causes of Hyponatremia in the Neuro-ICU

	SIADH	CSW
Mechanism	Increased secretion of ADH	Unknown; disturbance in atrial natriuretic peptide, BNP, and C-type natriuretic peptide; decreased renal reabsorption of Na
Volume status	Euvolemia (or small increase)	Hypovolemia
CVP	↑↔	↓
Serum sodium	↓	↓
Serum osmolality	↓	↓
Urine osmolality	↑	↑
Urine sodium	↑	↑
Urine volume	↓↔	↑
Tachycardia	Absent	May be present

SIADH = syndrome of inappropriate antidiuretic hormone secretion; CSW = cerebral salt wasting; ADH = antidiuretic hormone; BNP = brain natriuretic peptide; CVP = central venous pressure

Murphy-Human, Diringer MN. *J Pharm Pract* 2010;23(5):470-82.
Diringer MN, et al. *The Neurologist* 2006;12:117-26.

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Causes of SIADH

Category	Examples
Malignancy	Pulmonary tumor, mediastinal tumor, extrathoracic tumor
Pulmonary Disease	Infection (TB, pneumonia), cystic fibrosis, bronchiectasis
Other Causes	Postoperative setting, pain, severe nausea
CNS Disorders	Head trauma, SDH, SAH, stroke, meningitis, encephalitis, brain abscess, brain tumor, acute psychosis
Medications	Desmopressin, oxytocin, NSAIDs, nicotine, phenothiazines, TCAs, SSRIs, opioids, chlorpropamide, clofibrate, carbamazepine, oxcarbazepine, lamotrigine, cyclophosphamide, vincristine, diuretics

TB = tuberculosis; CNS = central nervous system; SDH = subdural hematoma; SAH = subarachnoid hemorrhage; NSAID = nonsteroidal anti-inflammatory drug; TCAs = tricyclic antidepressants; SSRIs = selective serotonin reuptake inhibitors

Diringer MN, et al. *The Neurologist* 2006;12:117-26.
Adrogue HJ, et al. *N Engl J Med* 2000;342(21):1584.
Liamis G, et al. *Am J Kidney Dis* 2008;52:144-153.

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Hyponatremia Treatment Approach

Assess:

- Timing of sodium decline
  - Acute ≤48 hours
  - Chronic >48 hours
- Degree of sodium decline
- Symptomatic or asymptomatic
- Volume status (hypo-, eu-, or hypervolemic)
- Water sources
  - Medications (IV piggybacks, infusions)
  - Nutritional intake (TPN, tube feeds)
- Medications which may potentiate ADH
- Underlying causes that may correct rapidly without treatment (ie; thiazide diuretics, DDAVP)

Limit rate of correction to ↓ ODS risk:

- <8-12 mEq/L in 24 h
- <18 mEq/L in 48 h

*Symptomatic patients:

- 0.75-1 mEq/L/h x first few hours, then ≤0.5 mEq/L/h

TPN = total parenteral nutrition; DDAVP = 1-deamino-8-D-arginine vasopressin (desmopressin); ADH = antidiuretic hormone; ODS = osmotic demyelination syndrome

Vaidya C, et al. *Cleve Clin J Med* 2010;77(10):715-26.
Schrier RW et al. *Curr Opin Crit Care* 2008;14:627-634.
Verbalis JG, et al. *Am J Med* 2007;120:S1-21.

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Treatment

Treatment	Hypovolemia	Euvolemia	Hypervolemia	Pearls
Fluid restriction		X	X	Concentrate fluids; IVPB to IVP, change to NS or PO when possible, caution in SAH, delayed effect
Diuretics		X	X	Monitor electrolytes (Mg, Phos, K), caution in SAH
Demeclocycline		X		Infrequently used for SIADH
Lithium		X		Infrequently used for SIADH (causes nephrogenic DI)
Fludrocortisone	X	X		Monitor K, glucose, option in SAH
Vaptans		X	X	Variable response, risk of overcorrection, prolonged effect
Normal saline	X			Fluid repletion for CSW
Hypertonic saline	X	X		May need central line, frequent sodium monitoring

Murphy-Human, Diringer MN. *J Pharm Pract* 2010;23(5):470-82.
Adrogue HJ, et al. *N Engl J Med* 2000;342(21):1584.

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Fludrocortisone

- Mineralocorticoid that enhances sodium retention
- 2023 aSAH AHA/ASA guidelines
  - "In patients with aSAH, use of mineralocorticoids is reasonable to treat natriuresis and hyponatremia." (COR 2a, LOE B-R)
- Typical dose: 0.1-0.2 mg BID
- Monitor hypokalemia, hyperglycemia
- Delayed onset
- Used in combination with other treatment modalities

Elledge SR, et al. *Clin Neurol Neurosurg* 2023;225:107568.
Hoh BL, et al. *Stroke* 2023;54(7):e314-e370.
Hasan D, et al. *Stroke* 1989;20(9):1156-61.

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AVP Antagonists (Vaptans)

	Conivaptan (Vaprisol®)	Tolvaptan (Samsca®)
Receptor(s)	V_{1a} & V_2	V_2
FDA-approved indication	Treatment of clinically significant euvolemic and hypervolemic hyponatremia	
Year approved	2005	2009
Formulation	IV	PO
Dose	Loading Dose: 20 mg over 30 min CI: 20-40 mg over 24 hours x4 days	15-60 mg daily
Metabolism	CYP3A4 substrates and inhibitors (conivaptan > tolvaptan)	
Elimination	Feces; <1% excreted unchanged in the urine	
Protein Binding	99%	
Half-life	3.1-7.8 h	6-8 h

Ghali JK, et al. *DDDT* 2009;3:253-68.
Decaux G, et al. *Lancet* 2008;371:1624-32.
Zmily HD, et al. *Int J Nephrol Renovasc Dis* 2011;4:57-71.
Human T. *Pharmacotherapy* 2011;31:518-24.

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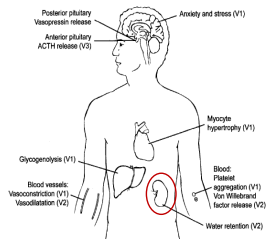
AVP Receptors

Receptor	Location	Function
V_{1a}	Vascular smooth muscle cells, hepatocytes, platelets, brain cells	Vasoconstriction, platelet aggregation, myocyte hypertrophy
V_{1b} (V_3)	Anterior pituitary gland	Mediate release of adrenocorticotropin hormone (ACTH)
V_2	Collecting ducts of the kidney	Mediate free water absorption, release of vWF

vWF = von Willebrand factor



Zmily HD, et al. *Int J Nephrol Renovasc Dis* 2011;4:57-71.
Ferguson JW, et al. *Clin Sci* 2003;105:1-8.

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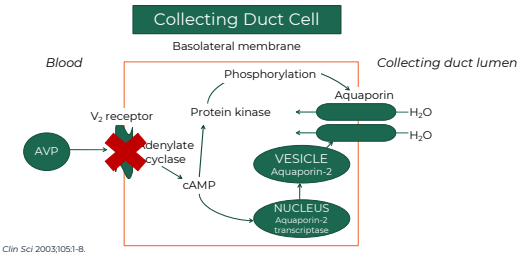
Renal Water Regulation



Ferguson JW, et al. *Clin Sci* 2003;105:1-8.

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Vaptans for Hyponatremia in Neurocritically Ill

Study	N	Treatment	Concomitant therapy	Sodium changes	Over-correction
Wright 2009	22	C bolus + infusion	50%	Na ↑ ≥6 mEq/L: 86% (avg time to goal: 13 h)	None
Murphy 2009	19	C bolus only	28%	Mean Na ↑ 5.8 mEq/L within 12 h In subgroup receiving only 1 dose in 72 h: - 75% ↑ of ≥4 mEq/L by 12 hrs - 69% maintained ↑ ≥4 mEq/L up to 72 hrs	5%
Der Nigoghossian 2017	36	C bolus +/- infusion (n = 5) or T (n = 31)	100%	Mean max Na ↑ 24 h following last dose: - 5.2 mEq/L C (p=0.05) - 7.9 mEq/L T (p<0.001). ↑ in Na sustained for 96 h, with majority of patients receiving a single dose	17% (n = 6 T, 0 C)

C = conivaptan; T = tolvaptan; NR = not reported

Wright WL, et al. *Neurocrit Care* 2009;11:6-13.
Murphy T, et al. *Neurocrit Care* 2009;11:14-19.
Der-Nigoghossian C, Lesch C, Berger K. *Pharmacotherapy* 2017;37(5):528-34.

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Salt Tabs

- Common dose: 1-2 g q6-8h
- 1 g NaCl tablet = 17 mEq Na
- 4 g PO q6h = 0.9% NaCl IV at 75 mL/hour
- May be poorly tolerated → nausea

Vaidya C, et al. *Cleve Clin J Med* 2010;77(10):715-26.
Verbalis JG, et al. *Am J Med* 2007;120:S1-21.

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Hypertonic Saline

	2% NaCl	3% NaCl	23.4% NaCl
mEq/L (Na)	342	513	4004
mOsm/L	684	1026	8008
How Supplied	Compounded	500 mL premix bag	30 mL vial
Administration	C/P	C/P[1]	C
Adverse effects	Hyperchloremia, acidosis, transient hypotension (23.4%), phlebitis, sodium overcorrection		

[1]Despite > 900 mOsm/L, many institutions allow peripheral administration of 3% NaCl; [2]12.5 g/50 mL vial; [3]100 g/500 mL premix bag

Jones GM, et al. *Am J Crit Care* 2016;26(1):37-42.
Torre-Healy A, et al. *Neurocrit Care* 2012;17:117-130.

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Hypertonic Saline

	0.9% NaCl	2% NaCl	3% NaCl	23.4% NaCl
mOsm/L	308	684	1026	8008
mEq/L (Na)	154	342	513	4004
30 mL	←	←	←	120 mEq
200 mL	31 mEq	68 mEq	103 mEq	
250 mL	←	←	128 mEq	
300 mL	46 mEq	103 mEq	154 mEq	
350 mL	←	120 mEq	180 mEq	

Forsyth LL, et al. *Pharmacotherapy* 2008;28:469-84.

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Peripheral Administration of 3% NaCl

	Jones 2017	Dillon 2018	Deveau 2023
N	213	66	706 administrations (422 patients)
Peripheral administration site			
Antecubital	64.3%	37%	22.8%
Forearm	16.9%	36%	14.3%[3]
Hand/wrist	18.8%	25%	0.6%[3]
Peripheral site needle gauge 18 or 20	93.9%	60%	68.9%
Duration of infusion (peripheral sites), median (IQR)	44.7 h (21.3-74.8)	14 h (4-30)	16 h (IRAE) vs 8 h (no IRAE)
Max infusion rate, median	30 mL/h (IQR 25-40)	50 mL/h (range 8-75)	30 mL/h (median)
Infusion-related reactions, n (%)	15 (7%)[1]	4 (6%)[2]	74 (10.5%)[4] infusions (14.2% patients)

IRAE = infusion related adverse event
[1]No thrombophlebitis, 26.3% had initial peripheral switched to central, 8/15 (53%) had cIV changed to alternate peripheral site, most events occurred at infusion rates ≤30 mL/hr; [2]Phlebitis and infiltration 2 (50%), erythema 1 (25%), edema <1 inch 1 (25%); [3]4.3% forearm/wrist as they were reported together, 0.6% hand; [4]1% phlebitis, 22% infiltration, 18% phlebitis + infiltration; [4]All IRAE except 1 were low grade

Jones GM, et al. *Am J Crit Care* 2017;26:37-42.
Dillon RC, et al. *J Intensive Care Med* 2018;33(1):48-53.
Deveau RF, et al. *Am J Emerg Med* 2023;63:27-31.

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Calculating Infusion Rates

Equations

- TBW (male) = 0.6 x weight (kg)
- TBW (female) = 0.5 x weight (kg)
- Na deficit = TBW x (Desired Na - Actual Na)
- Amount of Na needed to ↑ serum Na = TBW x desired Na ↑ (mEq/L/hr)

	0.9% NaCl	2% NaCl	3% NaCl	23.4% NaCl
mOsm/L	308	684	1026	8008
mEq/L (Na)	154	342	513	4004

TBW = total body water

Example

Gender	Weight	Actual Na	Desired Na
Male	70 kg	115	125

- TBW (male) = 0.6 x 70 kg = 42 L
- Na deficit = 42 L x (125 – 115) = 420 mEq Na
- Na needed to ↑ serum Na level by 1 mEq/L/hr = 42 L x 1 mEq/L/hr = 42 mEq/hr
- What is the infusion rate using 3% NaCl?
  - 42 mEq/hr x 1000 mL/513 mEq = 82 mL/hr
- How long should the infusion be continued?
  - Na deficit 420 mEq/42 mEq/hr = 10 hours
  - OR
  - Increase from 115 to 125 = 10 mEq/L total ↑
  - 10 mEq/L divided by 1 mEq/L/hr = 10 hours

3% NaCl infusion at 82 mL/hr should ↑Na from 115 to 125 in 10 hours (at a rate of 1 mEq/L/hr)

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Adrogue-Madias Formula

- ↑ in serum Na concentration with 1 L NaCl infusion (Solution = ↑ in mEq/L)

$$\frac{\text{Na in solution} - \text{Serum Na concentation}}{\text{TBW} + 1}$$

- Example: 1L 3% NaCl

$$\frac{513\ \text{mEq (Solution Na)} - 115\ \text{mEq (Serum Na)}}{42 + 1} = 9.3\ \text{mEq}$$

- If goal to ↑ 6 mEq/L in 6 hours: 6/9.3 = 0.645 L
- 645 mL of 3% NaCl over 6 hrs OR ~100 mL/h

Adrogue HJ, et al. *N Engl J Med* 2000;342(21):1581-9.

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Hypertonic Saline for Severe Hyponatremia

Severity of Hyponatremia	Dose	Goal
Seizures, coma/deep somnolence, high risk of herniation	3% NaCl 100-150 mL bolus, repeat as needed	Correct Na by 4-6 mEq/L within 1 h
Acute + moderate symptoms (confusion, headache, nausea)	3% NaCl 100-150 mL bolus or continuous infusion 3% NaCl 0.5-2 mL/kg/h	Correct Na by 4-6 mEq/L within 6 h

Rondon-Berrios H, Sterns RH. *Am J Kidney Dis* 2022;79(6):890-96.

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Hypertonic Saline for Severe Hyponatremia (<120 mEq/L)

Duration	Hypertonic Saline Dose	Initial Therapeutic Goal	Limit of Correction
Several hours	3% NaCl 100 mL bolus x3 prn severe symptoms	↑ Na 4-6 mEq/L in 6 h	Excessive correction not known to be harmful
1-2 days	3% NaCl 100 mL bolus x3 prn severe symptoms	↑ Na 4-6 mEq/L in 6 h	Avoid ↑ Na >10 mEq/L/day
Unknown or ≥2 days	3% NaCl 100 mL bolus if needed for seizures	↑ Na 4-6 mEq/L in 24 h Extra caution for conditions at high risk for ODS	Avoid ↑ Na >8 mEq/L/day Consider lowering again if limit exceeded, especially in patients with high risk of ODS

ODS = osmotic demyelination syndrome

Sterns RH. *N Engl J Med* 2015;372:55-65.

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DDAVP "Clamp"

- Use of concurrent administration of DDAVP with hypertonic saline to prevent free water diuresis following correction of hyponatremia
- Given to reduce overcorrection in patients
  - At high risk for ODS (chronic/severe hyponatremia, alcoholism, malnutrition, hypokalemia, cirrhosis)
  - At high risk for overcorrection (reversible cause of hyponatremia; hypovolemia, thiazide/SSRI discontinuation)
- Lack of consensus/data re: optimal timing, dosing, or patient selection
- Not helpful in hypervolemic hyponatremia and may worsen fluid overload
- Sample regimens:

Proactive Approach:	Reactive Approach:
• 3% NaCl 75 mL/hour + • DDAVP 1-2 mcg SQ/IV q8h scheduled +/- • Free water restriction (if able)	• 3% NaCl 75 mL/hour • DDAVP 1-2 mcg SQ/IV prn significant increase in UOP or serum Na

DDAVP = 1-deamino-8-D-arginine vasopressin (desmopressin); ODS = osmotic demyelination syndrome; SSRI = selective serotonin reuptake inhibitor; UOP = urine output

Sood L, et al. *Am J Kidney Dis* 2013;61(4):571-8.
AlShanableh Z, et al. *Kidney360* 2025;6(9):1462-71.

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Monitoring

- Serum sodium
  - Every 4-8 h initially
  - Every 8-12 hours as sodium stabilizes
  - More frequently if Na increases too quickly/slowly
- Urine output
- Adverse effects
  - Nausea/vomiting from salt tabs
  - Phlebitis from peripheral 3% NaCl
  - Hypokalemia with fludrocortisone, vaptans
  - LFTs with tolvaptan

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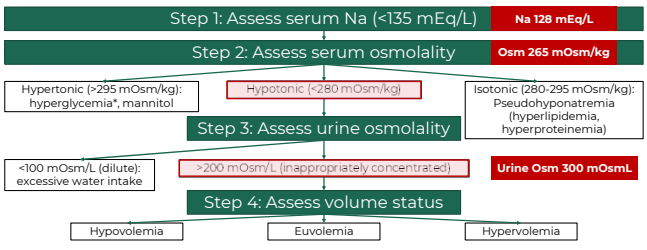
Diagnostic Algorithm for Hyponatremia



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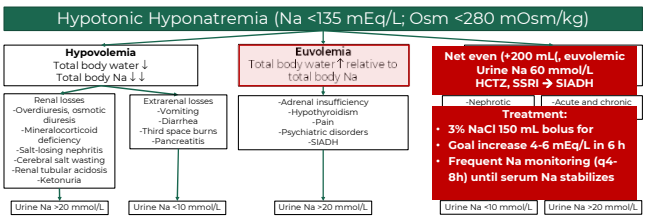
(Hypotonic) Hyponatremia



Schrier RW, et al. *Curr Opin Crit Care* 2008;14:627-634.

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Hyponatremia Treatment Summary

- Acute symptomatic hyponatremia should be treated with hypertonic saline boluses and/or infusion (usually 3% NaCl)
  - Goal increase 4-6 mEq/L in 6 h
  - May consider DDAVP scheduled or as needed in select cases for hypovolemic hyponatremia to prevent/manage overcorrection
- Asymptomatic hyponatremia should be treated based on etiology (fluids for hypovolemia, fluid restriction for eu-/hypervolemia, discontinue offending agents)
- Salt tabs may not be useful (minimal Na increase, poorly tolerated), vaptans should generally be avoided (unpredictable Na increase, risk of overcorrection)
- Fludrocortisone helpful adjunct in SAH
- Fluid restriction helpful after initial stabilization (not for SAH)
- Peripheral 3% NaCl safe at lower rates (~50 mL/h) and shorter durations (48-72 h)
- Frequent Na monitoring (q4-8h) until serum Na stabilizes

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Symptoms of Hypernatremia

- Thirst
  - May be impaired by reduced consciousness from brain injury/neurosurgery or sedation
- Lethargy
- Muscle weakness
- Confusion
- Seizures
- Coma
- Severity
  - Mild (Na >145-149 mEq/L)
  - Moderate (Na 150-160 mEq/L)
  - Severe (Na >160 mEq/L)
  - *Correlates with degree and timing (acute > chronic)

Murphy-Human, Diringer MN. *J Pharm Pract* 2010;23(5):470-82.
Bhat R, et al. *BJA Education* 2022;22(12):466-73.

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Causes of Hypernatremia

- Free water loss (diarrhea, osmotic diuresis)
- Excessive sodium intake (Na bicarb, hypertonic saline)
- Diabetes insipidus (DI)

Cause	Central/Neurogenic DI	Nephrogenic DI
Mechanism	Decrease in arginine vasopressin (AVP) secretion or decreased release from pituitary	Inadequate renal response to AVP
Cause	Tumors (pituitary adenomas, craniopharyngiomas) Tumor resection (triphasic response (polyuria-antidiuresis-polyuria) Vascular (expanding aneurysms, arteriovenous malformations, sinus thromboses, and intrathalamic hemorrhages) Head trauma Brain death	Drug toxicity (lithium, demeclocycline, gentamicin)

Murphy-Human, Diringer MN. *J Pharm Pract* 2010;23(5):470-82.

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DI Diagnosis

- Hypernatremia, Na >145 mEq/L
- Polyuria >300ml/h over two consecutive hours (>30 mL/kg/day)
- Urine osmolality <300 mOsm/kg
- Urine specific gravity <1.005 or 1.01
- High serum osmolality >305 mOsm/kg

*Often transient and recovers <1 week

Murphy-Human, Diringer MN. *J Pharm Pract* 2010;23(5):470-82.

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Calculations and Treatment

- Calculations
  - Free water deficit = TBW x [(serum Na/140)-1]
- Treatment
  - Free enteral water
  - Hypotonic IV fluids (D5W, 0.45% NaCl)
  - DDAVP
  - Vasopressin
- Consider limiting correction to 10-12 mEq/L/day

TBW = total body water

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IV Fluids

Fluid	Glucose (g/dL)	Sodium (mEq/L)	Chloride (mEq/L)	Potassium (mEq/L)	Osmolarity (mOsm/L)
Plasma	0.07-0.11	135-145	95-105	3.5-5.3	308
5% dextrose	5	0	0	0	252
0.45% NaCl	0	77	77	0	154
0.9% NaCl	0	154	154	0	308
Ringer's lactate	0	130	109	4	273
Plasma-Lyte	0	140	98	5	294

Moritz ML, Ayus JC. *N Engl J Med* 2015;373(14):1350-60.

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AVP Agonists

Drug	Mechanism	Formulation	Common Dose
DDAVP	Synthetic analogue of vasopressin (ADH), selective V2 receptor agonist	IV/SQ	1-2 mcg q8-12h
		Nasal	10 mcg q12h
		PO	0.05-0.1 mg (50-100 mcg) q12-24h
Vasopressin	V1/V2 receptor agonist	Continuous infusion	0.01-0.04 units/min

DDAVP = 1-deamino-8-D-arginine vasopressin (desmopressin); ADH = antidiuretic hormone

Murphy-Human, Diringer MN. *J Pharm Pract* 2010;23(5):470-82.

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Monitoring

- Serum sodium
  - Every 4-8 h initially
  - Every 8-12 hours as sodium stabilizes
  - More frequently if Na increases too quickly/slowly
- Urine output
  - Increases dramatically in DI, early marker before serum Na results
  - Should decrease rapidly after DDAVP; increasing UOP may indicate wearing off of DDAVP
- Urine specific gravity/Osm
  - Typically similar frequency as serum Na (for DI)

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Hypernatremia Treatment Summary

- Hypotonic fluids (D5W and 0.45% NaCl) +/- DDAVP first line treatment for DI
  - Dose DDAVP as needed to determine frequency before scheduling
  - Free water appropriate (preferred) for patients who are able to drink (can self regulate thirst, do not restrict)
  - Vasopressin rarely indicated due to adverse effect profile (sometimes used in brain death)
  - DDAVP IV/SQ first line for acute hypernatremia
    - Careful with IV → PO conversions (~1:100 conversion) 1 mcg IV → 100 mcg (0.1 mg) PO
  - Remember that DI often resolves within a week; titrate down/discontinue DDAVP before transfer out (or sign out a plan)
- Discontinuation/rate decrease of hypertonic saline if overly aggressive initial management

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Treatment Issues

- When to stop therapy?
- Switch, add, or wean?
- Sodium goals?
- How much to increase drips for sodium increases?
- How to avoid rapid increase/decrease?

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Pharmacist's Role

- Pharmacists play a key role in early recognition and management of hyponatremia
  - IVPB, drips: Change to NS (or PO) when possible
  - Initiate hypertonic saline? Help with initial calculations and monitoring requirements
  - Vaptan selection? Check for drug interactions and dosing

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Summary

- The diagnosis and management of sodium disorders requires special considerations for neurocritically ill patients such as higher Na goals, inability to fluid restrict, and confounding causes of hyponatremia
- Calculations offer a starting point, but may be inaccurate in ICU patients
- Hypertonic saline is used for acute, symptomatic hyponatremia; adjunctive fludrocortisone may be helpful for certain patients and the role of vasopressin antagonists is limited
- Hypotonic fluids and desmopressin are used to treat hypernatremia, however careful monitoring important to prevent overcorrection and hyponatremia

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Shaken with Salt: Managing Sodium Imbalances in Neurocritical Care

Karen Berger, PharmD, FASHP, FCCM, BCPS, BCCCP
kberger1@nova.edu

Thank you!

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