

Sodium & Water Assessment & Therapeutics

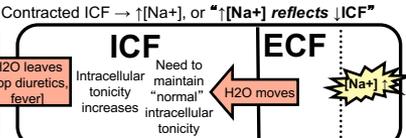
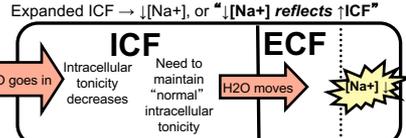
by Peter Loewen, B.Sc.(Pharm), ACPR, Pharm.D., R.Ph., FCSHP
V3.1 OCT 2018 updates at www.peterloewen.com

Assessing and managing Na/H2O disorders is complicated and requires a systematic approach.

My patient's serum [Na+] is abnormal and/or they seem to be "dehydrated"!

Serum [Na+] is the best reflection of ICF status.

Why does serum [Na+] reflect ICF and what does it mean?



TRAP: Never look at an elevated or low [Na+] and try to explain how that might cause ↑ or ↓ ICF. It doesn't, and it reinforces a misconception. Serum [Na+] REFLECTS what's happening in the ICF. The ICF will look after itself, with consequences for the ECF.

assess the ICF

START HERE!

assess the ECF (~volume + interstitial water)

Serum [Na+]
~135-145 mmol/L

Signs & Symptoms:
 ↓[Na+]: Cerebral edema, nausea/malaise, headache, lethargy, seizures, coma, noncardiogenic pulmonary edema
 ↑[Na+]: Rupture of cerebral veins, lethargy, weakness, irritability, twitching, seizures, coma

hypernatremia
(↓ ICF)

hyponatremia
(↑ ICF)

Common causes: water restriction (lack of access to water, loss of thirst response), diarrhea, vomiting, diabetes insipidus, acute diuresis with loop diuretic PLUS lack of or insufficient water intake.

ECF STATUS?

Hypovolemia/contracted ECF:
[JAMA. 1999;281:1022-1029]

1. **Postural changes** (lying-standing): severe dizziness, HR ↑ ≥30bpm, SBP ↓ ≥20mmHg
2. ↓JVP (<2cm ASA)
3. SCr/BUN <12 (or <10)
4. Urine [Na+] <20.30 mmol/L (if available)
5. ↓Urine output (<0.5 ml/kg/h)
6. Orbital depression
7. Skin tenting
8. Cool extremities
9. Dry mucous membranes
10. ↓capillary refill

Hypervolemia/excess ECF:
Edema (peripheral, pulmonary), ascites, ↑JVP, ↑BNP

Additional approaches to assessing hypovolemia vs. euvoolemia:
 Possibly greater diagnostic precision for detecting hypovolemia than clinical assessment alone:
 (1) If NOT on diuretics: measure **fractional excretion of Na+**: <1% = hypovolemia. [Arch Intern Med 1984;144:981-2]
 (2) If on diuretics or not: **fractional excretion of UREA** (<35% = hypovolemia. [Kidney Int 2002;62:2223-9] or **fractional excretion of URIC ACID** (<12% = hypovolemia [J Clin Endocrinol Metab 2008;93:2991-7])

ADH (arginine vasopressin, AVP) facts:
 • manufactured and released by the **posterior pituitary** (the "neurohypophysis")
 • ADH's purpose is to (1) help maintain blood pressure by retaining H2O during hypovolemia (inefficient mechanism), (2) prevent hyperosmolality during dehydration (efficient mechanism)
 • causes free H2O reabsorption from distal tubule. Similar effect to exogenous free H2O administration (i.e., can result in hyponatremia d/t expanded ICF). "ADH=D5W"
 • two stimuli for release: (1) serum osmolality (the "osmotic stimulus" - most sensitive stimulus), (2) significant volume (the "non-osmotic stimulus" - less sensitive stimulus)
 • ADH release turns off when serum osmolality is normal or low and it is euvolemic or hypervolemic. If it's ON during these states, it's inappropriate (SIADH/SAH)
 • loss of ADH secretion ability = **neurogenic diabetes insipidus (DI)**; blocked ADH activity at the site of action (eg, by lithium, demeclocycline) = **neurogenic DI**. when ADH is present, urine osmolality will be >100 mosmol/L
 • ADH does NOT make you thirsty (only ↑ plasma osmolality makes you thirsty)

MANAGEMENT:

1. Calculate total H2O deficit (the amount of H2O that would lower the patient's Na to 140 or 145 mmol/L. "free water deficit")
2. **ASSESS THE ECF**

3. Assess whether ICF, ECF, or both need to be repleted and the relative urgency of each.
4. Choose a free-water-containing crystalloid for replacement of ICF +/- NS for ECF repletion. D5W is most efficient Na-lowering crystalloid. Infuse at 50-200 ml/h.
5. Choose a ROUTE and RATE of administration: GOAL: reduce serum [Na+] by no more than ~0.5 mmol/L/h (i.e., ~12 mmol/L/day) to prevent ODS, though this is rare when correcting hyponatremia.
6. Reassess frequently (at least once daily depending on severity).

hypervolemic hyponatremia
Causes: HF, ascites, CKD, iatrogenic, primary polydipsia

MANAGEMENT:
 -treat the underlying cause
 -often DIURESIS is required
 -include ascites vs. CHF management principles

euvolemic hyponatremia
Causes: adrenal [cortisol] insufficiency (look for ↑ACTH), SIADH/SIAD

DIAGNOSIS OF SIADH/SIAD:
 Plasma osmolality <275 mOsm/kg + urine osmolality >100 mosmol/kg + urine [Na+] >20mEq/L + absence of thiazide diuretic [SMJ 2009;102:380-4, Am J Med 2013;126(10):51-42]. If on diuretic, add fractional excretion of Urine (FC) (>12% to rule in SIADH) [J Clin Endocrinol Metab 2008;93:2991-7], though definitive diagnosis can't be made until thiazide stopped. If uncertain about euvoolemia, give 500mL IV NS & remeasure serum [Na+].

Common Causes of SIADH/SIAD:

pain, vomiting, CNS injury / inflammation / tumor, pituitary tumors, any lung injury / inflammation / tumor, porphyria.
Drugs: carbamazepine, chlorpromazine, clofibrate, cyclophosphamide, interferons, ecstasy, opioids, oxytocin, PZTs, SSRIs, NSAIDs, TCAs, mirtazapine, venlafaxine, vincristine, vasopressin, demeclocycline, nicotine. **SIADH usually resolves when culprit drug is cleared.**

hypovolemic hyponatremia
Causes: volume depletion (millions of cases) with continued intake of hypotonic fluid (e.g. water)

MANAGEMENT:
 1. Manage **cause** (vomiting, diarrhea, etc.)
 2. Shut down ADH secretion by **restoring VOLUME** to the intravascular space.

IV-ADULTS: NS 250-1000ml over 15-60mins depending on severity, pt weight, age. **REASSESS ECF.** Caution if underlying heart failure. If necessary, follow with NS IV infusion @ 50-250 mL. D5-1/2NS requires 1.5x the volume as NS. Reassess frequently (≥ once daily) until hypovolemia +/- hyponatremia resolved.

ORAL: Water, WHO-ORS, water+salt, sports drinks, Rehydralyte (310 mOsm/kg), Pedialyte (250 mOsm/kg) [Contain 2.3 g/dL glucose, 45-90 mEq/L Na+, 30 mEq/L of base, and 20-25 mEq/L K+].

Hypovolemic Hyponatremia
 If hyponatremia is severe (<125 mmol/L) see "Treating severe hyponatremia" box.
 If hyponatremia not severe, treat **hypovolemia normally** and hyponatremia will resolve naturally via ADH shutdown → produce dilute urine → ICF depletion → raises serum [Na+].

Tip: When correcting hypovolemic hyponatremia (almost always caused by ADH secretion), it's not the Na+ in the crystalloid that raises the serum [Na+]. It's the crystalloid staying in the ECF (IV space specifically) → shuts off ADH secretion → produce dilute urine → deplete ICF → raises serum [Na+].

Diuretics and Na/H2O balance:

Thiazide: depletes a lot of Na, but not much H2O. Makes you pee roughly NS, not much of it.
Loop: makes you pee roughly 1/2NS
Spironolactone: Makes you pee NS, but not much of it. Doesn't usually disturb Na balance.
Melazozone: a thiazide that makes you pee a LOT of NS.

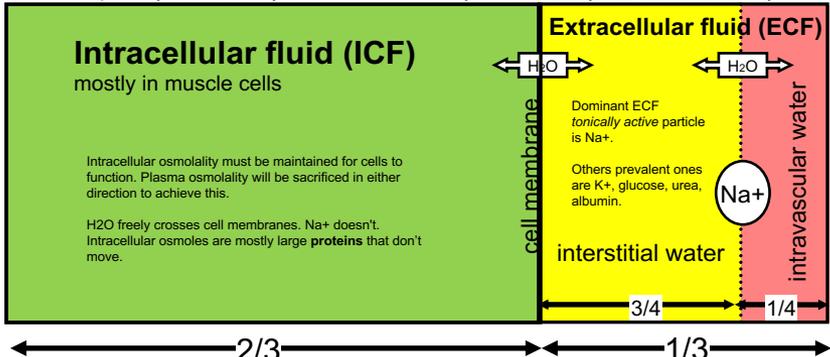
Trick: To remove volume while lowering Na (eg, hypervolemic hyponatremia): give melazozone + D5W, or furosemide + LOTS of D5W.

CPM/ODS (central pontine myelinolysis/osmotic demyelination syndrome): spastic quadriplegia and pseudobulbar palsy/paralysis (dysphagia, dysarthria, weakness of the tongue, emotional lability). Consciousness may be impaired. Lesions visible on CT or MRI. Outcomes vary from death to complete recovery, regardless of severity. No specific therapy except to avoid causing it. [Eur Neurol 2009;61:59-62, Eur J Intern Med 2008;19:29-31]. Incomplete known, but associated with initial Na+ <120 PLUS rise in serum Na+ by >25mmol/L or achieving normonatremia within first 48h [NEJM 1987;317:1190-1195]. Cause presumed to be cell death d/rate of correction of hyponatremia overwhelming cells' ability to restore lost intracellular organic osmoles ejected during hyponatremia. Very rarely caused by overcorrection of HYPERNatremia.

Where's your water?

Total body water (TBW) = 0.6* x total body weight

*More precisely: 0.45 for elderly female, 0.5 for non-elderly female or elderly male, 0.6 for non-elderly male.



Where does 1L of exogenous fluid end up?

Crystalloid / Colloid	ICF	ECF (intravascular)
Tap water, D5W	666mL	333mL (84mL)
NS (0.9% NaCl)	0	1000mL (250mL)
D5-1/2NS, 1/2NS	333mL	666mL (166mL)
2/3D5-1/3NS	445mL	555mL (139mL)
3% NaCl*	-2000mL	+3000mL (750mL)
Albumin 5% blood	0	1000mL (1000mL)
hetastarch, pentaspan	0	1000mL (1000mL)

*giving 1L of this would surely KILL a patient. These values are given for illustration/comparison purposes only.

Treating severe hyponatremia (<120 mmol/L) or hyponatremia with severe symptoms [NS&V, headache, CV distress, deep somnolence, seizures, coma (GCS<9)]. [Eur J Endocrinol 2014 Feb 4;170(3):G1-G47]. Adroge's formula underpredicts rise in [Na+] in 74% of cases [ClinJAmSocNephrol 2007;2:110-7].

TREATMENT: (based on Verbalis JG et al. AmJMed 2013;126:S1-S42 consensus guidelines)

ACUTE severe hyponatremia (<24h duration) with severe symptoms (risk of ODS):
 GOAL: rapid 4-6 mmol/L increase in serum [Na+]
 -100mL 3% NaCl IV over 10 mins, repeated twice at 30min intervals as needed
 -then allow serum [Na+] to correct to normal spontaneously (low risk of ODS), or if not correcting, move to approach below starting with Day2.
CHRONIC severe hyponatremia (>24h duration) with severe symptoms (risk of ODS):
 Usually caused by SIADH. Especially high risk of ODS in patients with serum Na+ <105 mmol/L, alcoholism, hypokalemia, malnutrition, advanced liver disease.
 -Day 1 goal: 4-6 mmol/L increase in serum [Na+] in first 6 hours. ("Rule of Sixes": "six a day makes sense for safety, so six in six hours for severe sx and stop." [AmJKidneyDis 2010;56:774-779]) using 100mL 3% NaCl IV over 10 mins, repeated twice at 30min intervals as needed.
 -Day2+: max 8-12 mmol/L/day increase in serum [Na+] (or 4-6 mmol/L if especially high-risk of ODS) using 3% NaCl IV infused at 0.5-2 mL/kg/h
 -max 10-12 mmol/L/24h increase in serum [Na+] (max 8 mmol/L/24h if especially high risk of ODS)
 -measure serum [Na+] q4-6h until serum [Na+] >125 mmol/L
 -implement standard SIADH treatment measures
 -excessive H2O diuresis can occur, but role of concurrent desmopressin + IV D5W is unclear. If used, stop when serum [Na+] exceeds ~128 mmol/L [Am J Kidney Dis 2013;61:571-578].