Sodium & Water Assessment & Therapeutics

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V2.11 SEP 2011 updates at www.peterloewen.com

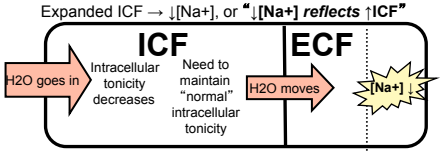
Assessing and managing Na/H2O disorders is complicated and requires a systematic approach.

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

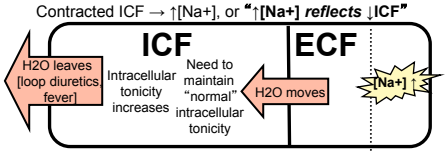
Serum [Na+] is the best reflection of ICF status.

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

Expanded ICF → ↓[Na+], or **"↓[Na+] *reflects* ↑ICF"**



Contracted ICF → ↑[Na+], or **"↑[Na+] *reflects* ↓ICF"**



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.

Free water deficit (L):
[([Na+] actual / [Na+] desired) -1] x TBW
http://www.medcalc.com/sodium.html

Assess the ICF

START HERE!

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)

Up to 38% incidence in hospitalized patients [Arch Intern Med. 2010;170(3): 294-302; Am J Med 2006;117:S30-5]. Most vulnerable: post-op, elderly, ICU, gen med. 67% of cases are ACQUIRED in hospital. OR death 1.66, 64% increase in LOS.

Common causes: diabetes insipidus, water restriction (lack of access, loss of thirst response), diarrhea, vomiting.

MANAGEMENT:
1. Calculate total H2O deficit (the amount of H2O that would lower the patient's Na from what it is to 140 or 145 mmol/L. ("free water deficit")
2. **ASSESS VOLUME/ECF STATUS**
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.
5. Choose a ROUTE and RATE of administration: GOAL: reduce serum [Na+] by *no more than* ~0.5 mmol/L/h (ie, ~12 mmol/L/day); some say 8 mmol/L/day). (osmotic demyelination syndrome-ODS, a.k.a. Central Pontine Myelinosis-CPM)

Diabetes Insipidus (DI):
Causes: idiopathic 30%, malignant/benign brain/pituitary tumors 25%, head trauma 16%, post cranial surgery 20%.
Goal of Therapy: Maintain urine volume <1 mL/kg/h and/or urine osmolality >500 mosm/L.
Therapeutic Options:
Neurogenic
1. Drink lots of water. 2. DDAVP 1-4 ug/d SC/IM/IV over 30 mins in 50ml NS (10-20 mcg IN q12-24h). 3. Thiazides ↓ urine volume (↑ urine osmolality, ↓ urine output by causing volume depletion → ↑ H2O retention via aldosterone & proximal Na reabsorption). 4. Restrict Na intake (to ↑ Na & H2O retention in proximal tubule). 5. Cause SIADH (Chlorpropamide 250 – 500 qd. Carbamazepine 400 –1200 /d, Clofibrate 500 tid/qid)
Nephrogenic #1, 3, and 4 above. If Li-induced, AMELORIDE 10mg/d can cure and prevent DI [Nat Rev Nephrol 2009;5, 270–276]

ECF STATUS?

Hypervolemic	Euvolemic	Hypovolemic
decompensated CHF, ascites, iatrogenic, psychogenic polydipsia	Adrenal insufficiency, ? hypothyroidism, **SIADH**	Volume depletion (millions of causes)

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

DIAGNOSIS of SIADH:
urine osmolality >100 mosm/kg AND urine [Na+] >20mEq/L
[SMJ 2009;102:380-4.]

Common Causes of SIADH:
pain, vomiiting, CNS injury/ inflammation/tumor, pituitary tumors, any lung injury/ irnflammation/tumor, porphyria.
Drugs: carbamazepine, chlorpropamide, clofibrate, cyclophosphamide, interferons, ecstasy, opioids, oxytocin, PTZs, SSRIs, NSAIDs, TCAs, mirtazapine, venlafaxine, vincristine, vasopressin/desmopressin, nicotine

MANAGEMENT of SIADH:
1. Identify & remove cause (tons of drug and non-drug causes)
2. H2O restriction (<1000 or <500 ml/d)
3. Furosemide
4. Salt liberalization (eg, >10g/d)
5. Fludrocortisone

Rarely:
6. Lithium
7. Demeclocycline
8. **Tolvaptan** (PO) [V2-antagonist]. Available in Canada as of Sept 2011. Conivaptan (IV/PO) not available yet.

MANAGEMENT:
Shut down AHD secretion by restoring VOLUME to the intravascular space.

When hyponatremia is severe (<125) and chronic (>48), highest risk for CPM/ODS upon correction. [Eur Neurol 2009;61:59-62]

After initial volume repletion, raise Na slowly: **GOAL**: raise serum [Na+] by *no more than* ~0.5 mmol/L/h (ie, ~12 mmol/L/day; some say 8 mmol/L/day).

Hot Tip:
-when correcting hpvolemic 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), which shuts off AHD secretion, which permits peeing dilute urine, which depletes ICF, which raises serum [Na+] (as water shifts from ECF to ICF to keep intracellular tonicity constant)

Assess the ECF (~volume+interstitial water)

Hypovolemia/contracted ECF:
[JAMA. 1999;281:1022-1029]
-Postural (lying→standing): severe dizziness, HR ↑≥30bpm, SBP↓≥20mmHg
-↓JVP
-SCr/BUN <12 (or <10)
-↓Urine output (<0.5 ml/kg/h)
-Orbital depression
-Skin tenting
-Cool extremities
-dry mucous membranes
-↓capillary refill

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

Alternative/backup approach to diagnosing hypovolemia;
Possibly greater diagnostic precision for detecting hypovolemia than clinical assessment alone.
If NOT on diuretics: measure fractional excretion of Na: <1% = hypovolemia. [Arch Intern Med 1984;144:981-2]
If on diuretics (or not): fractional excretion of UREA: <35% = hypovolemia. [Kidney Int 2002;;62:2223-9]

ADH (vasopressin) fast facts:
-manufactured and released by the posterior pituitary (the "neurohypophysis")
-designed to (1) help maintain blood pressure by retaining/ restoring H2O (inefficient mechanism), (2) prevent hyperosmolality
-causes free H2O reabsorption from distal tubule… similar effect to exogenous free H2O administration (ie, can result in hyponatremia d/t expanded ICF)
-two stimuli for release: (1)↑serum osmolality (the "osmotic stimulus"), (2) significant ↓volume (the "non-osmotic stimulus")
-turns off when serum osmolality is normal or low
-when you have none, it's called neurogenic diabetes insipidus (DI); when it's activity is blocked at the site of action (eg, by lithium, demeclocycline) it's called nephrogenic DI.
-when it's present, urine osmolality will be >100 mosm/kg
-does NOT make you thirsty (only↑plasma osmolality does this)

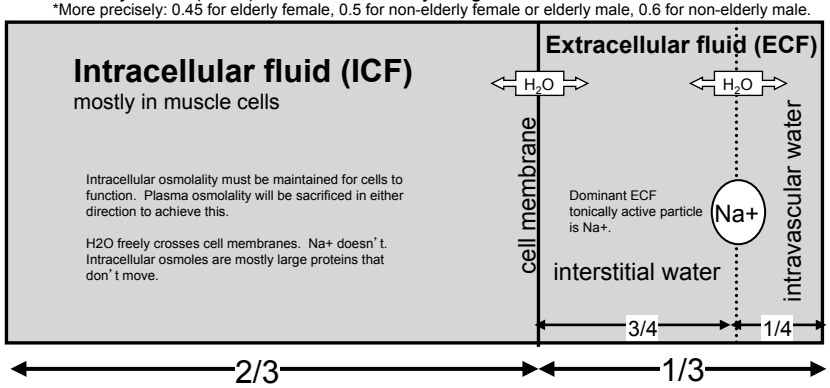
Diuretics and Na/H2O balance:
Thiazide: depletes a lot of Na, but not much H2O. Makes you pee roughly NS, not not much of it.
Loop: makes you pee roughly 1/2NS
Spironolactone: Makes you pee NS, but not much of it. Doesn't usually disturb Na balance.
Metolazone: a thiazide that makes you pee a LOT of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

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

CPM/ODS : spastic quadriparesis 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. [Eur Neurol 2009;61:59-62, Eur J Intern Med 2008;19:29-31.]

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	0 (1000mL)
Hetastarch, pentaspan	0	0 (all of it)

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

Hypertonic saline for severe hyponatremia (eg, with significant mental status changes or seizures):

Adrogue Formula:

$$\text{Change in serum } Na^+ = \frac{(\text{infusate } Na^+ + \text{infusate } K^+) - \text{serum } Na^+}{\text{total body water} + 1}$$

…where infusate [Na+] = 513 for 3%NS. 855 for 5%NS. 154 for NS. 130 for LR.
Tells you what 1L will do to serum [Na+]. Usually you want a ~5mmol/L initial change, and 0.5 mmol/L/h thereafter. Use this to determine how many mL of 3%NS is required to change the serum [Na+] by those amounts. **MAX RATE 100 mL/h.**
http://www.medcalc.com/sodium.html