Iponatremia in Medicina Interna

- ***Background.***

  L'iponatremia (ipotonica) è un disordine ipo-osmolare caratterizzato da un *eccesso di acqua corporea* rispetto ai soluti corporei.

'Because body water is the primary determinant of the *ECF*, disorders of body water homeostasis can be divided into **hypo-osmolar disorders**, in which there is an excess of body water relative to body solute, and hyper-osmolar disorders, in which there is a deficiency of body water relative to body solute.

Because sodium is the main constituent of *plasma osmolality*, these disorders are typically characterized by **hyponatremia** and hypernatremia, respectively.'

Verbalis JG, 2003

Photograph by D. Behrens

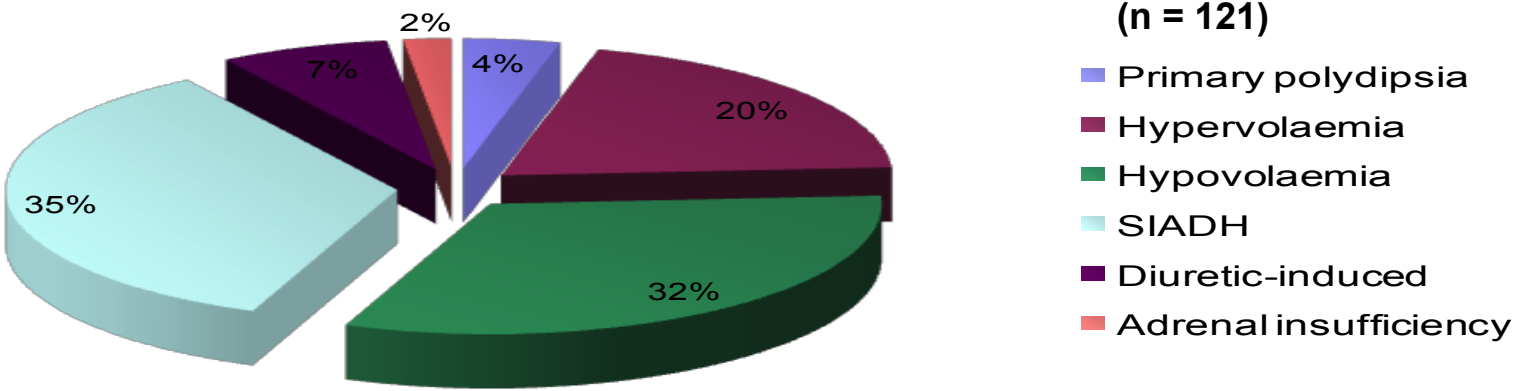
Hypotonic hyponatraemia is classified according to volume status

	Hypervolaemic hyponatraemia	Euvolaemic hyponatraemia	Hypovolaemic hyponatraemia
Total body water (TBW)[15]	↑ ↑	↑	↓
Total body sodium[15]	↑	↔	↓ ↓
Extracellular fluid (ECF) volume[16]	↑ ↑	↔	↓
Oedema[16]	Present	Absent	Absent
Cause[2-15]	Congestive heart failure, cirrhosis, nephrotic syndrome, renal failure (acute or chronic)	SIADH, glucocorticoid deficiency, hypothyroidism	*Renal solute loss:* Diuretic therapy, cerebral salt wasting, mineralocorticoid deficiency, salt wasting nephropathy *Extrarenal solute loss:* Vomiting, diarrhoea, pancreatitis, third space burns

2. Verbalis J, et al. *Am J Med*. 2007; 120(11 Suppl 1): S1-21.
15. Schrier RW, Bansal S. *Curr Opin Crit Care*. 2008;14:627-634.
16. Douglas I. *Cleve Clin J Med*. 2006;73(3):S4-S12.

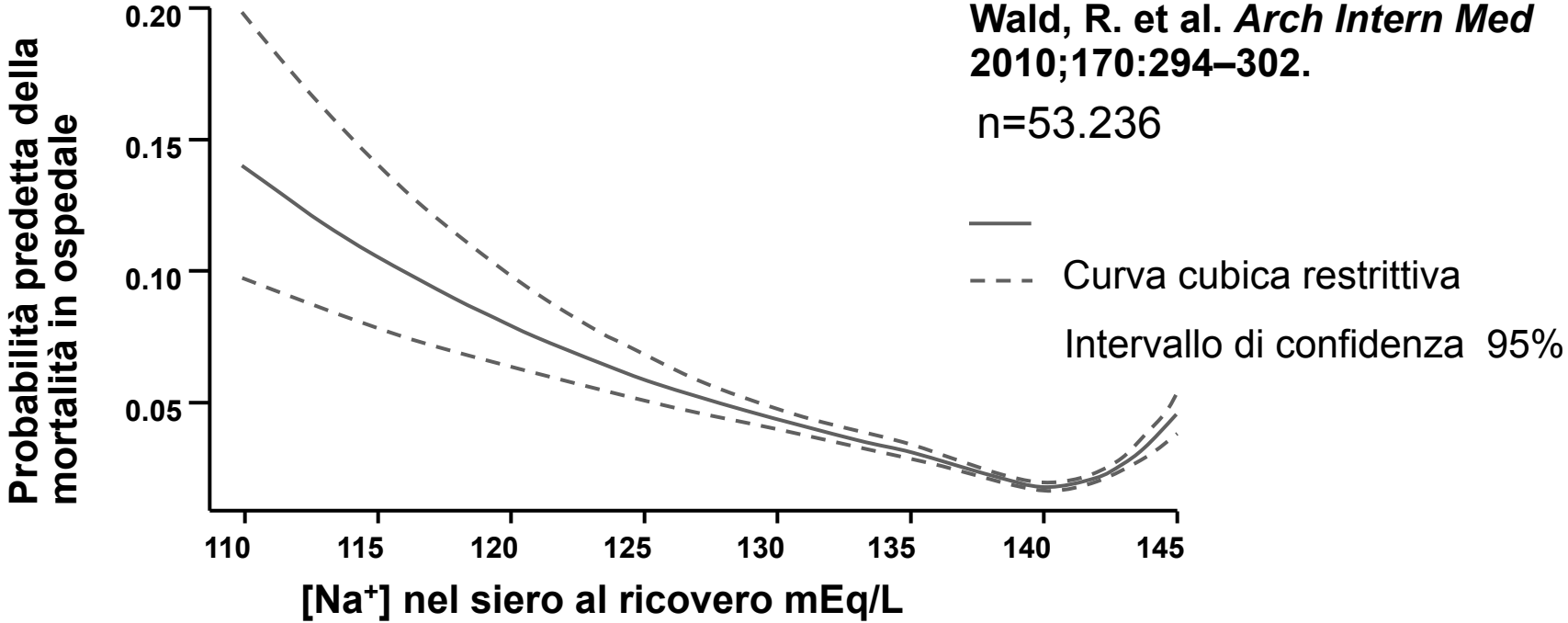
L'iponatremia può essere dovuta a diverse condizioni

Eziologia della iponatremia ([Na^+] siero < 130mmol/L) presso la Clinica Medica Universitaria di Würzburg[1]



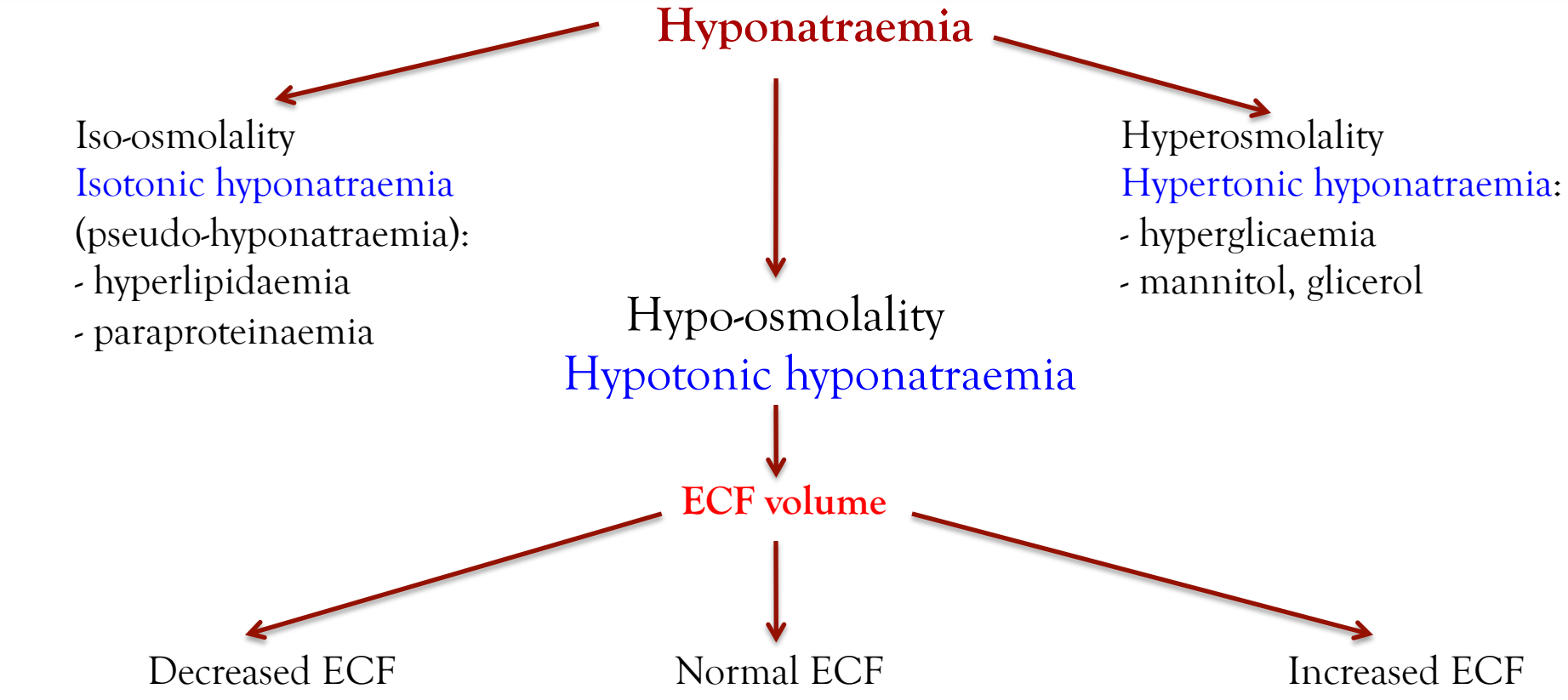
1. Fenske W, et al. *Am J Med.* 2010;123:652-657.

Relazione a forma di U tra la [Na^+] nel plasma al ricovero e la mortalità in ospedale[1]

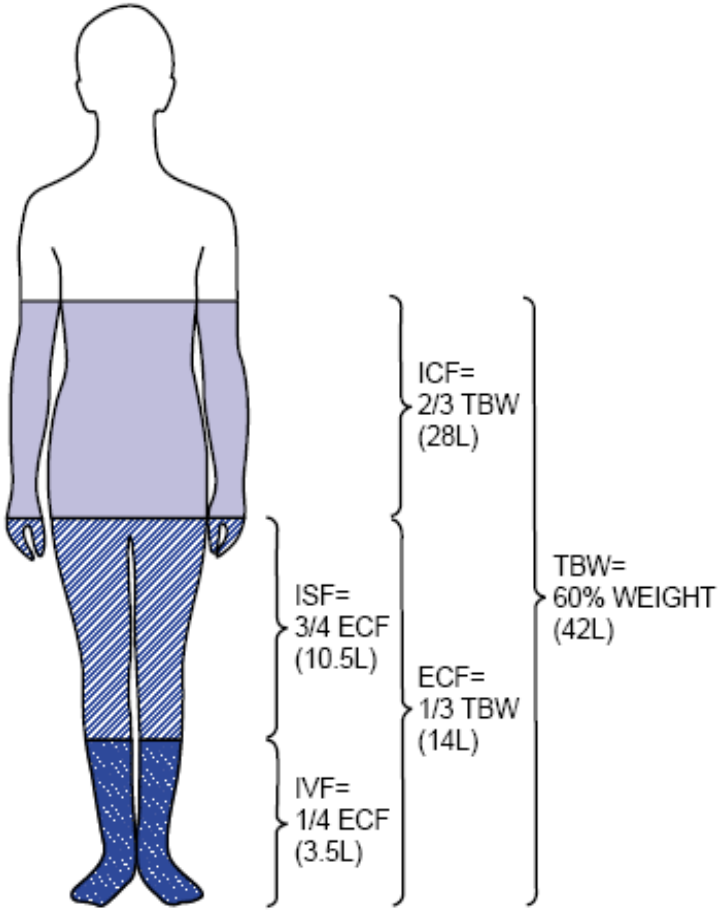


Adattato da: Wald R, et al. *Arch Intern Med.* 2010;170(3):294-302.

Hyponatraemia – first assessment



Body fluid compartments in man



Volemia

EABV (effective arterial blood volume)

J Verbalis, 2003

Parametri utili per il corretto inquadramento del paziente con iponatremia

- ***Osmolalità plasmatica***
- ***Osmolalità urinaria***
- ***Sodio urinario (su campione spot)***
- ***Valutazione dello stato del volume extracellulare !***

Criteria for the diagnosis of SIADH

Essential

- Decreased measured plasma osmolality (<275 mOsm/kg H_2O)
- Urinary osmolality > 100 mOsm/kg H_2O during hypo-osmolality
- Clinical euvolaemia
  - No clinical signs of volume depletion of extracellular fluid (e.g., no orthostasis*, tachycardia, decreased skin turgor, or dry mucous membranes)
  - No clinical signs of excessive volume of extracellular fluid (e.g., no oedema or ascites)
- Urinary sodium > 30 mmol/l with normal dietary sodium intake**
- Normal thyroid and adrenal function determined by both clinical and laboratory assessment
- No use of diuretic agents within the week prior to evaluation

Supporting

- Plasma uric acid < 4 mg/dl (< 0.24 mmol/l)
- Blood urea nitrogen < 10 mg/dl (< 3.57 mmol/l)
- Fractional sodium excretion > 1%; fractional urea excretion >55%***
- Failure to improve hyponatraemia after 0.9% saline infusion, or improvement of hyponatraemia with fluid restriction

* Orthostatic changes in blood pressure and pulse rate are defined as a ≥ 20 mm decrease in systolic BP and/or a ≥20 bpm increase in pulse rate upon going from a supine to a standing position.

** Although high urine sodium excretion generally occurs in patients with SIADH, its presence does not confirm the diagnosis, nor does its absence rule out the diagnosis; urine sodium can also be high in renal causes of solute depletion such as diuretic use or Addison's disease, and conversely some patients with SIADH can have low urinary sodium if they become hypovolaemic or solute depleted, which are conditions sometimes produced by imposed sodium and water restriction.

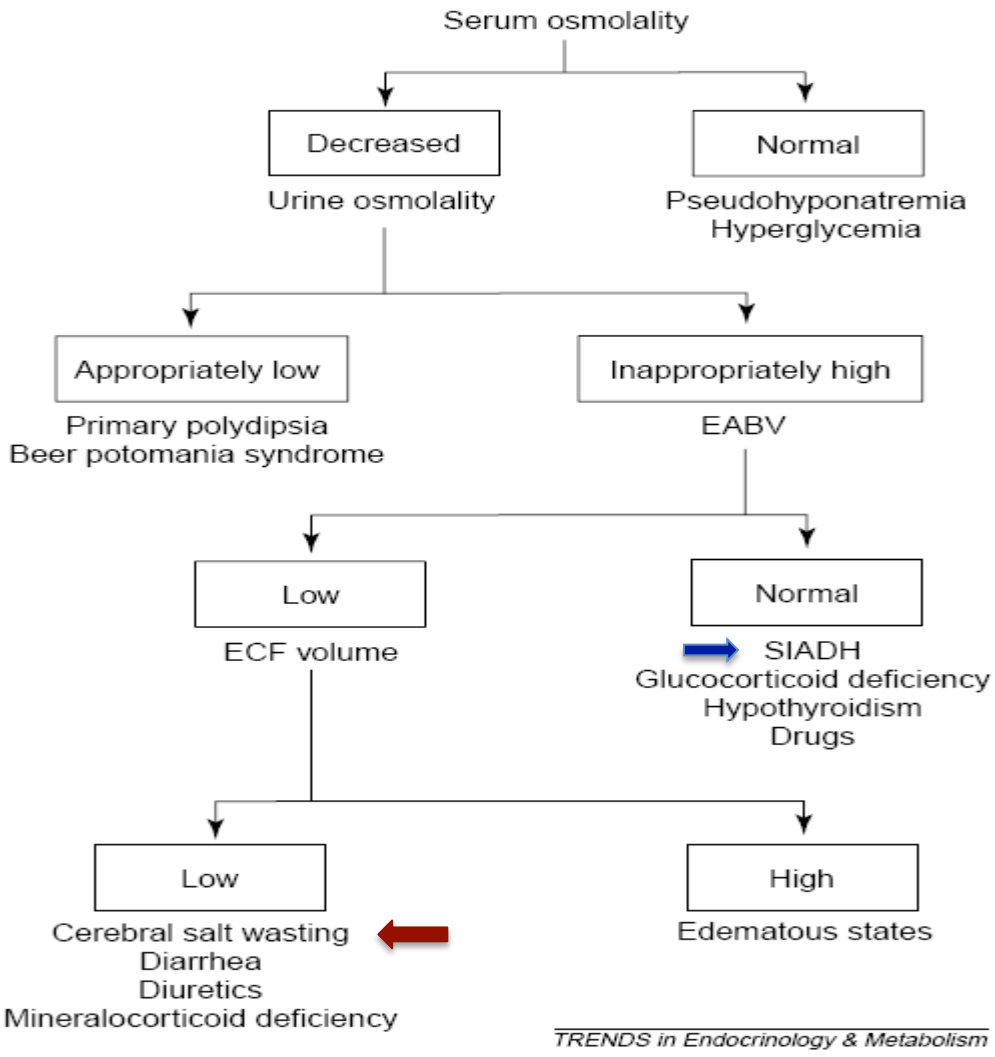
*** Fractional sodium excretion = (urinary sodium / plasma sodium) / (urinary creatinine / plasma creatinine) X 100;
Fractional urea excretion = (urinary urea / plasma urea) / (urinary creatinine / plasma creatinine) X 100.

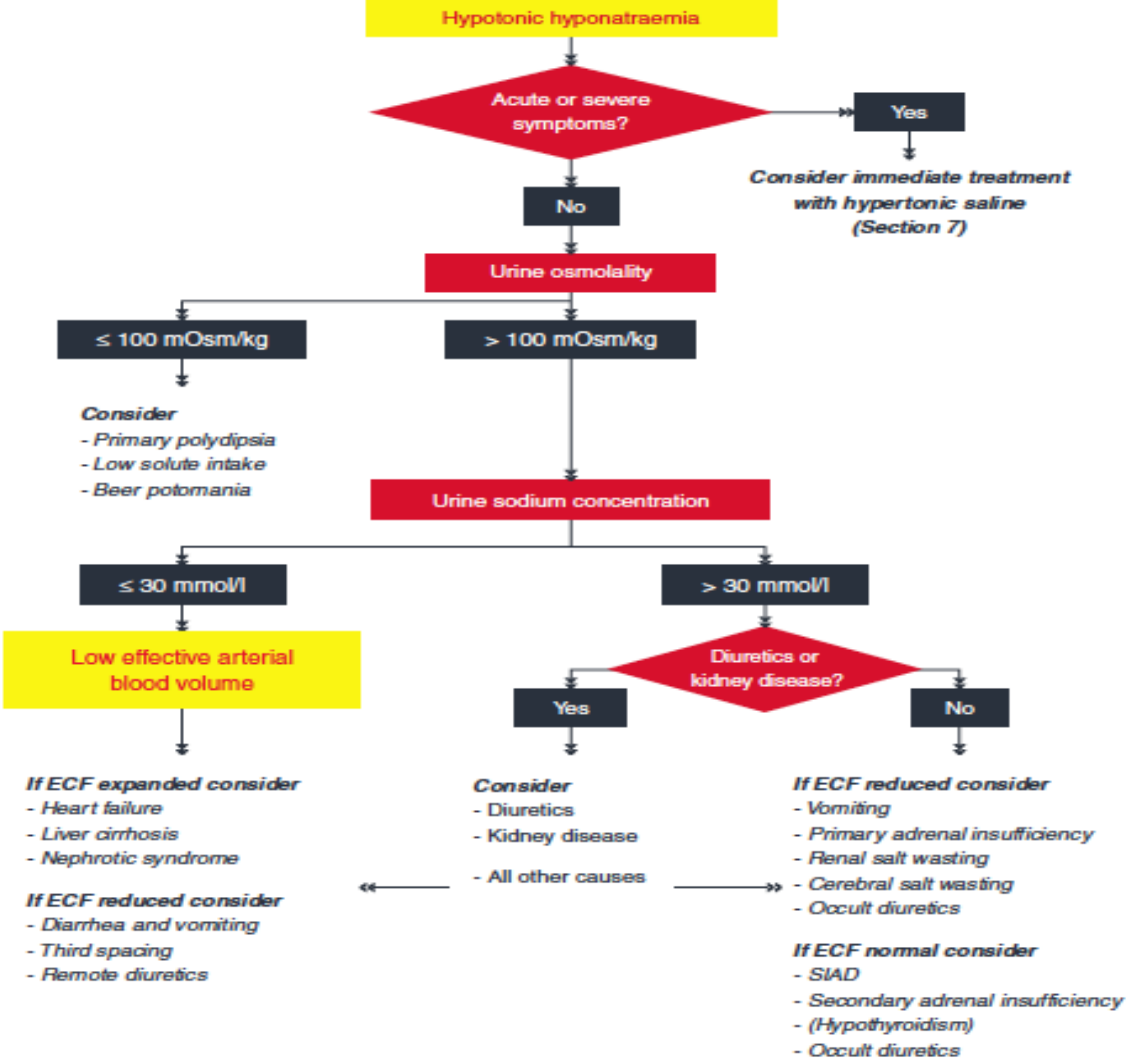
Developed with input from KOLs within the field of hyponatraemia and SIADH.

Approach to the hyponatraemic patient

EABV effective arterial blood volume
ECF extracellular fluid

Patient with extracellular fluid volume depletion:
- orthostatic
- dry skin
- light-headed





European Journal of Endocrinology (2014) 170, G1–G47

Signs and symptoms of hyponatraemia

- Anorexia/nausea
- Muscle cramps
- Headache
- <u>Central nervous system symptoms and signs</u>
  - Letargy/apathy
  - Disorientation, confusion, ataxia, gait disorder, falls
  - Tremulousness, agitation/delirium/vomiting → *treatment with hypertonic saline!*
  - Abnormal sensorium
  - Seizures
  - Coma (GCS < 9)
  - Depressed deep tendon reflexes
  - Pathologic reflexes
  - Focal neurologic deficits
  - Pseudobulbar palsy
  - Cheyne-Stokes respiration

Treatment of hyponatremia: a continuing challenge

Kidney International, Vol. 37 (1990), pp. 1006–1018

NEPHROLOGY FORUM

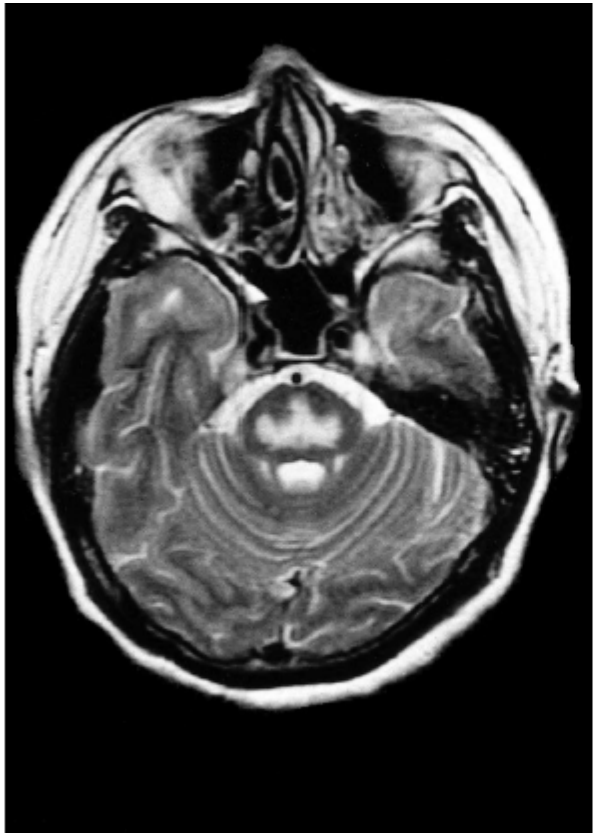
Treating hyponatremia: Damned if we do and damned if we don't

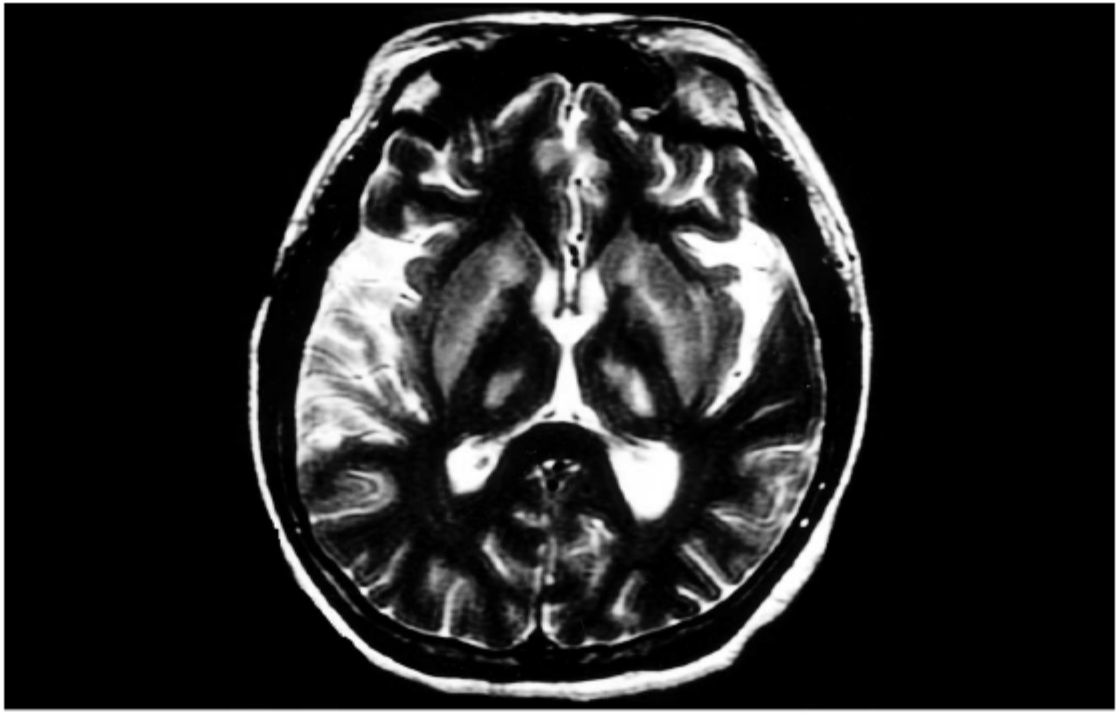
Principal discussant: TOMAS BERL

University of Colorado, Denver, Colorado

The risk of "wait-and-see" *(hyponatremic encephalopathy)*
and the risk of overtreatment *(osmotic demyelination syndromes)*

Osmotic demyelination syndromes





Clin Radiol 2002; 57: 800

Clinical practice guideline on diagnosis and treatment of hyponatraemia

European Journal of Endocrinology
(2014) 170, G1–G47

Goce Spasovski, Raymond Vanholder[1], Bruno Allolio[2], Djillali Annane[3], Steve Ball[4], Daniel Bichet[5], Guy Decaux[6], Wiebke Fenske[2], Ewout J Hoorn[7], Carole Ichai[8], Michael Joannidis[9], Alain Soupart[6], Robert Zietse[7], Maria Haller[10], Sabine van der Veer[11], Wim Van Biesen[1] and Evi Nagler[1] on behalf of the Hyponatraemia Guideline Development Group

SUPPLEMENT

THE AMERICAN JOURNAL of MEDICINE®

Diagnosis, Evaluation, and Treatment of Hyponatremia: Expert Panel Recommendations

Joseph G. Verbalis, MD,[a] Steven R. Goldsmith, MD,[b] Arthur Greenberg, MD,[c] Cynthia Korzelius, MD,[d] Robert W. Schrier, MD,[e] Richard H. Sterns, MD,[f] Christopher J. Thompson, MD, FRCPI[g]

[a]Georgetown University Medical Center, Washington, DC; [b]University of Minnesota, Minneapolis, MN; [c]Duke University Medical Center, Durham, NC; [d]Tufts University School of Medicine, Boston, MA; [e]University of Colorado, Denver, CO; [f]University of Rochester, Rochester, NY; [g]Royal College of Surgeons in Ireland School of Medicine, Dublin, Ireland.

The American Journal of Medicine (2013) 126, S1-S42

Clinical practice guideline on diagnosis and treatment of hyponatraemia

Severity	Symptom
Moderately severe	Nausea without vomiting Confusion Headache
Severe	Vomiting Cardiorespiratory distress Abnormal and deep somnolence Seizures Coma (Glasgow Coma Scale $\leq$8)

7.1.1.1. We recommend prompt i.v. infusion of 150 ml 3% hypertonic over 20 min (1D).

7.1.1.2. We suggest checking the serum sodium concentration after 20 min while repeating an infusion of 150 ml 3% hypertonic saline for the next 20 min (2D).

7.1.1.3. We suggest repeating therapeutic recommendations 7.1.1.1 and 7.1.1.2 twice or until a target of 5 mmol/l increase in serum sodium concentration is achieved (2D).

7.1.1.4. Manage patients with severely symptomatic hyponatraemia in an environment where close biochemical and clinical monitoring can be provided (not graded).

EJE 2014

Diagnosis, Evaluation, and Treatment of Hyponatremia: Expert Panel Recommendations

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Am J Med 2013

Expert Panel Recommendation: Treatment of Symptomatic Acute Hyponatremia

- Indications:
  - Self-induced acute water intoxication (eg, psychiatric diseases such as acute psychosis or schizophrenia, endurance exercise, "ecstasy" use);
  - Known duration of hyponatremia <24-48 hours (eg, postoperative);
  - Intracranial pathology or increased intracranial pressure;
  - Seizures or coma, regardless of known chronicity.
- Goal:
  - Urgent correction by 4-6 mmol/L to prevent brain herniation and neurological damage from cerebral ischemia.
- Recommended Treatment:
  - For severe symptoms, 100 mL of 3% NaCl infused intravenously over 10 minutes × 3 as needed;
  - For mild to moderate symptoms with a low risk of herniation, 3% NaCl infused at 0.5-2 mL/kg/h;
  - The rate of correction need not be restricted in patients with true acute hyponatremia, nor is re-lowering of excessive corrections indicated (**Figure 3**); however, if there is any uncertainty as to whether the hyponatremia is chronic versus acute, then the limits for correction of chronic hyponatremia should be followed (see section: *Current Recommendations for Rate of Correction of Hyponatremia*).

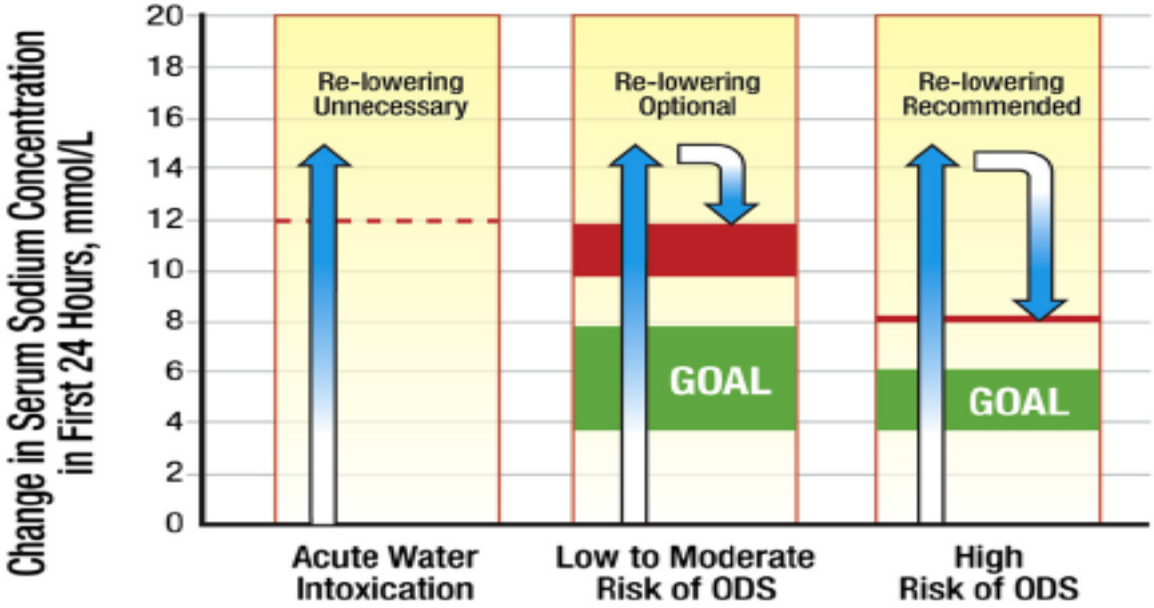

Figure 3 Recommendations for relowering of serum sodium concentration ($[Na^+]$) to goals (green) for patients presenting with serum $[Na^+]$ <120 mmol/L who exceed the recommended limits of correction (red) in the first 24 hours. Abbreviations: L = liter; mmol = millimole; ODS = osmotic demyelination syndrome.

Am J Med 2013

…to be continued

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