IPONATREMIA CRONICA: ANCORA SOTTOSTIMATA?

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Management of hyponatremia: definitions

**Definitions**

- Hyponatraemia: $\text{Na}^+ < 136$ mmol/l
- Severe hyponatraemia: $\text{Na}^+ < 120$ mmol/l
- Acute hyponatraemia: hyponatraemia known to be of less than 48 hours duration or developing at a rate of $> 0.5$ mmol/hour
- Chronic hyponatraemia: hyponatraemia known to be of more than 48 hours duration or developing at a rate of $< 0.5$ mmol/hour
- Tonicity (synonym: effective osmolality): that portion of total osmolality that has the potential to induce transmembrane water movement

Martin, JNNP 2004
What’s the cut-off for identifying “mild” hyponatraemia?

Is chronic hyponatraemia always mild/moderate?

Lancet 1998
Signs and symptoms of hyponatraemia

- Anorexia/nausea
- Muscle cramps
- Headache
- **Central nervous system symptoms and signs**
  - Letargy/apathy
  - Disorientation, confusion, ataxia, gait disorder, falls
  - Tremulousness, agitation/delirium
  - Abnormal sensorium
  - **Seizures**  
    *urgent treatment with hypertonic saline!*
  - Depressed deep tendon reflexes
  - Pathologic reflexes
  - Focal neurologic deficits
  - Pseudobulbar palsy
  - Cheyne-Stokes respiration
Diagnosis
Because the body water is the primary determinant of the osmolality of the ECF...
...and sodium is the main constituent of plasma osmolality...
Hyponatraemia is a hypo-osmolar disorder, in which there is an excess of body water relative to body solute.

Verbalis JG, 2003
Hypotonic hyponatraemia is classified according to volume status

<table>
<thead>
<tr>
<th></th>
<th>Hypovolaemic hyponatraemia</th>
<th>Euvolaemic hyponatraemia</th>
<th>Hypovolaemic hyponatraemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total body water (TBW)</td>
<td>↑↑</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Total body sodium</td>
<td>↑</td>
<td>↔</td>
<td>↓↓</td>
</tr>
<tr>
<td>Extracellular fluid (ECF) volume</td>
<td>↑↑</td>
<td>↔</td>
<td>↓</td>
</tr>
<tr>
<td>Oedema</td>
<td>Present</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Cause</td>
<td>Congestive heart failure, cirrhosis, nephrotic syndrome, renal failure (acute or chronic)</td>
<td>SIADH, glucocorticoid deficiency, hypothyroidism</td>
<td>Renal solute loss: Diuretic therapy, cerebral salt wasting, mineralocorticoid deficiency, salt wasting nephropathy</td>
</tr>
</tbody>
</table>

Iponatremia ipotonica

Introito di acqua in eccesso

Osmolalità delle urine

< 100 mOsm/kg

Cause frequenti:
- Polidipsia primaria
- Basso introito di soluti

> 100 mOsm/kg

Diluizione renale insufficiente

Sodio nelle urine

< 30 mOsm/kg

Ipovolemia
[Acqua corp. totale↑]
[Sodio corp. totale↑]

Iperolemia
[Acqua corp. totale↑]
[Sodio corp. totale↑]

Ipovolemia
[Acqua corp. totale↑]
[Sodio corp. totale↓]

Volume ECF

> 30 mOsm/kg

Volume ECF

Euvolemia
[Acqua corp. totale↑]
[Sodio corp. totale↑]

Perdita di soluti extrarenale:
- Perdita gastrointestinale (diarrea, vomito)
- Ustioni terzo spazio
- Pancreatite
- Muscolo traumatizz.

Disordini edematosi:
- Insufficienza cardiaca
- Cirrosi epatica
- Sindrome nefrotica

Perdita renale di soluto:
- Eccesso diuretico
- Nefrite con perdita di sale
- Diuresi osmotica (mannitolo)
- Deficit di mineralcorticoidi

Deficit di glicocorticoidi
- Ipotiroidismo
- Dolore
- Nausea
- SIADH

Patients with SIAD(H) are clinically euvolemic, but…
Criteria for the diagnosis of SIADH

**Essential**
- Decreased measured plasma osmolality (<275 mOsm/kg H₂O)
- Urinary osmolality > 100 mOsm/kg H₂O 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

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* 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.
SIAD(H) is a disorder in which renal water handling is impaired but renal sodium handling is normal.

Consider the response of a patient with SIAD(H) given 1 L of normal saline (308 mosm).

Assuming a urine osmolality of 616 mosm/L, the entire load of NaCl will be excreted in 500 ml of fluid. The remaining 500 ml of administered fluid will remain within the body and cause a further lowering of the serum sodium concentration.

In order to avoid worsening hyponatraemia in this setting, the osmolality of the fluid given must exceed the osmolality of the urine.

B. Palmer TEM, 2003
Fig. 1 Frequency distribution of serum sodium concentrations in patients at time of diagnosis with hypothyroidism (upper pane) and controls (lower pane).

hypothyroidism

controls

Warner MH et al Clin Endocrinol, 2006; 64: 598-99
Acronimi

SIADH: syndrome of inappropriate secretion of ADH (1957)

NSIAD: nephrogenic syndrome of inappropriate antidiuresis (2005)

SIAD: syndrome of inappropriate antidiuresis (2005)
Inactivating mutations: X-linked CNDI
Activating mutations: NSIAD

Autosomal recessive and dominant CNDI

Collecting tubule

Aquaporin-4 H2O channel
Aquaporin-3 H2O channel
Aquaporin-2 H2O channel

H2O

Stimulating G protein
Vasopressin type 2 receptor
Arginine vasopressin
Adenylate cyclase
Protein kinase A
A TP
Phosphoproteins

H2O
H2O
H2O
Treatment
The challenge of hyponatraemia

- Although morbidity varies widely in severity, serious complications can arise from:
  
  - the *disorder itself* (*hyponatraemic encephalopathy*)
  
  - as well as from *errors in management* leading to the *rapid shift in sodium* (*central pontine and extrapontine myelinolysis - the osmotic demyelination syndromes*).
Effects of hyponatraemia on the brain and adaptive responses *(NEJM 2000)*
MRI findings in central pontine myelinolysis (CPM) typically show a T2-weighted axial scan with a characteristic "bat-wing" appearance. This pattern is indicative of CPM and is consistent with findings from the publication in *Clin Radiol* 57: 800, 2002.
Panel 2: **Hyponatraemic patients at risk for neurological complications**

**Acute cerebral oedema**
- Postoperative menstruating females
- Elderly women on thiazides
- Children
- Psychiatric polydipsic patients
- Hypoxaemic patients

**Osmotic demyelination syndrome**
- Alcoholics
- Malnourished patients
- Hypokalaemic patients
- Burn victims
- Elderly women on thiazide diuretics

Maximum suggested correction of sodium in 24 hrs (Martin RJ, JNNP 2004)
Utilizzare la modalità di insorgenza dell’iponatremia secondaria a SIAD(H) come guida per la scelta del trattamento

Iponatremia

24-48 ore

Insorgenza graduale

> 48 ore

Sintomi severi

Sintomi lievi/moderati o paziente asintomatico

Sintomi lievi/moderati o paziente asintomatico

Tolvaptan

Restrizione idrica

Se non si conosce la rapidità con cui è insorta, l’iponatremia dovrebbe essere trattata come se fosse ad esordio graduale

Treatment of SIAD with severe symptoms (seizures, coma, respiratory distress) or moderate symptoms (nausea, disorientation, unsteady gait) if hyponatraemia is known to be acute (i.e. < 48 hrs duration)

Hypertonic saline
...The controversy as to how hyponatremic patients should best be treated can be traced to the fact that *not a single prospective, randomized, controlled trial* is designed to address the optimal management of this most common of electrolyte disorders. There are, therefore, *no clearly established and uniformly agreed-on national or international guidelines*, and those that are put forth in various publications are based primarily on retrospective observational analysis on a limited number of patients. None has the virtue of comparing prospectively two or more therapeutic options and monitoring for well-defined neurological outcomes in a randomized, controlled trial or even in a robust prospective, observational trial. Ultimately, *the published recommendations are largely opinion based* and reflect the experience of the various authors.’

Adrogué-Madias formula for estimating the effect of 1 litre of any infusate on serum sodium

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

*Total body water = body weight \times F

- F = 0.6 in non elderly men and children
- F = 0.5 in non elderly women and elderly men
- F = 0.45 in elderly women

Infusate Na in 0.9% saline = 154 mmol/l
Infusate Na in 1.8% saline = 308 mmol/l
Infusate Na in 3% saline = 514 mmol/l

Infusate Na in 200 ml 0.9% saline + 50 ml 11.68% saline (2 mmol/ml) = 523 mmol/l
Infusate Na in 11.68% saline = 2000 mmol/l
Infusate Na in Ringer’s lactate solution = 130 mmol/l
'It is good to make things simple, but not too simple'

Albert Einstein

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Editorial

The Adrogue-Madias Formula Revisited

Tomas Berl
Division of Renal Diseases and Hypertension, Department of Medicine, University of Colorado at Denver and Health Sciences Center, Denver, Colorado

The Adrogue-Madias Formula Revisited
Tomas Berl

- The primary shortcoming of the formula is *its failure to assess ongoing renal and extrarenal losses*. This is particularly critical in hypovolemic patients, when the nonosmotic release of vasopressin is no longer operant (because of the restoration of volume over 24-48 hrs) and a water diuresis ensues.

- The formula does not allow for the increase in serum sodium concentration that accompanies the administration of potassium in the potassium-depleted group (e.g., *role of potassium in hypokalemia-induced hyponatremia*).
Formulas for estimating the effect of any infusate on serum sodium
Treatment of SIAD with mild or asymptomatic hyponatraemia

- Fluid restriction alone
- Vaptans
Fluid restriction

<table>
<thead>
<tr>
<th>Chronic Hyponatremia</th>
<th>Urinary sodium+urinary potassium plasma sodium</th>
<th>Recommended fluid intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Restrict fluid intake</td>
<td>&gt;1</td>
<td>&lt;500 ml/day</td>
</tr>
<tr>
<td>Encourage dietary intake of salt and protein if hyponatremia continues</td>
<td>~1</td>
<td>500–700 ml/day</td>
</tr>
<tr>
<td>Demeclocycline, 300–600 mg twice daily, or urea, 15–60 g daily</td>
<td>&lt;1</td>
<td>&lt;1 liter/day</td>
</tr>
<tr>
<td>Vasopressin-receptor antagonists (if available)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 2. Algorithm for the Treatment of Hyponatremia Associated with SIAD.

The urine/plasma electrolyte ratio: a predictive guide to water restriction

Fig 1. Dependence of water clearance on daily solute excretion at low urinary osmolalities.

\[
c_{H_2O} = \frac{\text{Solute excretion}}{U_{osm}} \left(1 - \frac{U_{osm}}{P_{osm}}\right)
\]

\[
c_{H_2O_e} = \frac{\text{solute excretion}}{U_{osm}} \left(1 - \frac{U_{na} + U_k}{P_{na}}\right)
\]
Tolvaptan (Samsca)

- Samsca (tolvaptan, study name OPC-41061)
- Benzazepine derivative
  
- Oral Selective V2-Receptor Antagonist

Contraindications

- Hypersensitivity to the active substance or to any of the excipients
- Anuria
- Volume depletion
- Hypovolaemic hyponatraemia
- Hypernatraemia
- Patients who cannot perceive thirst
- Pregnancy
- Breastfeeding

Caso clinico

- Uomo di 82 anni inviato in P.S. per caduta a terra e stato confusionale, in terapia con aspirina a basso dosaggio (100 mg/die).
- Anamnesi patologica remota. Ernioplastica inguinale all’età di 42 anni. Vasculopatia cerebrale cronica documentata da RM eseguita qualche mese prima per caduta a terra.
- Anamnesi patologica recente. Ricoverato due volte in P.S. negli ultimi sei mesi per stato confusionale con caduta a terra e riscontro di iponatremia (123-128 mmol/L), trattata con infusione salina ipertonica per 24-48 ore.
- Esami di laboratorio. **Sodiemia: 121 mmol/L**; potassiemia: 3.9 mmol/L; emocromo e restanti esami di routine nella norma.
Caso clinico

- Quali esami/indagini mancano per definire la diagnosi?
  - Osmolarità plasmatica: 250 mOsm/kg H2O
  - Osmolarità urinaria: 388 mOsm/kg H2O
  - Sodio urinario: 78 mmol/L
  - Valutazione del volume dello spazio extracellulare: paziente clinicamente euvolemico
  - TSH: 2.8 mU/L
  - Ft4: 11 pg/ml
  - Cortisolemia: non ancora disponibile.

- Diagnosi?
- Cosa fare?
Caso clinico

• Cosa fare?
  – Soluzione salina ipertonica NaCl 3% (in attesa della cortisolemia)
  – Risalita della sodiemia (130 mmol/L: 9 mmol/L in 24 ore) con miglioramento delle condizioni cliniche
  – Nel frattempo, giunge il risultato della cortisolemia: 191 ng/ml

• Diagnosi: SIAD
Caso clinico

- **Cosa fare ora?**
  - Restrizione idrica: 800 ml/die
  - Nei 3 giorni seguenti: lieve discesa della sodiemia (128-129 mmol/L) con condizioni cliniche stabili.
  - Il 4° giorno il paziente comincia a lamentarsi della restrizione idrica
    - Sodiemia: 127 mmol/L
  - Si propone tolvaptan 15 mg/die (terzo ricovero per sodiemia in 6 mesi)
Caso clinico

- **Tolvaptan 15 mg/die**
  - La sodiemia si stabilizza attorno a 134-136 mmol/L nella settimana successiva.
  - Il trattamento è mantenuto per 30 giorni, poi viene interrotto, poiché nel frattempo viene pubblicato (30 aprile 2013) un comunicato della FDA, che consiglia di non superare il limite di 30 giorni per il rischio di epatotossicità nei trattamenti prolungati con tolvaptan, sulla scorta di dati emerse da studi sperimentali in corso per pazienti con malattia policisticà renale autosomica dominante (ADPKD).

- *In Europa tolvaptan può essere impiegato solo nella SIAD - a differenza di quanto avviene in U.S.A., dove il farmaco può essere utilizzato anche nelle iponatremie con aumentato volume del ECF (cirrosi, ecc...)*
Tolvaptan: aggiornamento di scheda tecnica

- **In Europa e in Italia** sono stati aggiornati i paragrafi relativi alle avvertenze speciali e alle precauzioni d’impiego, relativamente al rischio di disidratazione, alla epatossicità e all’uso dei diuretici.

- **Non è stato indicato alcun termine temporale** sull’uso del tolvaptan.
Unexplained Hyponatremia: Seek and You Will Find

Ewout J. Hoorn\textsuperscript{a} Daphne Hotho\textsuperscript{b} Robert Jan Hassing\textsuperscript{a} Robert Zietse\textsuperscript{a}

Nephron. Physiology, 2011
Case Report

A 60-year-old Indonesian man was referred for analysis of hyponatremia. His medical history included a lung operation for pneumothorax (1974), hypertension, stroke (2007), and chronic hepatitis C (genotype 2). He had a history of intravenous drug and alcohol use. He had been receiving treatment with peginterferon and ribavirin for chronic hepatitis C. Treatment was discontinued after 12 weeks because tuberculosis was suspected on routine X-ray (fig. 1). However, a pulmonologist considered tuberculosis unlikely on the basis of negative cultures, and absent pulmonary symptoms.
Fig. 1. Two chest X-rays made with approximately a 1-year interval (left during antiviral therapy for hepatitis C, right during our analysis). Both X-rays show an unspecified lesion in the right upper lobe, that appears stable over time, and that was reported to be a ‘fibrotic lesion’.
The pulmonary lesion proved stable over time and was interpreted as ‘fibrotic’ (fig. 1). During antiviral treatment, the hepatologist had noted hyponatremia, and referred the patient (fig. 2). At the time of referral, the patient complained of dizzy spells. He had lost weight, which he ascribed to a poor dietary intake because of problems with his dentures. He had not noticed fever or night sweats. He drank a total of four glasses of coffee, tea or water. He denied the current use of drugs or alcohol. He smoked 10 cigarettes per day (20 pack-years). He had no complaints of chest or abdominal pain, no nausea, vomiting, diarrhea, coughing, hemoptysis or sputum. His only medication was perindopril (4 mg/day) for hypertension. He had a low body mass index (14.8 kg/m²). His blood pressure was 130/85 mm Hg without orthostasis. His other vital signs were normal.
Physical examination was unremarkable: no increased jugular vein, normal pulmonary auscultation, no cardiac murmurs, no hepatosplenomegaly, no ascites, no peripheral edema, and no palpable abdominal masses. His initial laboratory data regarding electrolytes and kidney function are shown in table 2; figure 2 shows the course of serum sodium. Additional notable values included an elevated erythrocyte sedimentation rate (68 mm/h, normal range <20 mm/h), normocytic anemia (hemoglobin 7.9 mmol/l, normal range 8.6–10.5 mmol/l), and mildly elevated transaminases (maximum of one and a half times the upper limit of normal).
<table>
<thead>
<tr>
<th>Parameters</th>
<th>At referral</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Serum values</strong></td>
<td></td>
</tr>
<tr>
<td>Sodium, mmol/l</td>
<td>127</td>
</tr>
<tr>
<td>Potassium, mmol/l</td>
<td>4.3</td>
</tr>
<tr>
<td>Osmolality, mosm/kg</td>
<td>257</td>
</tr>
<tr>
<td>Creatinine, μmol/l</td>
<td>71</td>
</tr>
<tr>
<td>Urea, mmol/l</td>
<td>1.5</td>
</tr>
<tr>
<td>Uric acid, mmol/l</td>
<td>0.4</td>
</tr>
<tr>
<td><strong>Urine values</strong></td>
<td></td>
</tr>
<tr>
<td>Sodium, mmol/l</td>
<td>20</td>
</tr>
<tr>
<td>Potassium, mmol/l</td>
<td>82</td>
</tr>
<tr>
<td>Osmolality, mosm/kg</td>
<td>438</td>
</tr>
<tr>
<td>FE sodium, %</td>
<td>0.07</td>
</tr>
<tr>
<td>FE urea, %</td>
<td>40</td>
</tr>
<tr>
<td>FE uric acid, %</td>
<td>3.7</td>
</tr>
</tbody>
</table>
**Table 1. Diagnostic criteria for SIADH**

<table>
<thead>
<tr>
<th>Essential features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased effective serum osmolality (&lt;275 mosm/kg)</td>
</tr>
<tr>
<td>Urinary osmolality &gt;100 mosm/kg but usually &gt; serum osmolality¹</td>
</tr>
<tr>
<td>Clinical euvolemia</td>
</tr>
<tr>
<td>Urinary sodium &gt;40 mmol/l with normal dietary salt intake</td>
</tr>
<tr>
<td>Normal thyroid and adrenal function</td>
</tr>
<tr>
<td>No recent use of diuretics</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Supplemental features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum uric acid &lt;0.24 mmol/l</td>
</tr>
<tr>
<td>Serum urea &lt;3.6 mmol/l, low normal serum creatinine</td>
</tr>
<tr>
<td>Fractional sodium excretion &gt;1%, fractional urea excretion &gt;55%</td>
</tr>
<tr>
<td>Failure to correct hyponatremia after 0.9% saline infusion</td>
</tr>
<tr>
<td>Correction of hyponatremia through fluid restriction</td>
</tr>
<tr>
<td>Abnormal water-loading test (excretion &lt;80% of a 20 ml/kg water load in 4 h)</td>
</tr>
<tr>
<td>Elevated vasopressin levels despite hypotonicity and clinical euvolemia²</td>
</tr>
</tbody>
</table>
The patient had chronic hyponatremia that was characterized by hypotonicity, a low urine sodium, a very low fractional sodium excretion, and a high urine osmolality (table 2). Our initial differential diagnosis focused on explaining the combination of low urine sodium and high urine osmolality. Causes of hyponatremia that are characterized by this combination include liver cirrhosis.

In summary, liver cirrhosis seemed very unlikely.
This forced us to reconsider the diagnosis. SIADH re-emerged as a possibility. Although one of the essential criteria of SIADH is a urine sodium >40 mmol/l (table 1), this requires a normal dietary sodium intake, which our patient did not have. Therefore, we administered sodium chloride tablets (3 g/day), which increased urinary sodium, but did not treat hyponatremia (table 2; fig. 2).
### Table 2. Laboratory values

<table>
<thead>
<tr>
<th>Parameters</th>
<th>At referral</th>
<th>During sodium supplementation</th>
<th>Reference values</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Serum values</strong></td>
<td></td>
<td></td>
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<tr>
<td>Sodium, mmol/l</td>
<td>127</td>
<td>129</td>
<td>135–145</td>
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<tr>
<td>Potassium, mmol/l</td>
<td>4.3</td>
<td>4.0</td>
<td>3.5–5.0</td>
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<tr>
<td>Osmolality, mosm/kg</td>
<td>257</td>
<td>261</td>
<td>275–300</td>
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<tr>
<td>Creatinine, μmol/l</td>
<td>71</td>
<td>72</td>
<td>65–115</td>
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<tr>
<td>Urea, mmol/l</td>
<td>1.5</td>
<td>2.7</td>
<td>2.5–7.5</td>
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<tr>
<td>Uric acid, mmol/l</td>
<td>0.4</td>
<td>0.3</td>
<td>0.2–0.42</td>
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<tr>
<td><strong>Urine values</strong></td>
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<tr>
<td>Sodium, mmol/l</td>
<td>20</td>
<td>83</td>
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<tr>
<td>Potassium, mmol/l</td>
<td>82</td>
<td>63</td>
<td>–</td>
</tr>
<tr>
<td>Osmolality, mosm/kg</td>
<td>438</td>
<td>446</td>
<td>–</td>
</tr>
<tr>
<td>FE sodium, %</td>
<td>0.07</td>
<td>0.68</td>
<td>–</td>
</tr>
<tr>
<td>FE urea, %</td>
<td>40</td>
<td>53</td>
<td>–</td>
</tr>
<tr>
<td>FE uric acid, %</td>
<td>3.7</td>
<td>7.4</td>
<td>–</td>
</tr>
</tbody>
</table>

FE = Fractional excretion.
**Fig. 2.** ‘NaCl’ means the period of time that the patient received sodium chloride supplementation.
Fig. 3. Computed tomography of the lungs showing an air crescent sign around a soft tissue mass (circles). Also visible are extensive emphysematous lesions, bronchiectasis and pleural widening.

Final diagnosis: SIAD due to pulmonary aspergillosis
Case report - Conclusions

The importance of an extensive analysis as described above is not only that hyponatremia can be an early sign of potentially treatable underlying disease, but also that it is increasingly recognized that chronic hyponatremia is not benign. For example, patients with chronic hyponatremia have attention deficits and gait instability, causing them to fall four times more often than matched controls [28]. In addition, chronic hyponatremia was recently identified as an independent cause of osteoporosis [29].

Hoorn EJ, Nephron. Physiology, 2011
The Bellaria Hospital’s jazz band

Giorgio Frank (trumpet and conductor)

Diego Mazzatenta
Matteo Zoli
Ernesto Pasquini
Vittorio Sciarretta
Marco Faustini Fustini
Antonella Bacci