5° Messaggio PRATICO

Chi e Come Trattare ?

Optimal Strategies for Correcting Serum Sodium Levels

- *The best method for determining an initial rate for hypertonic saline infusion is also controversial*
- *Many authorities recommend using furosemide (20 to 40 mg intravenously) with saline because it promotes free-water excretion and prevents extracellular-fluid volume expansion*. Loop diuretics also increase the rate of increase in the serum sodium level.

$$130 - 120 = 10 \times [0.6 \times 70 = 42] = 420\ mEq$$

Infondere

Fisiologica 3% : *70 - 140 ml/h capaci di > il Na di 1-2 mEq/h*
1 Litro = 513 mEq *140 - 280 ml/h capaci di > il Na di 2-4 mEq/h SE COMA o CONVULSIONI*
25 - 70 ml/h capaci di > il Na di 0.3-1 mEq/h SE SINTOMI SFUMATI

Cio' consente anche di decidere il volume da infondere a seconda del quadro clinico.
correzione non ecceda 12-14 mEq nelle 24 ore = 0.5 mEq/h e 18 mEq/48 ore

- ***L'approccio metodologicamente piu' corretto, è quello di calcolare le MODIFICAZIONI della SODIEMIA indotte dall'INFUSIONE di 1 L di SOLUZIONE IPERTONICA...***

NEJM,2007,356:2064-2072

Come calcolare la quantità di Sodio da infondere ?

- Porsi come OBIETTIVO INIZIALE il raggiungimento di una Sodiemia di 125-130 mEq/L

- Sapendo il contenuto di Na delle due Soluzioni "Fisiologiche"…
  154 mEq/L in quella allo 0.9 gr%
  513 mEq/L in quella al 3 gr %

SI PUO' CALCOLARE QUALE SARA' la VARIAZIONE della SODIEMIA del SOGGETTO INFONDENDO 1 litro della Soluzione al 3% secondo la seguente Formula :

$$\frac{\text{Sodio Infuso} - \text{Sodiemia Paziente}}{\text{TBW (0.6 x Peso Corporeo)} + 1\text{ L}}$$

$$\frac{513 - 120}{(0.6 \times 70) + 1} = 9.1\ \text{mEq/L}$$

FISIOLOGICA al 3% ???

da 500 cc di Fisiologica allo 0.9%

che contengono 4.5 gr di NaCl
sottrarre 110 cc = 1.0 gr.di NaCl
aggiungere 5 fl da 20 mEq di NaCl (1.17g)= 11.7 gr.di NaCl

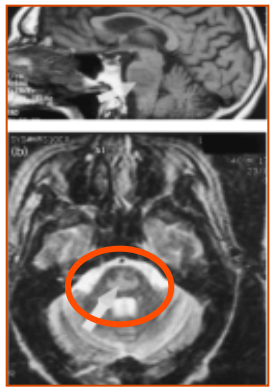
Si ottiene una soluzione di 500 cc con circa 15 grammi di NaCl , cioe' una soluzione al 3% di NaCl

Concentrazione di Na in 1 L delle diverse soluzioni per infusione e.v.

- **Sol salina NaCl 0,9% (fisiologica): 154 mEq/l**
- **Sol ipertonica NaCl 1,8%: 308 mEq/l**
- **Sol ipertonica NaCl 3%: 513 mEql/l**
- **Sol elettrolitica reidratante: 140 Na+ mEql/l**
- **Ringer lattato: 130 mEq/l**
- **Soluzione glucosata 5%: 0 mEq/l**

- **NaCl fl da 10 ml (2 mmol/ml): 20 mEq/l**

Quali devono essere i tempi di infusione



Infondendo quindi
1 L di Fisiologica al 3%
(513 mEq di Na) aumenteremo
la Naemia del Soggetto di **9.1 mEq/L**
(portandola da 120 a 129 mEq/L)

Per EVITARE che la VARIAZIONE sia TROPPO BRUSCA e quindi comporti l'insorgenza della MIELINOLISI PONTINA , OCCORRE che l'INFUSIONE di questi 9.1 mEq di Sodio avvenga in modo graduale :

all'inizio : 0.5 mEq /ora
(9.1/0.5 = *18 ore*)
Il litro di soluzione salina al 3% che contiene 513 mEq, capace di modificare la Sodiemia di 9.1 mEq/l,deve essere infuso *in 18 ore = a 55 ml/h*

successivamente : 1 mEq / ora
(9.1/1.0 = *in 9 ore a 110 ml/h*

MedCalc: Hyponatremia & Hypernatremia

http://www.medcalc.com/sodium.html

Patient's Sodium : mEq/L

Rate of Na Correction : mEq/L/hr

Patient's Weight : kg

Patient is a : man

Calculate using : Adrogue formula

Reimposta

IVF Rate : cc/hr for hours

IV Fluids : 0.9% NaCl (NS)

Correct for:

Fever ?

Insensible Loss ?

6° Messaggio PRATICO

Chi e Come Trattare ?

Hyponatraemia secondary to SIAD * (Europe)

Severe symptoms
(e.g., seizures, respiratory distress, coma)

- Hypertonic saline

Moderate symptoms
(e.g., nausea, confusion, unsteady gait, disorientation)

- Hypertonic saline
- *Tolvaptan*

Mild symptoms or asymptomatic
(e.g., mild neurocognitive symptoms, depression)

- Fluid restriction
- If fluid restriction fails or is not tolerated consider tolvaptan treatment
- Consider tolvaptan as a first choice in particular situations

SAMSCA 15 – 30 mg

Peri A. J Clin Endocrinol Metab, 2013

Elementi per la Diagnosi dell'Iposodiemia

- *Stato del SODIO*

  Perdite Renali

  Perdite ExtraRenali

  Nessuna Perdita

- *Stato del VOLUME*

Determinazione del Na Urinario "Spot"

Segni della Disidratazione

- secchezza della cute che si solleva in pliche e delle Mucose
- ipotomia dei bulbi oculari
- calo ponderale
- ipotensione arteriosa
- emoconcentrazione

Misurazione PVC

(o Ecografia della Vena Cava Inferiore)

Determinazione del Na Urinario "Spot"

6° Messaggio PRATICO

ZONA "GRIGIA fra 20 e 40 mEq

Na U > a 40 mEq

- *CON SEGNI di DISIDRATAZIONE* :
  Iposodiemia da Perdita Renale
  CSW (S.Cerebrale da Perdita di Sali) ,
  Addison Acuto
- *SENZA SEGNI di DISIDRATAZIONE* :
  SIAD, IPOTIROIDISMO
  GRAVE, DEFICIT di MINERALCORTICOIDI
  (+IperK), INSUFFICIENZA RENALE CRONICA
  Polidipsia, Potomania, Dolore , Polmoniti ,
  Insufficienza Respiratoria Acuta , Ventilazione
  a Pressione Positiva

Na U < a 20 mEq

- *CON SEGNI di DISIDRATAZIONE* :
  Iposodiemia da Perdita Extra Renale
  (Diarrea,Vomito …
  Compartimentalizzazione)
- *CON EDEMI*
  Cirrosi ,
  Scompenso Congestizio ,
  S. Nefrosica

Sinossi per il Management dell'Iposodiemia

IPOSODIEMIA

Anamnesi , Storia Clinica

In "assenza" di Elementi Anamnestici

IPOSODIEMIA da DILUIZIONE
Cirrosi,Scompenso,Sindrome Nefrosica

IPOSODIEMIA da DISIDRATAZIONE
Vomito,Diarrea,Diuretici ecc.

Sodio Urinario

> 20 - 40 mEq/L

Misurazione PVC o Ecografia della Cava I.

< 6 cm H_2O

> 6 cm H_2O

Ci si deve preoccupare delle Alterazioni dell'H_2O

Restrizione Idrica nel primo caso

Idratazione nel secondo

IPONa IPOVOLEMICA
Cerebral Salt Wasting
Rimpiazzo di Liquidi e Trattamento dell'IpoNa+

IPONa EUVOLEMICA
SIAD
Restrizione Idrica + Trattamento dell'IpoNa+

SENZA MAI DIMENTICARSI dell'IPOSURRENALISMO

Mai come in questo campo
(MA VALE comunque SEMPRE…!!!)
occorre ricordare una *massima* di Socrate :

SE PENSATE che la CONOSCENZA COSTI…

NON AVETE IDEA di QUANTO MAGGIORE SIA
il COSTO dell'IGNORANZA… !!!

ADESSO
FATTI,
NON PAROLE!

Soluzioni Reidratanti ed Idro-Elettrolitiche

"Alcalinizzanti"	pH	Osm. mOsm/l	Na mEq/l	K mEq/l	Cl mEq/l	HCO3
Elettrolitica Reidratante 1	**5.5-7.0**	**312**	**120**	**3.6**	**104**	**52**
2	**5.0-7.0**	**294**	**133**	**14**	**99**	**48**
3	**5.0-7.0**	**307**	**140**	**10**	**103**	**47**
Altre						
Elettrolitica Bilanciata con Gluc.	**5.0-7.0**	**390**	**40**	**13**	**40**	**16**
Ringer	**5.0-7.0**	**309**	**147**	**4**	**155**	**-**

La Problematica Clinica di Maggior Interesse e di Maggior Difficolta' Decisionale è senz'altro quella di Identificare le IPOSODIEMIE "NORMOVOLEMICHE" e di DIFFERENZIARLE

SIADH
(S. da inappropriata Antidiuresi)
CSW
(cerebral salt wasting)

Ipopituitarismo misconosciuto
Insufficenza Surrenalica del Paz. Critico

Insufficenza Surrenalica Cronica
(Deficit di MineralCorticoidi)
Ipotiroidismo Grave
Insufficienza renale cronica.
Polidipsia, Potomania, Dolore ,
Polmoniti , Insufficienza Respiratoria Acuta,
Ventilazione a Pressione Positiva

The Syndrome of Inappropriate Antidiuresis

Osmolarita' Plasmatica = 280 - 300 mOsm/kg

P osm = 2x [Na] pl + glicemia (mg/dl) / 18
+ (azotemia (mg/dl)/2.8)

2 x 124 + 84/18 + (43/2.8) = 253 mOsm/kg
(268)

Osmolalità urinaria (U-Osm) 400 - 500 mOsm/Kg

(da 50 a 1400 mOsm/Kg a seconda dell'idratazione)

Il peso specifico e l'osmolalità urinaria hanno tra loro una buona correlazione, *con un rapporto di 1 a 35, dopo il mille*.

Es.	1000	0
	1003	105
	1010	350
	1020	700

NEJM,2007,356:2064-2072

Cause di inappropriata secrezione di ADH (SIAD)

NEOPLASIE

Polmone
- Small cell
- Mesotelioma
- Orofaringe

Tratto gastroenterico
- Stomaco
- Duodeno
- Pancreas

Tratto Genito-urinario
- Uretere, vescica
- Prostata
- Endometrio

Altre:
- Timomi
- Linfomi
- Sarcomi

MALATTIE POLMONARI

Infezioni:
- Batteriche e Virali , Ascessi ,
- Tubercolosi
- Micosi

Asma

Fibrosi cistica

Insufficienza respiratoria con ventilazione a pressione positiva

DISORDINI del SNC

Patologia vascolare / espansiva
- Ematoma subdurale
- Emorragia subaracniodea
- Stroke
- Tumori cerebrali
- Traumi cerebrali
- Idrocefalo
- Trombosi dei seni cavernosi

Infezioni:
- Encefaliti
- Meningiti
- Ascessi cerebrali
- Aids

Altro:
- Sclerosi multipla
- S. di Guillain-Barré
- S. di Shy Drager
- Porfiria acuta intermittente

DA DIFFERENZIARE con la CSW

ALTRE CAUSE

Nausea severa

Dolore intenso

Stato post-operatorio

Esercizi fisici prolungati (maratoneti…)

Forma genetica (sindrome nefrogenica da inappropriata antidiuresi)

Forma idiopatica

Farmaci

Modificata da Ellison and Berl, NEMJ, 2007

Cause Farmacologiche di inappropriata antidiuresi (SIAD)

Farmaci che stimolano il rilascio o potenziano l'azione di AVP

- **Antidepressivi :**
  - triciclici *(amitriptilina, desipramina, protriptilina)*
  - inibitori selettivi del re-uptake della serotonina
  - inibitori delle monoamine-ossidasi
- **Antipsicotici :**
  - fenotiazine *(tioridazina, trifluoperazina)*
  - butirrofenoni *(aloperidolo)*
  - aripiprazolo
  - clozapina ? *(rare segnalazioni in passato; dati più recenti indicano,viceversa, la possibilità del miglioramento dell'iponatremia nel paziente schizofrenico con polidipsia psicogena)*
- **Antiepilettici**
  - carbamazepina, oxcarbazepina
  - valproato di sodio
  - lamotrigine
- **Agenti antineoplastici**
  - vincristina, vinblastina *(raramente)*
  - cisplatino *(frequentemente)*, carboplatino *(raramente)*
  - ciclofosfamide i.v., melfalan, ifosfamide
  - methotrexate
  - interferone alfa e gamma
  - levamisole
  - pentostatina
  - anticorpi monoclonali
- **Antidiabetici**
  - clorpropamide.
  - tolbutamide
  - rosiglitazone
- **Antibiotici:**
  - trimetoprim-sulfametossazolo;
  - ciprofloxacina,
  - cefoperazone/sulbactam,
  - rifabutin
- **Miscellanea**
  - anti-infiammatori non steroidei *(inibitori della sintesi di prostaglandine)*
  - oppiacei
  - tramadolo
  - nicotina
  - clofibrato
  - ACE-inibitori
  - amiodarone, lorcainide, propafenone
  - amlodipina
  - MDMA *(ecstasy)*
  - Teofillina
  - Imatinib
  - sibutramina
  - inibitori della pompa protonica *(omeprazolo)*

Farmaci analoghi della AVP

- desmopressina
- ossitocina
- vasopressina

SIAD
ECF espanso

Encefaliti
Meningiti
ESA
Ascessi cerebrali
Stroke
Ematomi
Neoplasie
Chirurgia SNC

CSW
ECF contratto

It has been postulated that CSW is a centrally mediated process, possibly via secretion of natruretic peptides or disrupted sympathetic neural input to the proximal tubules Scattered case reports in the pediatric population demonstrated suppressed plasma renin activity and plasma aldosterone concentration in CSW, while plasma aldosterone concentration usually remained normal or high in SIADH

Dati di Laboratorio	*SIAD*	*Cerebral Salt Wasting*
Sodiemia	*RIDOTTA*	
Sodiuria	*> 40 mmol/L*	
Osmolarita' Plasmatica	*RIDOTTA*	
Osmolarita' Urinaria	*INAPPROPRIATAMENTE ELEVATA*	

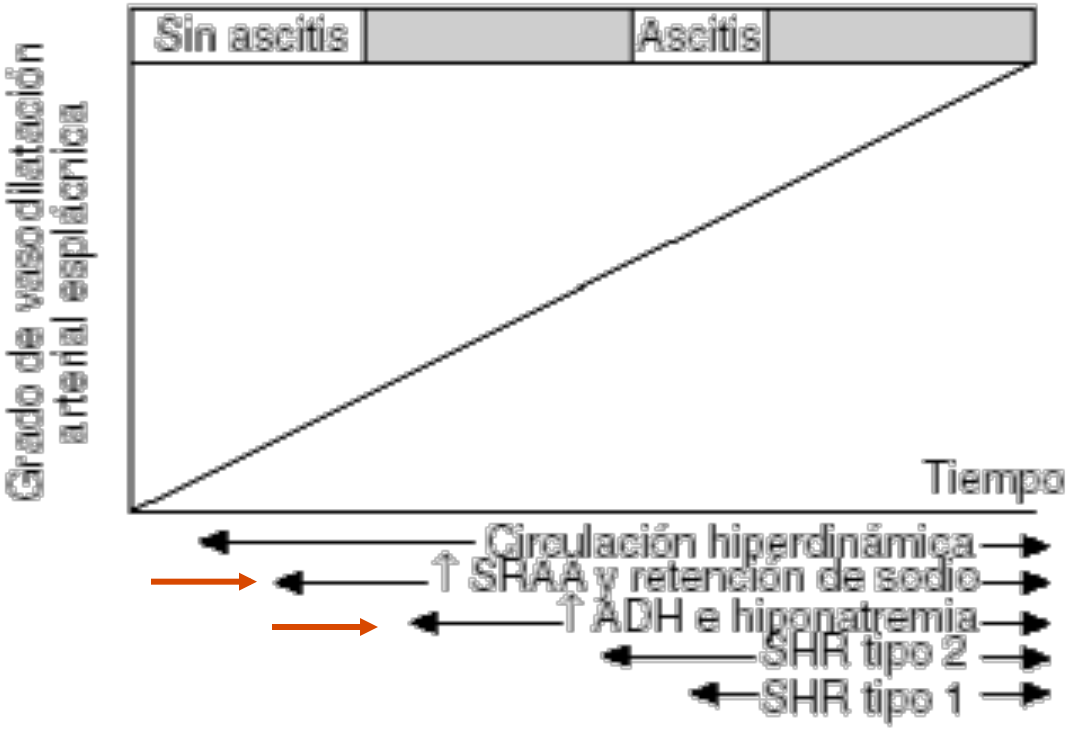
Successful Treatment of Adult Cerebral Salt Wasting With Fludrocortisone
Arch Intern Med. 2008;168(3):325-326.

Opzioni Terapeutiche per la SIAD

- *Demeclociclina (Ledermicina) :*
  interactúa con la AVP en el riñón y *produce una diabetes insípida nefrogénica reversible*.
  Debe administrarse a dosis de *600-1.200 mg/día*, teniendo en cuenta que el efecto es dependiente de la dosis, desapareciendo tras la retirada del fármaco.
  Se debe vigilar la función renal y su *utilidad en hiponatremias crónicas es limitada porque tarda algunas semanas en ejercer su efecto*.
  Existe dificultad de disponer del fármaco en nuestro país.
- *Diuréticos de asa* :
  si la restricción hídrica no es suficiente. De elección es la *furosemida* en dosis de *40-80 mg / día* y deben administrarse suplementos de magnesio y potasio.
- *Fludrocortisone (Florinef)*
  0.05- 0.2mg P.O 2 times/day
- *Carbonato de litio :*
  interactúa con la AVP en el riñón *produciendo una diabetes insípida nefrogénica*, aunque con más efectos colaterales que la demeclociclina.
  Sólo es efectivo en el 20% de los pacientes. No está aconsejado su uso por los efectos tóxicos adyuvantes.
- *Análogos de la vasopresina:*
  poseen función antagonista *inhibiendo competitivamente la acción de la vasopresina a nivel del receptor, provocando un aumento en la excreción renal del agua*.
  Existen varios compuestos en fase experimental

Endocrinol Nutr. 2007 ; 54:23-33.

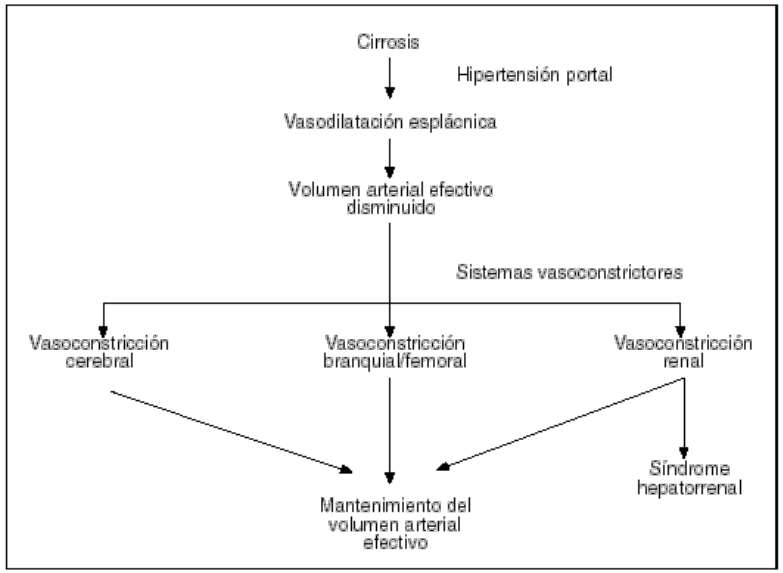
♪
내분비내과♪
임상실습학생♪
이인경♪



Esquema que muestra la evolución clínica en el tiempo de los parámetros hemodinámicos y hormonales de los pacientes cirróticos.

SRAA: sistema renina-angiotensina-aldosterona;
ADH: hormona antidiurética;
SHR: síndrome hepatorrenal.

Hipótesis del infrallenado arterial y activación de sistema de vasoconstrictores de manera compensadora en diferentes regiones



Gastroenterol Hepatol. 2004 ; 27 (Supl 4) :26-39.

Approccio Pragmatico-Laboratoristico

Table 4: Possible causes of hyponatremia according to acid-base status and serum potassium level

Acid base status	Potassium status; cause: Hyperkalemia (potassium level > 5.0 mmol/L)	Normokalemia (potassium level 3.5–5.0 mmol/L)	Hypokalemia (potassium level < 3.5 mmol/L)
Metabolic acidosis	Renal failure Adrenal insufficiency		Diarrhea
Metabolic alkalosis			Vomiting Diuretic therapy
Normal pH (7.35–7.45)		SIADH Compulsive polydipsia Cortisol deficiency Hypothyroidism	

Hyponatremia of Long or Unclear Duration

- *The treatment of hyponatremia with an unclear duration and nonspecific symptoms or signs (e.g., headache or lethargy) is particularly challenging.*
- *Some reports suggest a high risk if patients are not treated aggressively;*
  Ayus JC, Arieff AI. Chronic hyponatremic encephalopathy in postmenopausal women: association of therapies with morbidity and mortality. JAMA 1999;281:2299-2304
- *Others suggest that rapid correction increases morbidity or mortality.*
  Sterns RH. The treatment of hyponatremia: first, do no harm. Am J Med 1990;88:557-560
- *Unlike patients with acute hyponatremia, those with hyponatremia of longer duration have a documented risk of osmotic demyelination if the serum sodium level is corrected by more than 12 mmol per liter over a period of 24 hours. This disorder, which includes both **central pontine and extrapontine myelinolysis**, begins with lethargy and affective changes (generally after initial improvement of neurologic symptoms with treatment), followed by mutism or dysarthria, spastic quadriparesis, and pseudobulbar palsy. Case series and experimental data indicate that this complication may result from rapid correction of hyponatremia that has been present for more than 48 hours.*

NEJM,2007,356:2064-2072

Acute Symptomatic Hyponatremia

- *The most important factors dictating the management of SIAD are the severity of the hyponatremia, its duration, and the presence or absence of symptoms*
- *For symptomatic patients* with *severe hyponatremia* known to have *developed within 48 hours*, clinical experience suggests that *rapid treatment is warranted*. An increase in serum sodium levels of less than 10 mmol o mEq/per liter is usually sufficient to reduce the symptoms and prevent complications
  The goal is to raise the serum sodium level by 0.5 to 2 mmol o mEq/per liter per hour by infusing 3% saline; these recommended rates are guided by data from case series, in the absence of data from randomized trials, but they are widely accepted.
- Many experts believe that *the magnitude of correction during the first 24 hours* of treatment should be *no more than 8 to 12 mmol o mEq/ per liter*, and *during the first 48 hours no more than 18 to 25 mmol o mEq/per liter*, even when the hyponatremia is acute

NEJM,2007,356:2064-2072

Farmaci e SIAD

- Desmopressina
- Ossitocina
- Derivati Oppioidi
- Nicotina
- Clofibrato
- Lisinopril
- Vin
- Cicl
- Esc
- Eparina
- Fenotiazine
- Triciclici
- SSRI
- Carbamazepina
- Inibitori delle

UFH is reported to decrease plasma and urinary aldosterone concentrations by directly decreasing aldosterone production.[1] The mechanism is controversial, but may be related to both a decrease in the direct synthesis of aldosterone within the zona glomerulosa, as well as a decrease in the number of angiotensin-II receptors within the zona glomerulosa.[1] As a result of aldosterone inhibition, hyponatremia and hyperkalemia may be detected within 1–3 days of the initiation of UFH. This was the case in our pa-

Mortality after Hospitalization with Mild, Moderate, and Severe Hyponatremia

Characteristics of Hospitalized Individuals with and without Hyponatremia							
	Sodium Concentration (mEq/L)						*P* Value
	135 - 144 (82,377)	< 135 (12,562)	130 - 134 (10,469)	125 - 129 (1591)	120 - 124 (353)	< 120 (149)	
Mean age ± SD, years	63.1	67.0	66.0	71.5	72.8	73.1	< .001
Female (%)	51.1	51.2	50.8	51.4	55.5	66.4	.83
Major diagnostic category (%)							
Circulatory system: surgical	16.7	17.8	18.7	15.0	7.9	4.0	.002
Circulatory system: medical	9.0	8.2	7.9	10.1	9.9	10.1	.006
Musculoskeletal system: surgical	12.2	8.3	8.9	5.8	3.7	2.0	< .001
Nervous system: surgical	5.0	3.3	3.5	2.3	1.7	0.7	< .001
Nervous system: medical	5.7	4.2	3.9	6.1	5.7	1.3	< .001
Respiratory system: medical	5.1	7.5	6.8	10.7	13.0	10.7	< .001

Am J Med **2009**, 122 , 9 : 857-865

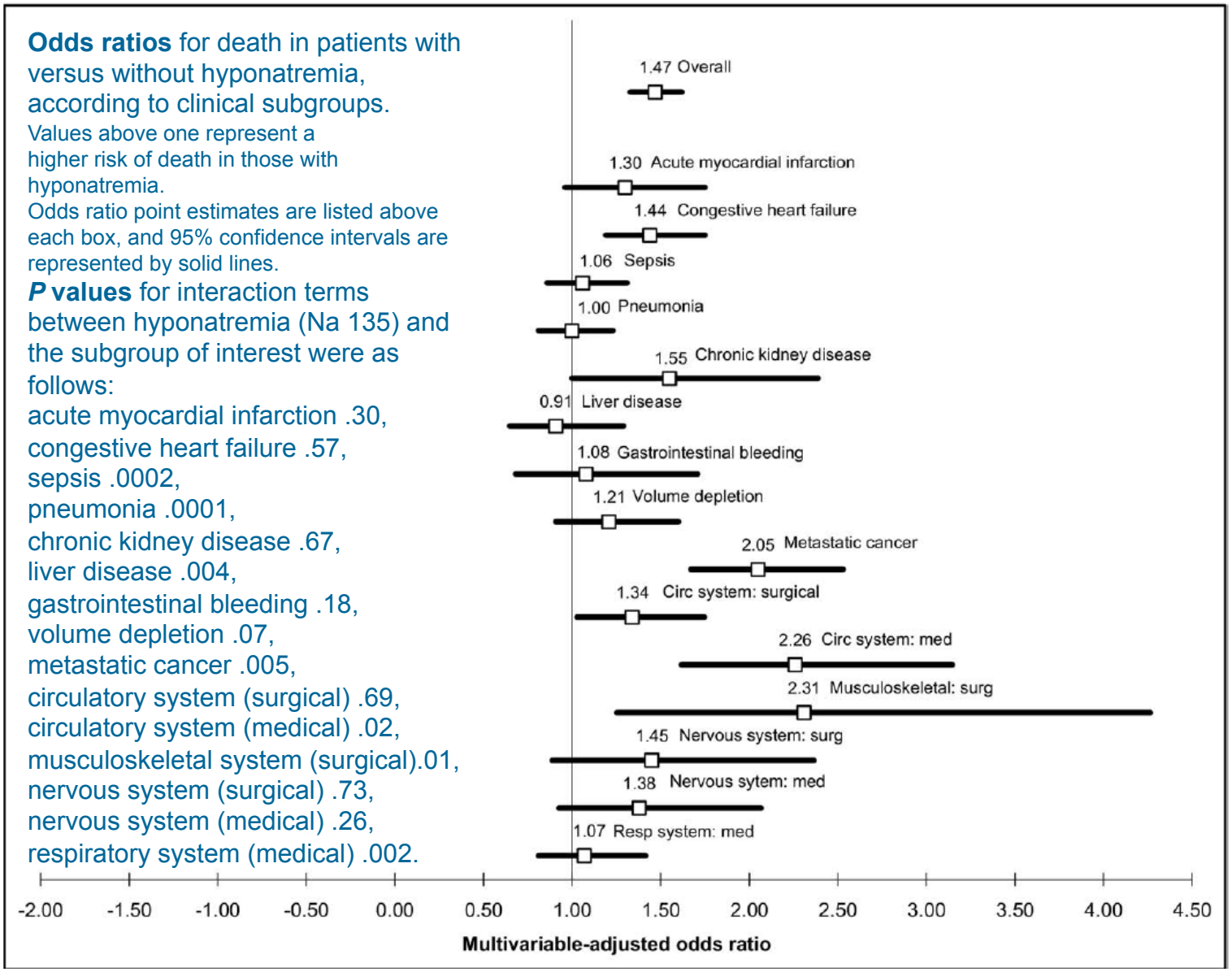
Mortality after Hospitalization with Mild, Moderate, and Severe Hyponatremia

Mortality in Patients with and without Hyponatremia						
	Sodium Concentration (mEq/L)					
	135-144 (82,377)	< 135 (12,562)	130-134 (10,469)	125-129 (1591)	120-124 (353)	< 120 (149)
Crude in-hospital mortality (%)	2.4	5.4	4.8	8.9	8.5	6.7
Crude 1-year mortality (%)	11.7	21.4	19.8	28.5	33.1	22.2
Crude 5-year mortality (%)	42.3	54.8	53.6	61.0	60.6	59.7

Am J Med 2009, 122 , 9 : 857-865

Mortality after Hospitalization with Mild, Moderate, and Severe Hyponatremia

Odds ratios for death in patients with versus without hyponatremia, according to clinical subgroups.
Values above one represent a higher risk of death in those with hyponatremia.
Odds ratio point estimates are listed above each box, and 95% confidence intervals are represented by solid lines.
***P* values** for interaction terms between hyponatremia (Na 135) and the subgroup of interest were as follows:
acute myocardial infarction .30,
congestive heart failure .57,
sepsis .0002,
pneumonia .0001,
chronic kidney disease .67,
liver disease .004,
gastrointestinal bleeding .18,
volume depletion .07,
metastatic cancer .005,
circulatory system (surgical) .69,
circulatory system (medical) .02,
musculoskeletal system (surgical).01,
nervous system (surgical) .73,
nervous system (medical) .26,
respiratory system (medical) .002.



Am J Med **2009**, 122 , 9 : 857-865

Mortality after Hospitalization with Mild, Moderate, and Severe Hyponatremia

Table 4 In-hospital Mortality in Selected Subgroups of Patients with and without Hyponatremia

	Sodium Concentration (mEq/L)					
Condition	Total n (% Mortality)	135-144	130-134	125-129	120-124	<120
Sepsis	2632 (25%)	1 (ref)	1.00 (0.79-1.26)	1.36 (0.88-2.11)	1.65 (0.64-4.24)	0.38 (0.04-3.21)
Pneumonia	4761 (16%)	1 (ref)	0.98 (0.78-1.23)	1.09 (0.71-1.69)	1.70 (0.71-4.08)	—
Liver disease	1462 (16%)	1 (ref)	0.73 (0.48-1.10)	1.32 (0.71-2.45)	2.63 (1.00-6.94)	0.56 (0.07-4.83)
Metastatic cancer	6612 (7%)	1 (ref)	1.78 (1.41-2.24)	3.25 (2.20-4.81)	3.43 (1.61-7.33)	4.80 (1.27-18.17)
Circulatory system (medical)	8421 (3%)	1 (ref)	2.19 (1.52-3.17)	2.73 (1.41-5.28)	1.35 (0.26-6.90)	2.97 (0.35-25.16)
Musculoskeletal system (surgical)	11,079 (0.6%)	1 (ref)	2.10 (1.08-4.07)	4.60 (1.35-15.73)	—	—
Respiratory system (medical)	5153 (7%)	1 (ref)	1.03 (0.75-1.40)	1.38 (0.81-2.35)	0.82 (0.25-2.66)	0.60 (0.07-5.35)

Sodium values corrected for admission glucose. Values are shown for subgroups of patients in whom statistically significant interaction was detected for the association between hyponatremia (Na <135) and in-hospital mortality. *P* values for interaction terms were: sepsis .0002, pneumonia <.0001, liver disease .004, metastatic cancer .005, circulatory system (medical) .02, musculoskeletal system (surgical) .01, respiratory system (medical) .002.

Am J Med **2009**, 122 , 9 : 857-865

Incidence

- *Hyponatremia* is the most common electrolyte abnormality seen *in general hospital patients*, with an *incidence of about 1%* in the US.
- In a study of blood samples taken from approximately 30 000 patients in a Papua New Guinea hospital over 23 months, 1% of the samples showed **hyponatremia**. In this population, **hyponatremia** was more common *in medical (38%) and pediatric (35%) patients*

In this study, over one-quarter of the affected patients had severe hyponatremia (serum sodium level <120 mEq/L) .

The clinical conditions thought to have caused **hyponatremia**, in descending order of importance, included
- **diarrhea and vomiting** (29%),
- **renal failure** (12%),
- **CNS infections**
- **trauma** (12%), and
- **pulmonary infections** (9%).

- **In a study of 184 episodes** of **severe hyponatremia** (serum sodium level 120 mEq/L) in several hospitals in the US and UK, *21% of patients had **acute hyponatremia** (3 days' duration), and 79% of patients had **chronic hyponatremia** (>3 days' duration).*

The causes of **hyponatremia** included
- **overhydration** (21%), often due to chemotherapy or following surgery;
- **liver failure** (9%);
- **renal failure** (9%);
- **drugs** (9%);
- **SIADH** (8%);
- **cardiac failure** (7%); and
- **multiple factors** (22%).

Clouding of consciousness affected 76% of patients with **hyponatremia**; 11% experienced coma. **The incidence of coma** was more strongly **associated with acute** rather than chronic **hyponatremia**
Other hyponatremic complications included chronic signs (including hemiparesis; 6.0%), seizures (3.3%), tremor (1.0%), hallucinations (0.5%), intellectual impairment without clouding of consciousness (0.5%), and acute psychosis (0.5%).
In all, 8 patients (4.3%) died as a direct result of their electrolyte disturbance (acute **hyponatremia**, 1 patient; chronic **hyponatremia**, 7 patients).

The Annals of Pharmacotherapy: 2003 , 37, 1, : 1694-1702

Alterazioni del SODIO

Possono quindi essere un
disordine dell'Acqua
e non una carenza/eccesso del Sale

e quindi possono riflettere
Modificazioni del Volume Plasmatico e
del Volume Arterioso Efficace

Vasopressin-Receptor Antagonist Therapy

- *A more recent option for treating SIAD is Conivaptan (Vaprisol, Astellas Pharma), a vasopressin-receptor antagonist approved by the Food and Drug Administration in 2005 for intravenous treatment of euvolemic hyponatremia and approved in 2007 for intravenous treatment of*

Table 3. Vasopressin-Receptor Antagonists.*

Drug	Dose of Drug	Vasopressin Receptor	Route of Administration	Urinary Volume	Urinary Osmolality	Sodium Excretion over 24 hr
Conivaptan (Vaprisol, Astellas Pharma)†	20–40 mg daily	V_{1A} and V_2	Intravenous	Increased	Decreased	No change

During the week after discontinuation of tolvaptan on day 30, hyponatremia recurred *NEJM, 2006,355:2099-2112*

* Data are adapted from Lee et al.[35]
† Conivaptan was approved for clinical use in 2005 by the Food and Drug Administration.

moderate-to-severe hyponatremia and symptoms but not seizures, delirium, or coma, which would warrant the use of hypertonic saline. Infusion-site reactions are common (occurring in as many as 50% of patients, according to the package insert for the drug), and its metabolism by the 3A4 isoform of cytochrome P450 (CYP3A4) can result in drug interactions

NEJM,2007,356:2064-2072

Cause di inappropriata secrezione di ADH (SIAD)

- ***Neoplasie maligne***
  a) *Carcinoma bronchiale*, pancreatico, uretrale, prostatico, vescicale.
  b) Linfoma e leucemia
  c) Timoma e mesotelioma

- ***Disordini del SNC***
  a) Traumi , Infezioni
  b) Stroke , Emorragie
  c) Tumori , Psicosi Acuta
  d) Porfiria
  Da DIFFERENZIARE con la CWS

- ***Disordini polmonari***
  a) TBC
  b) Polmonite
  c) Ventilatori a pressione positiva

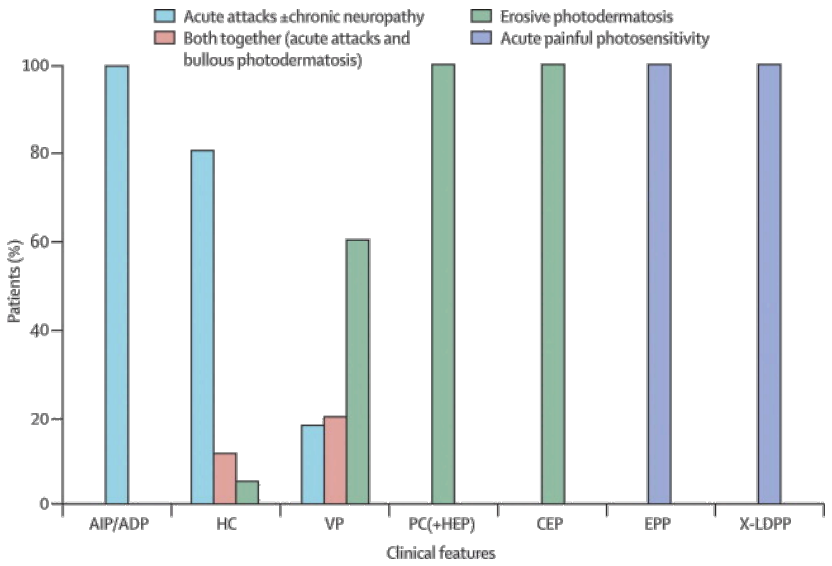
- ***Molti farmaci***
  inducono secrezione di ADH

- ***Decorso post-operatorio***

- ***Dolore Intenso,***
- ***Beer potomania***

Acute porphyrias (2

Clinical features of porphyrias



AIP = acute intermittent porphyria.
ADP = 5-aminolaevulinic acid (ALA) dehydratase porphyria.
HC = hereditary coproporphyria.
VP = variegate porphyria.
PCT = familial and sporadic porphyria cutanea tarda.
HEP = hepatoerythropoietic porphyria.
CEP =congenital erythropoietic porphyria.
EPP = erythropoietic protoporphyria.
X-LDPP = X-linked dominant erythropoietic protoporphyria.

Presentation

- Porphyric attacks begin with a **prodromic phase** including **minor behavioural changes** such as **anxiety, restlessness,** and **insomnia**.
- Most people with **acute attacks present** with **severe abdominal pain**, but this pain might also be felt in the back or thighs.
- **Nausea**, **vomiting**, and **constipation** are common.
- **Tachycardia**, **excess sweating**, and **hypertension**, which are symptoms of increased sympathetic activity, are often present.
- **Physical examination shows no abnormalities and X-ray analysis is normal or shows mild ileus of the bowel in most cases**.
- During acute attacks, patients frequently become dehydrated and electrolyte imbalanced.
- ***Hyponatraemia attributable to inappropriate antidiuretic hormone secretion syndrome develops in 40% of cases, and when severe can lead to convulsions***.
- **Seizures** in acute attacks can develop because of hyponatraemia or hypomagnesaemia or as a manifestation of porphyria.
- Occasionally, **excretion of red or dark-coloured urine** helps physicians with their investigations.

The Lancet, 375, 9718: 924 - 937, 13 March 2010

SIAD
ECF espanso

Encefaliti
Meningiti
ESA
Ascessi cerebrali
Stroke
Ematomi
Neoplasie
Chirurgia SNC

CSW
ECF contratto

Dati di Laboratorio	SIAD	Cerebral Salt Wasting
Sodiemia	RIDOTTA	
Sodiuria	> 40 mmol/L	
Osmolarita' Plasmatica	RIDOTTA	
Osmolarita' Urinaria	INAPPROPRIATAMENTE ELEVATA	

IPOSODIEMIA "NORMO"VOLEMICA

(Non Edemi-Non Ascite)

El síndrome pierde-sal cerebral (SPSC) se define como ***la pérdida renal de sodio debida a enfermedad intracraneal que ocasiona hiponatremia y disminución del volumen extracelular***.

Se ha descrito en **pacientes neuroquirúrgicos** especialmente en aquellos que presentan **hemorragia subaracnoidea**, en quienes su aparición aumenta el riesgo de **vasospasmo sintomático**.

Aunque menos frecuente, en pacientes con **meningoencefalitis tuberculosa y meningitis carcinomatosa, y meningoencefalitis de etiología viral y infecciones del SNC**

El mecanismo por el cual un trastorno intracraneal produce SPSC no se conoce bien.

La hipótesis fisiopatológica más aceptada implica **la disrupción de la inervación nerviosa del riñón, así como la elaboración de un factor natriurético que ocasionaría una pérdida de sodio en el túbulo contorneado distal**, con la consiguiente disminución del volumen extracelular

Med Clin (Barc). 2007;128:278-9.

Sodio Urinario

> 20 – 40 mEq/L

In an emergency department study, ultrasound measurements of the inferior vena cava correlated with central venous pressure.

Ann Emerg Med 2010 Mar 55:290

< 6 cm H_2O

Con Segni di Disidratazione

> 6 cm H_2O

Senza Segni di Disidratazione

IPONa IPOVOLEMICA

Cerebral Salt Wasting

IPONa EUVOLEMICA

SIADH

RIMPIAZZO dei LIQUIDI

RESTRIZIONE dei LIQUIDI