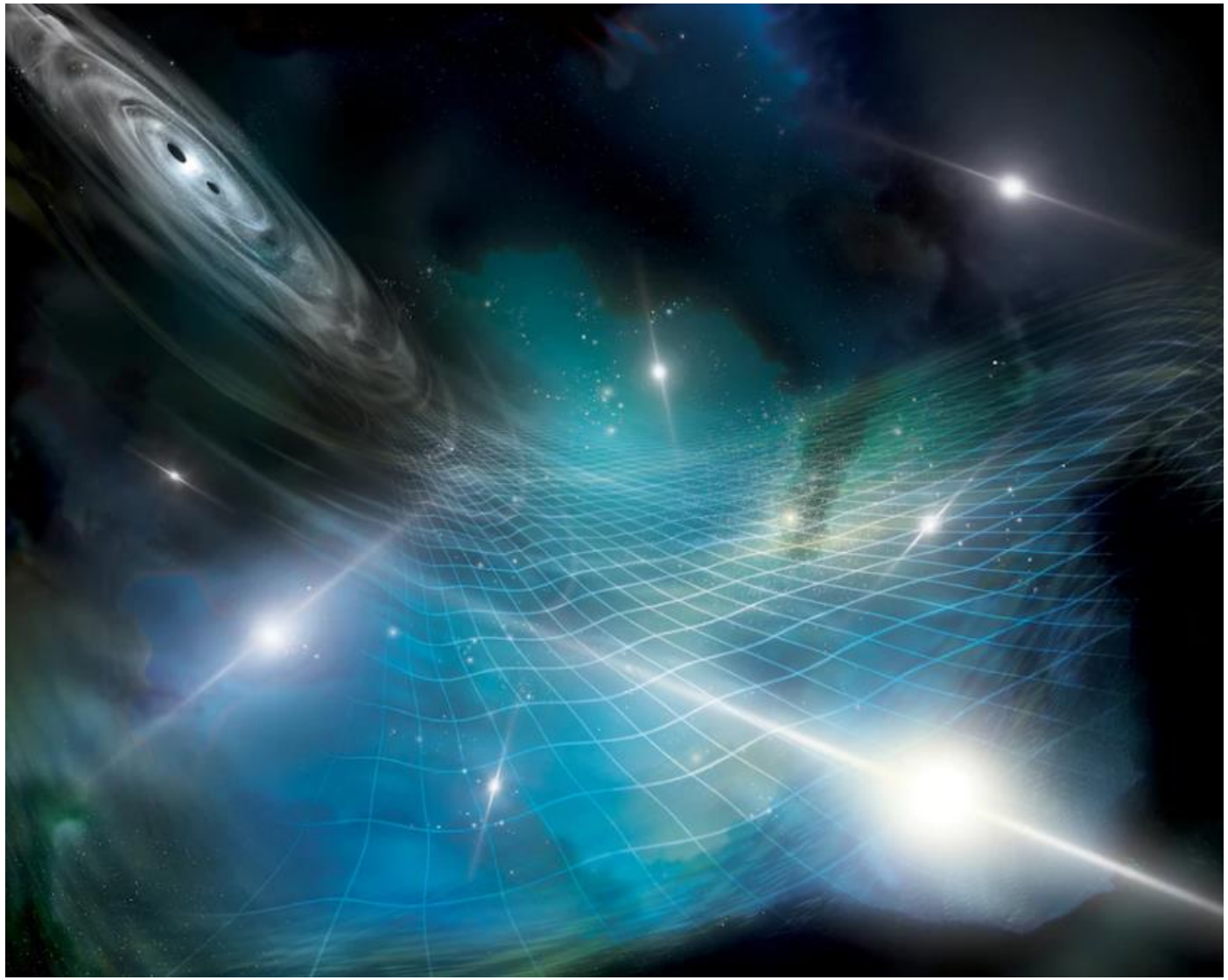
The plasma sodium is determined by spacetime.

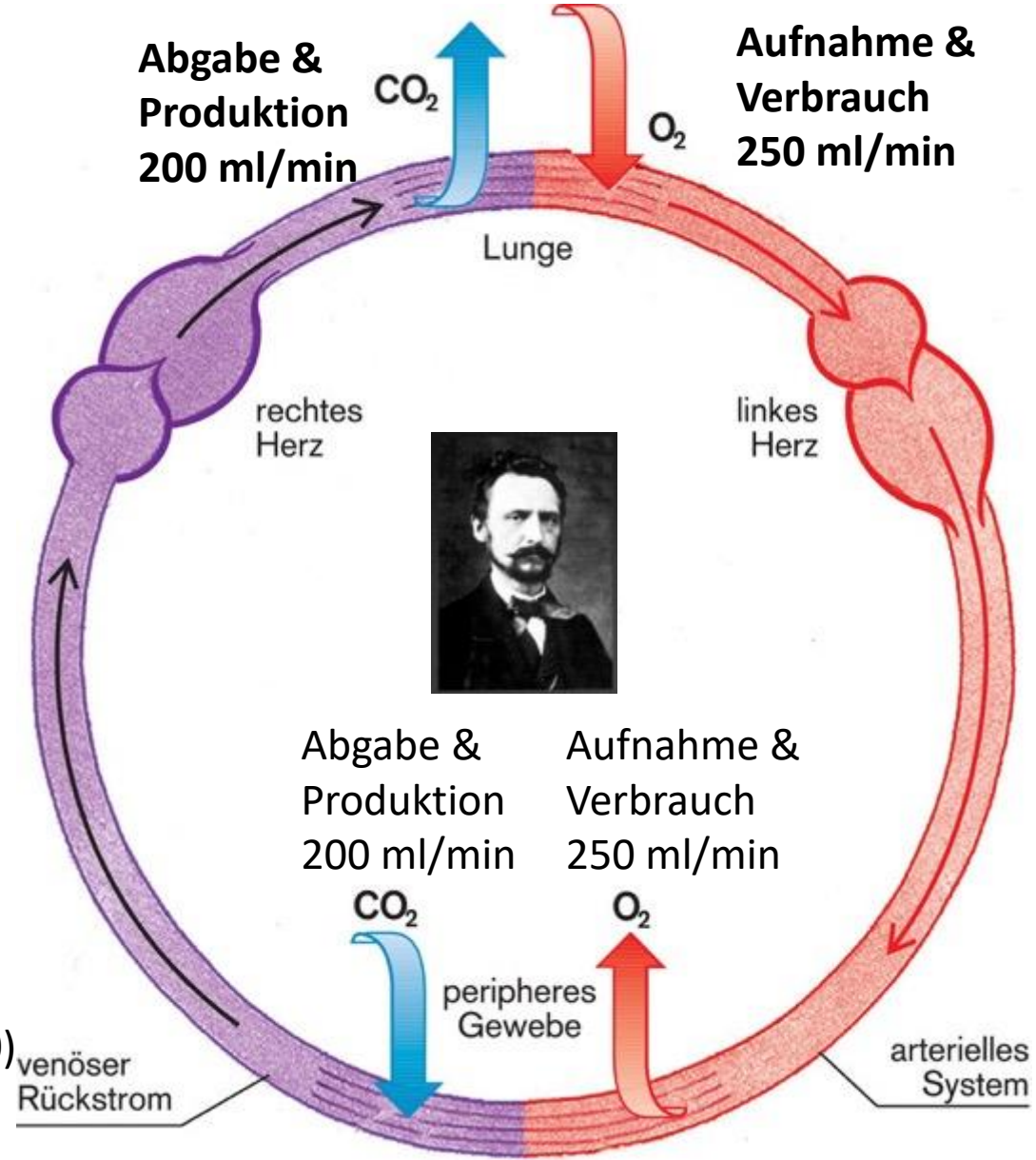


31-year-old man comes to ER in coma. 10-day history of nausea and vomiting. Body builder, but drugs are denied by wife. BP 110/76 mm Hg, HR 100/min, RR 20/min. Thrashes around after sternal rub.

Arterial blood gases comprised pH 7.49, $PaCO_2$ 18, PaO_2 122 (both mm Hg), HCO_3 14 mmol/L.

- H^+ ion concentration in nmol/L?
- Alveolar PAO_2 and ventilation in L/min?
- Acid-base disturbance?
- Compensation adequate?

Circulation and Fick‘s Principle



Inhalt
150 ml O_2/L
Blut

540 ml CO_2/L
Blut

Inhalt
200 ml O_2/L
Blut

500 ml CO_2/L
Blut

$HZV = CO_2$ Abgabe

(Ven 540 – Art 500)

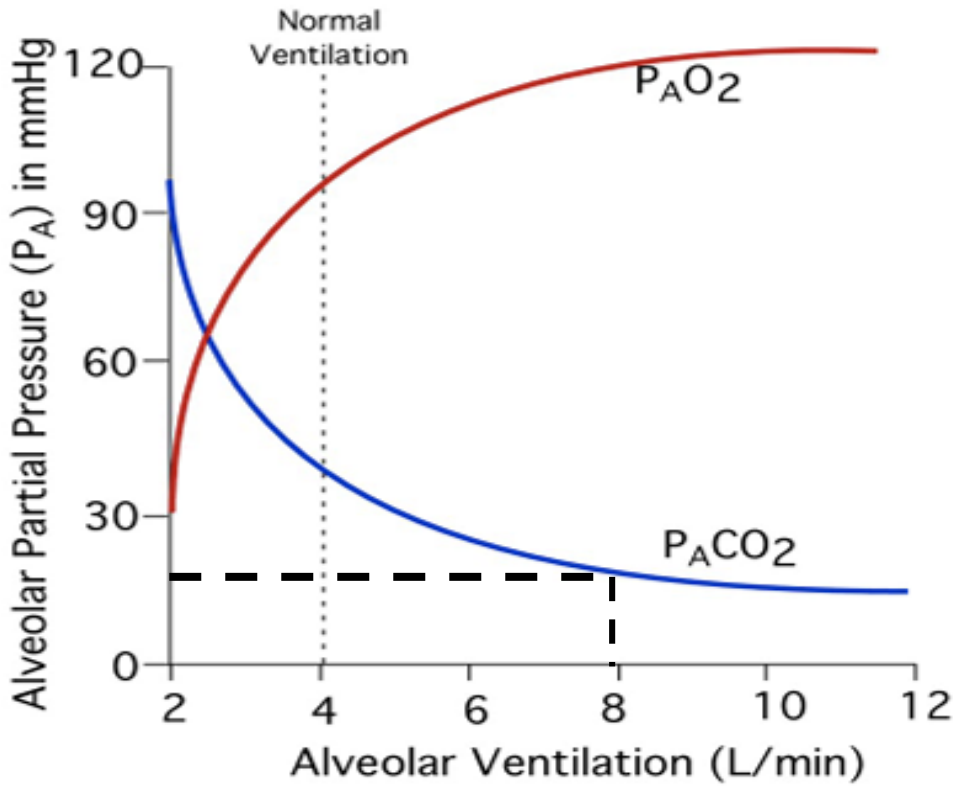
$HZV = O_2$ Aufnahme

(Art 200 – Ven 150)

I have no idea why this patient had a respiratory alkalosis. Presumably, it was centrally driven.

$H = (24 \times PCO_2)/HCO_3$

$PAO_2 = 150\text{-}PaCO_2/0.8$

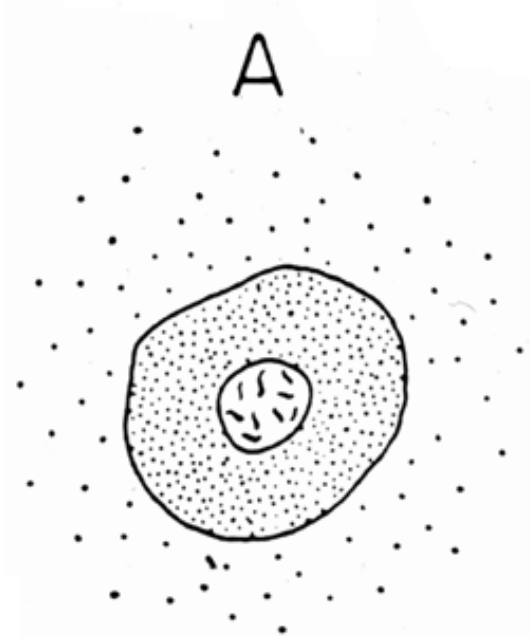


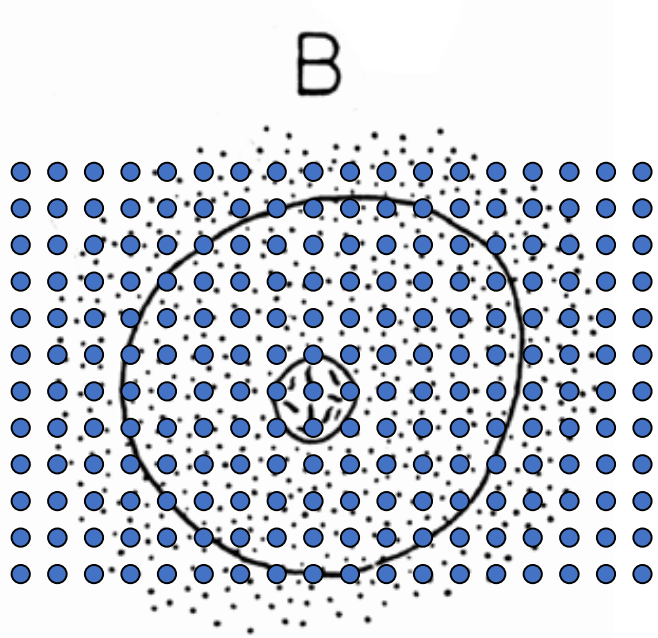
Well-tanned skin, dark palmar creases, and gingival pigment were present.

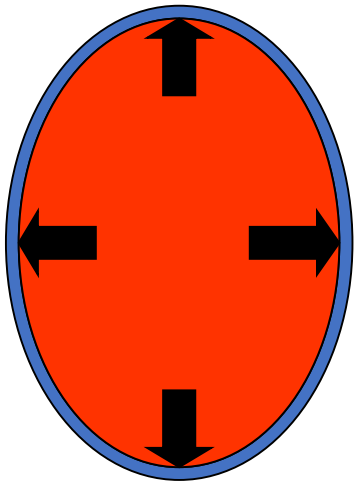
Na was 93, K 4.5, Cl 73, ^{i}Ca 1, glucose 5 (all mmol/L).

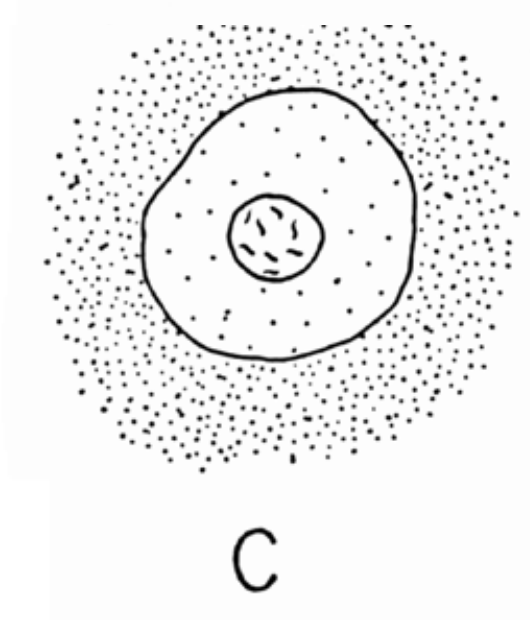
- How can you tell if he is getting better or worse?
- What would you order to decide the question?
- What is the Edelman equation?

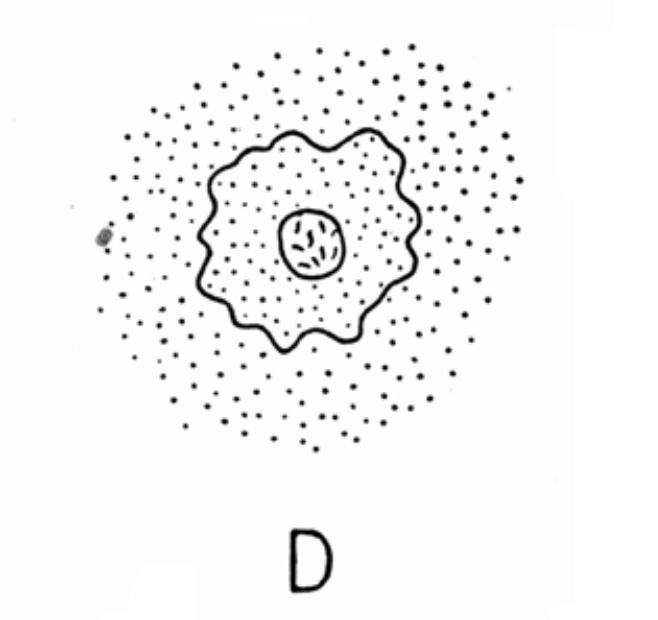
Do we understand osmolality and tonicity?

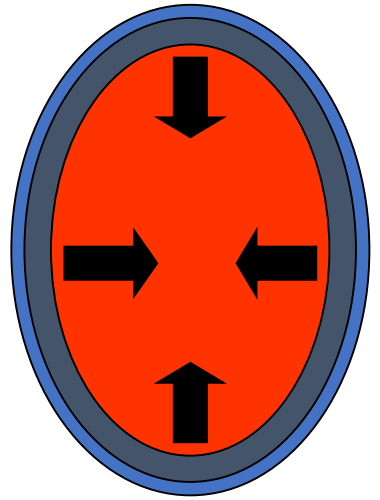




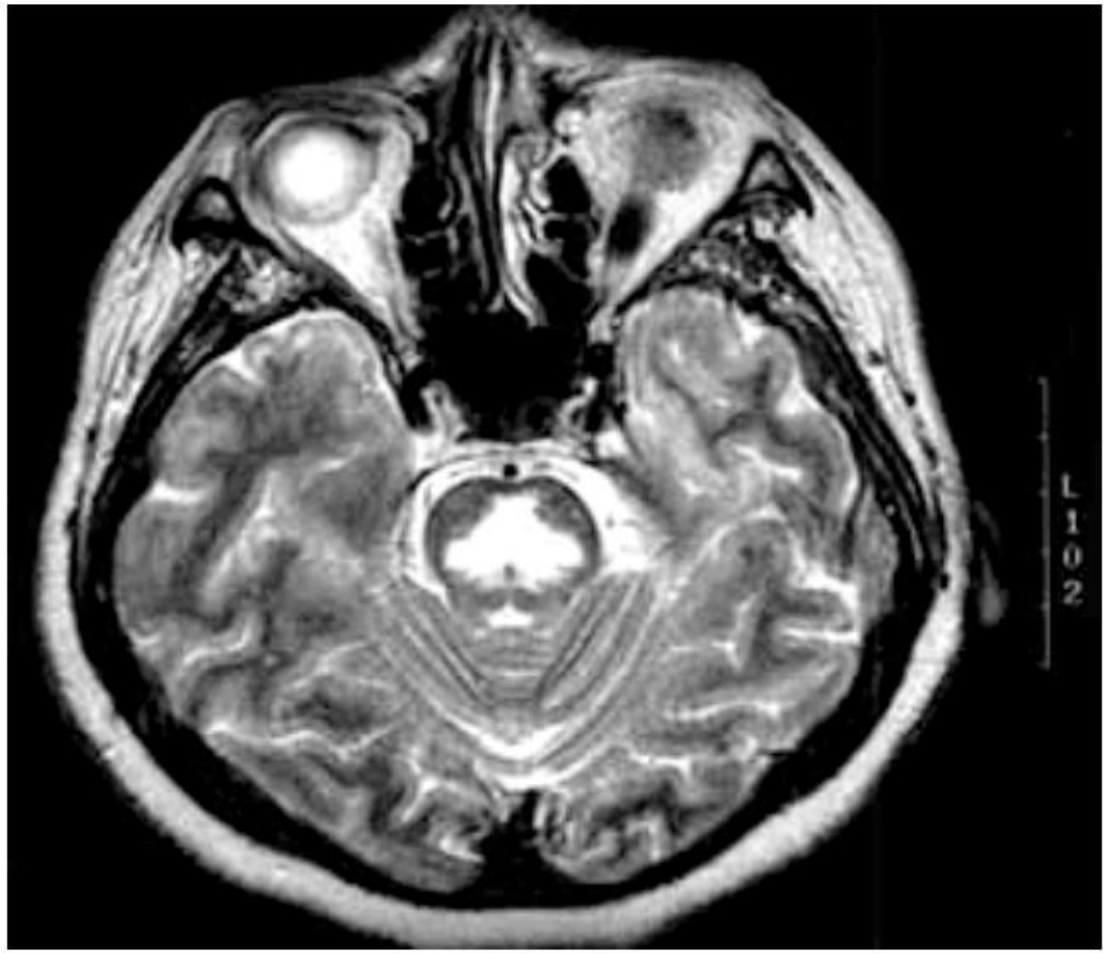








We do not want osmotic demyelination syndrome (ODS)!



T2-weighted MRI, Pons largely destroyed.

Central pontine myelinolysis

„Locked-in syndrome“

Recommendations read, „stay low and go slow“

But are they right?

Ann Int Med 1997;126:57

The plasma sodium is determined by spacetime, (Na_e and K_e).

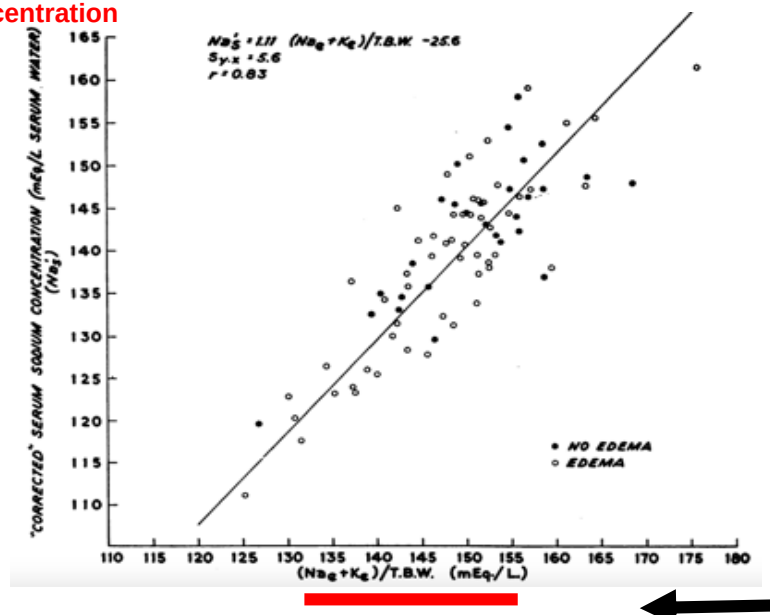
J Clin Invest 1958

INTERRELATIONS BETWEEN SERUM SODIUM CONCENTRATION, SERUM OSMOLARITY AND TOTAL EXCHANGEABLE SODIUM, TOTAL EXCHANGEABLE POTASSIUM AND TOTAL BODY WATER [1]

By I. S. EDELMAN,[2] J. LEIBMAN,[3] M. P. O'MEARA,[4] AND L. W. BIRKENFELD [5]

(From the Department of Medicine, University of California School of Medicine, and the San Francisco Hospital, San Francisco, Calif.)

Serum Na+ Concentration



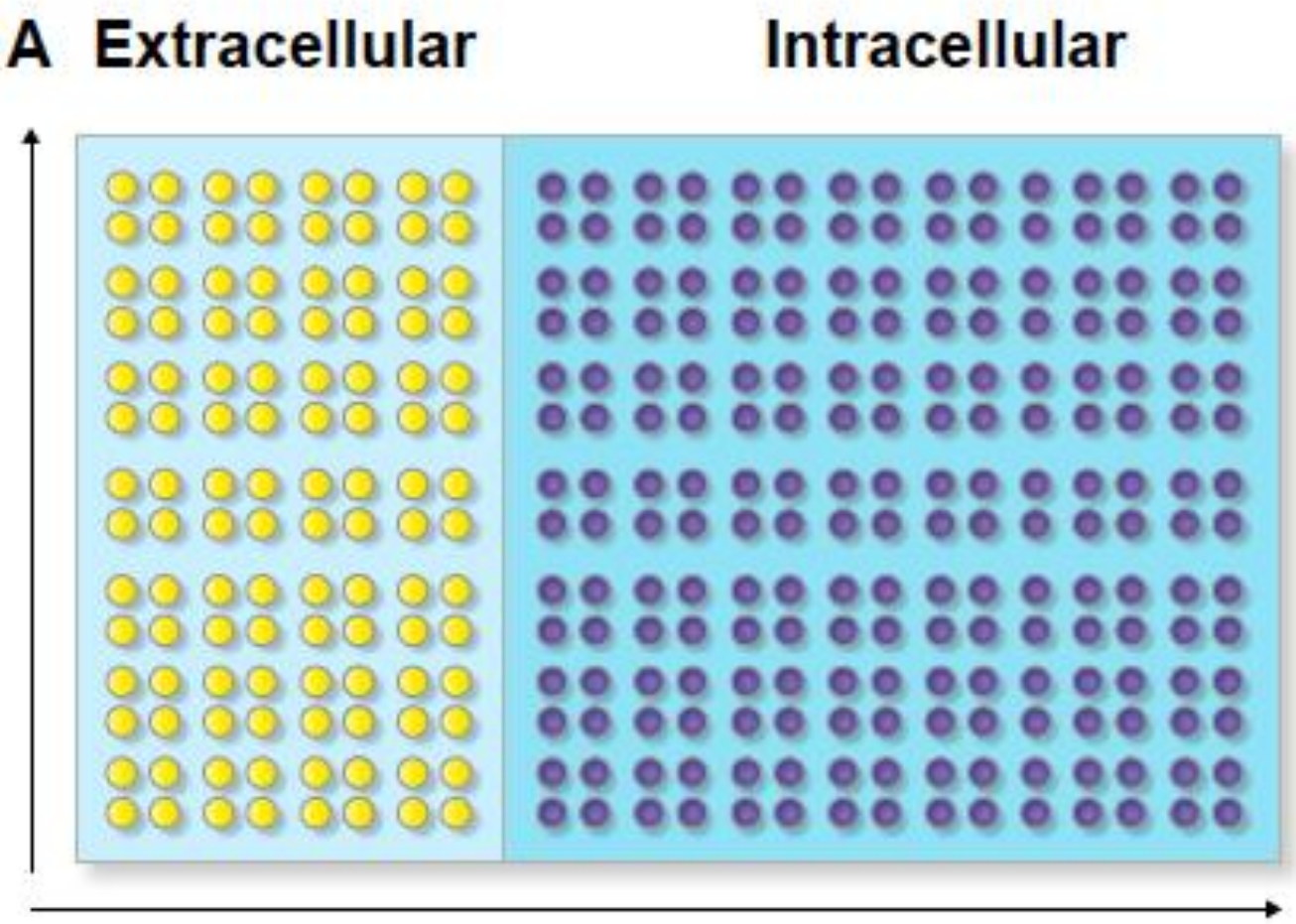
How was this done?

D_2O, Na^{24}, K^{42}

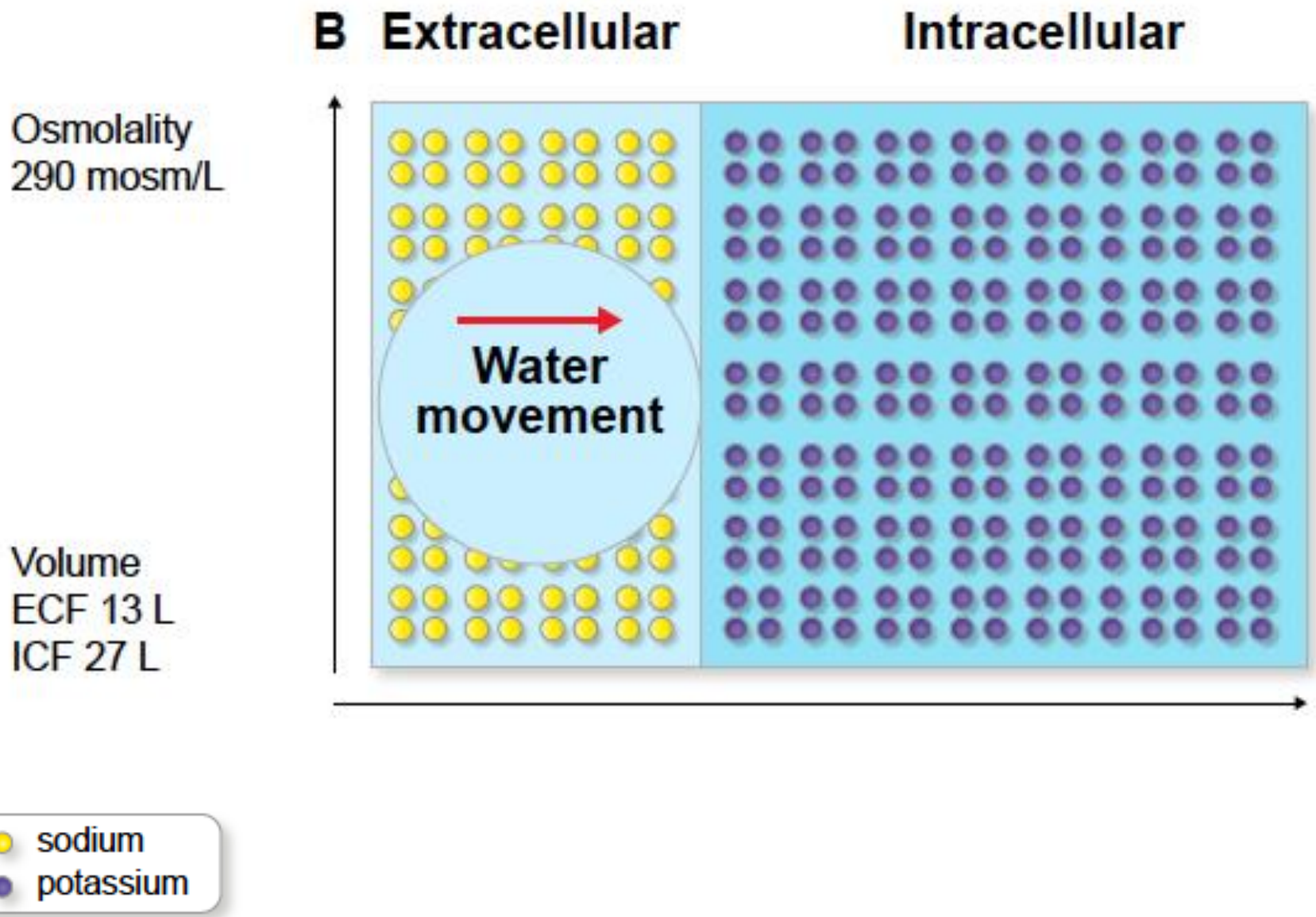
Edelman et al. introduced an explicit model to describe plasma $[Na^+]$ in a population as $[Na^+] = \alpha \cdot (\text{exchangeable } Na^+ + \text{exchangeable } K^+)/(\text{total body water}) - \beta$.

$$\text{Serum Na} \approx \frac{Na_{exch} + K_{exch}}{TBW\ H_2O}$$

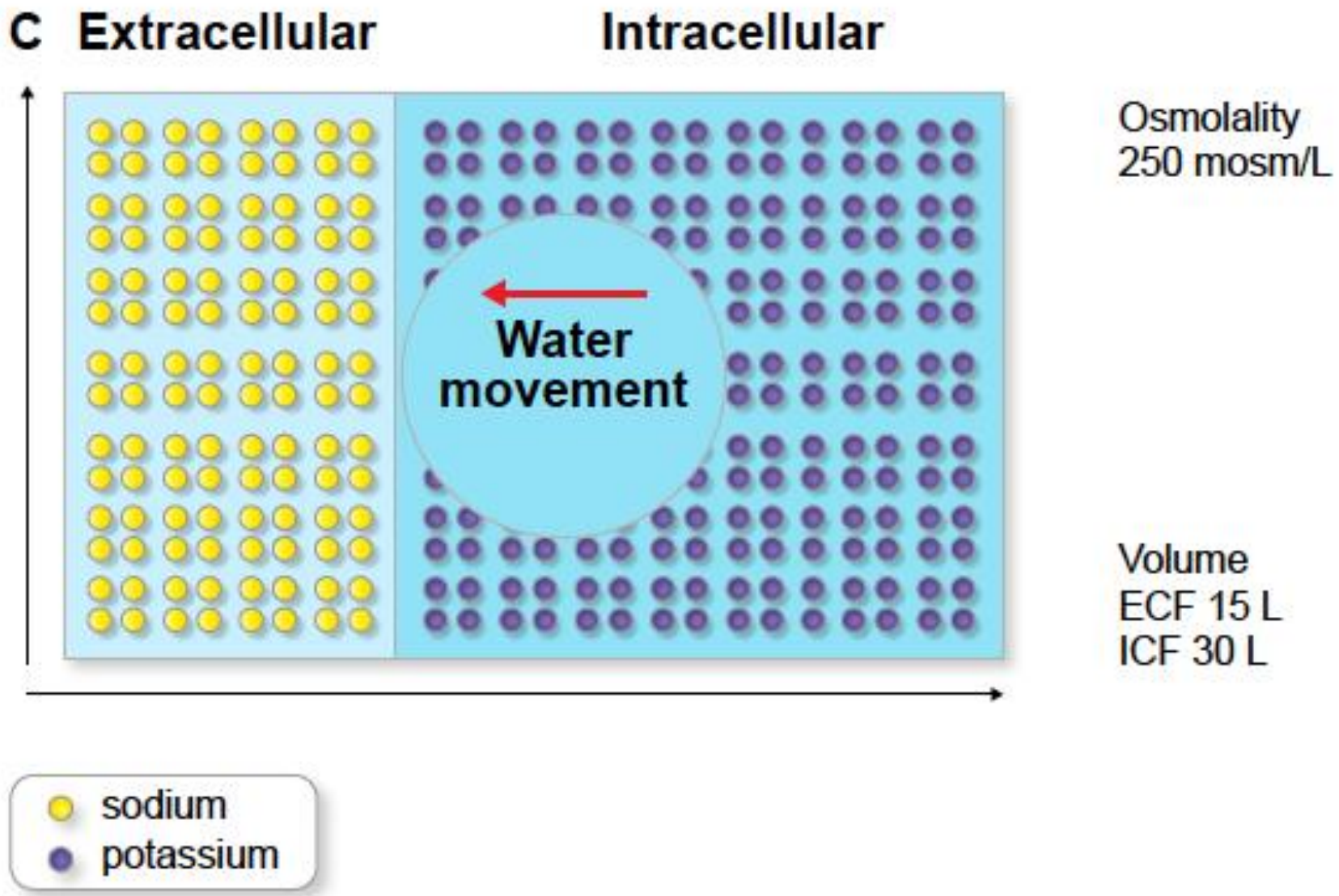
Aside from nonosmotic Na storage, we have (Na_e and K_e).



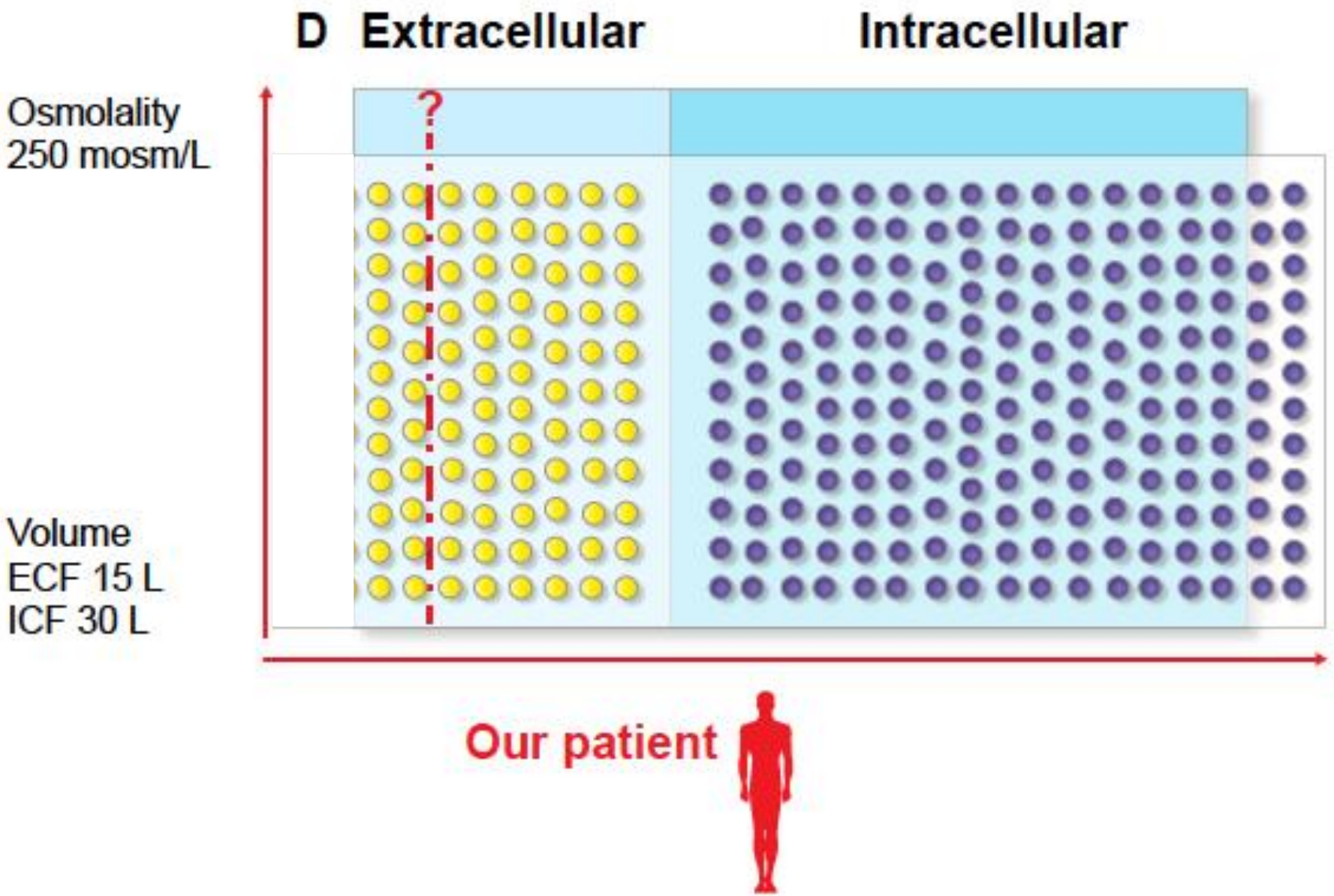
Were I just to lose sodium, we have (Na_e and K_e).



Were I just to lose potassium, we have (Na_e and K_e).



Our patient is an example of (Na_e and K_e) spacetime!

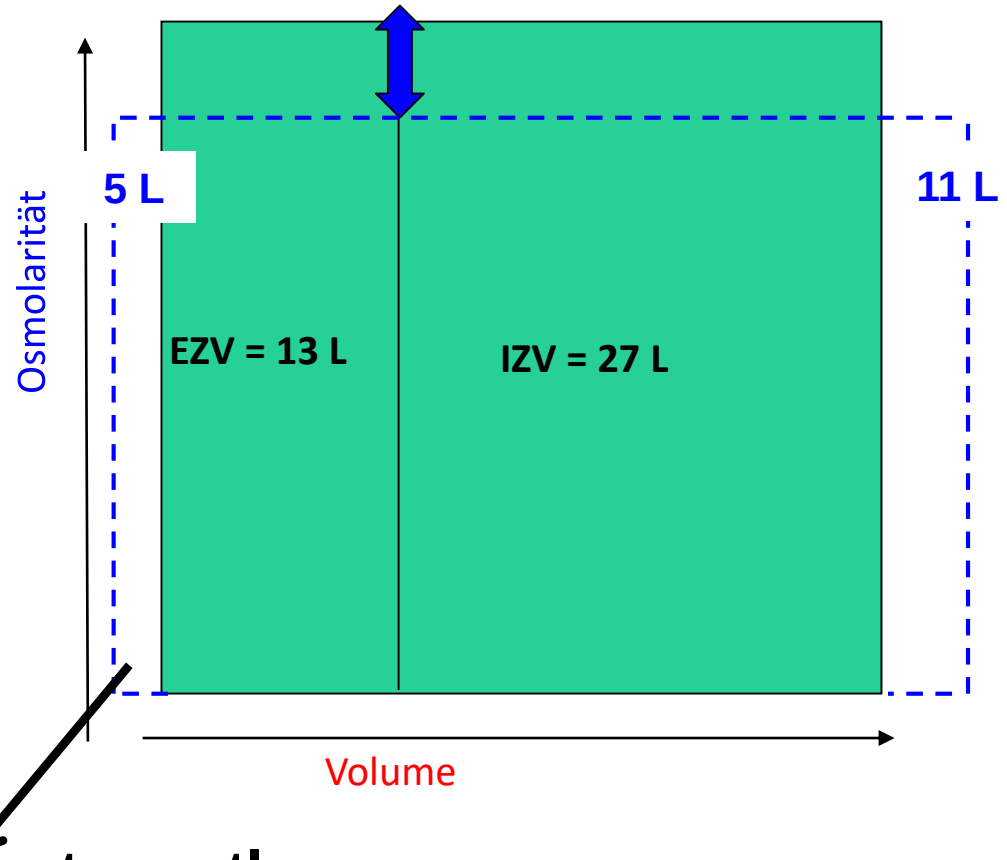


Can we „guesstimate“ how much extra water he has on board?

Water Excess = TBW -{(actual serum Na/ desired serum Na) x TB

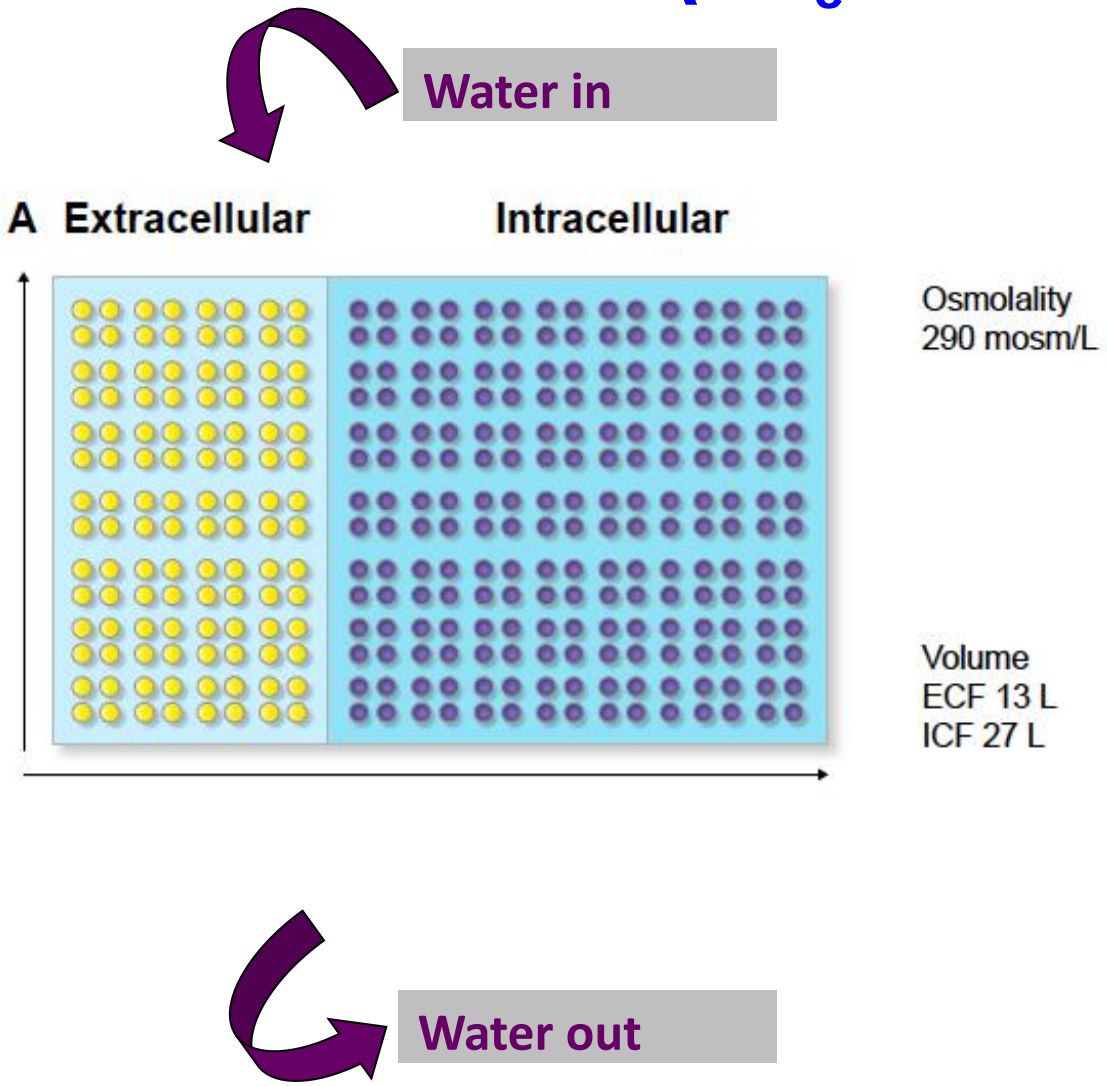
At 70 kg → 16 L Excess!!

(kind of true)



We do not exactly know his ECF

Thus, plasma Na depends on Na, K, and TBW. (Na_e and K_e) spacetime!

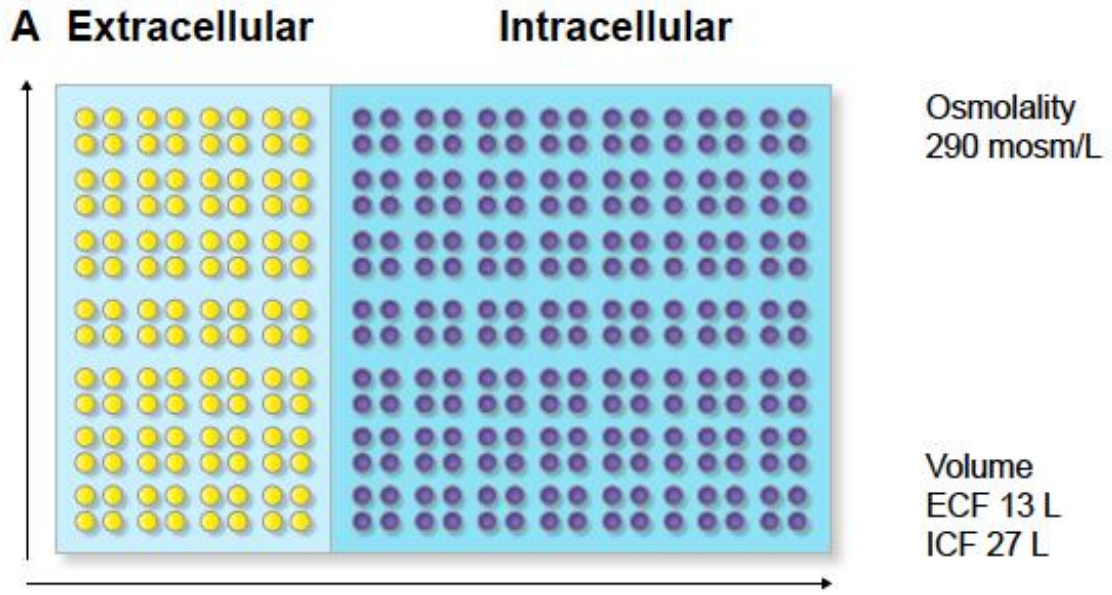


$$\text{Serum Na} \approx \frac{Na_{exch} + K_{exch}}{TBW\ H_2O}$$

Na

K

$$\text{Serum Na} \approx \frac{Na_{exch} + K_{exch}}{TBW\ H_2O}$$

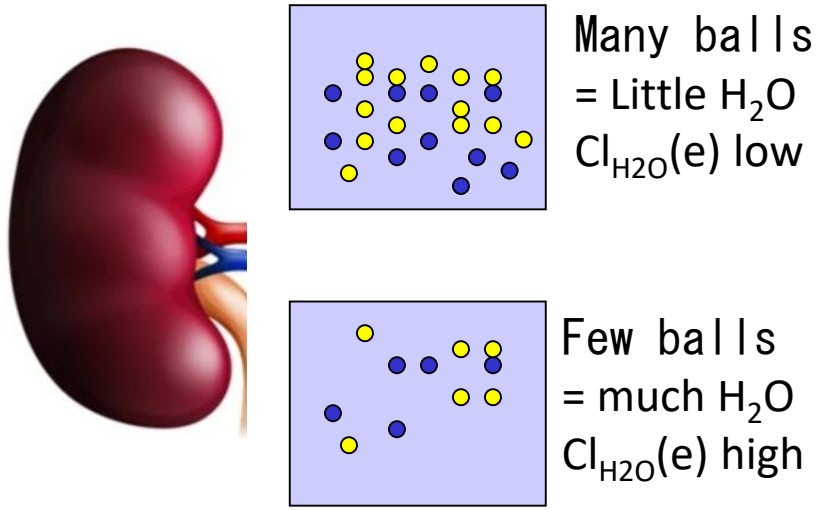


$$\text{Clearance } H_2O \text{ (e)} = V\ \left(1 - \frac{UNa+UK}{SNa}\right)$$

★

If UNa+UK >SNa, the Cl_{H2O}(e) neg and serum Na must fall

If UNa+UK < SNa, the Cl_{H2O}(e) pos and serum Na must increase



In a spontaneous urine sample, the UNa was 85 and UK 95 (mmol/L) with urinary osmolarity 889 mosm/L.

- Is he getting worse or better?
- How fast will his sodium change?
- What will you do therapeutically?
- What diagnostic tests are indicated?

$$\text{Clearance } H_2O \text{ (e)} = V \left(1 - \frac{UNa+UK}{SNa}\right)$$

The random plasma cortisol level was 146 nmol/L (lower limit of normal) with prolactin 777 mIU/L (10-fold elevated) and ACTH (markedly elevated). The aldosterone was <37 ng/L (below detection limit), the renin concentration >329 (markedly elevated).

- What acid-base disorder would you have expected?
- What complications would you expect (or fear)?

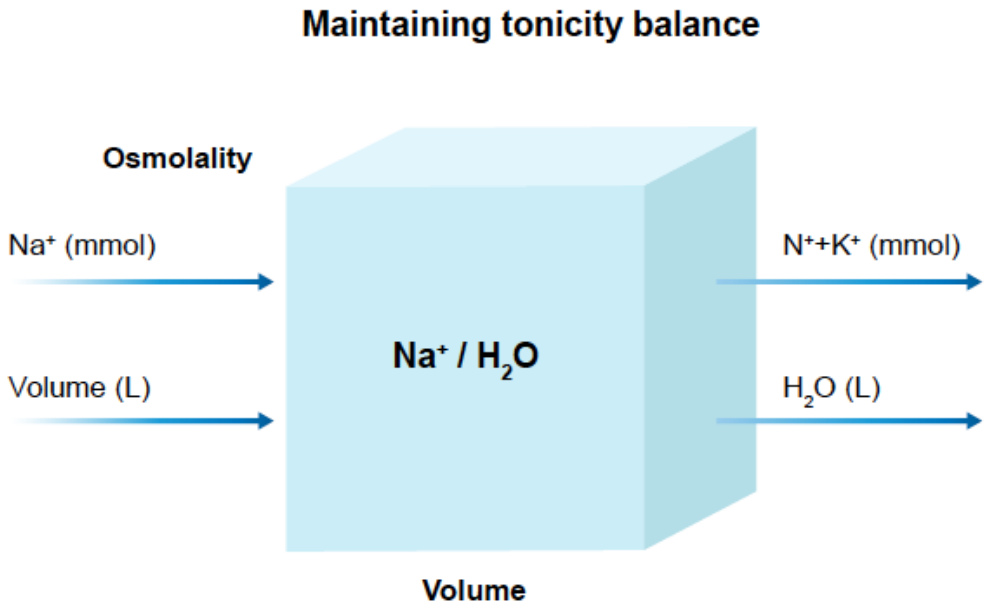
Our goal was to control tonicity balance (spacetime).

Na

K

$$\text{Serum Na} \approx \frac{Na_{exch} + K_{exch}}{TBW\ H_2O}$$

$$\text{Clearance } H_2O \text{ (e)} = V\ \left(1 - \frac{UNa+UK}{SNa}\right)$$

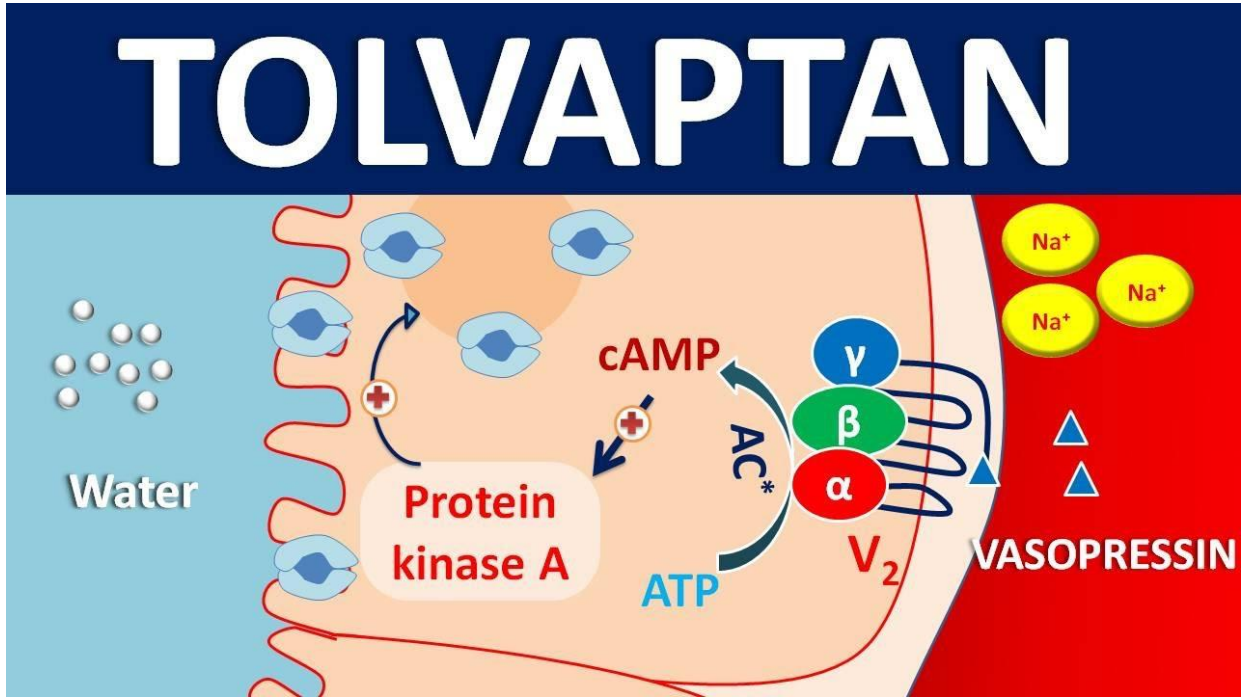


If UNa+UK >SNa, the Cl_{H2O}(e) neg and serum Na must fall

If UNa+UK < SNa, the Cl_{H2O}(e) pos and serum Na must increase

Two treatment options

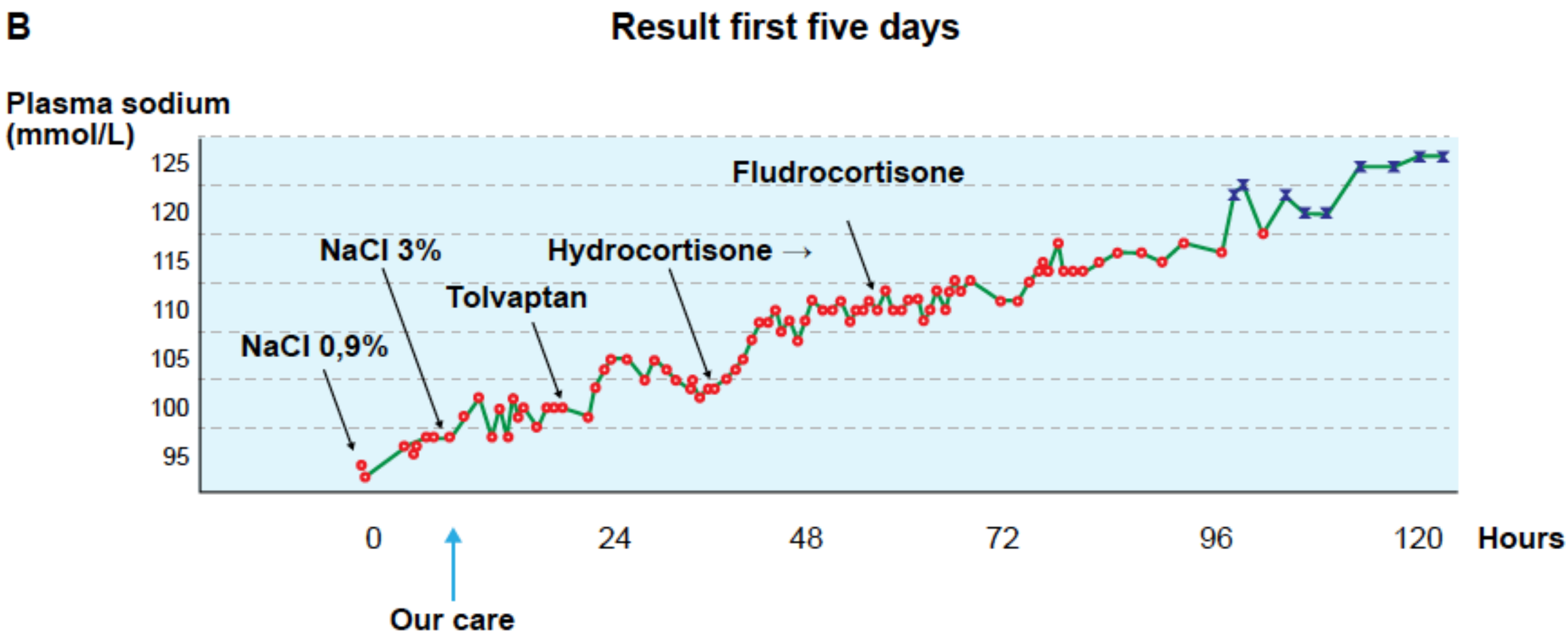
Concentration: mmol/L Na
3% Hypertonic NaCl: 513



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

(Kind of true)

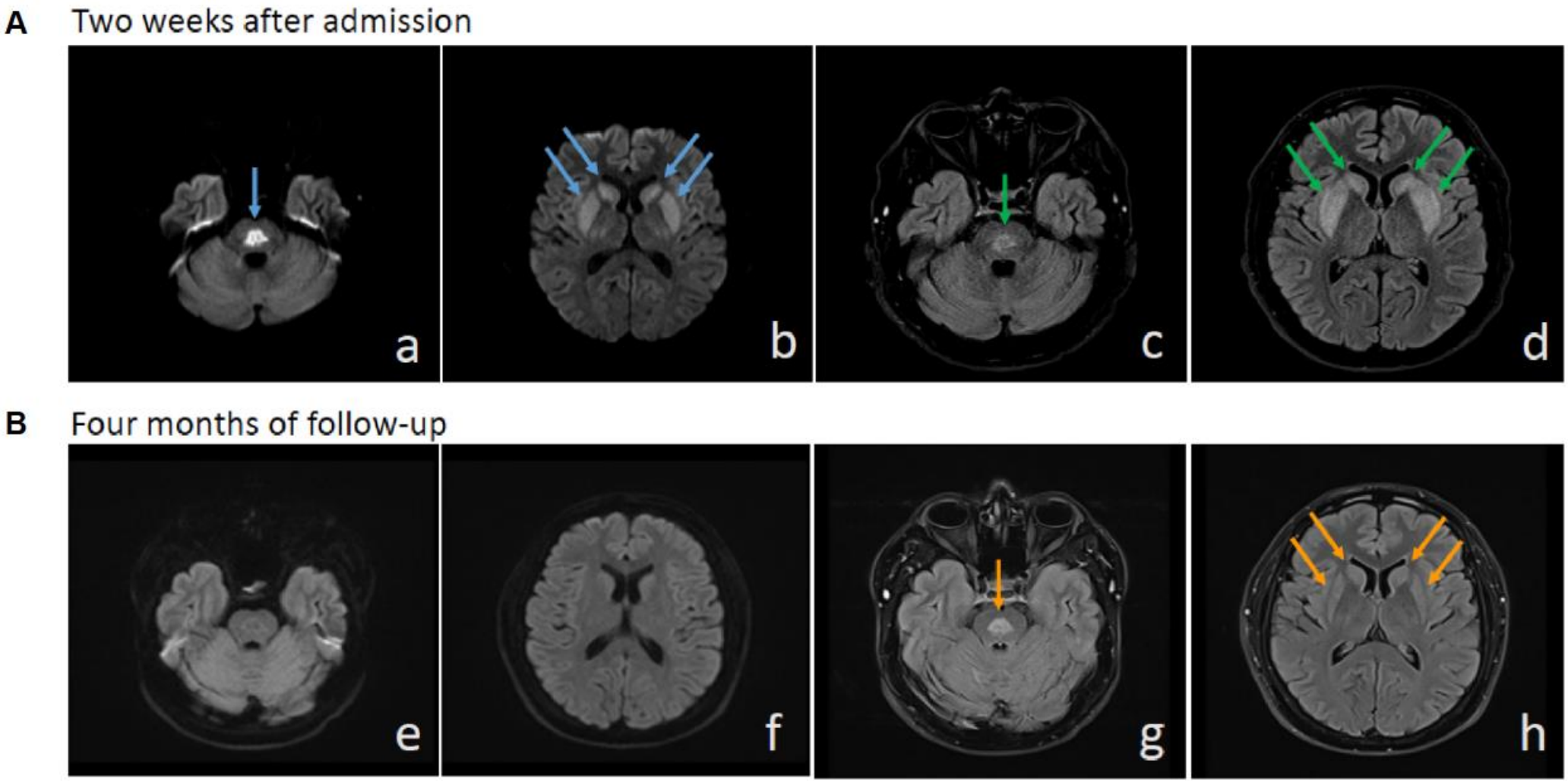
We raised the serum sodium slowly according to spacetime.



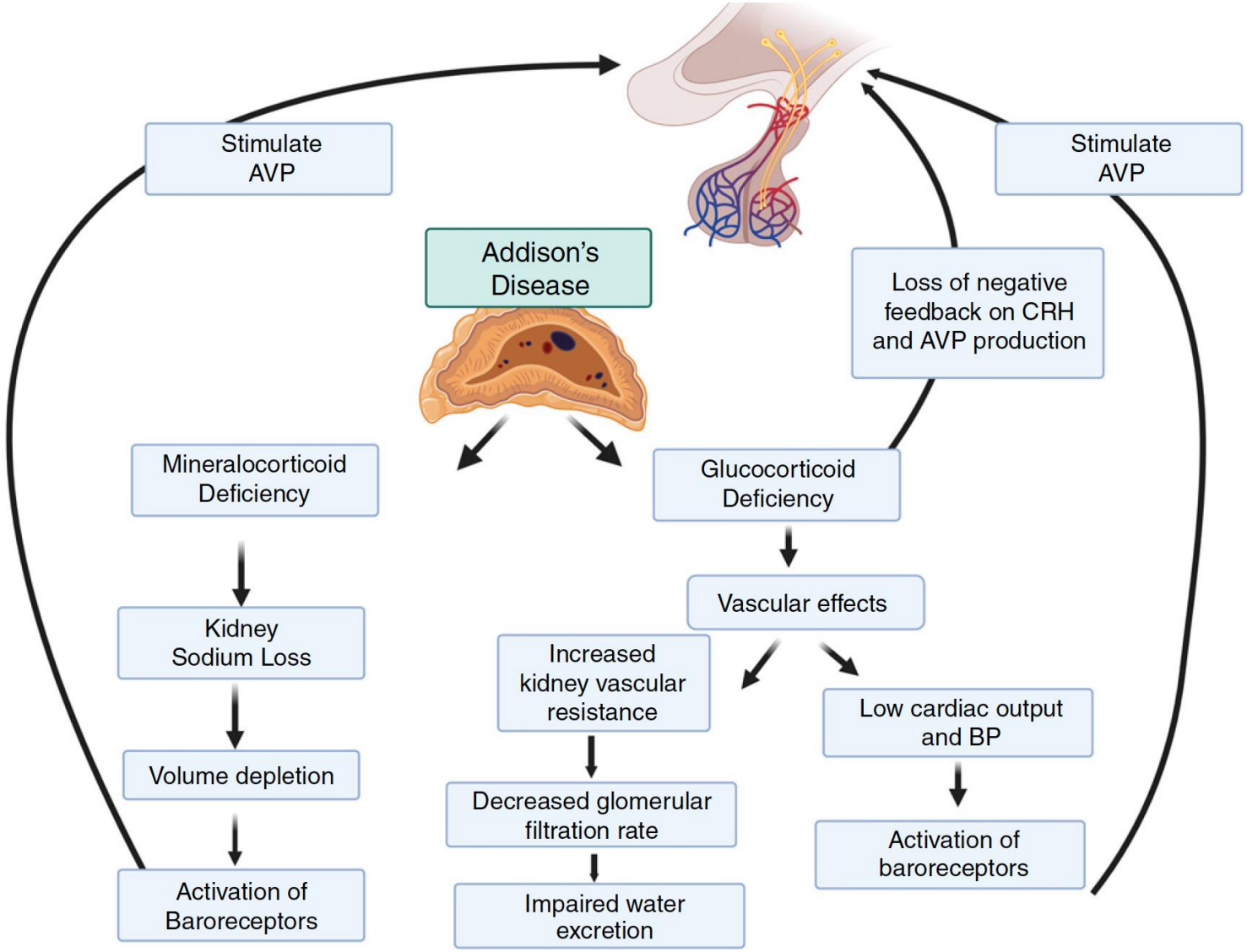
Magnetic resonance imaging (MRI) shortly after admission was normal. After hydrocortisone administration, the patient became combative and aggressive with coprolalia. We embarked on a decidedly conservative course to gradually increase the plasma sodium to viable values and hoped to avoid pontine myelinolysis.

- Does „slow“ sodium correction avoid ODS?

Admitting MRI was normal, at two weeks ODS; however, at four months – recovery, ie. spacetime.



Mechanisms of hyponatremia in Addison's disease.



The problem here is „too much water" and far less „not enough salt"

The Edelman formula is correct (however Na_e).

Seeing the sodium in a patient with hypernatremia

Christoph Kopp[1,2], Peter Linz[2], Matthias Hammon[3], Christof Schöfl[4], Martin Grauer[4], Kai-Uwe Eckardt[1], Alexander Cavallaro[3], Michael Uder[3], Friedrich C. Luft[5] and Jens Titze[1,2,6]

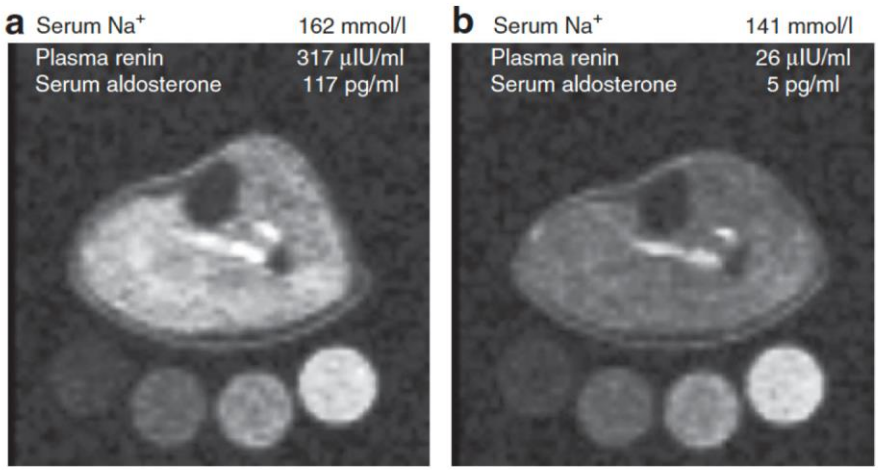


Figure 1 | ^{23}Na magnetic resonance imaging of calf muscle. A patient with hypernatremia before (**a**) and after (**b**) correction to a normal serum Na^+ concentration. The standards are below the calf muscle and contain Na^+ concentrations of 10, 20, 30, and 40 mmol/l. A remarkable decrease in the muscle Na^+ content occurs with correction of serum Na^+ concentration, plasma renin, and serum aldosterone.

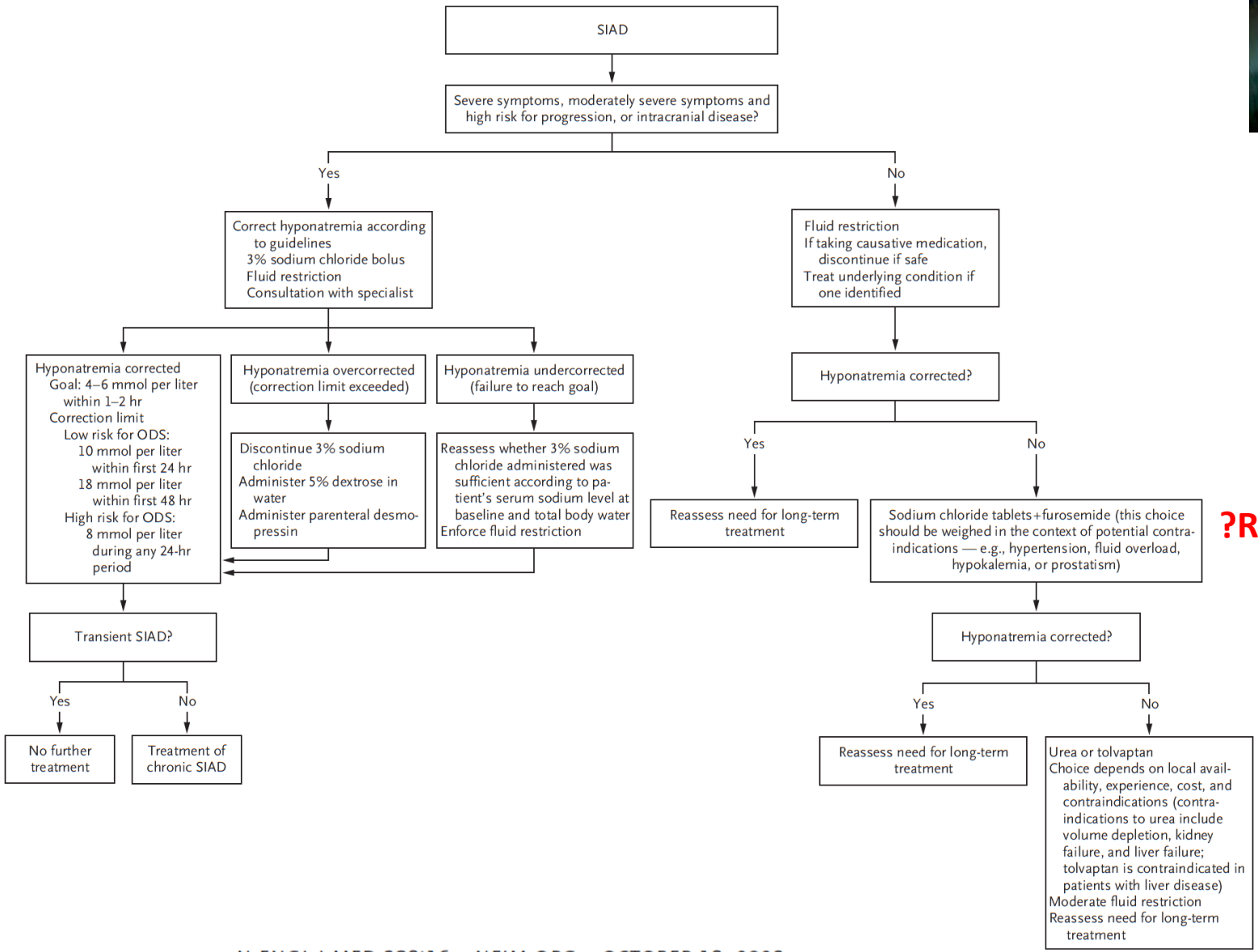
What do we mean with „exchangeable“?

Kopp C et al. Kidney Int. 2012

The Syndrome of Inappropriate Antidiuresis

Horacio J. Adrogué, M.D., and Nicolaos E. Madias, M.D.

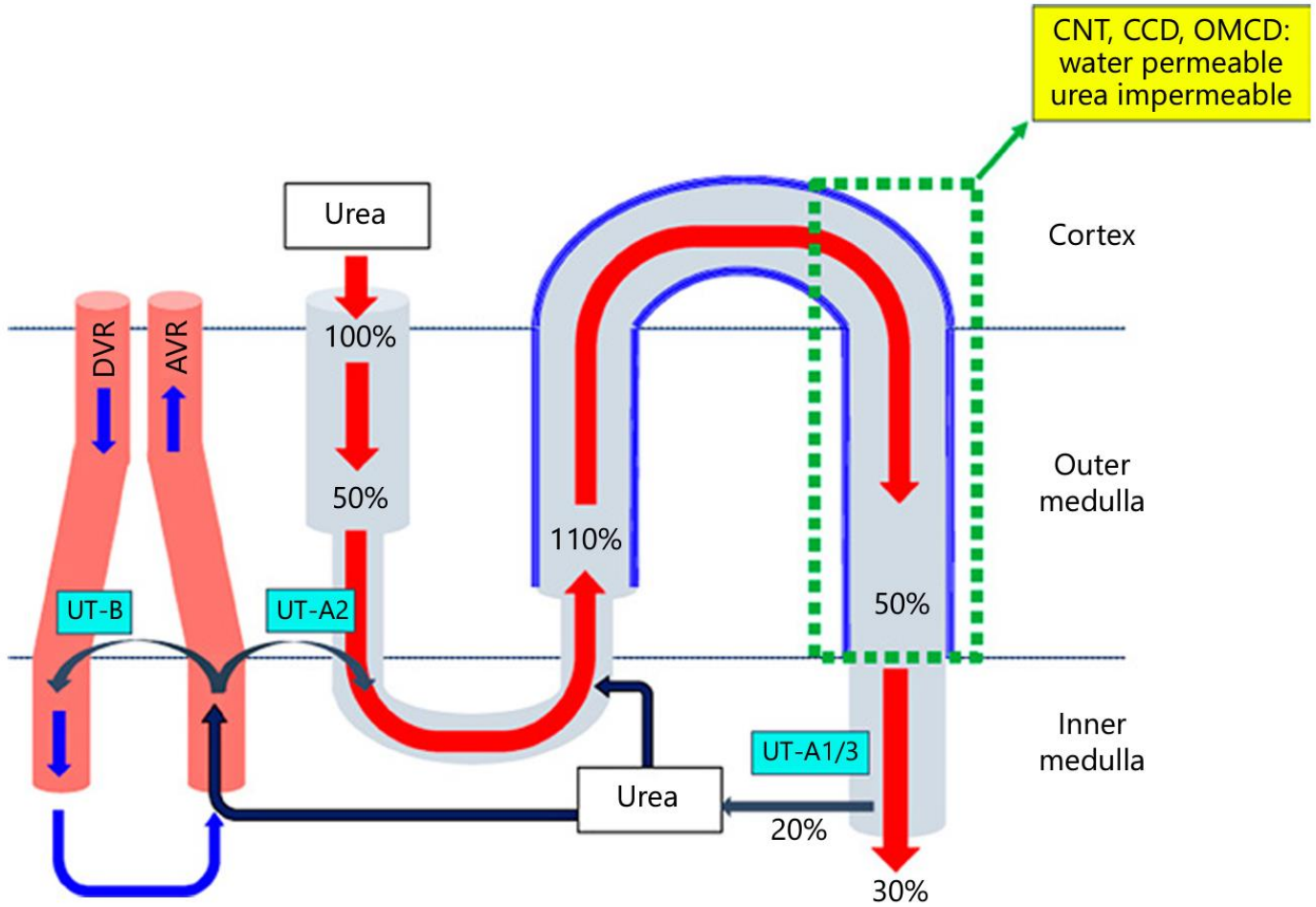
K is not mentioned in this scholarly review



?Really

What about urea? (for chronic SIAD)

Renal handling of urea. Urea is freely filtered by the glomerulus. About half of filtered urea is reabsorbed in the proximal tubule. Urea is secreted into the lumen of the thin limbs (urea recycling) increasing urea concentration at the beginning of the thick ascending limb. DVR, descending vasa recta; AVR, ascending vasa recta; UT-B, urea transporter UT-B; UTA2, urea transporter UT-A2; UT-A1/A3, urea transporters UT-A1 and UT-A3; CNT, connecting tubule; CCD, cortical collecting duct; OMCD, outer medullary collecting duct.

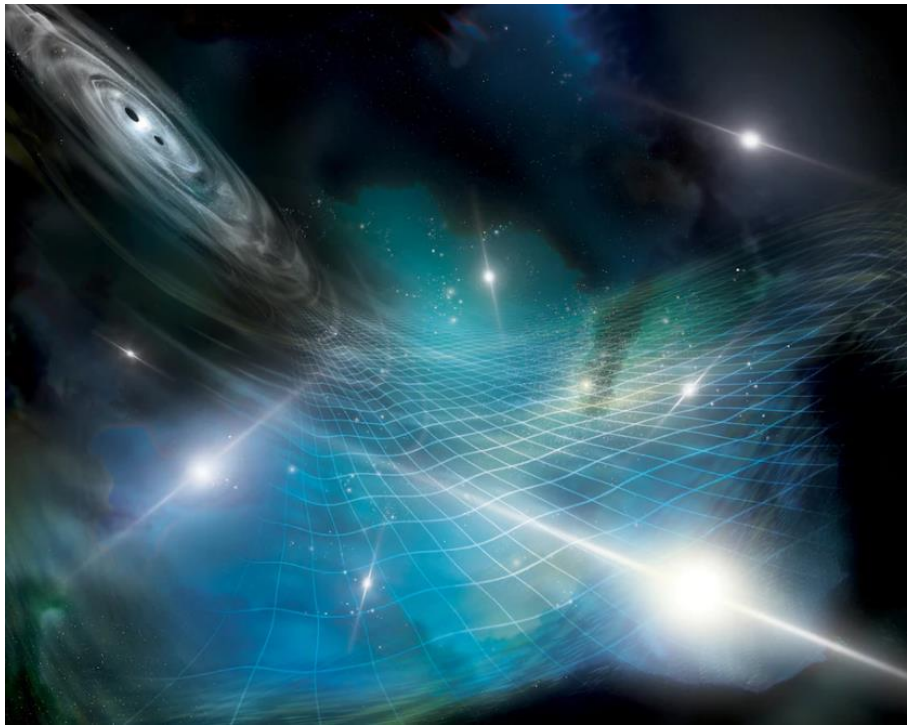


Teaching points.

- The patients do not always do what we want.
- Addison‘s disease can cause profound hyponatremia; hyperkalemia is present in about half the cases. I would expect metabolic acidosis from hypoaldosteronism. However, the CNS controls acid-base (to a degree).
- The key to hyponatremia revolves around the Edelman equation. So please measure not only Na in urine but also K.
- Above all – hyponatremia is a water problem, NOT a salt problem!

  Avoid the immediate reflex of “dumping in salt!!
- The „rate of correction“ remains a matter of debate (Salsa Study).
- ODS is not precluded by „slow“ correction.
- Exchangeable includes „relative“ areas such as skin and proteoglycans.

friedrich.luft@charite.de



Why do all the pundits, experts, etc. even in N Engl J Med, solely measure UNa and not UK?

Because they have no idea about spacetime!

If UNa+UK >SNa, the Cl_{H2O}(e) neg and serum Na must fall

If UNa+UK < SNa, the Cl_{H2O}(e) pos and serum Na must increase

$$\text{Clearance } H_2O \text{ (e)} = V \left(1 - \frac{UNa+UK}{SNa}\right)$$