Significance of Na^+, K^+ and Cl^- investigation

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Sodium cation

Sodium balance and distribution

Na^+ concentration in plasma	135 - 145 mmol/L
Na^+ concentration in cell	3 - 10 mmol/L
Na^+ intake	140 - 260 mmol/day (8 - 15 g NaCl)
Na^+ renal excretion	120 - 240 mmol/day
Na^+ excretion via GIT	10 mmol/day
Na^+ excretion via sweat	10 - 80 mmol/day
Na^+ total excretion	140 - 260 mmol/day

The concentration gradient between ECF and ICF is maintained principally by the Na+/K+ pump.

Assessment of plasma concentration

- anamnesis, clinical symptoms
- S-osmolality: $2x[Na^+] + [glucose] + [urea]$ (ca. 285 mmol/kg)
- Tonicity : $2x[Na^+] + [glucose]$
- Evaluation of extracellular volume (dehydration, euvolemia, edema)
- S – albumin
- U - Na^+
  - ADH: water reabsorption (distal convoluted tubule)
  - aldosterone: reabsorption of Na^+ (+ H_2O) and excretion of K^+,H^+
  - atrial natriuretic peptide: excretion of Na^+ (and water)

Definitions of plasma sodium imbalance

- **hyponatremia** – the Na^+ concentration in the serum is below the physiological range
  - mild 130 - 135mmol/L
  - moderate 120 - 130 mmol/L
  - severe < 120 mmol/L
- *acute* – last less than 48 hours or the increase in plasma concentration is higher than 0.5 mmol/L/h
- *chronic* - last more than 48 hours or the increase in plasma concentration is lower than 0.5 mmol/L/h

TIME DIVISION IS NECESSARY FOR THE SPEED OF THERAPY!

- **hypernatremia** – the Na^+ concentration in the serum is above the physiological range, severe above the 155 mmol/L

Hyponatremia

- one of the most common electrolyte imbalance
- symptoms depend on the severity of hyponatremia and the speed of development
- symptomatic hyponatremia – 33% mortality or permanent brain damage, in chronic form 25%

Symptoms of hyponatremia

- brain edema, increased intracranial pressure, myelinolysis, nausea or vomiting, lung edema with hypoxia
- no signs if the development of hyponatremia is slow
- beware kids and older people – weaker symptoms even in severe hyponatremia
- **risk factors**: hypoxemia (vicious circle), female sex (estrogens), alcoholism, hepatopathy , et al.

Hyponatremic encefalopathy

hyponatremia in ECF

↓

movement of water into cells including brain cells

↓

brain edema

↓

compensational mechanisms decrease the osmolality of ICF (24 – 48 hours)

↓

reduction of brain edema

beware of quick therapy!!

Hyponatremic encefalopathy II.

quick increase of plasma concentration (e.g., rapid correction of hyponatremia)

↓

plasma becomes relatively more osmotic compared to ICF

↓

movement of water from ICF back to ECF

↓

dehydration of brain cells

↓

syndrome of central pontine and extrapontine myelinolysis (osmotic demyelination syndrome)

Types of hyponatremia

Osmolality = 2[Na^+] + [glucose] + [urea]

Isoosmolar / Isotonic	Hyperosmolar / Hypertonic	Hypoosmolar / Hypotonic (90%)
pseudohyponatremia (interference of lipids and proteins using some types measurement)	Hyperglycemia Mannitol Ethylene glycol	low ECF volume (hypovolemic) increased ECF volume (hypervolemic) normal ECF volume (euvolemic / isovolemic)

Hyperosmolar hyponatremia

- every increase in plasma glucose concentration by 5 mmol/L above the physiological range decreases the plasma sodium concentration by approx. 1.5 mmol/L
  - correction formula:

$P_{Na}^{x} = P_{Na}^{+} / (1 - P_{Glc} * f)$

f = 0,002

P_{Na}^{x} corrected plasma sodium concentration

P_{Na}^{+} measured plasma sodium concentration

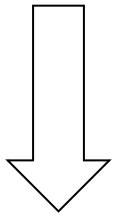
P_{Glc} measured plasma glucose concentration

INFOLAB - Kumulativní nález

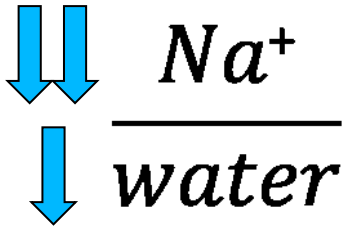
06/08/2014	06/08/2014	06/08/2014	06/08/2014	06/08/2014	06/08/2014
				Gluk= 50.3+	
				CRP = 2.8	
				Na = 120-	
				K = 5.8+	
				Cl = 66-	
cPGl= 54.2+		cPGl= 54.0+			cPGl=> 33 mm
	Udus=negativ				
	U-pH= 5.0				
	U-CB= 1				
	UGlu= 4+				
	UKet= 2+				
	UUro=normáln				
	UBil= 0				
	UKrv= 1				
	Leuk= 0				
	Uhus= 1.014-				

Hypoosmolar hyponatremia

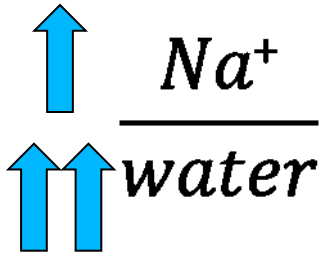
- relative imbalance between the volume of ECF and the amount of sodium cations included



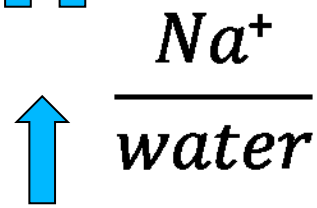
[Na $^{+}$]



hypovolemic



hypervolemic



euvolemic

Hypovolemic hypoosmolar hyponatremia

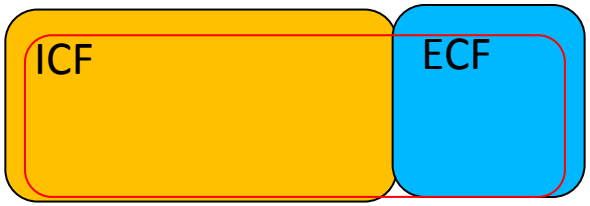
- Na^+ loss is higher than loss of free water (volume of ECF is reduced)
- **Extrarenal loss**

  diarrhea, vomiting, burns

  third spacing of fluid (ileus, peritonitis, fistulas, burns, etc.)
- **Renal loss**

  diuretics

  aldosterone deficiency



- **Signs**

  Dehydration, risk of kidney failure and blood circulation
- **Therapy**

  isotonic saline

Hypervolemic hypoosmolar hyponatremia

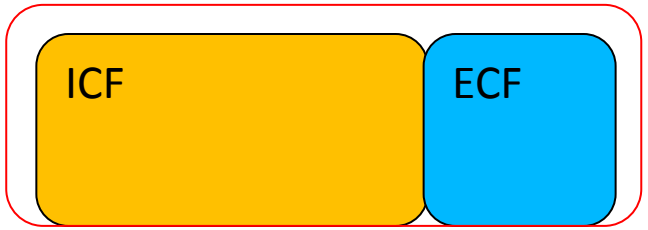
- retention of water of hypoosmotic fluid
- **Nonrenal causes**

  cirrhosis, heart failure, nephrotic syndrome with the development of edema (hypoalbuminemia)
- **Renal causes**

  acute renal failure
- **Signs**

  edemas, gain of weight
- **Therapy**

  fluid restriction, water restriction, diuretics



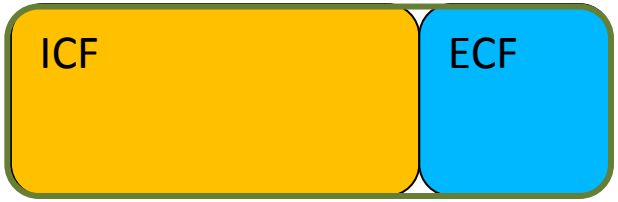
Isovolemic hypoosmolar hyponatremia

- retention of pure water with later redistribution into intracellular space

- **Syndrome of inappropriate antidiuretic hormone secretion (SIADH)**

  brain trauma, pneumonia, lung cancer

  drugs – carbamazepine, barbiturates, hydrochlorothiazide



- **Therapy**

  water intake restriction, antagonists of ADH receptors

Basic notes to therapy

- it is important to:
  - judge the severity of hyponatremia, time course of sodium levels and cause of hyponatremia
  - assess the ECF volume and osmolality
- treat the cause of hyponatremia if possible
- consider the correction (max. **8 – 12 mmol/L/ 24h** in symptomatic patients, in asymptomatic even slower)
- monitor the level of plasma sodium concentration hourly

Calculation of sodium deficit

deficit Na^+ = m (in kg) *** F * (140 – measured plasma Na^+ concentration)**

(F = 0.6 for men a 0.55 for women)

- **target value of plasma sodium concentration**: half of the distance between measured value of plasma sodium concentration and value 140 mmol/L

deficit Na^+_{target} = m (in kg) *** F * (target value of plasma sodium concentration - measured plasma Na^+)**

Hypernatremia

- most common cause of increased osmolality
- very often caused by water deficit rather than sodium cation excess
- hyperosmolality cause the movement of water from ICF to ECF with dehydration of (brain) cells
- compensational mechanism is the increase of solute particles in brain cells
- rapid therapy cause brain edema

Signs of hypernatremia

- mostly neurological – because of the water movement in brain cells
  - thirst
  - irritability, spasticity, aggressivity, insomnia, hyperventilation, coma → death
  - intracranial bleeding (volume changes of brain tissue)

Causes of hypernatremia

category	example
decreased body sodium (loss of water > Na^+)	extrarenal: sweating, diarrhea renal: osmotic diuresis (diabetes mellitus)
normal body sodium (loss of pure water)	extrarenal: fever renal: diabetes insipidus
increased body sodium (retention of Na^+ > water)	steroid treatment, Cushing‘s syndrome, increase intake of sodium (iatrogenic application of hyperosmolar saline, provoking of vomiting by salt solution, castaways adrift at sea)

Therapy of hypernatremia

- the same rules as in therapy of hyponatremia (cause, severity, time course)
- typical treatment is rehydration, oral or intravenous (combination of 5% glucose and saline according to estimated loss of water and sodium) or diuretics (in case of retention of water and Na^+)

Potassium cation

Potassium balance and distribution

K^+ concentration in plasma	3.8 – 5.2 mmol/l
K^+ concentration in cell	100 - 160 mmol/l
K^+ concentration in urine	30 - 80 mmol/l
intracellular reserve	3200 mmol
extracelullular reserve	60 mmol
K^+ intake	50 - 100 mmol/24 h.
K^+ excretion	50 - 100 mmol/24 h.

K^+ is the main intracellular cation – at least 95% of the body's potassium is found inside the cells

Plasma potassium concentration and pH

- they are dependent (decrease of pH by 0.1 increase plasma potassium concentration by approx. 0.6 mmol/L)
- more accurate is Kazda's formula :

Plasma potassium concentration = 33,05 – 3,87*plasma pH

- pH = 7 matches the plasma potassium concentration 6 mmol/L and pH = 7.7 matches the plasma potassium concentration 3.3 mmol/L

AND IF THE VALUES DO NOT MATCH EACH OTHER?

Definitions of plasma potassium imbalance

- **<u>hypokalemia</u>** – the plasma K^+ concentration is below the physiological range
  - mild 3.0 – 3.5 mmol/L
  - moderate 2.5 – 3.0 mmol/L
  - severe < 2.5 mmol/L
- **<u>hyperkalemia</u>** – the K^+ concentration in the serum is above the physiological range
  - mild 5.5 – 6.5 mmol/L
  - moderate 6.5 – 7.5 mmol/L
  - severe > 7.5 mmol/L

Types of hypokalemia

- Altered internal distribution
- Altered external balance
  - deficient intake of K^+
  - excessive losses of K^+
- Other
  - artefact (collection of blood from a vein near to site of IV infusion)

Hypokalemia must not be equated with depletion of body K^+. Although most patients with K^+ depletion have hypokalemia, acute changes in the distribution of K^+ in the body can offset any effects of depletion or excess.

Hypokalemia due to altered internal distribution of K^+

- altered internal distribution = shift of K^+ into cells
  - alkalosis
  - insulin (beware of hypokalemia after starting the treatment of diabetic ketoacidosis)
  - adrenaline (e.g. after MI)
  - cellular incorporation of K^+ (parenteral re-feeding, rapidly proliferating leukemic cells)

Hypokalemia due tu altered external balance

- deficient intake of K^+
  - chronic and severe malnutrition, anorexia nervosa
- excessive losses of K^+ from the renal tract
  - hyperaldosteronism, diuretic therapy, renal tubular acidosis, Bartter‘s syndrome
- excessive losses of K^+ from the GI tract
  - vomiting, diarrhea or laxative abuse, fistula

Signs of hypokalemia

- muscle weakness, spasms
- disturbances of cardiac conduction
- constipation or paralytic ileus
- disturbed concentration of urine and polyuria

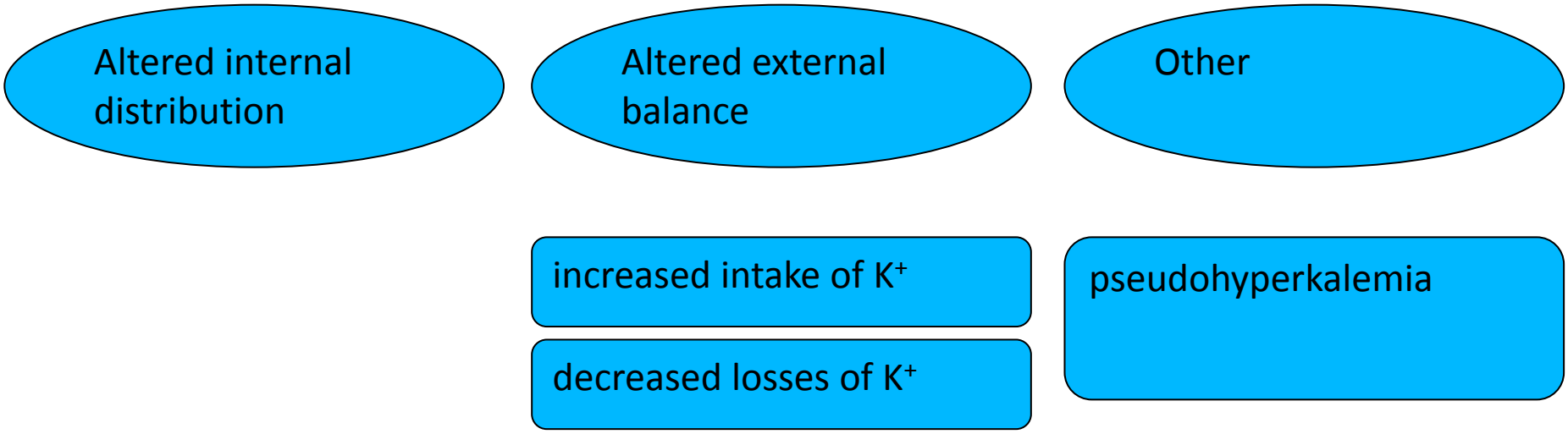
Principles of therapy

- measure the plasma magnesium concentration – it is necessary for activity of Na^+/K^+ ATPase
- calculate the deficit of potassium

$$K_{deficit} \text{ (in mmol)} = (K_{normal\ lower\ limit} - K_{measured}) \times \text{body weight (kg)} \times 0.4$$

- correction depends strongly on the kidney function
- IV administration is recommended in severe hypokalemia or if the plasma potassium level is not responding to oral administration
- maximal dose is 10 - 20 mmol/L/h
- 7.5% KCl contents 1mmol/L of K^+ in 1 ml
- check the plasma potassium concentration hourly

Types of hyperkalemia



Causes of hyperkalemia

- altered internal distribution
  - acidosis, uncontrolled diabetes mellitus (lack of insulin), cellular necrosis
- increased intake
  - rare, only in combination with renal insufficiency
- decreased excretion
  - renal diseases, mineralocorticoid deficiency

Pseudohyperkalemia

- increased amount of potassium in plasma that occurs due to excessive leakage of K^+ from cells during or after blood is drawn
  - excessive use of tourniquet
  - lack in processing the blood after the collection
  - hemolysis
  - leukocytosis (> $50 \cdot 10^9$/l)
  - trombocytosis (> 750-$1000 \cdot 10^9$/l)

Principles of therapy

- increase of shift of K+ into cells (glucose + insulin, alkalization, correction of hyponatremia)
- diuretics in nonrenal causes
- calcium gluconate (counter the neuromuscular effect of hyperkalemia)
- renal dialysis in severe hyperkalemia

Practical notes to therapy

- plasma potassium concentration must be judged together with clinical condition of patients (ECG!), acid – base balance, renal functions and possible K+ depletion
- hypokalemia with acidosis and hyperkalemia with alkalosis are potentially critical
- hypokalemia with increased potassium in urine is usually caused by renal disorder, hypokalemia with decreased excretion fraction of potassium has usually extrarenal cause. Conversely in hyperkalemia.
- therapy of hyperkalemia must be quick with monitoring of electrolyte balance every half an hour.

Chloride anion

Chloride balance and distribution

Cl^- concentration in plasma	98-107 mmol/L
Cl^- concentration in cell	3 mmol/L
Cl^- intake	140-260 mmol /24h (8-15 g NaCl)
Cl^- renally excretion	120-240 mmol / 24h
Cl^- excretion via intestines	10 mmol / 24h
Cl^- excretion via sweat	10-80 mmol / 24h
Cl^- total excretion	140-260 mmol / 24h

Chlorides and acid-base balance

- chlorides are necessary for the calculation of anion gap and unmeasured anions

- **corrected chlorides** – reflect the influence of hydration on plasma chloride concentration (how would be the plasma chloride concentration if the plasma sodium concentration is 140 mmol/l)

$$\text{Corrected chlorides} = [Cl^-] \times (140 \div [Na^+])$$

Hypochloremia

- is an electrolyte disturbance in which there is an abnormally low level of the chloride ion in the blood (< 98 mmol/l)
- accompanied by hypochloremic alkalosis, hypokalemia, and usually hyponatremia

Causes:

- **Nonrenal:**
  - loss of GI fluids – vomiting, fistula in proximal part of GIT
- **Renal:**
  - increased renal excretion of Cl^- – polyuric stage of renal failure, a massive treatment with diuretics

- **Treatment:** correction of the underlying cause, saline, 7.5% KCl if the hypokalemia is also present

Hyperchloremia

- is an electrolyte disturbance in which there is an abnormally elevated level of the chloride ion in the blood (> 107 mmol/l)
- often combined with metabolic acidosis and hypernatremia
- **Causes:** infusion therapy, diarrhea, kidney diseases (e.g. renal tubular acidosis), overactivity of the parathyroid glands etc.
- **Treatment:** correcting the underlying cause, restriction of intake, diuretics (rarely)

Thank you for your attention.