Pathophysiology of water and ion metabolism

Ágnes Haris MD, PhD
Budapest
Sudden disaster on a Sunday afternoon .....  

- 84 years old female, admitted to hospital 12 days earlier because she had had diarrhoea for 3 days  
- On admission she looked volume depleted, had low BP (90/50 mmHg)  
- Laboratory results: Hgb 9.86 g%, serum Na 134 mmol/l, K 3.0 mmol/l, BUN 21.9 mmol/l, creatinine 182 umol/l  
- She got 0.9% NaCl infusion+KCl for 3 days the BP normalized (118/59 mmHg), the labs: Na 141 mmol/l, K 3.6 mmol/l, BUN 4.1 mmol/l, creatinine 86 umol/l  
- The gastroenterology team decided to go on with GI work up in order to look for the cause of anemia
Sudden disaster on a Sunday afternoon ..... 

- Scheduled for colonoscopy on Monday (plan to preparing her by Fleet enema on Sunday evening)
- Instruction by the nurse on Sunday morning: „no solid food to eat, only fluids to drink”
- On Sunday morning – complaints free, ambulating, „looked nervous”
- In the afternoon: she suddenly lost her consciousness, had a convulsion, did not respond even to pain, had uncoordinated movements in all her extremities. Repeatedly vomited.
Sudden disaster on a Sunday afternoon ..... 

- Urgent labwork: serum Na 117 mmol/l, K 2,9 mmol/l, 
  BUN 2,4 mmol/l, cretinine 98 umol/l 
- Urinary osmolality 431 mOsm/kg, urinary Na 164 
  mmol/l, K 44 mmol/l hrs, 900 ml/12 hrs 
- Brain CT: 
  - no major abnormality can be seen 
- She remained unconscious in the next day: 
  Neurological examination: 
  - no primary neurological abnormality, 
  EEG: diffuse functional cortical abnormality
Sudden disaster on a Sunday afternoon ..... 

- Why was she mildly hyponatremic on admission?
- Why had she severe hyponatremia 12 days later?
- What do you think about the urinary osmolality of 431 mOsm/kg?
- And about the urinary Na of 164 mmol/l?
- What is your suggestion for treatment on the day of admission?
- What would you give on the 12th day? How much?
Hyponatremia

ADH secretion + Water intake

Both need to be present

Why ???

Why is ADH secreted in spite of hypoosmolality?
Where is the water coming from?

Is this an acute or a chronic condition?
ADH secretion

- In physiologic conditions
  - increased osmolality
  - increased serum Na

- In pathophysiologic conditions
  - stress, anxiety, pain, fever, nausea, vomiting
  - severe hypovolemia due to
    - fluid loss
    - diuretic use
  - effective volume depletion
  - SIADH
  - medications
Treatment on the first day

- The major stimulus for ADH was the volume depletion
- 0.9 % NaCl infusion shuts off the stimulus for ADH secretion
- How do you know this? The urine with high osmolality (evidence for ADH secretion) changes to less concentrated urine → the patient becomes able to excrete free water → the low serum osmolality and low serum Na are increasing and get normalized
- Hypertonic Na infusion is unnecessary and dangerous
Treatment on the 12th day

- Acute, severe hyponatremia, causing convulsion, coma, vomiting → very likely cerebral edema
- Urine osmolality: 431 mOsm/kg means - strong influence of ADH
- Urine Na: 164 mmol/l means - no volume depletion
- Treatment: 3% NaCl infusion
- How much?
Treatment on the 12th day

- Weight of the patient: 72 kg. Body water: 42 l
  In order to elevate her serum Na by 1 mmol/l, she needs 42 mmol Na
  In order to elevate serum her Na by 5 mmol/l, she needs 210 mmol Na
  It means 408 ml of 3% NaCl infusion
- Follow urinary Na loss and replace it
- Check electrolytes frequently
Treatment on the 12th day

- She got 300 ml 3% NaCl infusion (154 mmol) and 4 g KCl
- 4 hours later serum Na 119 mmol/l, K 3,2 mmol/l
- During Sunday night 300 ml 3% NaCl infusion (154 mmol) and 4 g KCl
- On Monday morning 300 ml 3% NaCl infusion (154 mmol)
- In 24 hours: serum Na 130 mmol/l, K 3,9 mmol/l
- Urinary losses in 24 hrs: 230 mmol Na and 62 mmol K
- In summary she got 462 mmol Na in the 1st 24 hrs
- Next day: serum Na 134 mmol/l, she regained consciousness
- Two days later: serum Na 140 mmol/l
Acute hyponatremia

ADH secretion + Water intake

Both need to be present

Why ???

Why is ADH secreted in spite of hypoosmolality?
- stress, anxiety, pain, fever, nausea, vomiting,
  typically in a perioperative situation

Where is the water coming from?
- hypotonic fluid intake, very often iv. infusions
Generation of EFW - Desalination

Balance:
Water intake: 2000 ml
Na⁺ intake 308 mmol
Excreted free water: 1000 ml
Excreted Na⁺: 308 mmol

No reason to retain NaCl
Persistent ADH action: 1 L electrolyte free water is retained in the body, which causes hyponatremia

1000 ml Salsol infusion
154 mmol Na⁺

1000 ml Salsol infusion
154 mmol Na⁺

Body

Urine 1000 ml
Na⁺ excretion 308 mmol
More tests than thoughts....

- 69 yrs female, in her past medical history:
  - 1990. Resection of malignant lung tumor
  - For 2 years hypertension, osteoporosis
  - Meds: indapamide, aspirin, carvedilol, vitamin D, Calcium suppl.
- 2008. october
  - dizziness, headache, unsteadiness, repeated falls
  - Once she invited guests, treated them, made conversation, but later did not remember these events
- SeNa  oct. 3.  141,   dec.19.  126,
  oct.29.  119,   febr.20.  120 mmol/l.
  nov.17. 124,
More tests than thoughts....

- Tests because of her complaints (oct-febr):
  - head CT, 2x head MRI, neurosurgical consultation (some traumatic contusions)
  - chest XR and CT, mammography, abdominal US, carotid art. doppler scan, neurological examination

- Modification of the therapy:
  - Indapamide changed to ramipril+hydrochlorothiazide
  - Increased salt and fluid (!) intake suggested (although the patient did not wish to drink much)

- **What is wrong with this lady?**
Not so difficult....

- Febr. 20. Nephrology consultation: discontinue the thiazide, continue increased salt intake but limit fluid intake
- March 10. Free of complaints - SeNa 140 mmol/l.
The most frequent causes of hyponatremia

Clayton et al. Q.J.Med 2006

- Hyponatremia was found in 108 of the 9622 patients admitted to internal medicine department in 6 months

- Etiology
  - **Thiazide diuretics** - 29 cases
  - **Congestive heart failure** - 27 cases
  - **Liver cirrhosis** - 21 cases
  - In further cases: volume depletion, medications, malignancies, lung- and cerebral diseases, hypothyroidism, Addison disease, hypoNa postoperatively, primary polydipsia and chronic renal failure

- During the hospitalization 20% of the patients died
Risk factors for thiazid-induced hyponatremia

Chow et al. Q.J. Med 2003

- Between 1996-2002, 223 thiazide caused hyponatremic patients were observed.
- SeNa: 98-128 mmol/l (mean 116±7 mmol/l).
- Average length of treatment 1-4479 day! (mean 105 day)
  - 42.8% indapamide,
  - 15.4% HCT+triamterene
  - 16.1% HCT,
  - 8.4% bendrofluazide
  - 17.3% HCT+amiloride,
- Thiazides were administered mainly for hypertension.
- Risk factors for developing hyponatremia: age, low body weight, hypokalemia.
Pathomechanism of thiazid-induced hyponatremia

- In most cases ADH secretion could not be explained by volume depletion!
- When thiazide is taken, the medulla can achieve high concentration – little ADH is enough to produce concentrated urine
- Decreased urinary dilution capacity in the elderly
- Increased fluid intake due to increased thirstiness (?)
- Decreased salt intake – advised medically sec.to HTN (?)
- Na\(^+\)-K\(^+\) transcellular shift in hypokalemia
- Activation of AQP-2 channels in cortical tubules due to thiazides – individual sensitivity (?)
Do cirrhotic patients need sodium in hyponatremia?

- 70 yrs old male, treated on an internal medicine department. He is a regular alcohol drinker, has liver cirrhosis, oedema on the legs and huge ascites.
- On admission: serum Na 132 mmol/l, K 4.2 mmol/l, BUN 5.7 mmol/l, creatinine 82 umol/l.
- Initial treatment: 100 mg spironolactone, 160 mg furosemide, 50 mg ethacrynic acid, 50 mg hydrochlorothiazide, 3 g KCl.
- In three days BW 115 → 111 kg, Na 132 → 125 mmol/l, creatinine 82 → 126 umol/l.
- Treatment: furosemide discontinued, others continued, + 5 g NaCl in Ringer infusion.
Do cirrhotic patients need sodium in hyponatremia?

- In the next three days: BW → 120 kg, SeNa → 117 → 109 mmol/l, creatinine → 270 umol/l,
- Even more NaCl given
- Consultation asked for nephrology service because oliguria, deteriorating renal functions: SeNa 112 mmol/l, K 3,8 mmol/l, BUN 8,8 mmol/l, creatinine 307 umol/l
  Urinary Na excretion 2 mmol/day, K 8,6 mmol/day
- How would you manage this patient?
Hyponatremia in cirrhotic patients

Splanchnic vasodilatation, ↓ systemic vascular resistance, ↓ MAP

Baroreceptor activation - „effective volume depletion”

↑ secretion of the „hypovolaemic hormones”

Renin → Ang.II.  ADH  Norepinephrine

Other factors causing hyponatremia:
- overgenerous diuretic treatment
- too much fluid intake (e.g. Beer drinkers)
Hyponatremia in congestive heart failure

↓ cardiac output, ↓ systemic blood pressure

Baroreceptors sense low perfusion pressure (in the carotid sinus, aortic arch, afferent arterioles in the kidneys)
„effective volume depletion”

↑ secretion of the „hypovolaemic hormones”

Renin → Ang.II.  ADH  Norepinephrine

Other factors causing hyponatremia:
Low cardiac output, high level of Ang II. → increased thirstiness
Disturbed free water clearance – effects of the "hypovolaemic hormones"

- Ang.II
- Norepinephrine

↓ GFR

↓ Isosomolar Na and water reabs.

Free water delivery into the distal nephron ↓
→ free water excretion ↓

↑ ADH

↑ free water reabs.

↑ AQP-2 expression
Hyponatremia in cirrhotic patients

- Severity of hyponatremia is proportional to the prognosis
- Correction of hyponatremia does not change the hemodynamical, pathophysiological abnormalities
- Mild hyponatremia usually does not cause any complaints, do not have to be treated (≥125 mmol/l)
- Treatment: decrease fluid intake in order to achieve negative fluid balance
- „Delicate” diuretic administration, mainly loop diuretics (if peripheral edema present, ↓BW: by 1-2 kg/d, if only ascites: <0.5 kg/d)
- Hypertonic saline infusion is contraindicated !!
- Vasopressin receptor antagonists: aquaretics (vaptans)
Therapy in CHF

- Survival is proportional to the degree of hyponatremia
- Its correction does not improve the prognosis of CHF
- ACEI/ARB
  - Cardiac output improves
  - ACEI decreases ADH’s effectivity in the cortical collecting duct, therefore water reabsorption ↓
  - Decreased thirstiness
- Moderate fluid restriction
- Administration of moderate doses of loop diuretics
- Vasopressin receptor antagonists: aquaretics (vaptans)
A case of SIADH

- 66 years old male, ALL diagnosed 9 months ago
- Got monthly bolus cytostatic treatments
- Developed aspergillus pneumonia - Rx intaconazole
- Admitted secondary to feeling unwell, weak, dizzy, but he was ambulating, can properly communicate
- Labs: Na 117 mmol/l, K 3,5 mmol/l, Cl 85 mmol/l, bicarb 23 mmol/l, BUN 6,5 mmol/l, creatinine 75 umol/l, BS 8,3 mmol/l, serum osmolality 237 mOsm/kg, urinary Na 83 mmol/l, osmolality 456 mOsm/kg, normal TSH
- According to his chart: serum Na 123-133 mmol/l previously
- Why does he have ADH? Acute or chronic?
Chronic hyponatremia

ADH secretion + Water intake

Both need to be present

Why ???

Why is ADH secreted in spite of hypoosmolality?
- hypovolemia due to fluid loss, diuretic use, effective volume depletion, SIADH, medications

Where is the water coming from?
- usually not extraordinarily huge fluid intake
Inappropriate ADH secretion - SIADH

- **Malignancies**
  - small lung cell carcinoma
  - prostate, uterus cc.
  - pancreas, duodenum cc.
  - leukemia, lymphoma

- **Medications**
  - dDAVP, oxytocin, NSAID
  - antidepressants,
  - narcotics, nicotine
  - cytostatics
  - chlorpropamide
  - carbamazepine

- **Central nervous syst.dis.**
  - Tumors, abscess
  - infections
  - Demyelinization diseases
  - SAH, trauma

- **Lung diseases**
  - TBC, aspergillosis
  - pneumonia, abscess
  - obstructive lung disease
  - ventilation
Vaptans

- Vasopressin receptor antagonists – increase electrolyte-free water excretion
- Conivaptan (V1a and V2), tolvaptan, satavaptan, lixivaptan (V2 receptor antagonists)
- Indicated (in general) in euvolemic and hypervolemic hyponatremia
- Contraindicated in hypovolemic hyponatremia
- Overcorrection of hyponatremia has to be avoided!
- Very expensive drugs
Tolvaptan – EVEREST trial
Gheorghiade M et al., JAMA 2007. 297:1332

- Short and long term administration of tolvaptan
  - randomised controlled trial
  - 4133 patients admitted with chronic heart failure
- Body weight, dyspnea, edema ↓, serum Na ↑ more in patients who received tolvaptan
- But no effect on mortality, comparing to placebo
- Mental functioning showed small but significant improvement in the tolvaptan group
Tolvaptan – SALT1 and SALT2 trials
Schrier RW et al. NEJM 2006. 355:2099

- Two multicenter RCTs for 30 days
- Tolvaptan 225 pts, placebo 223 pts with SIADH, CHF, and cirrhosis
- Serum Na increased more in the tolvaptan group
- Hyponatremia recurred after tolvaptan was discontinued
- Patients in the tolvaptan group had increased thirst, dry mouth, increased urination
Hyponatremia in chronic renal failure

- **Our case:** 72 years old lady, regularly seen on clinic
  - eGFR 10 ml/min
  - Nausea, vomiting, feeling unwell
  - Se Na 129 mmol/l, urine output 3400 ml/day

- **On the next visit:**
  - Se Na 135 mmol/l
  - Urinary osmolality 284 mOsm/kg
  - Urine output 2800 ml/day

- **Why was she hyponatremic?**
What does the maximal urinary diluting capacity mean?

- Healthy persons:
  - Minimal urine osmolality: 50-80 mOsm/kg
  - Average solute excretion: 600-900 mOsm/day
    (300-450 mmol Na, K + the anions, and 300-450 urea)

- How much can we drink without the risk of hyponatremia?
  - Solute excretion / diluting capacity / L
    - 900 mOsm and 50 mOsm /kg = 18 L
    - 600 mOsm and 80 mOsm /kg = 7.5 L
    - 200 mOsm and 50 mOsm /kg = 4 L

- Beer potomania („Tea and toast” hyponatremia):
  - Low protein and salt intake, therefore low osmolar excretion and too much fluid intake
Hyponatremia in chronic renal failure

- The urine is „isostenuric” \( \approx 300 \text{ mOsm/kg} \)
- The kidneys are not able to dilute significantly better (nor concentrate)
- If the daily solute excretion 900 mOsm – maximally 3 L fluid can be excreted, without causing hyponatremia
- But on low protein and low salt diet the daily solute excretion ↓, therefore exaggerated fluid intake can cause hyponatremia
- Therapy: adjust fluid intake to the actual diluting capacity of the kidneys
What kind of i.v. infusion has to be given in hypernatremia?

- 81 yrs old male patient, admitted to hospital because of volume depletion and pneumonia. He was febrile, desoriented.
- Lab results: serum Na 156 mmol/l, K 5,0 mmol/l, BUN 22 mmol/l, creatinine 173 umol/l, glucose 6,1 mmol/l.
- Chest XR: pneumonia and pulmonary congestion
- Initial treatment: 500 ml of Ringer lactate infusion and 500 ml 5% glucose infusion
- Was this appropriate? What kind of change do you expect in serum Na concentration?
What kind of i.v. infusion has to be given in hypernatremia?

Next morning:
- Serum Na 157 mmol/l, osmolality 330 mOsm/kg
- Urinary Na 40 mmol/l, K 48 mmol/l, osmolality 463 mOsm/kg
(24 hrs collection could not be done)
What kind of i.v. infusion has to be given in hypernatremia?

- **Na balance**
  - the patient excreted 40 mmol/l sodium,
  - intake by RL: 67 mmol
    (Ringer lactate contains 132 mmol/l)

- **Treatment on the following day**
  1500 ml 5% glucose infusion, and he was eating and drinking a little
  Serum Na 159 mmol/l

- **Why? What can we do now?**
What kind of i.v. infusion has to be given in hypernatremia?

- Checking again the urinary excretion: Na 11 mmol/l, K 9,5 mmol/l osmolality 439 mOsm/kg
- He was excreting very little Na
- He was not able to increase his urine osmolality
- We gave 40 mg furosemide i.v. and 2500 ml 5% glucose infusion daily
- The urinary Na excretion increased to 52 mmol/l, K excretion to 30,2 mmol/l
- The serum Na decreased gradually and in 3 days normalized to 137 mmol/l
Sodium balance in diabetes insipidus

Balance:

- Water intake: 4000 ml/24 hr
- Na⁺ intake: 272 mmol
- Excreted water: 4000 ml/24 hr
- Excreted Na⁺: 140 mmol/24 hr

The patient retains 33 mmol Na⁺ by each L of infusion. In 24 hours, 132 mmol Na⁺ surplus created in the body.

4000 ml Rindex 5 infusion
68 mmol/l Na⁺

Body

4000 ml urine
Na⁺ concentration 35 mmol/l, osmolality 150 mOzm/kg
Hypokalemia – where does this huge amount of K go?

- A 62 yrs old female
- PMHx: collagen colitis – she had been well for years
- She presented with profuse, watery diarrhoea, several times daily. In the last days nausea and vomiting also occurred
- On admission: severely volume depleted, very weak, completely anuric, BP 60/40 mmHg.
Hypokalemia – where does this huge amount of K go?

- Labs on admission:
  Na 124 mmol/l, K 1,8 mmol/l, BUN 31,5 mmol/l, creatinine 665 umol/l

<table>
<thead>
<tr>
<th>Days</th>
<th>KCl g/day</th>
<th>HD-Dialysate K</th>
<th>Serum K</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
<td>3 mmol/l</td>
<td>1,5</td>
</tr>
<tr>
<td>2</td>
<td>14</td>
<td>3 mmol/l</td>
<td>2,3</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
<td>-</td>
<td>2,6</td>
</tr>
<tr>
<td>4</td>
<td>14</td>
<td>-</td>
<td>3,0</td>
</tr>
<tr>
<td>5</td>
<td>14</td>
<td>-</td>
<td>3,6</td>
</tr>
<tr>
<td>6</td>
<td>10</td>
<td>-</td>
<td>3,8</td>
</tr>
</tbody>
</table>
Hypokalemia – where does this huge amount of K go?

- Why did she need so much K?
  \[(83 \text{ g} = 1079 \text{ mmol})\]
- Did this patient have renal K wasting tubulopathy?
Hypokalemia – first step in differential diagnosis

- Urinary K excretion
  - In our patient: 19,5 mmol/day
    18,8 mmol/day

- TTKG – transtubular K gradient

\[
\frac{\text{Urine K}}{\text{Serum osmolality}} \times \frac{\text{Serum K}}{\text{Urine osmolality}}
\]

- In our patient: 4,9
Hypokalemia – where does this huge amount of $K$ go?

- Body weight of the patient: 60 kg
  Extracellular water: 10 l
  Intracellular water: 20 l

- K content of EC: $10 \times 4 = 40 \text{ mmol}$
  K content of IC: $20 \times 150 = 3000 \text{ mmol}$
An other hypokalemic patient ...

- 48 years old male
- PMHx: hypertension since his age of 30
- His mother, his sister and his son also have HTN
- Serum potassium between 2.5-2.8 mmol/l for years
- Meds on the first consultation: 20 mg amlodipin, 2x20 mg enalapril+hydrochlorothiazide, 4 mg prasosin, 2x2 g KCL
- Labs: serum Na 145 mmol/l, K 2.9 mmol/l, CN 7.7 mmol/l, creatinine 100 umol/l
- What kind of tests would you order?
An other hypokalemic patient ...

- 24 hr urinary Na: 262 mmol/day
  24 hr urinary K: 104 mmol/day
  urinary osmolality: 678 mOsm/kg
- TTKG 15,8
- What is the differential diagnosis?
An other hypokalemic patient ...

- Renin and aldosterone levels: repeatedly normal
- RAS, glucocorticoid overproduction excluded
- Rx: spironolactone – no change
- **What is your diagnosis and how would you treat this patient?**
• Continually open ENaC
• Familiar HTN
• Suppressed renin and aldosterone
• Rx: amiloride, triamterene

Liddle syndrome
Is this an emergency?
Life threatening hyperkalemia

- 82 years old female with HTN, DM, and CRF
- Serum creatinin earlier 150 umol/l
- Rx: 20 mg lisinopril, 20 mg spironolactone, 5 mg amiloride, 50 mg hydrochlorotiazide, 100 mg metoprolol, trimetroprim-sulfamethoxasol for one week
- Extremely week, unable to walk, than respiratory insufficiency developed
- Labs: serum Na 133 mmol/l, K 10,0 mmol/l, Cl 102 mmol/l, HCO3 18 mmol/l, kreat 265 umol/l, CN 31,5 mmol/l, Vc 26,4 mmol/l, urinary K 16 mmol/l.
- **How many reasons did she have for hyperkalemia?**
Inhibitors of renal potassium excretion

↓ Renin
  - metoprolol

↓ Ang II.
  - ACEI

↓ GFR
  - acute on chronic renal insufficiency

Decreased Na⁺ delivery

↓ aldosterone
  - spironolactone

↓ ENaC
  - amiloride
  - trimetoprim

(Lack of insulin
  - decreased K intake by cells)
Acid-base disorders
A bicarbonate of 2.3 mmol/l

- 78 yrs old male
  - PMHx: diabetes mellitus, hypertension
  - admission in very poor condition: desoriented, Kussmaul-breeding, BP 88/52 mmHg, oligo-anuric

- Serum Na 139 mmol/l, K 5,8 mmol/l, Cl 99 mmol/l
  BUN 39 mmol/l, creatinine 504 umol/l,
  bicarb 2,3 mmol/l

- What should we do?
A bicarbonate of 2.3 mmol/l

- Blood-gas analysis:
  - pH 6.97
  - HCO₃⁻ 2.3 mmol/l
  - pCO₂ 10.2 mmHg

- What kind of acid-base disorder is this?
A bicarbonate of 2.3 mmol/l

- Decrease in bicarbonate
  \[25 - 2.3 = 22.7 \text{ mmol/l}\]

- Respiratory compensation: delta pCO2
  \[40 - pCO_2 = 40 - 10.2 = 29.8 \text{ mmHg}\]

- Anion gap
  \[\text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-) = 139 - (99 + 2.3) = 37.7 \text{ mmol/l}\]
The patient has:
- high anion gap metabolic acidosis

His lactate level:
- 12.2 mmol/l

He was taking metformin, which caused lactic acidosis

He was dialysed, survived, but remained dialysis dependent
Types of anion gap acidosis

Gain of acids

Endogenous acid production
- ketoacidosis
- L-lactic acidosis (A and B-types)
- D-lactic acidosis
- advanced renal failure

Exogenous acids
- ethylene glycol
- methanol
Glucose

Glucose-6-phosphate

Piruvate

Oxygen is necessary for the ATP production in the mitochondria. „A” type L-lactic acidosis develops, when there is no oxygen supply, therefore ATP is not produced. The consequence: increased glycolysis and lactate production.

Mitochondria

Acetyl-CoA

Citrate cycle

CO₂ + H₂O + ATP

NADH

NAD⁺

Lactate dehydrogenase

Lactate - + H⁺

NADH

NAD⁺

Piruvate dehydrogenase
The most frequent causes of „B” type L-lactic acidosis
A 42 yrs old male patient consulted by nephrology service
He was admitted to the hospital secondary to rapidly deteriorating physical condition the previous day
Medical Hx: joint problems, hip replacement, on NSAIDs, aethyl abusus

Labs on admission:
-Serum Na 138 mmol/l, K 2,9 mmol/l, Cl 121 mmol/l, BUN 24,8 mmol/l, creatinine 432 umol/l, Hgb 9,6 g%
-Blood gas analysis: pH 7,29, bicarbonate 10,8 mmol/l, pCO2 14,2 mmHg

Gastroscopy revealed bleeding from gastric ulcers

What kind of acid-base disorder is this?
Deteriorating pH

- Decrease in bicarbonate
  \[25 - 10,8 = 14,2 \text{ mmol/l}\]

- \(\text{delta pCO2}\)
  \[40 - \text{pCO}_2 = 40 - 14,2 = 25,8 \text{ mmHg}\]

- Anion gap
  \[\text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-) = 138 - (121 + 10,8) = 6,2 \text{ mmol/l}\]
Deteriorating pH

- Treatment: he got proton pump inhibitor, Na-bicarbonate infusion and furosemide, but did not improve

- Blood gas analysis few hours later:
  pH 7.19, bicarb 9.1 mmol/l, pCO2 24.3 mmHg
  (previous: pH 7.29, bicarb 10.8 mmol/l, pCO2 14.2 Hgmm)

- What happened to the pH?
Deteriorating pH

- Next day:
  pH 6.84, bicarb 9.7, pCO2 57.6 mmHg
  (previous: pH 7.29, bicarb 10.8 mmol/l, pCO2 14.2 Hgmm
   pH 7.19, bicarb 9.1 mmol/l, pCO2 24.3 mmHg)

- What kind of acid-base disorder is this now?
Acidosis

pH ↓

- HCO₃⁻ ↓
  metabolic acidosis
  pCO₂ ↓
  respiratory compensation
  1:1

- pCO₂ ↑
  respiratory acidosis
  HCO₃⁻ ↑
  metabolic compensation
  1:0,3
Alkalosis

\[ \text{pH} \uparrow \]

- **HCO_3^- \uparrow**
  - **metabolic alkalosis**
    - **pCO_2 \uparrow**
      - **respiratory compensation**
        - \(1:0.7\)
  - **pCO_2 \downarrow**
    - **respiratory alkalosis**
      - **HCO_3^- \downarrow**
        - **metabolic compensation**
          - \(1:0.5\)
A complicate case

■ 33 yrs old male patient

■ PMHx: ileocecal reticulosarcoma, ileum and colon resection, irradiation colitis, moderate chronic renal failure, recently proved distal renal tubular acidosis

■ Medical Hx: has usually 3-4 bowel movements/day
   Had several GI tests performed recently, and severe, watery diarrhoea developed
   Admitted in a very poor condition, severely volume depleted

■ Labs: Serum Na 142 mmol/l, K 2.99 mmol/l, Cl 119 mmol/l, BUN 7.6 mmol/l, creatinine 224 umol/l,

■ Blood gas analysis: pH 7.19, bicarb 12.0 mmol/l, pCO2 32 mmHg
A complicate case

- What kind of acid-base disorder is this?
- Why is he hypokalemic?
A complicate case

- Combined metabolic and respiratory acidosis
  - delta bicarbonate: $25 - 12 = 13$ mmol/l
  - delta pCO$_2$: $40 - 32 = 8$ mmHg

- Anion gap: $142 - (119 + 12) = 9$
  (lactate level $1.03$ mmol/l)

- Urinary K excretion $9.9$ mmol/l
  - non-renal K loss

- Is this acidosis due to gastrointestinal bicarbonate loss or renal abnormality?
Differential diagnosis of non-anion gap metabolic acidosis

Low plasma bicarbonate level

Gastrointestinal bicarbonate loss

Renal tubular abnormality

- pRTA
- insufficient NH$_4^+$ production
- dRTA

Urine Cl$^-$ $>>$ Na$^+$+K$^+$ (refers to NH$_4^+$ production)
Physiologic bicarbonate reabsorption in the proximal tubule. pRTA develops due to reduced indirect bicarbonate reabsorption.
Bicarbonate-ammonia production is necessary for H⁺ excretion.
dRTA develops if the H⁺ secretion is disturbed in the collecting duct.
Gastrointestinal disease diagnosed by blood pH

- A 41 year-old male patient, admitted to hospital secondary to nausea, vomiting and epigastric pain
- On admission he looked severely volume depleted, had a BP of 96/58 mmHg
- Labs: serum Na 123 mmol/l, K 3.5 mmol/l, BUN 24 mmol/l, creatinine 355 umol/l,
- Blood gas analysis: pH 7.65, bicarb 43 mmol/l, pCO2 55.2 mmHg.
- What is your diagnosis?
Gastrointestinal disease diagnosed by blood pH

- Metabolic alkalosis, hyponatremia and hypokalemia, acute renal failure
- According to the clinical picture – suspicion of pylorus stenosis
- Gastroscopy confirmed this abnormality (ulcer causing pylorus stenosis)
- Therapy: 0.9 % NaCl infusion, KCl replacement, PPI
- Labs one week later: serum Na 143 mmol/l, K 5.1 mmol/l, CN 9.5 mmol/l, creatinine 128 umol/l, pH 7.39, bicarb 24.8 mmol/l, pCO2 44 mmHg.