Acid-base mysteries explained

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Hydrogen ion concentration pH 7.4

- In plasma 40 nmol/l (compared to mmol for other electrolytes M, mmol, µmol, nmol)
- In cells about 60 nmol/l
- Concentration is expressed as pH (puissance hydrogen)
- \( \text{pH} = \log1/H \)
- Water has pH 7.0 or \( 1 \times 10^{-7} \) M or 0.000 000 1 M or 100 nmol/l
- Plasma has pH 7.4 or \( 1 \times 10^{-7.4} \) or 40 nmol/l
[H+] = 7.XY  80-XY=H+

"puissance" Hydrogen
Sorensen & Hasselbalch

pH
Log 1/[H]

[H] nanomol/l
To convert pH to H (nmol/l) between pH values 7.20 and 7.60 subtract the last two digits behind the pH decimal value from 80

<table>
<thead>
<tr>
<th>pH</th>
<th>nmol/l</th>
<th>Calculation</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.60</td>
<td>20</td>
<td>80 - 60 = 20</td>
</tr>
<tr>
<td>7.50</td>
<td>30</td>
<td>80 - 50 = 30</td>
</tr>
<tr>
<td>7.40</td>
<td>40</td>
<td>80 - 40 = 40</td>
</tr>
<tr>
<td>7.30</td>
<td>50</td>
<td>80 - 30 = 50</td>
</tr>
<tr>
<td>7.20</td>
<td>60</td>
<td>80 - 20 = 60</td>
</tr>
<tr>
<td>7.10</td>
<td>90</td>
<td>extrapolate</td>
</tr>
<tr>
<td>7.00</td>
<td>100</td>
<td>water = 100</td>
</tr>
<tr>
<td>6.90</td>
<td>125</td>
<td>seldom</td>
</tr>
</tbody>
</table>
Buffer systems minimize pH changes: (Weak acid + excess conjugate base)

There are many buffer systems
\( \text{H}_2\text{CO}_3 + \text{HCO}_3 \) system provides about 60%
Hemoglobin provides about 35%
All the buffer systems are in equilibrium with each other

If we have to components to any one, we can calculate the pH relationships

\( \text{HCO}_3 \) system is an open system since we can manipulate both \( \text{PaCO}_2 \) and \( \text{HCO}_3 \)

\( \text{(HB)} \quad \text{B}^- \)
Alveolus: \( \text{gasCO}_2 \) (\( \text{PACO}_2 \) 38 mm Hg) 20 mmol/min

Alveolar capillary
\( \text{dCO}_2 \) (\( \text{PvCO}_2 \) 45 mm Hg; \( \text{PaCO}_2 \) 40 mm Hg)

Solubility coefficient
\( \text{PaCO}_2 \times 0.03 = 40 \text{ mmHg} \)

Endproducts of metabolism 20 mmol/min

\[ \text{dCO}_2 + \text{H}_2\text{O} \]

\[ \text{H}^+ \text{ 80 mmol/d; NH}_4\text{Cl and fixed acids} \]

\[ \text{Hb and other buffers} \]

\[ \text{Liver from AA and urea cycle} \]

\[ \text{H}_2\text{CO}_3 \leftrightarrow \text{H}^+ + \text{HCO}_3^{-} \]

\[ 1.3 \text{ mmol/l} \quad 40 \text{ nmol/l} \quad 24 \text{ mmol/l} \]
Lawrence Joseph Henderson (* 3. June 1878 in Lynn, MS, USA; † 10. Februar 1942 in Cambridge) was an American chemist and biologist.

He wanted this:
\[ H = \frac{24 \times pCO_2}{HCO_3} \]

(Henderson Formula)

\[ [H] = 24 \left( pCO_2 \right) = \frac{24 \times 40}{HCO_3} = 40 \text{ nmol/l} \]

Karl Albert Hasselbalch (* 1. November 1874 in Aastrup, Denmark; † 19. September 1962) was a physical chemist.

Henderson got this:
\[ \text{pH} = 6.1 + \log \frac{HCO_3}{0.03 \times PCO_2} \]

Ever seen one of your staff solving this thing on the wards?
Base excess (BE): The amount of acid or base that would be necessary, to titrate the pH value back to a value of 7.40.

Standard BE: Calculates the same assuming that the Hb = 5 g/dl.

Standard pH (Hasselbalch): The pH under standardized conditions assuming: PCO₂ 40 mm Hg, Temp 37 °C, und O₂ 100 % Sat.

Standard Bicarbonate: Defined as the metabolic component. It represents the HCO₃⁻ value: were the PCO₂ 40 mm Hg; Temp 37 °C, und O₂ 100 % Sat.

OK for 1950, but times have changed. Many physicians have not.
Acid-base „balance“

pH 7.4
[H] 40

7.20
60

7.60
20

PaCO₂ 40 mm Hg (respiratory)

HCO₃ 24 mmol/l (metabolic)
Acidemia = pH<7.35
Alkalemia = pH>7.45

• Acidosis and Alkalosis are syndromes (disease)
• Metabolic acidosis or alkalosis is primarily a bicarbonate problem
• Respiratory acidosis or alkalosis is primarily a PaCO$_2$ problem
• If the primary disturbance is metabolic, then the compensatory response will be respiratory
• If the primary disturbance is respiratory, then the compensatory response will be metabolic
Acute metabolic acidosis

pH 7.4
[H] 40

PaCO₂ 40 mm Hg (respiratory)

HCO₃⁻ 7 mmol/l (metabolic)

This pan got smaller
The respiratory component ($H_2CO_3$) is controlled by the lungs; we measure it as $PaCO_2$.

The lungs excrete 20,000 mmol of CO$_2$ per day.

The CO$_2$ content of a 70 kg person is 110 L.

The PaCO$_2$ reflects the alveolar ventilation.

\[ ClCr = \frac{UCrxV}{SCr} \]

\[ V_{ALV} \approx \frac{gCO_2 \times V}{PCO_2} \]
28 year-old man, who 2 weeks ago developed polyuria, polydypsia, lethargy, and weakness. In emergency department, his temperature is 38°C. BP is 90/50 mm Hg; HR 120/min; Resp 30/min

Patient #1

- Creatinine 400 µmol/l (n<105)
- Urea 40 mmol/l (n<9)
- Na 137 (norm 136-144), Cl 105 (n 95-105), K 4 (n 3.5-5.2) (mmol/l)
- Glucose 30 (n<11) mmol/l
- Urine stick Ketone ++++
- pH 6.97, PaCO₂ 18 mm Hg, PaO₂ 125 mm Hg (room air), HCO₃ 4 (n24) mmol/l

What could kill this patient within the next hour or so? You are offered his pH, his glucose, his bicarbonate, his creatinine, his failure to embrace the correct religion, his volume-depletion (shock)?
Acute metabolic Acidosis

H₂O + CO₂ ↔ H₂CO₃

pH / .4

[H] 40

7.20

60

7.00

100

H⁺ + HCO₃⁻

7.60

20

HCO₃⁻ 4 mmol/l (metabolic)

PaCO₂ 40 mm Hg (respiratory)

H⁺ = 24 x \( \frac{40}{4} \) = 240 nmol/l ≈ pH 6.62

This pan collapsed
Respiratory compensation comes within minutes

\[ H^+ = 24 \times \frac{18}{4} = 108 \text{ nmol/l} \approx \text{pH 6.97} \]

\[ \text{pH 7.4} \]
\[ [H] 40 \]

\[ 7.20 \]
\[ 7.60 \]
\[ 60 \]
\[ 20 \]

This pan is actively reduced

- 1 mm Hg \( \text{PaCO}_2 \)

- 1 mmol/l \( \text{HCO}_3^- \)

\( \text{PaCO}_2 \) 18 mm Hg (respiratory)

\( \text{HCO}_3^- \) 4 mmol/l (metabolic)
Metabolic acidosis is a HCO$_3^-$ problem; only two mechanisms can be responsible

H$_2$O + CO$_2$ $\rightleftharpoons$ H$_2$CO$_3$ $\rightleftharpoons$ H$^+$ + HCO$_3^-$

- Gain
- Loss

• Either gain of strong acid
  – In that case the, H$^+$ require an accompanying anion.
  – HCO$_3^-$ be lost from the body.
  – Then we need to find out where the HCO$_3^-$ could be going.
The "metabolic component is the HCO₃⁻ ion in plasma; The cations = anions in terms of their electrical charge meq/meq (mval/mval).

UK = 10 mmol/l
Na = 140 mmol/l

UK = K+Ca+Mg and + Proteins

UA = 18 mmol/l
HCO₃⁻ = 24 mmol/l
Cl = 104 mmol/l

UA = Albumin 12 mmol/l, PO₄, SO₄, and others
Metabolic acidosis with increased anion gap

**Normal**

- Na: 140
- UA: 6
- HCO₃: 25
- Cl: 104
- Total: 146

**Elevated UA**

- Na: 137
- UA: 6
- HCO₃: 34
- Cl: 105
- Total: 143

**Elevated Cl**

- Na: 140
- UA: 6
- HCO₃: 12
- Cl: 117
- Total: 146
Strong acid $H_2SO_4$

H ion must have a conjugate base

HCO$_3^-$ (conjugate base) losses
Wide anion gap after Adolph Kussmaul

- Ketoacidosis
- Uremia
- Salicylic acid (aspirin)
- Methanol
- Ethylene glycol
- Uremie (zwei mal für Anfänger)
- Lactic acidosis

There are very few others; the concept counts. These must be differentiated within 20 min.
Metabolic acidosis with increased and nonincreased UA

Normal

Increased UA

Increased Cl
Metabolic acidosis with a non-increased UA: Where did the $\text{HCO}_3^-$ go???
How does one lose $\text{HCO}_3^-$ ??
(Count the holes: Try lower GI tract or kidney)

- How does one lose $\text{HCO}_3^-$ ??
- (Count the holes: Try lower GI tract or kidney)
- Diarrhea
- Pancreatico-Cutaneous fistula
- Gall bladder drainage
- Kidney cannot reabsorb bicarbonate (proximal)
- Kidney cannot excrete hydrogen ion (distal)
- Not enough kidney left to excrete $\text{NH}_4^+$ (chronic renal failure)
Acute metabolic alkalosis: how can this happen?

pH 7.4
[H] 40

7.20
60

PaCO₂ 40 mm Hg (respiratory)

HCO₃ 60 mmol/l (metabolic)

7.60
20
Case: A 56 year-old alcoholic woman was admitted with “several days” of abdominal pain with vomiting. She had a history of ulcer disease and pancreatitis. She smoked 2 packs daily since age 12 yr. She had lost 10 kg. BP 100/70 mm Hg, HR 100/min RR 8/min, abdominal tenderness, EKG long QTc with “U” waves

- Na 125, K 2.6, Cl 54, HCO₃ 60 (mmol/l), pH 7.61, PaCO₂ 70, PaO₂ 65 (mm Hg)
- PCr 7 mg/dl, BUN 80 mg/dl, Blood sugar 65 mg/dl
- Amylase elevated
- Gastroscopy, duodenal ulcer with pyloric narrowing

- Primary disturbance ?
- Compensatory response ?
- Hypokalemia ?
- Urinary electrolytes ?
- Treatment ?
Compensated metabolic alkalosis: what are the penalties?

PaCO$_2$ 60 mm Hg (respiratory)

PaO$_2$ 68 mm Hg

pH 7.4

[H] 40

7.20

60

7.60

20

HCO$_3$ 60 mmol/l (metabolic)
Metabolic alkalosis (a HCO₃⁻ problem) can come about in only two ways

- H⁺ can be lost from the body
  - In this case, the H⁺ has an accompanying anion, namely chloride
- HCO₃⁻ can be gained inappropriately
  - Some crazy people actually eat HCO₃⁻ !!
  - HCO₃⁻ may be gained because H⁺ is being excreted by the kidney in exchange for Na reabsorption (mineralocorticoid effect)
How must this patient reabsorb Na? Only 54 mmol/l
Can be reabsorbed as NaCl, the rest must rely on H exchange
Why metabolic alkalosis is self-sustaining until the Cl deficit is replaced

UNaV, UCIV, UKV depend on intake
H is 80 mmol/d as NH3 and fixed acids

UNaV is low
UCIV is zero
H and K losses are high (paradoxical aciduria)
How do you know that this patient does not have underlying chronic respiratory acidosis?

- What is the appropriate compensation for metabolic alkalosis?
- Is the ECF volume contracted - and if so, why?
- Is the renal response appropriate?
- How can I test for chronic lung disease in this patient?
- What is the alveolar-arterial $O_2$ gradient?

**Patient had protracted vomiting**

BP 100/70, HR 100  
Na 125, K 2.6, Cl 54, $HCO_3$ 60 (mmol/l),  
PCr 7 mg/dl, BUN 80 mg/dl, Sugar 65 mg/dl  
mOsm = $2(125+2.6) + 65/18 + 80/2.8 = 280$

UNa= 10, UK 37, UCl = 1 (mmol/l)  
Uosm = 450  
TTKG = U/P K / U/P Osm  
TTKG around 7  
$PAO_2=150-(60 \times 1.25)=75$  
A:a 75-68=7 mm Hg  
No lung disease
Chronic compensated metabolic alkalosis

pH 7.4
[H] 40

PaCO₂ 44 mm Hg (respiratory)

HCO₃ 34 mmol/l (metabolic)
Volume expansion with metabolic alkalosis; No hypotension, no hypochloremia, yes hypertension; Patients usually have a serum Na on the „high“ side of normal

BP 150/110 mm Hg
Na 144 mmol/l
Cl 101
HCO₃ 34
K 3.2

TBW 40 L
mOsm 300
ECF 13 L
ICF 27 L

Patient had primary aldosteronism
Normal electrolyte relationship (left) compared to our patient (right)
Questions to ask when patients have metabolic alkalosis

• Is the ECV contracted?
• If the ECV is contracted, why?
• If the ECV is contracted, what is the renal response? The urine should be chloride free. If not, suspect diuretics
• If the ECV is not contracted, look for high aldosterone levels, high renin states, or primary hyperaldosteronism
Acid-base „balance“

pH 7.4
[H] 40

7.20 60

7.60 20

PaCO$_2$ 40 mm Hg (respiratory)

HCO$_3$ 24 mmol/l (metabolic)
pH 7.4
[H] 40

PaCO₂ 80 mm Hg (respiratory)
HCO₃ 24 mmol/l (metabolic)
The respiratory component \((H_2CO_3)\) is controlled by the lungs; we measure it as \(PaCO_2\).

The lungs excrete 20 000 mmol of \(CO_2\) per day.

The \(CO_2\) content of a 70 kg person is 110 L.

The \(PaCO_2\) reflects the alveolar ventilation.

\[
PaCO_2 \approx \frac{1}{V_{ALV}}
\]

\[
V_{ALV} \approx gCO_2 \times \frac{V}{PCO_2}
\]
Acid-base „balance“

pH 7.4
[H] 40

7.20 60

7.60 20

PaCO₂ 89 mm Hg (respiratory)

HCO₃ 47 mmol/l (metabolic)
### Measured values

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.329</td>
</tr>
<tr>
<td>pCO₂</td>
<td>89.8 mm Hg</td>
</tr>
<tr>
<td>pO₂</td>
<td>32.4 mm Hg</td>
</tr>
<tr>
<td>SO₂</td>
<td>52.5%</td>
</tr>
<tr>
<td>Hct</td>
<td>54%</td>
</tr>
<tr>
<td>Hb</td>
<td>18.8 mg/dl</td>
</tr>
<tr>
<td>Na⁺</td>
<td>138 mmol/l</td>
</tr>
<tr>
<td>K⁺</td>
<td>4.17 mmol/l</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>84.6 mmol/l</td>
</tr>
<tr>
<td>Glu</td>
<td>7.2 mmol/l</td>
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</tbody>
</table>

### Calculated values

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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<tbody>
<tr>
<td>BEecf</td>
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<tr>
<td>BE</td>
<td>14.5 mmol/l</td>
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<tr>
<td>SBC</td>
<td>36.9 mmol/l</td>
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<tr>
<td>HCO₃⁻</td>
<td>47.7 mmol/l</td>
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<tr>
<td>TCO₂</td>
<td>50.4 mmol/l</td>
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<tr>
<td>A</td>
<td>44.6 mm Hg</td>
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<tr>
<td>A-aDO₂</td>
<td>12.3 mm Hg</td>
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<tr>
<td>a/A</td>
<td>0.7</td>
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<tr>
<td>An.Gap</td>
<td>10.0 mmol/l</td>
</tr>
<tr>
<td>P50</td>
<td>27.9 mm Hg</td>
</tr>
<tr>
<td>O₂ Cap</td>
<td>24.2 ml/dl</td>
</tr>
<tr>
<td>O₂Ct</td>
<td>12.8 ml/dl</td>
</tr>
</tbody>
</table>

*Temperatur-abhängig*
Respiratory acidosis (a PaCO$_2$ problem) can come about by decreasing alveolar ventilation

- CO$_2$ and therefore H$_2$CO$_3$ is retained by the body
- The compensatory response must be metabolic, namely an increase in HCO$_3$
Acid-base balance summary

- Understand H\(^+\) concentration and pH
- Understand the H\(_2\)CO\(_3\) and HCO\(_3\) buffering system
- Understand the primary disturbance and the compensatory response (1:1, 1:0.7, or 1:0.3)
- Know what compensation is appropriate
- Understand the anion gap and gain of H\(^+\)
- Understand gain of HCO\(_3\) through loss of HCl or increased Na vs. H exchange
- Know alveolar ventilation - gain and loss of PaCO\(_2\)