How this all started

Fascination for Physiology
(Kidney, Electrolytes and Water)

Intrigued by dogma's
(in an era of Evidence Based Medicine)

The 'Bicarbonate Challenge'
(my 'fight' with a neonatologist)

I love Teaching

Upside down
World Map

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LEGEND
Capital ■ City, Town ●

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SOUTH ATLANTIC OCEAN

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NEW CALEDONIA

TONGA

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VANUATU

FIJI

SAMOA

TUVALU

KIRIBATI

NAURU

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SOLOMON ISLANDS

PAPUA NEW GUINEA

INDONESIA

MICRONESIA

NORTHERN MARIANAS

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FINLAND

UNITED KINGDOM

IRELAND

ICELAND

DENMARK

NORTH ATLANTIC OCEAN

SOUTH ATLANTIC OCEAN

ARCTIC OCEAN

GREENLAND

Case: Newborn (GA 38 w)

Day 1 postoperative (*gastroschisis*)
→ Circulatory Failure
→ Fluid Therapy (NaCl 0,9% & FFP) & Dopamine.

	RESULT
Na^+	131 mmol/L
K^+	5.5 mmol/L
Cl^-	110 mmol/L
Albumine	16.0 g/L
Lactate	**6.6 mmol/L**
pH	**7. 1**
pCO_2	**4.0 kPa = 30 mmHg**
HCO_3^-	**9.0 mmol/L**
sBEc	**-16.3 mmol/L**

Lactate Acidosis due to **anaerobic metabolism and SHOCK**

Traditional Interpretation (1)

Committee of the New York Academy of sciences 1965

Interpretation

Step 1

Na$^+$	131 mmol/L
K$^+$	5.5 mmol/L
Cl$^-$	110 mmol/L
Albumine	16.0 g/L
Lactate	**6.6 mmol/L**
pH	**7. 1**
pCO$_2$	**4.0 kPa = 30 mmHg**
HCO$_3$$^-$	**9.0 mmol/L**
sBEc	**-16.3 mmol/L**

pH = ?

-log [H+]

Acidemia: pH < 7.36 ([H+] > 44 nmol/L)

Alkalemia: pH > 7.44 ([H+] < 36 nmol/L)

Traditional Interpretation (1)

Committee of the New York Academy of sciences 1965

Interpretation	
Na$^+$	131 mmol/L
K$^+$	5.5 mmol/L
Cl$^-$	110 mmol/L
Albumine	16.0 g/L
Lactate	**6.6 mmol/L**
pH	**7. 1**
pCO$_2$	**4.0 kPa = 30 mmHg**
HCO$_3$$^-$	**9.0 mmol/L**
sBEc	**-16.3 mmol/L**

Step 1

pH = ?

-log [H+]

Acidemia: pH < 7.36 ([H+] > 44 nmol/L)

Alkalemia: pH > 7.44 ([H+] < 36 nmol/L)

Traditional Interpretation (2)
Committee of the New York Academy of sciences 1965

Interpretation

Step 2

Acidosis:
A primary abnormal process that, in the absence of compensatory mechanisms, causes an acidemia.

pH can be normal

Alkalosis:
A primary abnormal process that, in the absence of compensatory mechanisms, causes an alkalemia.

pH can be normal

Acidosis
or
Alkalosis

Respiratory

Metabolic

$\Delta\ pCO_2$

Determinants

$\Delta\ HCO_3^-$

Traditional Interpretation (2)

Buffer reserve

$\underset{\text{Base}}{HCO_3^-} + \underset{\text{Proton}}{H^+} \rightleftarrows H_2CO_3 \rightleftarrows \underset{\text{Water}}{H_2O} + \underset{\substack{\text{Carbo}\\\text{DiOxide}}}{CO_2}$

volatile Acid

METABOLIC ACIDOSIS

= ↓ *HCO$_3$*

= *BASE deficit*

H$^+$

An ACID is a Proton-Donor

$\underset{}{^-O-\overset{\overset{O}{\|}}{C}-R} \longleftarrow \underset{\text{Metabolic Acid}}{H O -\overset{\overset{O}{\|}}{C}-R}$

Traditional Interpretation (2)

Base *Proton* *Water* *Carbo DiOxide* *Lung Disease or Hypo-ventilation*

$$HCO_3^- + H^+ \rightleftarrows H_2CO_3 \rightleftarrows H_2O + CO_2 \uparrow$$

RESPIRATORY ACIDOSIS

= ↑ CO_2

= NORMAL HCO_3

Traditional Interpretation (2)
Committee of the New York Academy of sciences 1965

Interpretation	Determinants	Step 2

Respiratory: Δ pCO_2 **Metabolic**: Δ HCO_3^-

$$H^+ + HCO_3^- \leftrightarrow H_2CO_3 \leftrightarrow H_2O + CO_2$$

$$H^+ = K \times \frac{pCO_2}{[HCO_3^-]}$$

$$pH = pK + \log \frac{[HCO_3^-]}{S \times pCO_2}$$

Acidosis *or* Alkalosis

Henderson-Haselbalch equation

Traditional Interpretation (2)

Boston 'rule of thumbs' **Narins et al. 1980**
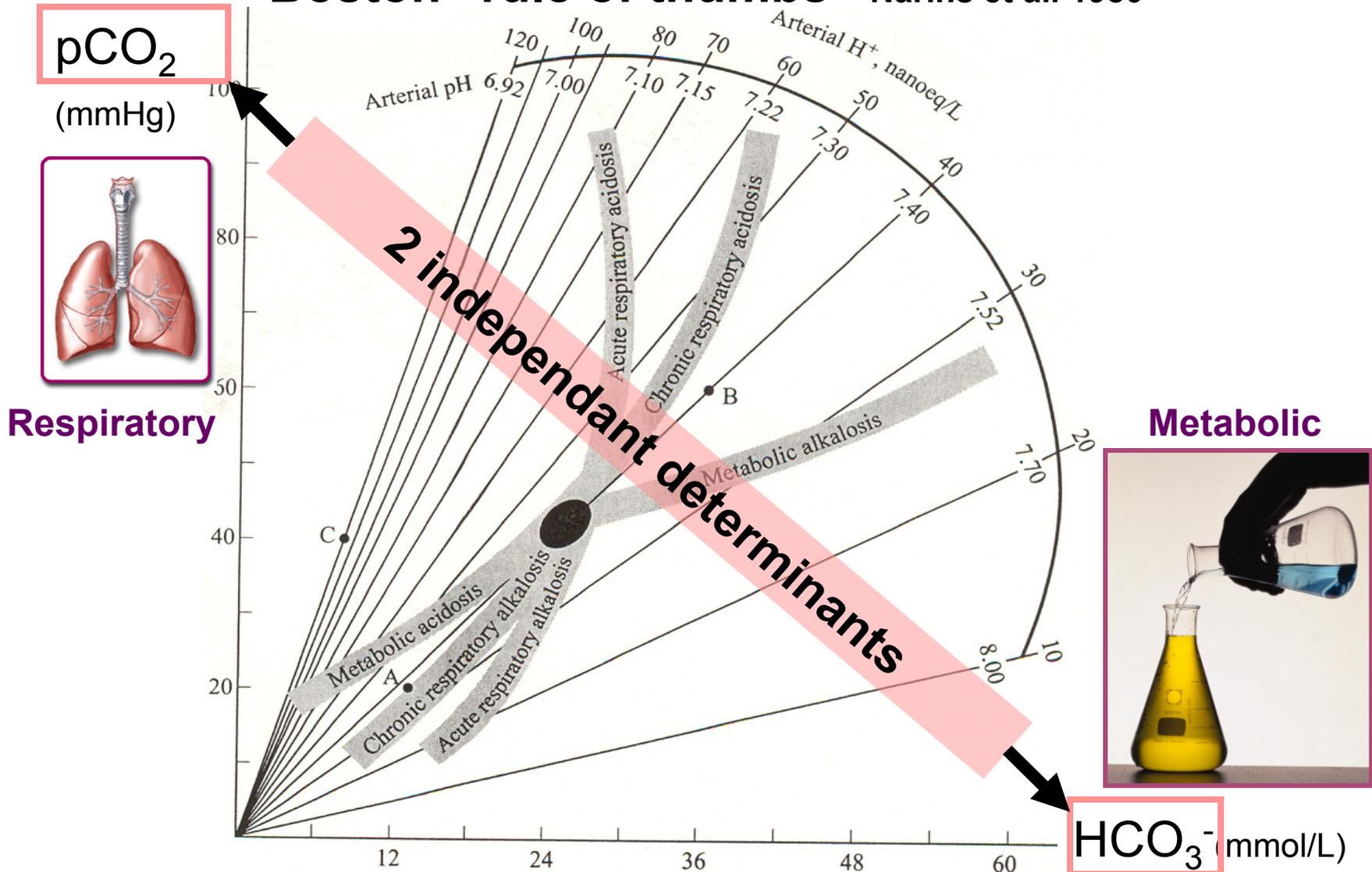
Traditional Interpretation (2)

Base   *Proton*   *Water*   *Carbo DiOxide*

Buffer reserve

$$HCO_3^- + H^+ \rightleftarrows H_2CO_3 \rightleftarrows H_2O + CO_2$$

volatile Acid

METABOLIC ACIDOSIS

= ↓ HCO_3

= *BASE deficit*

H⁺

An ACID is a Proton-Donor

$$\overset{\displaystyle O}{\underset{\displaystyle -O-\overset{\|}{C}-R}{}}$$
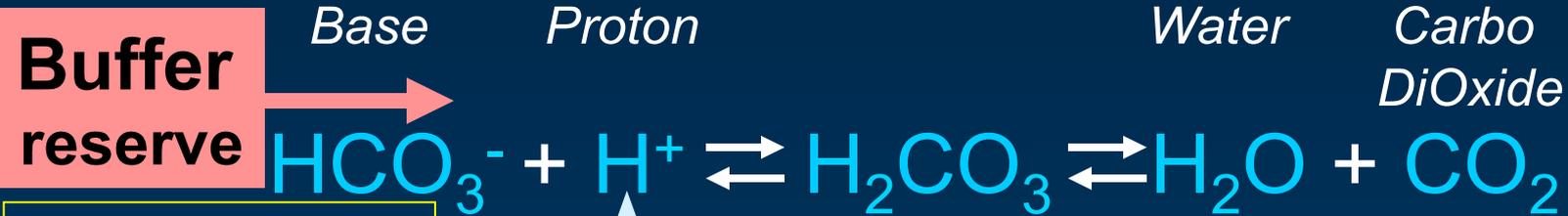
$$\overset{\displaystyle O}{\underset{\displaystyle HO-\overset{\|}{C}-R}{}}$$
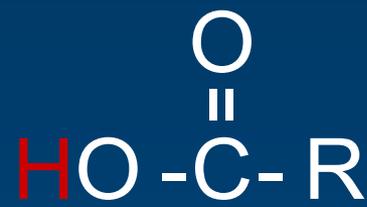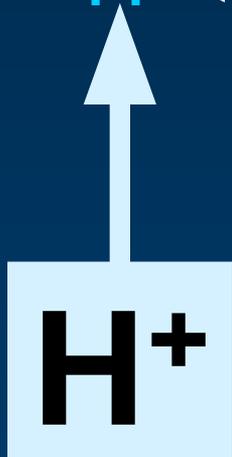
Metabolic Acid

Traditional Interpretation (2)

$H_3C-C-C-O^- \ H^+$ (HO, O, H)

Lactic Acid

$HCO_3^- + Na^+$

$H_3C-C-C-O^-Na^+$ (HO, O, H)
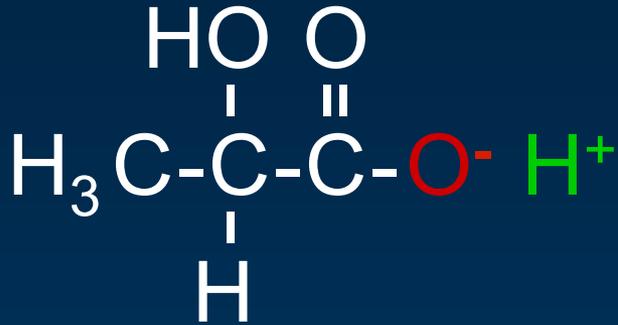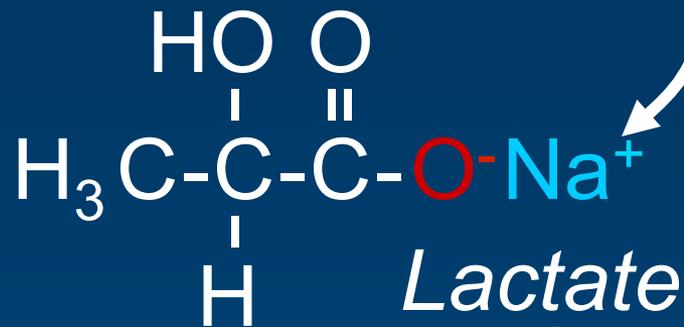
Lactate

$\downarrow$

Metabolism

$H_2CO_3 \rightleftharpoons H_2O + CO_2$

$\downarrow$

Expired

Traditional Interpretation (3)

Committee of the New York Academy of sciences 1965

| Interpretation | | Stap 3 |

Compensation
A secundary, normal process that in case of an acidosis or alkalosis, 'strives' for a normalization of pH

Compensation ?

Acid-Base abnormality   Compensation

| Metabolic Acidosis | $[HCO_3^-] \downarrow$ | *Hyperventilation* → | $pCO_2 \downarrow$ | Respiratory |
| Metabolic Alkalosis | $[HCO_3^-] \uparrow$ | *Hypoventilation* → | $pCO_2 \uparrow$ | *Fast* |

| Respir. Acidosis | $pCO_2 \uparrow$ | → | $[HCO_3^-] \uparrow$ | Renal |
| Respir. Alkalosis | $pCO_2 \downarrow$ | → | $[HCO_3^-] \downarrow$ | *Slow* |

Traditional Interpretation (3)

Committee of the New York Academy of sciences 1965

Interpretation

Stap 3

Compensation
A secundary, normal process that in case of an acidosis or alkalosis, 'strives' for a normalization of pH

Compen sation ?

Complete

pH normal

Incomplete

pH abnormal

Correction
Full disappearence of the primary process that initially had caused the acidosis or alkalosis

Correction

Traditional Interpretation (4)

Committee of the New York Academy of sciences 1965

| Interpretation | *In Metabolic Acidosis* |

Anion Gap

= [Non-Measured anions] = $[Na^+]+[K^+]-([Cl^-]+[HCO3^-])$

	Na^+	K^+	Cl^-	$HCO3^-$	
	140	4	105	24	mmol/L
Electro-neutrality	144		129	15	

Anion Gap • > 95 % Plama-proteins

Normal AG = 12-20 mmol/L

Anion Gap ?

Normal AG   **High AG**

Traditional Interpretation (4)

Committee of the New York Academy of sciences 1965

| Interpretation | *In Metabolic Acidosis* |

Step 4

Normal Anion Gap Metabolic Acidosis
= ↓ $[HCO_3^-]$ = ↑ $[Cl^-]$

	Na$^+$	K$^+$	Cl$^-$	HCO3$^-$	
	140	4	115	14	mmol/L

Electro-neutrality

| 144 | 129 | 15 |

| Causes |

Loss of Bicarbonate (Renal, Gut)

- Tubular immaturity
- Intestinal Secretion

Excess of Chloride

- Chloride infusion

Anion Gap ?

Traditional Interpretation (4)
Committee of the New York Academy of sciences 1965

| Interpretation | *In Metabolic Acidosis* |

Step 4

Normal Anion Gap Metabolic Acidosis
= ↓ $[HCO_3^-]$ = ↑ $[Cl^-]$

$$R\text{-}H \leftrightarrow R^- + H^+$$

Na^+ K^+ Cl^- $HCO3^-$

| 140 | 4 | 105 | 14 | mmol/L |

Electro-neutrality

| 144 | 119 | 25 |

Causes
- Lactate acidosis
- Keto-acidosis (diabetes mellitus)
- Intoxication
- Organic acidemia
- Renal Failure

Anion Gap ?

p.leroy@mumc.nl   November 22nd 2018

Traditional Interpretation

↓

"pH Life = Simple"

Acid = Proton-Donor (H$^+$)

Buffer (HCO$_3^-$) = Proton-Acceptor

Equation (Henderson-Hasselbalch) → pCO$_2$

Anion Gap (shows us the "*acid enemy*")

Is this all really true?

Traditional Interpretation
Committee of the New York Academy of sciences 1965

| Interpretation | *In Metabolic Acidosis* |

Na$^+$	131 mmol/L
K$^+$	5.5 mmol/L
Cl$^-$	110 mmol/L
Albumine	16.0 g/L

Lactate	**6.6 mmol/L**	→ *'Added' ACID*
pH	**7. 1**	→ *Acidemia*
pCO$_2$	**4.0 kPa = 30 mmHg**	→ *Incomplete Compensation*
HCO$_3$$^-$	**9.0 mmol/L**	→ *Metabolic Acidosis*
sBEc	**-16.3 mmol/L**	→ *Buffer Deficit*

? **Anion Gap = (131+5.5)-(110+9.0) = 17.5 = Normal !??**

Problem 1

What is an "*Acid*"

ACID   Brönsted & Lowry 1920: "a [H+] donor"

$$[HA] \Leftrightarrow [H^+] + [A^-]$$

<u>ACID</u> = a proton donor

Problem (1) The concept "<u>Acid</u>"

<u>NaCl 0.9%</u> induces *in vivo* a metabolic acidosis!

Is NaCl 0,9% an H^+ donor?

5L Serum

155 mmol Na^+

155 mmol Cl^-

1 Liter H_2O^-

pH=7.4

$[Na^+]=$**140** mmol/L

$[Cl^-]=$**100** mmol/L

$\Delta=$ **40**

1L NaCl 0.9%

6L

$[Na^+]=$**143** mmol/L (+3)

$[Cl^-]=$**109** mmol/L (+9)

$[H^+] > [OH^-]$

pH ↓ < 7.4

$\Delta=$ **34**

Hyperchloremic Acidosis

p.leroy@mumc.nl

November 22nd 2018

The roles for **Water, Electrolytes** and **Albumine**

$$H_2O \rightleftharpoons H^+ + OH^-$$

The roles for **Water, Electrolytes** and **Albumine**

Addition of Na⁺

$$Na^+$$

$$\downarrow$$

$$H_2O \rightleftharpoons H^+ \ + OH^- \longrightarrow NaOH$$

Strong Base

$$\downarrow$$

Metabolic ALKALOSIS

The roles for **Water, Electrolytes** and **Albumine**

Addition of Cl^-

$$Cl^-$$

$$\downarrow$$

$$H_2O \rightleftharpoons H^+ + OH^- \rightarrow HCl$$

Strong Acid

$$\downarrow$$

Metabolic ACIDOSIS

The roles for **Water, Electrolytes** and **Albumine**

Serum

[Water]	[Zouten]	[H$^+$]

mmol/L 55300   Na 140   0,00004

Cl 100

K 4

1.382.500.000   **3.500.000**   **1**

The abundance of water and electrolytes ?

HumorHound.com

Ignoring an abundance is quite <u>delicate</u> and not without a certain <u>risk</u>…

The roles for **Water**, **Electrolytes** and **Albumine**

$$H_3PO_4$$
Fosfaat

$$H_2O \rightleftharpoons H^+ + OH^-$$

Weak Acids

$$H_nAlbumine$$

Problem 2

"*pH*" is non-sense

"*pH*" is non-sense

pH 7.4

$$pH = -log_{10} [H^+]$$

$$[H^+] = 10^{-pH}$$

=40 nEq/L

ELECTRODE POTENTIAL (mV)

500

100^0C (74mV / pH UNIT)

50^0C (64 mV / pH UNIT)

0^0C (54 mV / pH UNIT)

ISOPOTENTIAL POINT

$[H^+]= 1 \times 10^{-7}$ Eq/L

0

-500

0   7   14

"*pH*" is non-sense

pH 7.4

$$pH = -\log_{10} [H^+]$$

$$[H^+] = 10^{-pH}$$ =40 nEq/L

$$pH = \log_{10} \{1/[H^+]\}$$

$[H^+] > 1$ Eq/L	$[H^+] = 1$ Eq/L	$[H^+] = 0$
$-\infty \leftarrow pH$	$pH = 0$	$pH = +\infty$

pH = double non-linear transformation of [H$^+$]

pH has <u>no dimension</u> (-∞ ↔ +∞)

pH creates <u>confusion</u>

Problem (2)   "*pH*" is non-sense

$$H_2O \rightleftharpoons H^+ + OH^-$$

$$[OH^-] = [H^+]$$

Acid-Base neutral

Temp	0 °C	25 °C	37 °C	100 °C
10^{-7} Eq/L	0,34	1,0	2,1	8,8
pH	7.5	7.0	6.8	6.1

Is water (an) ACID ?

"*pH*" is non-sense

$$H_2O \rightleftharpoons H^+ + OH^-$$

$$[OH^-] = [H^+]$$ Acid-Base neutral

Temp	0 °C	25 °C	37 °C	100 °C
10^{-7} Eq/L	0,34	1,0	2,1	8,8
pH	7.5	7.0	6.8	6.1

[H$^+$] may ↑ <u>WITHOUT</u> the addition of [H$^+$] !!!

"*pH*" is non-sense

Modern Definitions (Stewart, Kellum, Elbers 2009)

Acid Solution	$[H^+] > [OH^-]$

Alkalic Solution	$[H^+] < [OH^-]$

Neutral Solution	$[H^+] = [OH^-]$

Acid	Substance that causes a ↑ $[H^+]$

Base	Substance that causes a ↓ $[H+]$

Henderson-Hasselbalch is Incomplete

$$pH = pK + \log \frac{[HCO_3^-]}{S_{CO_2} \times pCO_2} \quad \textit{(Henderson-Hasselbalch)}$$

Mathematical transformation

$$\log pCO_2 = -pH + \log [HCO_3^-] / K \times S_{CO_2}$$

Buffer Curve – Van Slyke 1921

$$y = -ax + b$$

Linear relationship between **log pCO$_2$** and **pH**

Problem 4

How to assess buffering ?

(…how to assess the extent of the <u>metabolic component</u>)

Buffer

Swan & Pitts experiment
(1954)

Dogs: infusion 14 mmol H^+/L B_{ody} W_{ater}

pH 7.44 $\longrightarrow$ **pH 7.14**

$[H^+]$ 36 nmol/L $\longrightarrow$ **$[H^+]$ 72 nmol/L**

14.000.000 nmol - 36 nmol

=

13.999.964 nmol were buffered

99,99974%

$[HCO_3^-]$: a **measure** for Metab Acidosis?

Buffer reserve

Volatile Acid

$$HCO_3^- + H^+ \rightleftharpoons H_2CO_3 \rightleftharpoons H_2O + CO_2$$

H⁺

Acid

Problem (4) $[HCO_3^-]$: a **measure** for Metab Acidosis?

1

Respiratory: Δ pCO$_2$ Metabolic: Δ HCO$_3^-$

Buffer

Loss

Independent determinant   **Dependent determinant**

2 **[HCO$_3$] is partly determined by pCO$_2$**

(e.g. acute respiratory acidosis)

Problem (4) [HCO$_3^-$]: a **measure** for Metab Acidosis?

$[HCO_3^-]$: a **measure** for Metab Acidosis?

➡️ **Search for a CO_2-independent measure of the buffer status (buffer-reserve)**

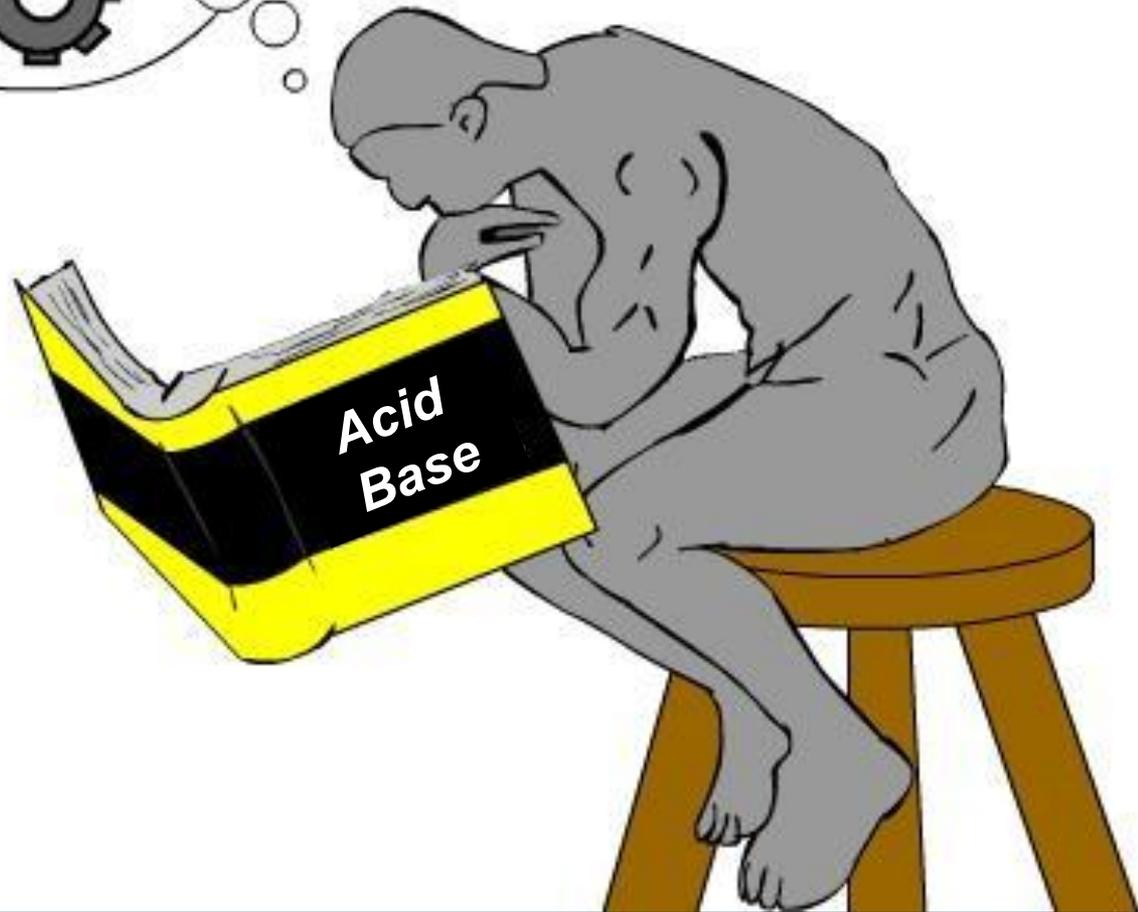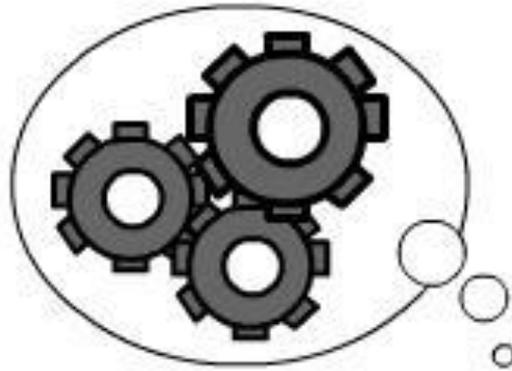| Singer&Hastings (1948): (~Faraday)	Van Slyke (1920s): *Standard Bicarbonate*
Buffer = [Pos Ions] - [Neg Ions]	= $[HCO_3^-]$ after equilibration to pH 7.4 and pCO_2 40 mmHg

BUFFER = $[HCO_3^-]+[A^-]$*

Base-forming

Acid-forming

Mainly Na^+

Mainly Cl^-

* Weak Acids **(proteins, phosph.)**

$[HCO_3^-]$: a **measure** for Metab Acidosis?

➡️ **Search for a CO$_2$-independent measure of the buffer status (buffer-reserve)**

Singer&Hastings (1948): (~Faraday)	Van Slyke (1920s): *Standard Bicarbonate*

Calculated	Siggaard-Andersen 1960: *Base Excess*

= represents the amount of **acid** or **alkali** that must be added to 1 liter of blood exposed in vitro (at 37°C) to a pCO$_2$ of 40 mmHg to achieve the average normal pH of 7.40.

→ Positive BE, if *acid* is required (pH>7.4)

→ Negative BE, if *alkali* are required (pH<7.4)

By use of the "*van Slyke*" equation

Problem (4)   [HCO$_3^-$]: a **measure** for Metab Acidosis?

BE = {[HCO$_3^-$] - 24.4 + ((2.3 x [Hgb] +7.7) x (pH-7.4))} x {1-(0.023 x [Hgb])}   *("Van Slyke Equation")*

BE still CO$_2$ dependent

Base Excess vs pH. Series: 17.2, 8.6, 4.6, SBEc

Kellum Crit Care 2005;9:500-507

SBEc= {[HCO$_3^-$]- 24.4 + ((8.3 x [Alb] x 0.15) + (0.29 x [Phosph.] x 0.32))} x (pH-7.4)   *Wooton 2003*

Weak Acids !

Problem (4) $[HCO_3^-]$: a **measure** for Metab Acidosis?

➡️ **Search for a CO_2-independent measure of the buffer status (buffer-reserve)**

SBEc is the best measure for the assessment of the metabolic component in acid-base disorders

NEW PROBLEM

Excess buffering ?
Other Acids ?
Lactate Acidosis ?

Lactate	**6.6 mmol/L**	**+ 5.6** mEq/L
pH	7. 1	
pCO_2	4.0 kPa = 30 mmHg	
HCO_3^-	9.0 mmol/L	
sBEc	**-16.3 mmol/L**	**-16.3** mEq/L

SOLUTIONS !

Acid
Base

Na⁺, K⁺, Ca⁺⁺, Mg⁺⁺

Strong Pos Ions

Strong Neg Ions

Cl⁻, Lactate⁻

Difference

Unmeasured Acids

Albumin PO₄⁻⁻

H₂O

Weak Acids

pH

[H⁺]

pCO₂

HCO₃⁻

H₂CO₃

Extra Cellular Buffer

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November 22nd 2018

Peter Stewart

1921-1993

1981: "*How to understand Acid Base Physiology*"

What is the role of bicarbonate in acid-base balance?
The answer is simply: <u>none!</u>

$[H^+]$ and $[HCO3-]$ are dependent variables, determined by other independent variables

An increase of $[H^+]$ does NOT need the addition of H^+ to the body fluid

<u>Physico-Chemical</u> approach

<u>Quantification</u> of all contributing factors

Edition 2009

www.acidbase.org

acidbase.org

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Electroneutrality: [+] = [-]

$$[Na^+]+[K^+]+[Ca^{++}]+[Mg^{++}]+[H^+]$$

$$= [Cl^-]+[Lact^-]+[HCO_3^-]+[A^-]+[CO_3^{-2}]+[OH^-]$$

$$[Na^+]+[K^+]+[Ca^{++}]+[Mg^{++}]-[Cl^-]-[Lact^-]+[H^+]$$

$$= [HCO_3^-]+[A^-]+[CO_3^{-2}]+[OH^-]$$

$$SID+[H^+]$$

$$= [HCO_3^-]+[A^-]+[CO_3^{-2}]+[OH^-]$$

"Conservation of charge"

Electroneutrality: [+] = [-]

"Conservation of mass" | $HA \Leftrightarrow H^+ + A^-$

$[A_{tot}] = [HA] + [A^-]$

4 equilibrium reactions

Water

$[OH^-] \times [H^+] = K_w'$

Weak Acids

$[A^-] \times [H^+] = K_a \times [HA]$

Bicarbonate ion

$[H^+] \times [HCO_3^-] = K_i' \times S \times pCO_2$

(Henderson-Hasselb.)

Carbonate ion

$[H^+] \times [CO_3^{-2}] = K_3 \times [HCO_3^-]$

Stewart equation → [H$^+$] as the only unknown

Stewart Equation

$$a[H^+]^4 + b[H^+]^3 + c[H^+]^2 + d[H^+] + e = 0$$

Strong Ion Difference (SID*)

Total [Weak Acids]
(albumin & Phosphate)

a = 1

b = SID + K_a

c = K_a x {[SID] + [A_{tot}] − K_w' − (K_i' x S x pCO_2)}

d = −{K_a x (K_w' + (K_i' x S x pCO_2)) − (K_3 x K_i' x S x pCO_2)}

e = −K_a x K_3 x K_i' x S x pCO_2

Strong
POS Ions

Strong
NEG Ions

SID*= [Na]+[K]+[Ca]+[Mg] − [Cl]−[Lact]

Stewart Equation

$$a[H^+]^4 + b[H^+]^3 + c[H^+]^2 + d[H^+] + e = 0$$

$$pH = pK_i' + \log \frac{[SID] - K_a \times [A_{tot}]/K_a + 10^{-pH}}{S \times pCO_2}$$

pCO_2, SID and $[A_{tot}]$ are <u>Independent</u> variables

pH, $[H^+]$ and $[HCO_3^-]$ are <u>Dependent</u> variables

SID* = [Na]+[K]+[Ca]+[Mg] - [Cl]-[Lact]

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Strong Ion Difference (SID)

$$\downarrow \text{[SID]} \longrightarrow \uparrow \text{[H}^+\text{]} \longrightarrow \downarrow \text{pH}$$

Ca^{++}
Mg^{++}
K$^+$

Lactate$^-$

Na$^+$

Cl$^-$

\+

\-

= **S**trong **I**on **D**ifference (SID)
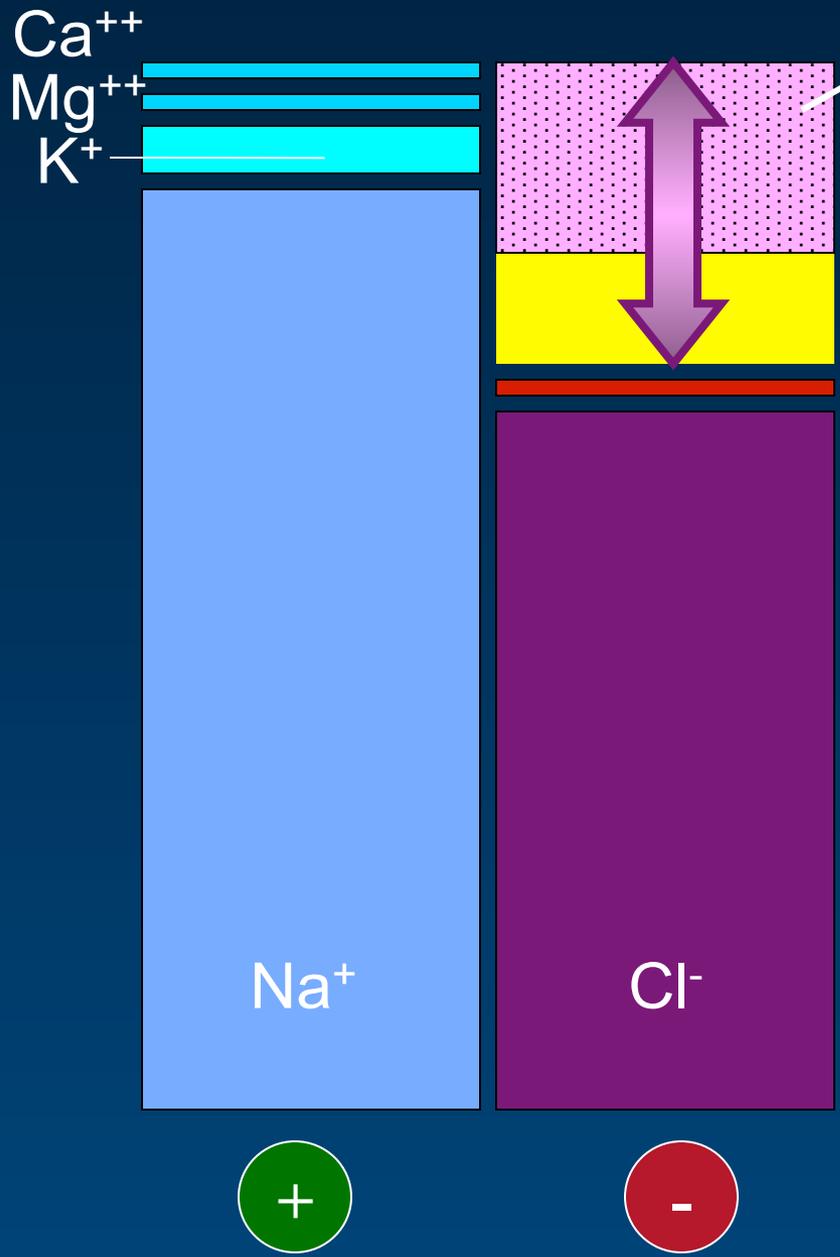= [Na]+[K]+[Ca]+[Mg]-[Cl]-[Lact]
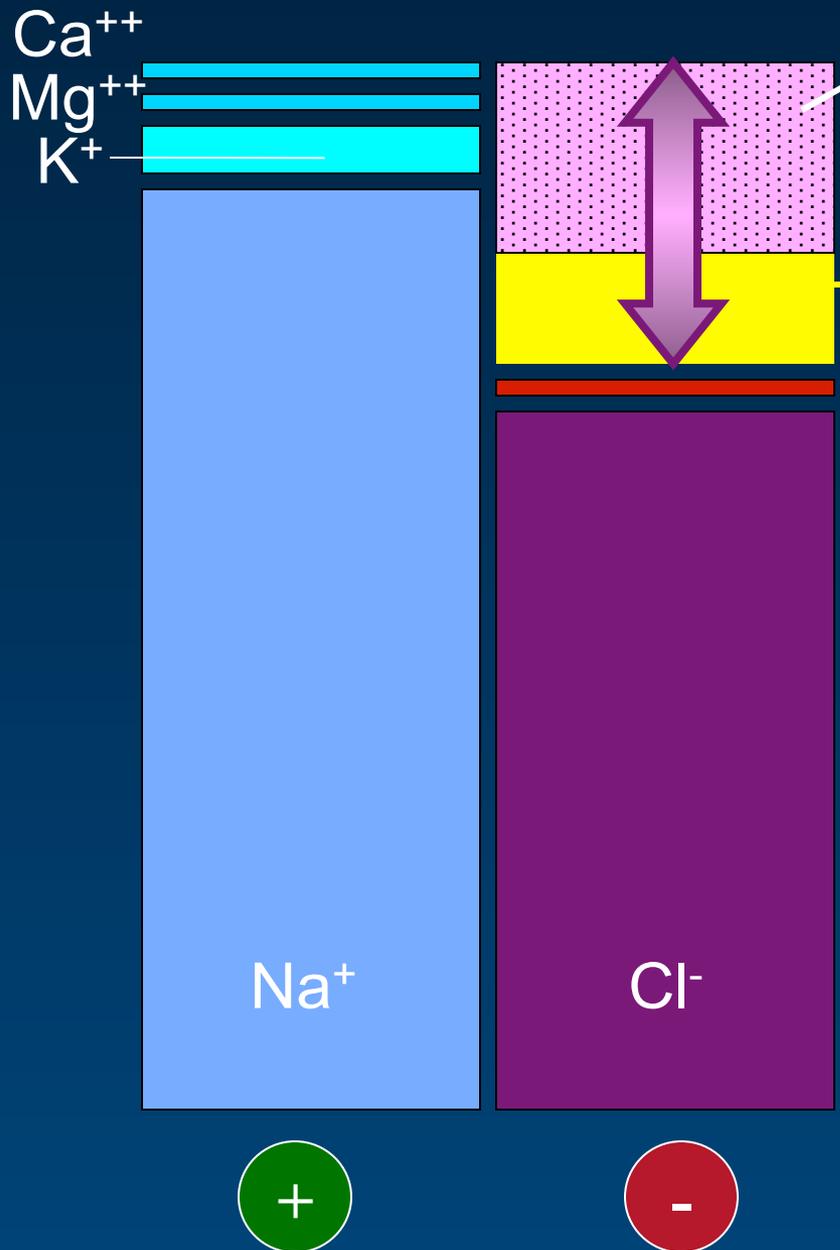
EFFECTIVE SID (SID_e)=
(Bi)carbonate

Phosphate

Albumin (A⁻)

$$SID_e = -2.46 \times 10^{-8} \times pCO_2/10^{-pH}$$
$$+ [Alb] \times 0.123 \times (pH-0.631)$$
$$+ [PO^{4-}] \times (pH-0.469)$$
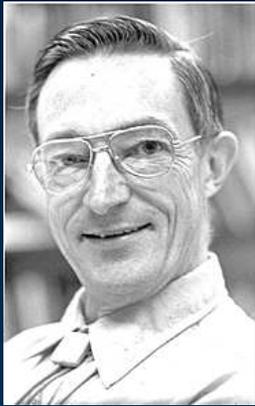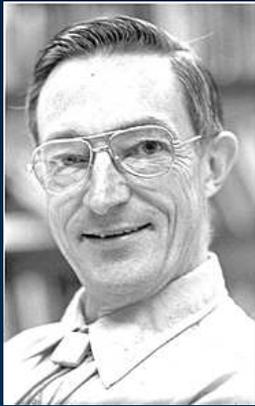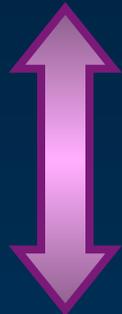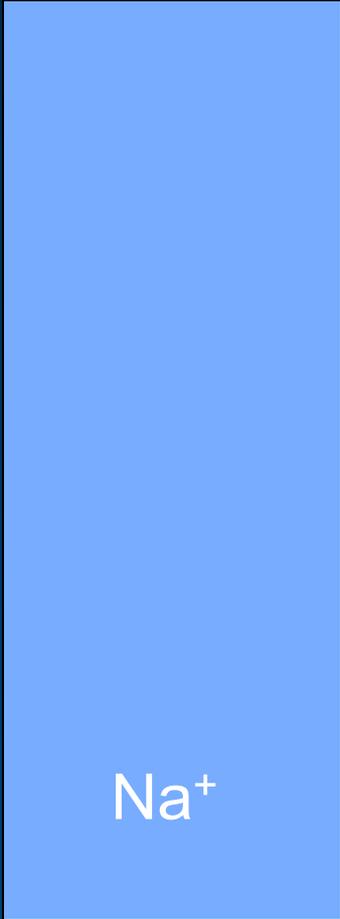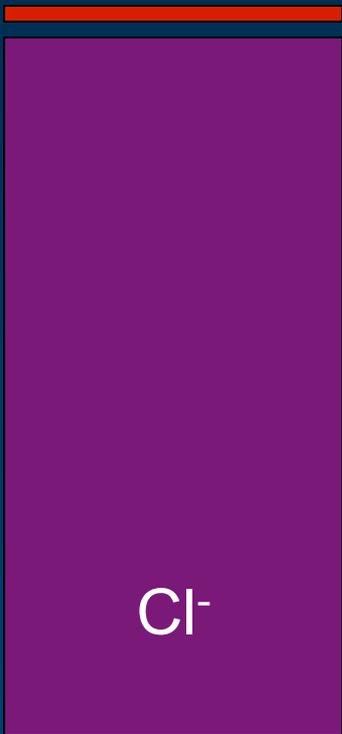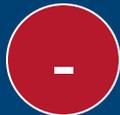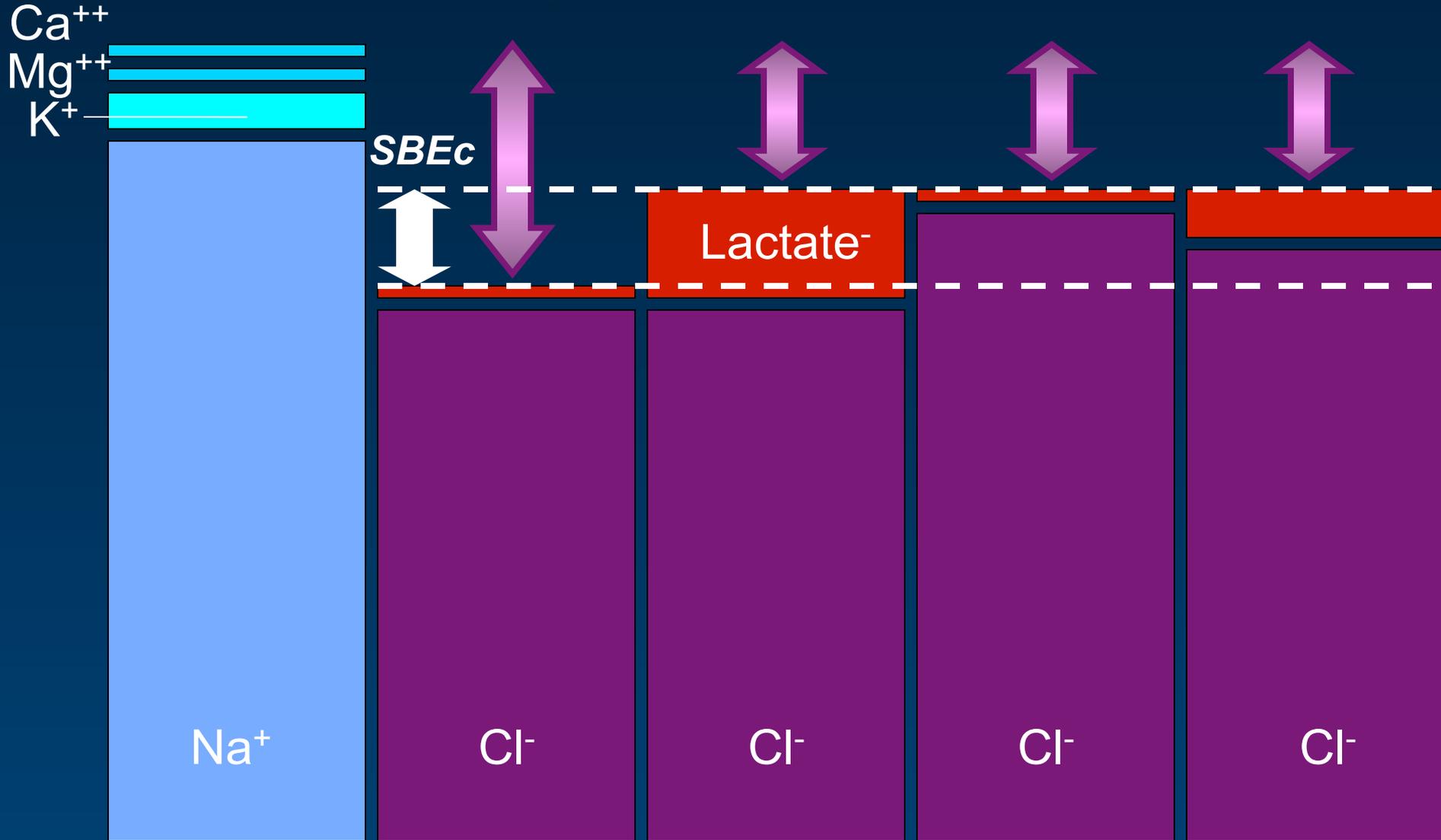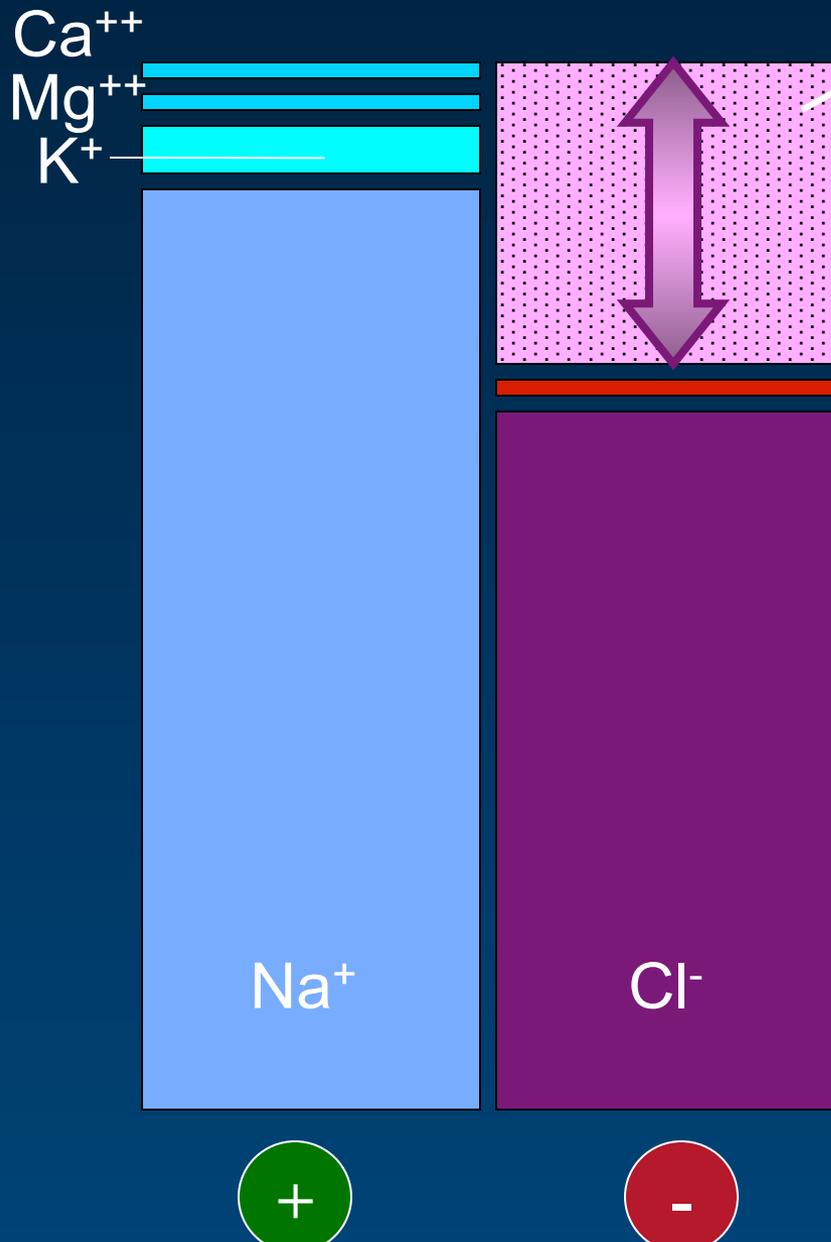
$= $ ▦ $\quad SID_a = SID_e$

Normal ± 40 mmol/L

= **S**trong **I**on **D**ifference (SID)
= [Na]+[K]+[Ca]+[Mg]-[Cl]-[Lact]
= **Apparent** SID (SID_a)

Ca⁺⁺
Mg⁺⁺
K⁺

Na⁺

Cl⁻

+

-

Ca^{++}
Mg^{++}
K$^+$

Na$^+$

Cl$^-$

(+)

(-)

EFFECTIVE SID (SID$_e$)=
(Bi)carbonate

Phosphate

Albumin (A$^-$)

SID$_e$= -2.46 x 10^{-8} x pCO$_2$/10^{-pH}
+ [Alb] x 0.123 x (pH-0.631)
+ [PO^{4-}] x (pH-0.469)

SID$_a$> SID$_e$

>

= **S**trong **I**on **D**ifference (SID)
= [Na]+[K]+[Ca]+[Mg]-[Cl]-[Lact]
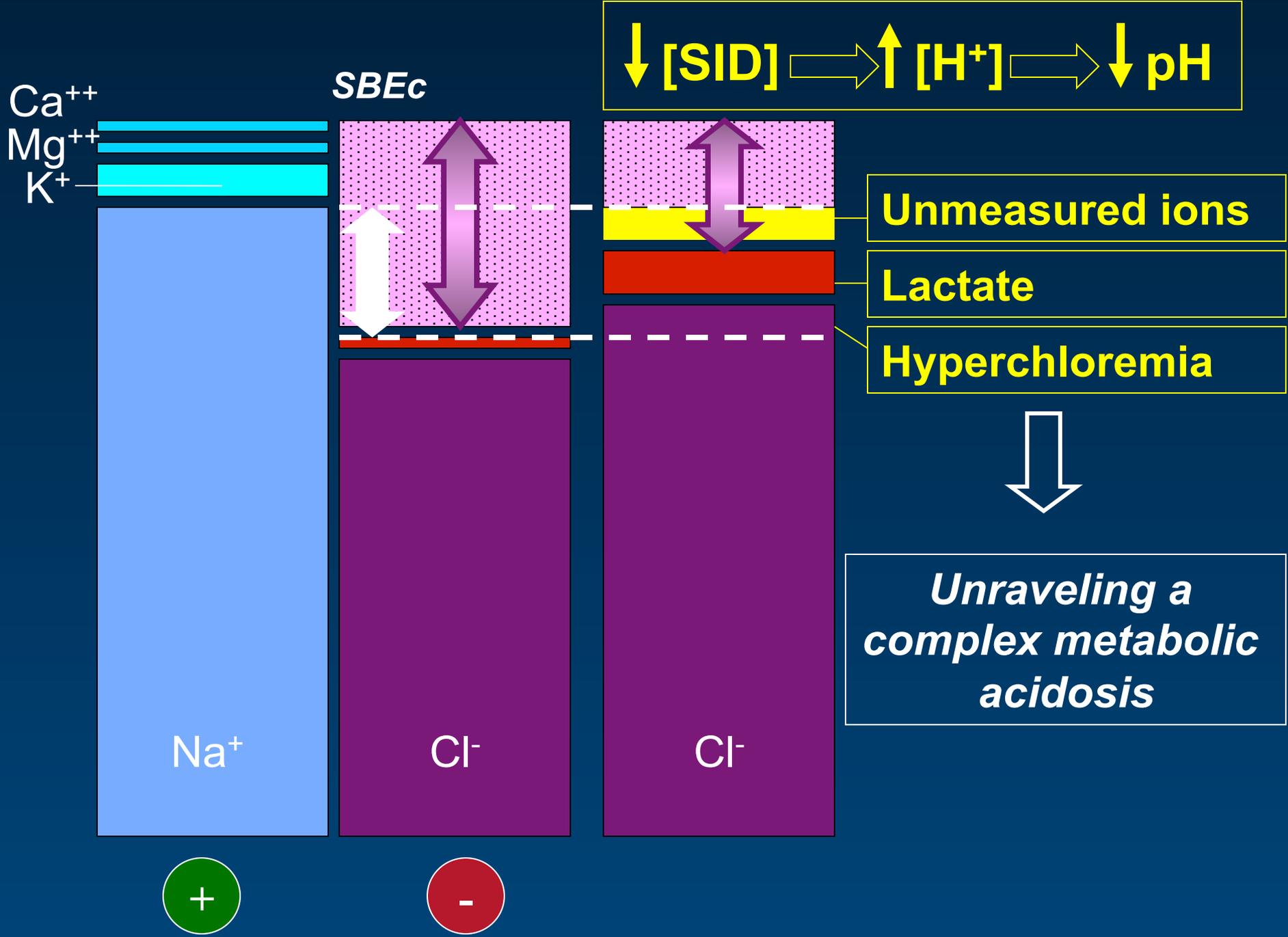= **Apparent** SID (SID$_a$)

EFFECTIVE SID (SID_e)

Strong Ion Gap (SIG) =
UNMEASURED ANIONS

(Citrate, D-lactate, ketoglutarate, pyroglutamate, succinate, toxins, unknown metabolites,…)

$SID_a > SID_e$

SIG = SID_a - SID_e

= **S**trong **I**on **D**ifference (SID)
= [Na]+[K]+[Ca]+[Mg]-[Cl]-[Lact]
= **Ap**parent SID (SID_a)

Ca^{++}
Mg^{++}
K^+

Na^+ Cl^-

+   -

	Result
Na^+	131 mmol/L
K^+	5.5 mmol/L
Cl^-	110 mmol/L
Albumin	16.0 g/L

| **Lactate** | **6.6 mmol/L** | **+ 5.6** mEq/L |

pH	**7. 1**
pCO$_2$	**4.0 kPa = 30 mmHg**
sBEc	**-16.3 mmol/L**	**-16.3** mEq/L

10.7 mEq/L Acids are **not** explained

SID$_a$ = [Na]+[K]+[Ca]+[Mg]-[Cl]-[Lact] = 22.8 (Normal = 40)

SID$_e$ = Calculation based on [HCO$_3^-$], [PO^{4-}] en [Alb$^-$] = 22.7

SIG = 0.1 ≈ 0 ⟶ <u>NO</u> unmeasured Negative Ions
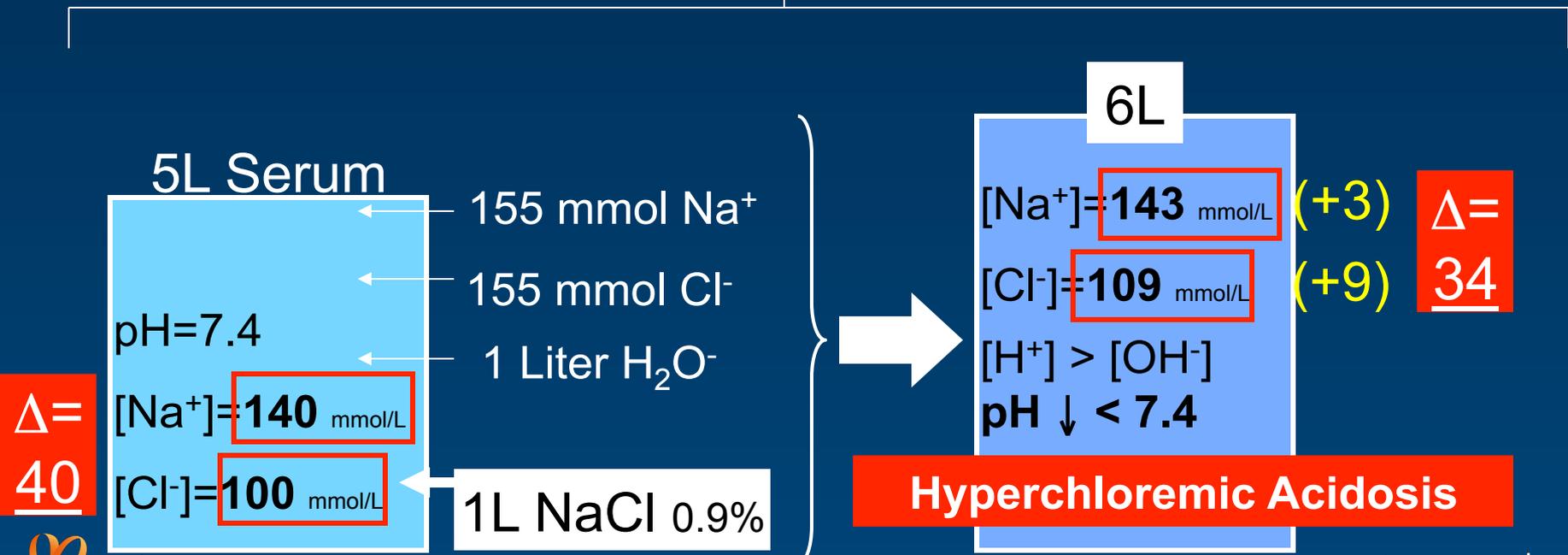
Problem (1) What is an "_Acid_"?

NaCl 0.9% generates _in vivo_ an acidosis !

Because **SID** is decreased !
(as we have increased [Cl$^-$]…)

5L Serum

155 mmol Na$^+$

155 mmol Cl$^-$

pH=7.4

1 Liter H$_2$O$^-$

[Na$^+$]=**140** mmol/L

Δ=40

[Cl$^-$]=**100** mmol/L

1L NaCl 0.9%

6L

[Na$^+$]=**143** mmol/L (+3)

[Cl$^-$]=**109** mmol/L (+9)

Δ=34

[H$^+$] > [OH$^-$]

pH ↓ < 7.4

Hyperchloremic Acidosis

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November 22nd 2018
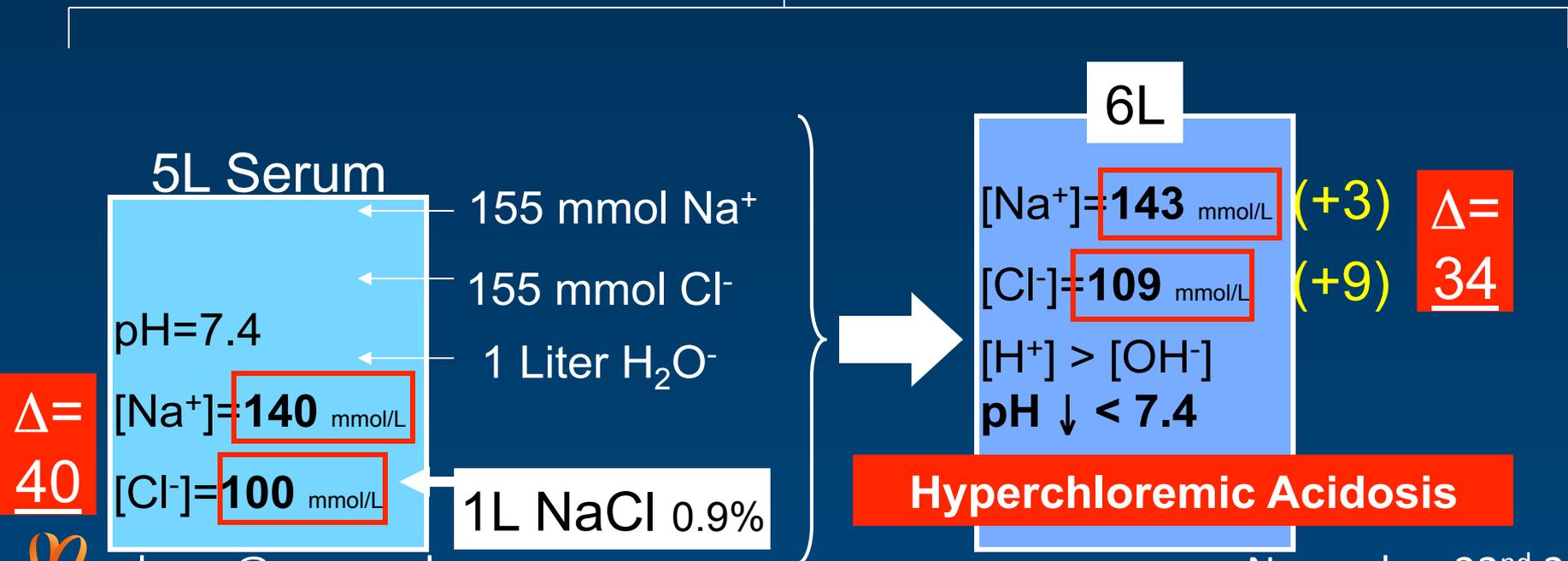
NaCl 0.9% generates *in vivo* an acidosis…

NaCl 0.9% generates *in vivo* an acidosis…

Metabolic acidosis in patients with severe sepsis and septic shock:
A longitudinal quantitative study   **Crit Care Med 2009;37:2733**

Danilo T. Noritomi, MD, PhD; Francisco G. Soriano, MD, PhD; John A. Kellum, MD, PhD;
Sylas B. Cappi, MD; Paolo J. C. Biselli, MD, PhD; Alexandre B. Libório, MD, PhD; Marcelo Park, MD, PhD

Conclusions: Patients with severe sepsis and septic shock exhibit a complex metabolic acidosis at intensive care unit admission, caused predominantly by hyperchloremic acidosis, which was more pronounced in nonsurvivors.

# <u>NaCl 0.9%</u> generates *in vivo* an acidosis…

Pediatric Critical Care

Hyperchloremia is the dominant cause of metabolic acidosis in the postresuscitation phase of pediatric meningococcal sepsis*

Ellen O'Dell, MRCPCH; Shane M. Tibby, MRCP; Andrew Durward, FCP; Ian A. Murdoch, FRCP

Conclusions: Hyperchloremic acidosis is common and substantial after resuscitation for meningococcal septic shock. Recognition of this entity may prevent unnecessary and potentially harmful prolonged resuscitation. (Crit Care Med 2007; 35:2390–2394)

NaCl 0.9% generates *in vivo* an acidosis…
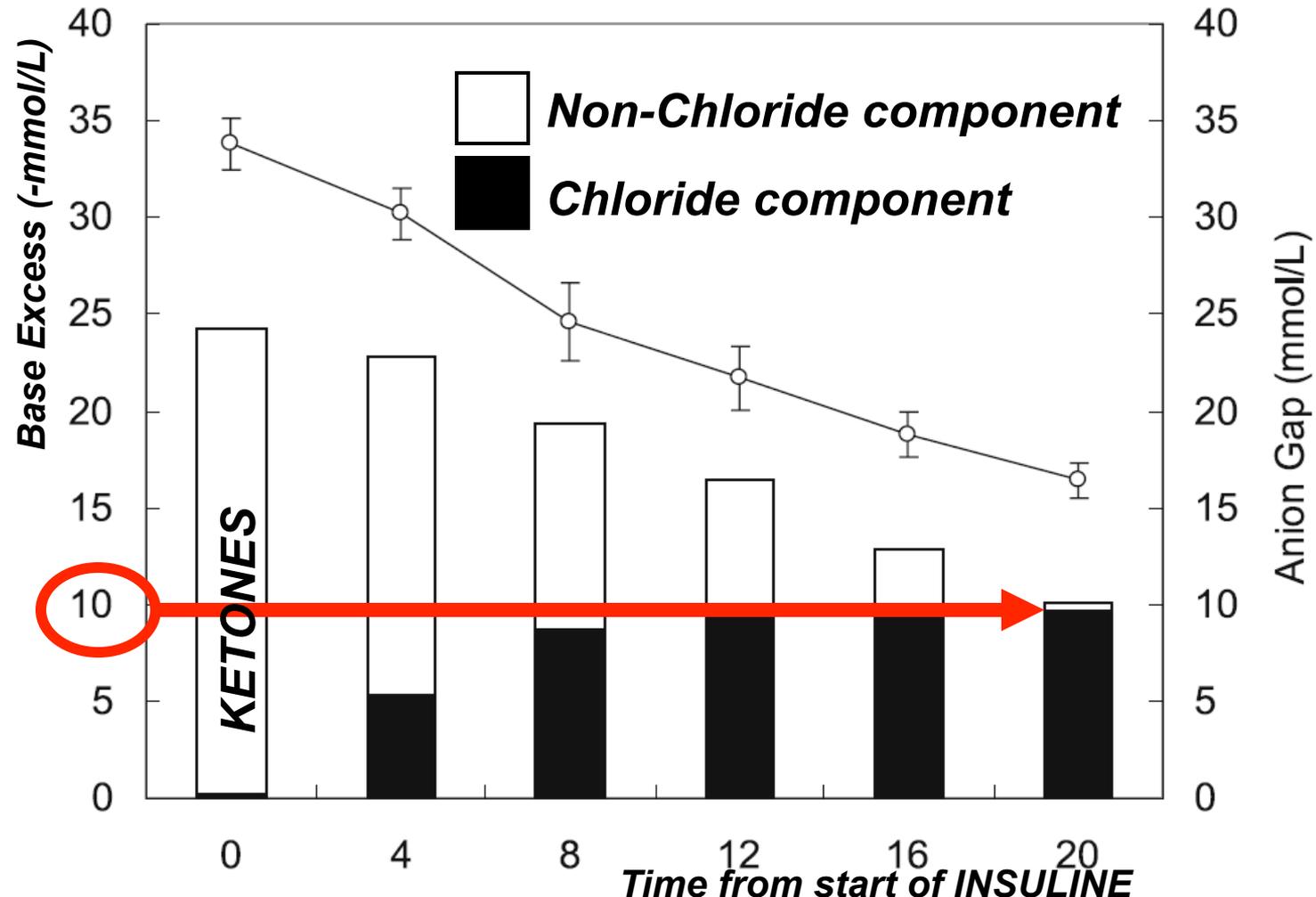
Taylor et al. ICM 2006; 32: 295

Hyperchloremic Acidosis Increases Circulating Inflammatory Molecules in Experimental Sepsis*

John A. Kellum, MD, FCCP; Mingchen Song, MD, PhD; and Eyad Almasri, MD

The strong ion gap predicts mortality in children following cardiopulmonary bypass surgery*

Andrew Durward, FCP; Shane M. Tibby, MRCP; Sophie Skellett, MRCP; Conal Austin, FRCS; David Anderson, FRCS; Ian A. Murdoch, FRCP

Conclusions: An elevated strong ion gap occurs commonly following bypass surgery and appears to be superior to lactate as a mortality predictor. (Pediatr Crit Care Med 2005; 6:281–285)

Hyperchloremic acidosis (data from literature)

Kidney	**oliguria**
	Hyperkalemia
	Renal vasoconstriction
Blood	**Coagulopathy**
Gut	**↓ splanchnic circulation**
	Vomiting & Nausea (post-operat)
	Intestinal Injury
Brain	**Decreased ability in abstract thinking**

Alexis Hartmann

JAMA 1934: Gastro-enteritis in children

→ Earlier recovery in Ringer-Lactate group (=Hartmann's solution) compared to NaCl 0.9%

J. Trauma 2009; 66:1045

Persisting Metabolic Acidosis → **Fluid therapy** *(NaCl 0.9%)*

The next day...

	Result
Na$^+$	129 mmol/L (131)
K$^+$	7.0 mmol/L (5.5)
Cl$^-$	100 mmol/L (110)
Albumine	16.0 g/L (8.0)
Hb	4.8 mmol/L
Lactate	**8.5 mmol/L**
pH	**6.9**
pCO$_2$	**4.0 kPa = 30 mmHg**
sBEc	**-18.3 mmol/L**

Anion GAP = 29.0

+ 7.5 mEq/L

-18.3 mEq/L

10.8 mEq/L Acids are **not** explained

SID_a = [Na]+[K]+[Ca]+[Mg]-[Cl]-[Lact] = 30.8 (Normal = 40)

SID_e = Calculated using [HCO$_3^-$], [PO^{4-}] en [Alb$^-$] = 25.1

SIG = 5.6 !!! (Unknown Acids…)

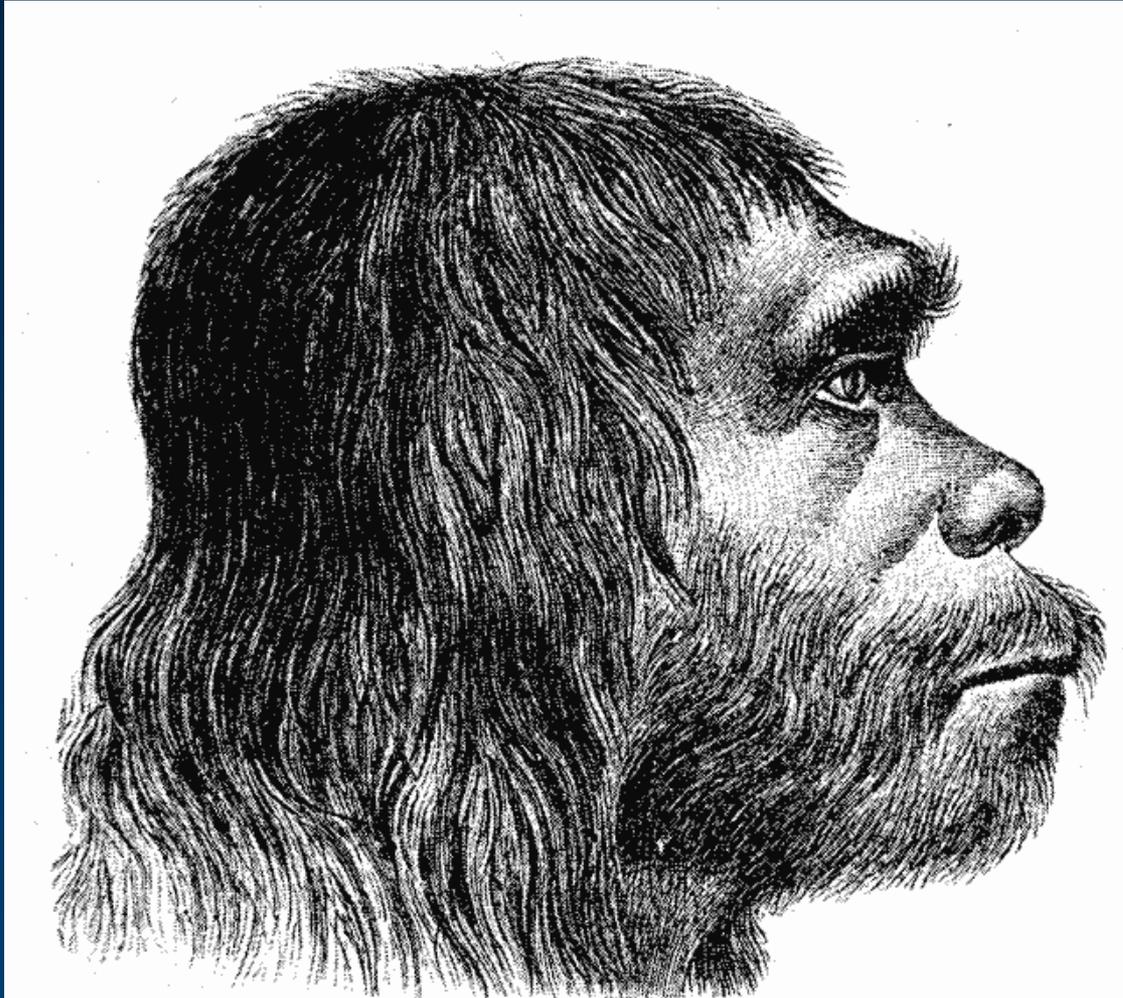# Henderson-Hasselbalch

(Over) Simplification

Threatens the mental proces

Undeserved leading role for HCO_3^-
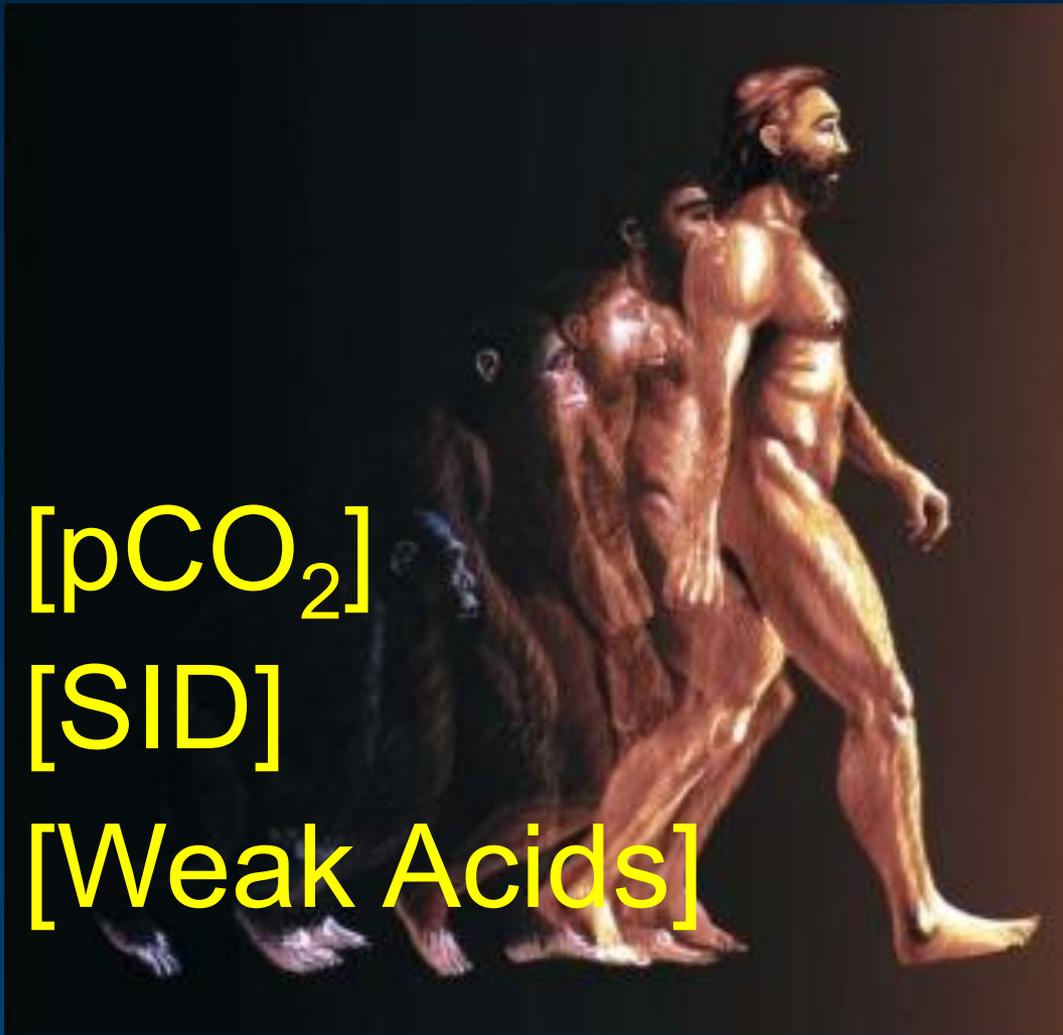
Ignores important players

Henderson-Hasselbalch

(Over) Simplification

Threatens the mental proces

Undeserved leading role for HCO_3^-
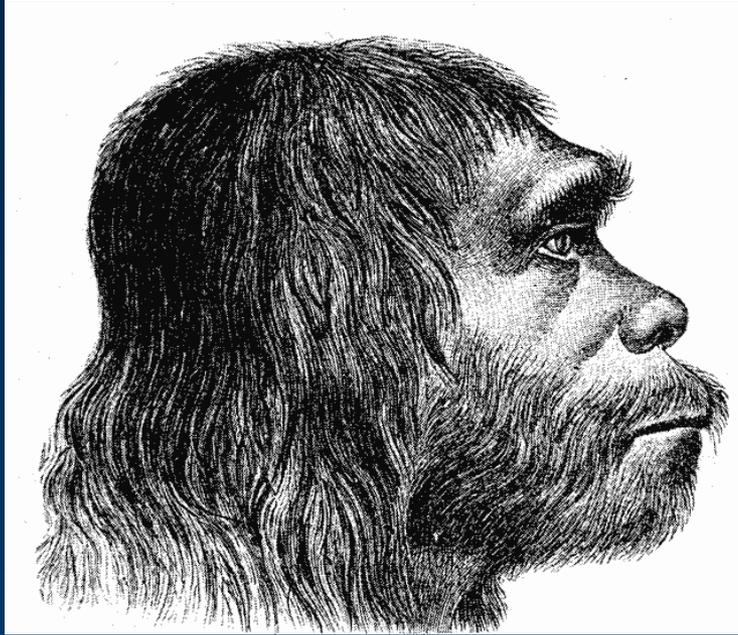
Ignores important players

Stewart-Approach

[pCO$_2$]
[SID]
[Weak Acids]

Unravels the role of different players

Explains Lactate acidosis

Explains Hyper-chloremic acidosis

H$^+$ en HCO$_3^-$ are (only) dependent variables

Conclusion: Metabolic acidosis

Qualitative approach

Henderson-Hasselbalch

Quantitative approach

Stewart

We remain confused as ever….

but on a higher level…

And on more difficult things !