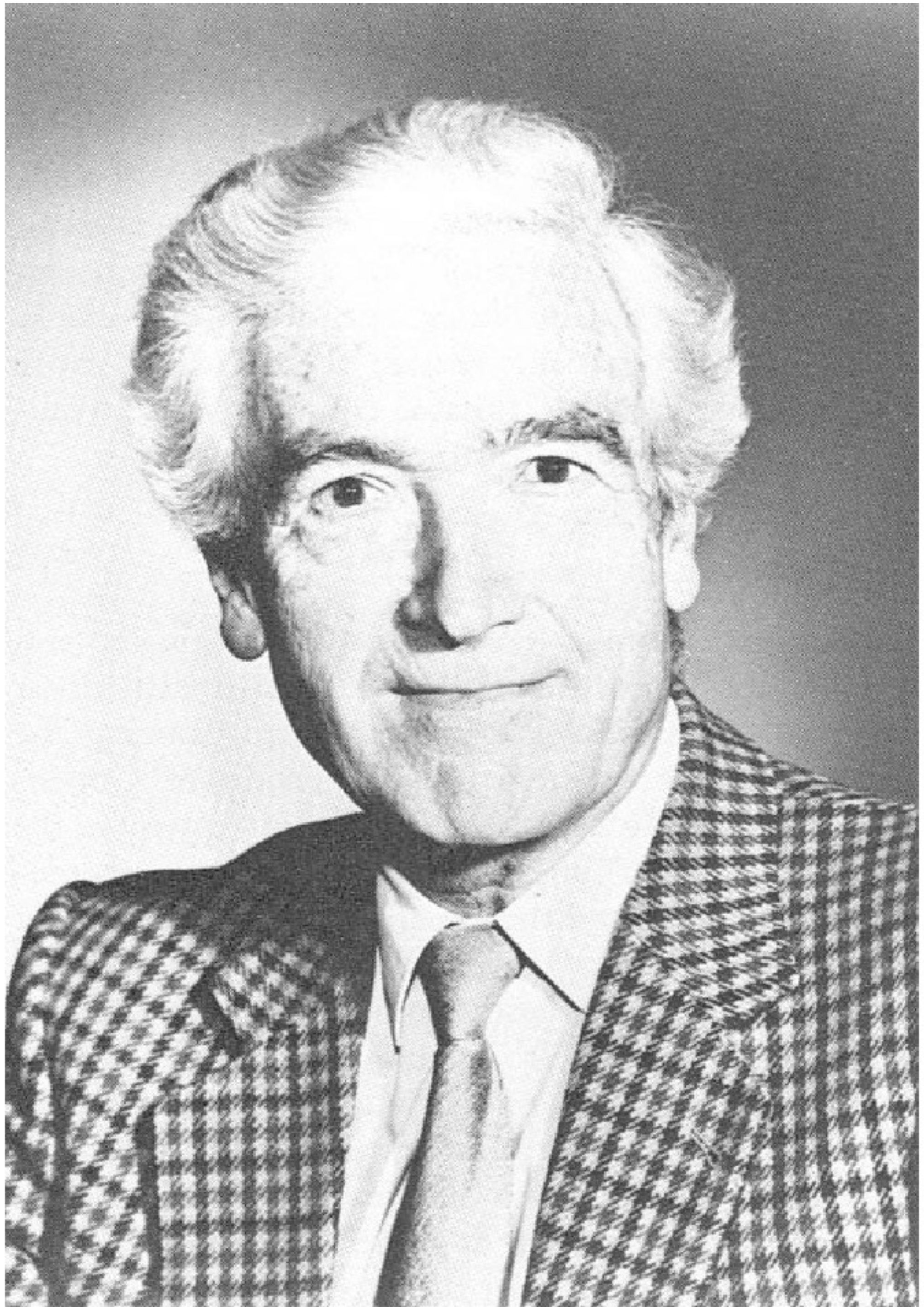
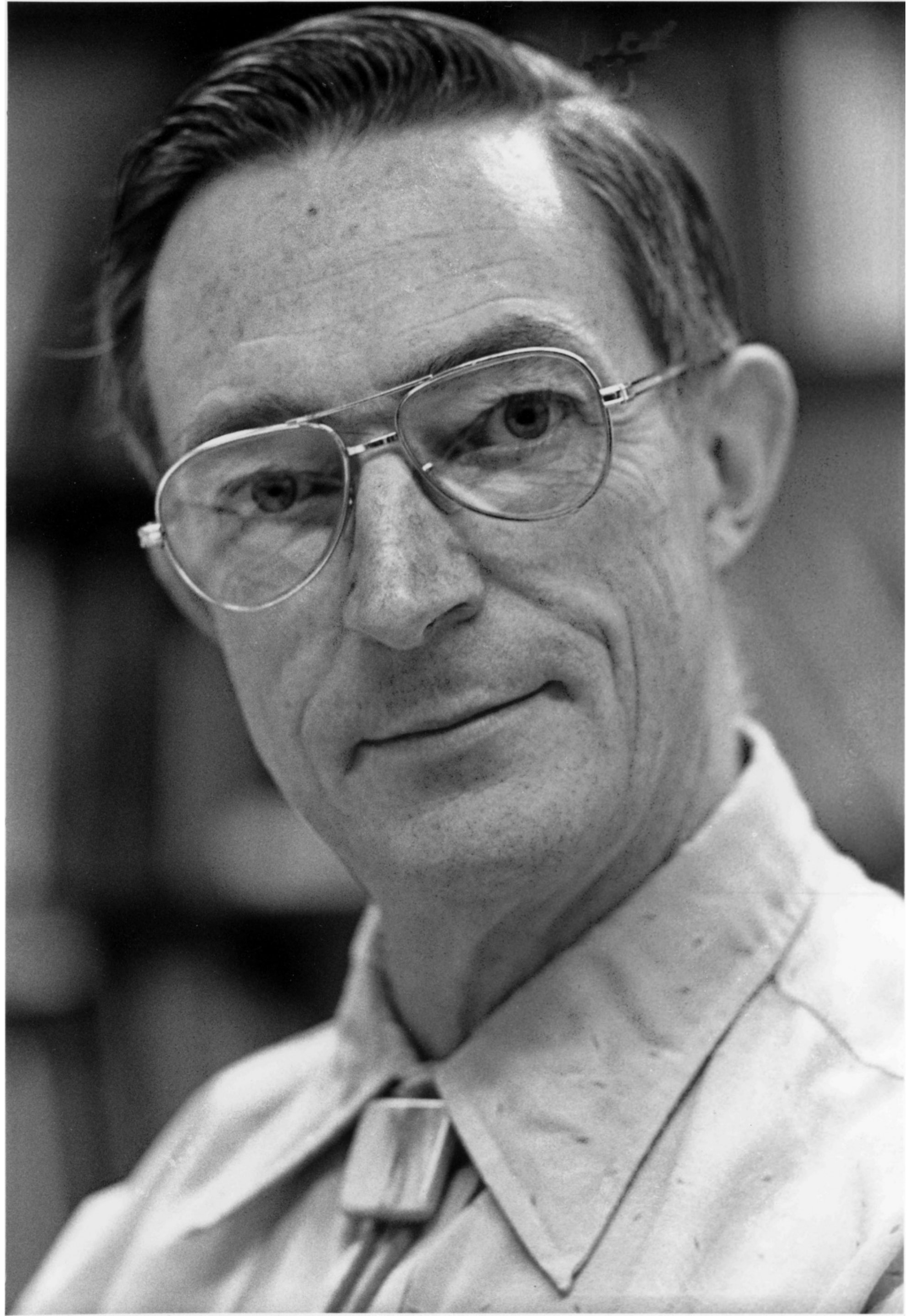
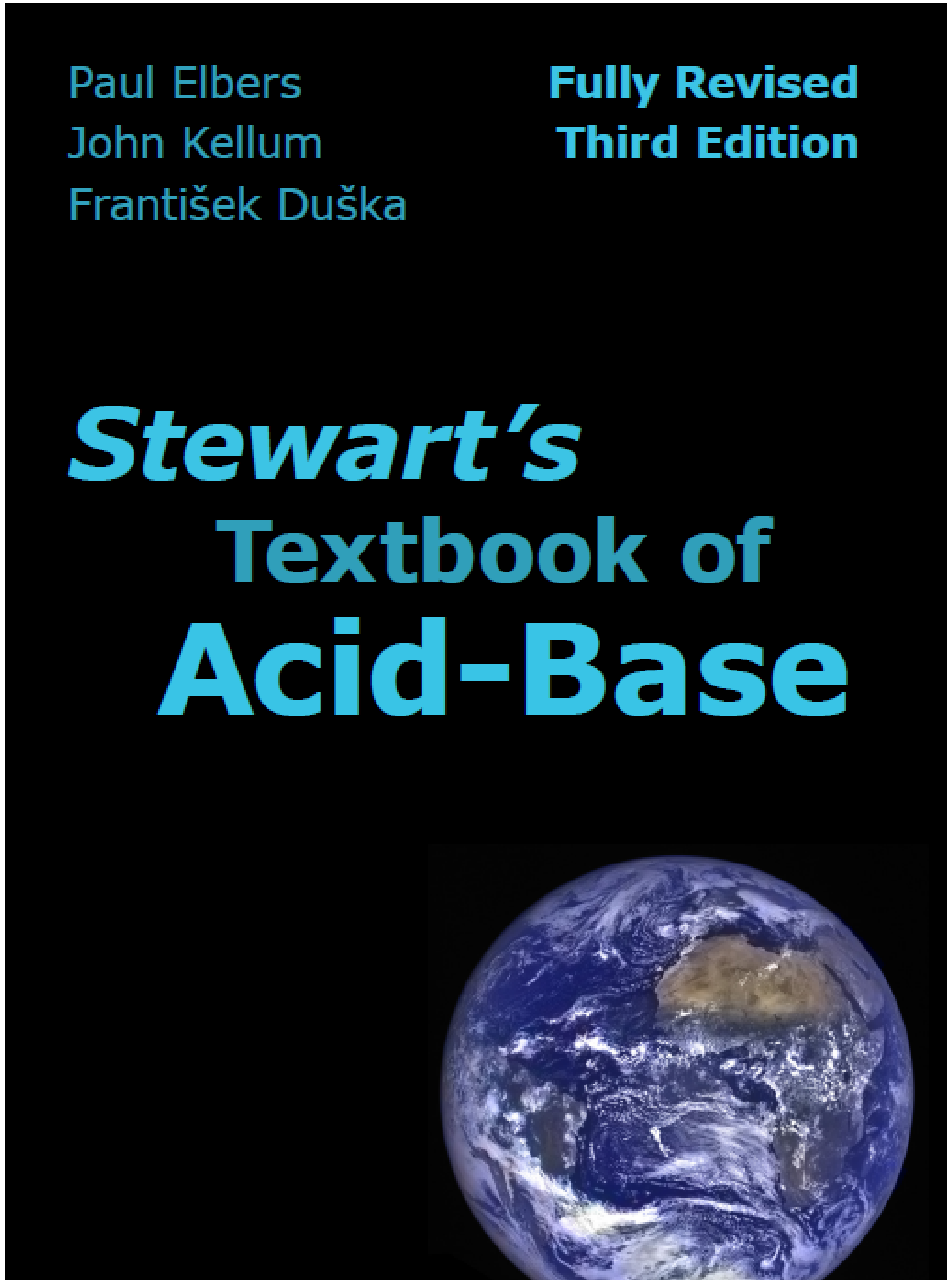
Stewart or Astrup?

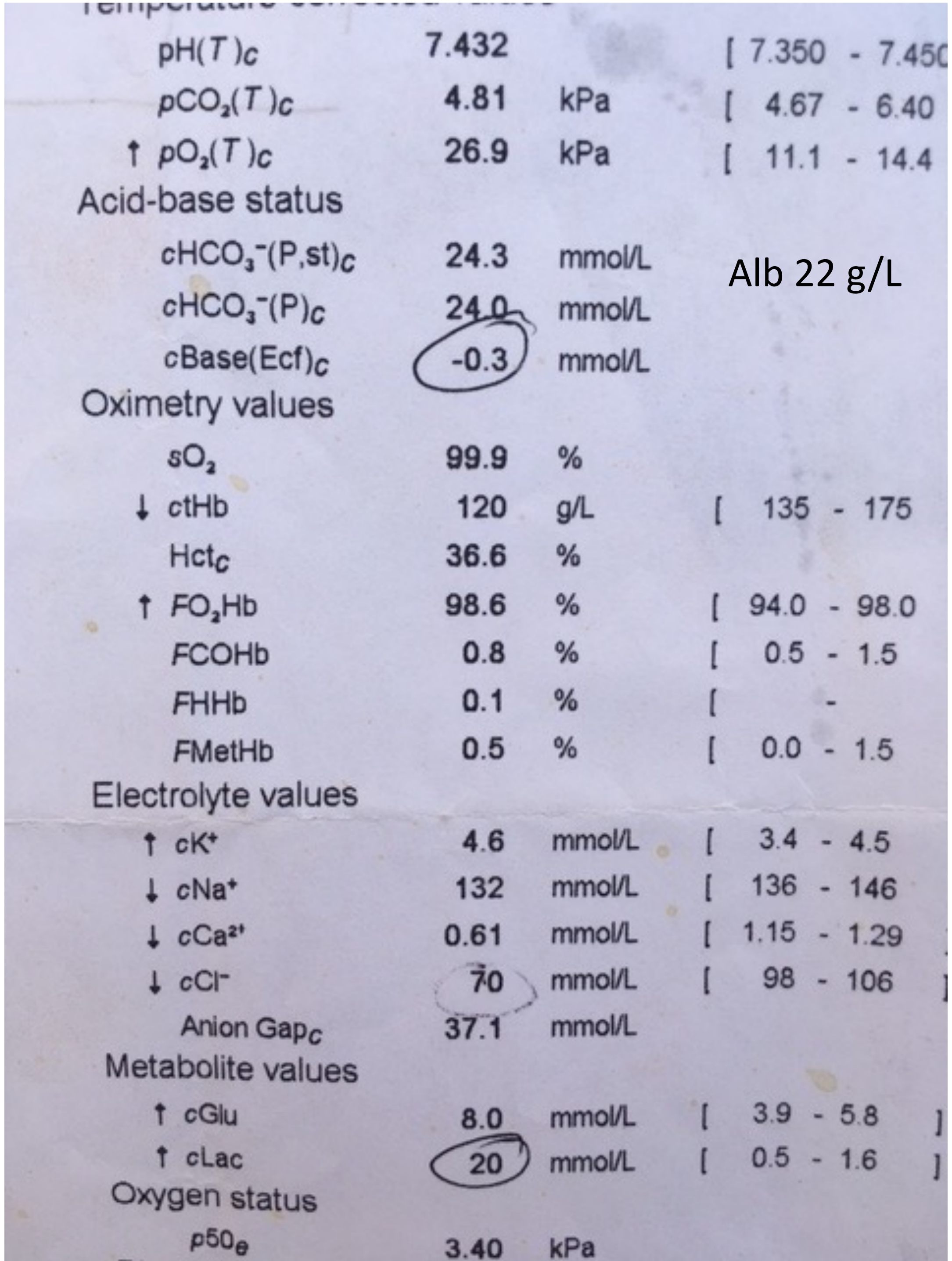
František Duška

Conflict of interests

- Director of Summer School of Clinical Acid Base, sponsored by 4-EU Alliance Programme and Radiometer, ltd., Copenhagen, Denmark
- Co-editor (with P. Elbers, J. Kellum) of Stewart's Acid Base, 3rd ed.
- No other COI





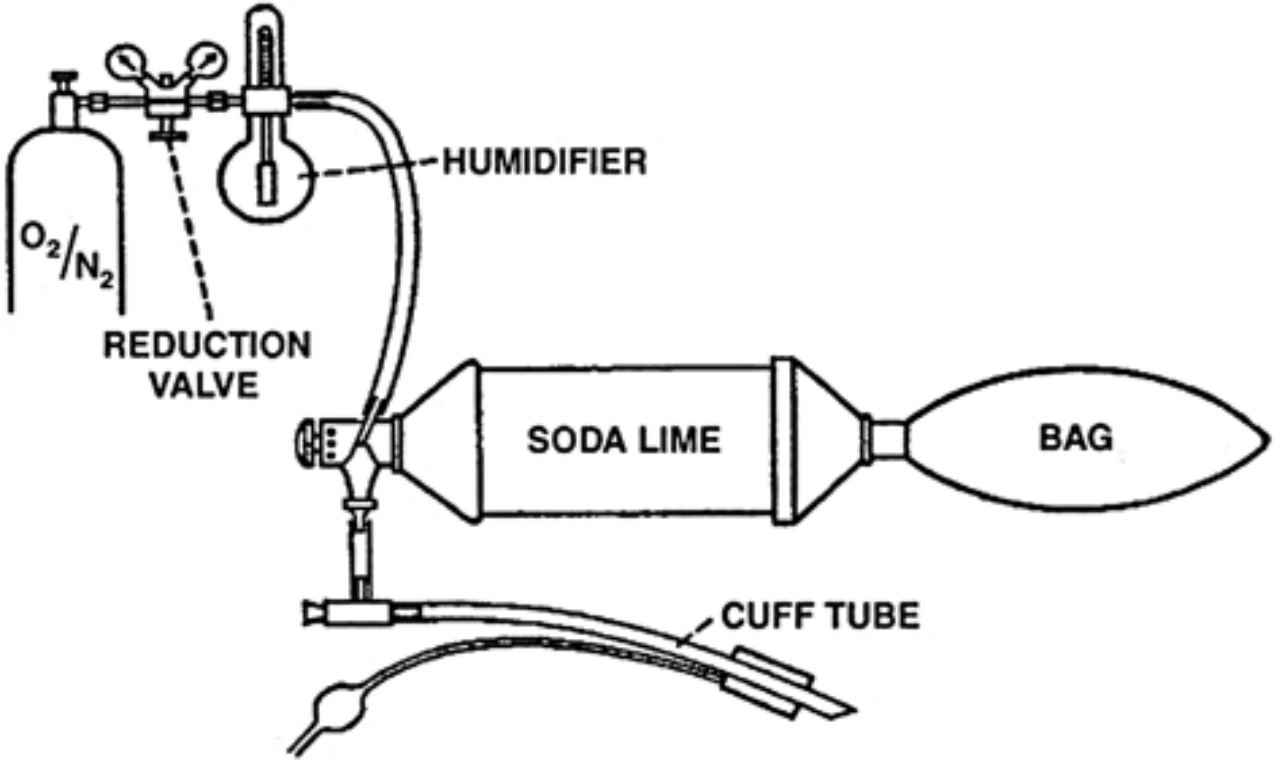
pH(T)c	7.432		[7.350 - 7.450
pCO₂(T)c	4.81	kPa	[4.67 - 6.40
↑ pO₂(T)c	26.9	kPa	[11.1 - 14.4
Acid-base status			
cHCO₃⁻(P,st)c	24.3	mmol/L	
cHCO₃⁻(P)c	24.0	mmol/L	
cBase(Ecf)c	-0.3	mmol/L	
Oximetry values			
sO₂	99.9	%	
↓ ctHb	120	g/L	[135 - 175
Hctc	36.6	%	
↑ FO₂Hb	98.6	%	[94.0 - 98.0
FCOHb	0.8	%	[0.5 - 1.5
FHHb	0.1	%	[-
FMetHb	0.5	%	[0.0 - 1.5
Electrolyte values			
↑ cK⁺	4.6	mmol/L	[3.4 - 4.5
↓ cNa⁺	132	mmol/L	[136 - 146
↓ cCa²⁺	0.61	mmol/L	[1.15 - 1.29
↓ cCl⁻	70	mmol/L	[98 - 106]
Anion Gapc	37.1	mmol/L	
Metabolite values			
↑ cGlu	8.0	mmol/L	[3.9 - 5.8]
↑ cLac	20	mmol/L	[0.5 - 1.6]
Oxygen status			
p50e	3.40	kPa	

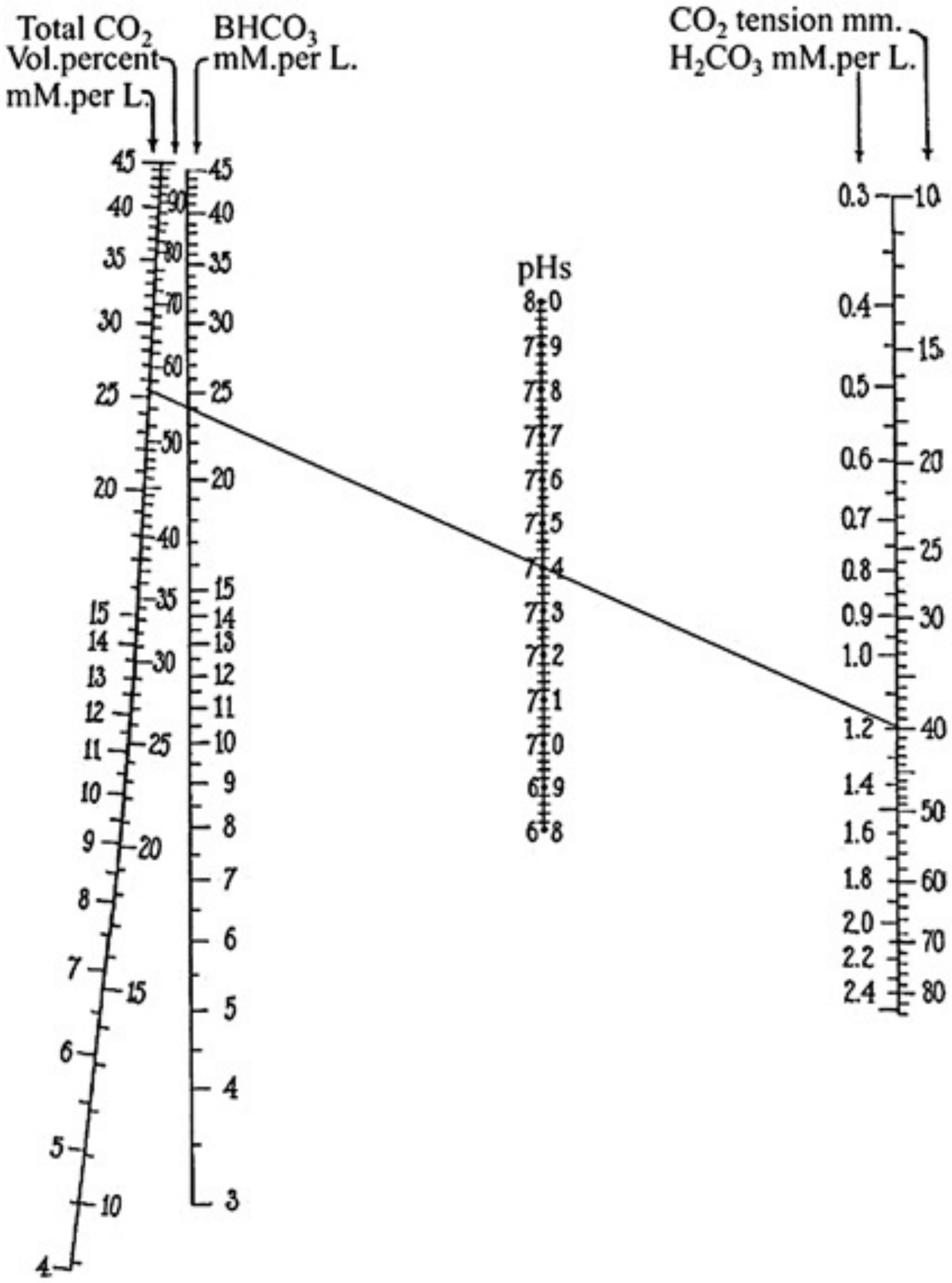
Alb 22 g/L

34-years-old, alcoholism, self-neglect, Now presents with after 3 days off legs. Vomiting, confused.

First blood gas in emergency room

Copenhagen 1952




Total CO_2
Vol.percent
mM.per L.
$BHCO_3$
mM.per L.
pHs
CO_2 tension mm.
H_2CO_3 mM.per L.

Classical approach to acid base

- Assessment of bicarbonate buffer based on Henderson-Hasselbalch equation

$$pH = 6.1 + \log \frac{[HCO_3^-]}{\alpha * pCO_2}$$

Metabolic disorders ([HCO₃⁻])

↓= acidosis

↑= alkalosis

Respiratory disorders (pCO₂)

↓= alkalosis

↑= acidosis

<u>Compensation</u> = the other system's response to primary disorder (to the same direction, hence pH closer to normal)

Challenges of bicarbonate-based approach

- Bicarbonate changes with pCO_2
- Bicarbonate does not reflect severity of acidosis due to varying non-carbonic buffers
- Mixed disorders
  - Respiratory with metabolic
  - Within one system

pCO_2 affects HCO_3^-

↓ pH	7,351		7.158	
pCO2	5,73	kPa	9.65	kPa
↑ pO2	17,8	kPa	25.5	kPa
Hodnoty oximetrie				
ctHb	136	g/L	133	g/L
↑ sO2	99,4	%	99.3	%
↑ FO2Hb	98.0	%	97.9	%
FMetHb	0,4	%	0.7	%
FCOHb	1,0	%	0.7	%
Hodnoty elektrolytů				
cK+	4,1	mmol/L	4.4	mmol/L
cNa+	145	mmol/L	146	mmol/L
cCa2+	1,04	mmol/L	1.08	mmol/L
↑ cCl-	114	mmol/L	114	mmol/L
Hodnoty metabolitů				
↑ cGlu	5,7	mmol/L	5.7	mmol/L
? cLac	1,3	mmol/L	1.1	mmol/L
Hodnoty korigované na teplotu				
pH(T)	7,351		7.158	
pCO2(T)	5,73	kPa	9.65	kPa
pO2(T)	17,8	kPa	25.5	kPa
Statusy kyslíku				
ctO2,c	18,9	Vol%	18.7	Vol%
p50,e	3,71	kPa	4.62	kPa
Acidobasický status				
cBase(B),c	-1,9	mmol/L	-4.5	mmol/L
cBase(Ecf),c	-1,8	mmol/L	-3.0	mmol/L
cHCO3-(P,st),c	22,9	mmol/L	[illegible]	mmol/L
cHCO3-(P),c	23,8	mmol/L	25.7	mmol/L
[illegible]	[illegible]	mmol/L	10.3	mmol/L
ctCO2(B),c	21,5	mmol/L	24.4	mmol/L
ctCO2(P),c	25,1	mmol/L	27.9	mmol/L
ctO2,c	18,9	Vol%	18.7	Vol%

The two blood gases are from same patient done 10 min apart.

In between the patient underwent APNEA TEST

pCO2 increased (5.73→9.65 kPa)
pH decreased (7.351→ 7.158)
HCO3- increased (23.8 →25.7)

Why BICARB increased???

Why Base Excess?

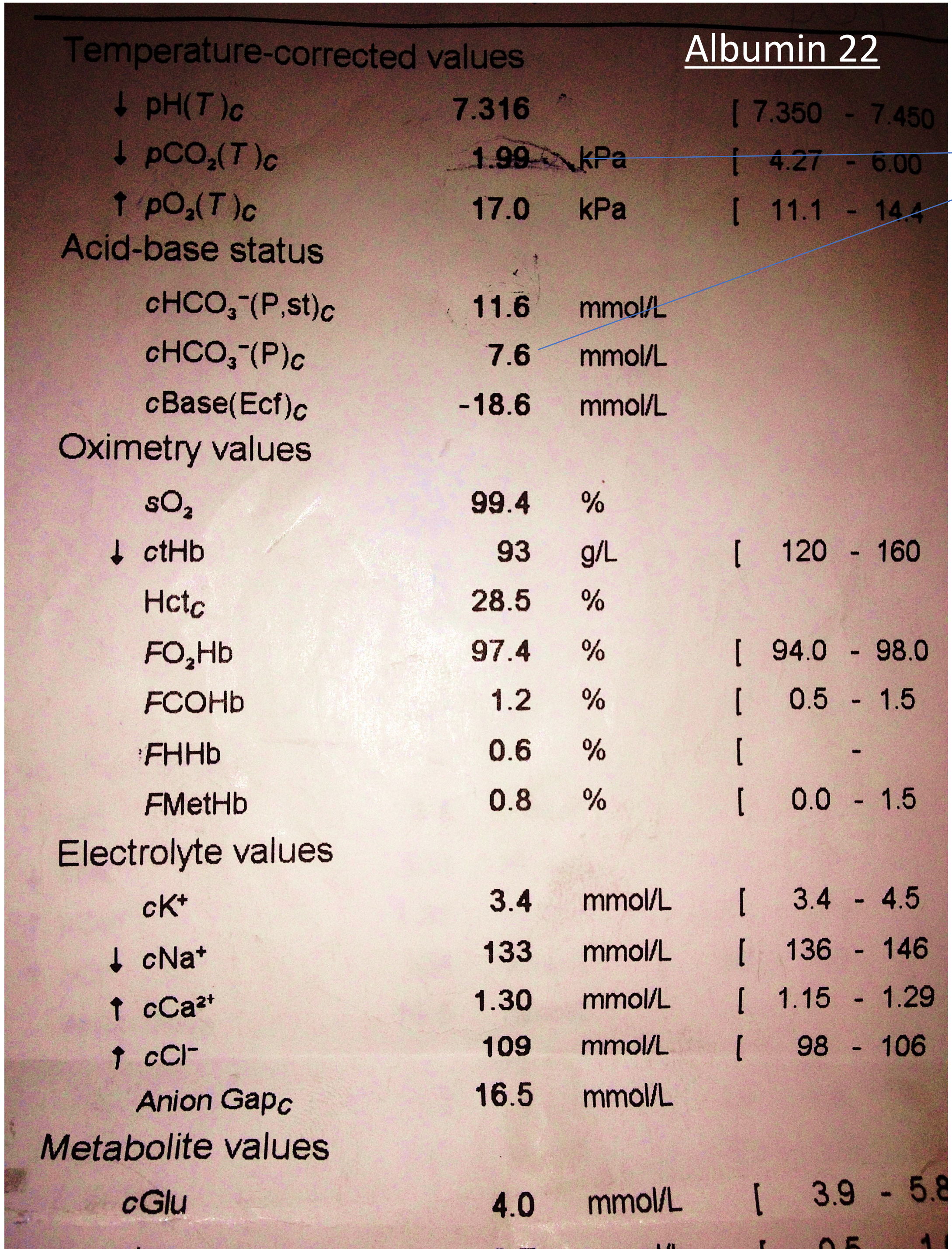
- Henderson&Hasselbalch fails to quantify the magnitude of $[HCO_3^-]$ change unless pCO_2 is held constant.

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

- Consequence: acute CO_2 retention causes instant HCO_3^- elevation (i.e. before renal HCO_3- retention occurs)
- Solution:
  - Concept of standard bicarbonate (Jorgensen&Astrup, 1957)
  - Concept of Base Excess: reflects roles of non-carbonic buffers

Challenges of bicarbonate-based approach

- Bicarbonate changes with pCO_2 Solved by standard bicarbonate.
- Bicarbonate does not reflect severity of acidosis due to varying non-carbonic buffers Solved by Base excess
- Mixed disorders
  - Respiratory and metabolic: Solved by “Boston rules” Help to distinguish compensation from superimposed disorder
  - Mixed disorders within one system



Albumin 22

Temperature-corrected values			
↓ $pH(T)_c$	7.316		[7.350 - 7.450
↓ $pCO_2(T)_c$	1.99	kPa	[4.27 - 6.00
↑ $pO_2(T)_c$	17.0	kPa	[11.1 - 14.4
Acid-base status			
$cHCO_3^-(P,st)_c$	11.6	mmol/L	
$cHCO_3^-(P)_c$	7.6	mmol/L	
$cBase(Ecf)_c$	-18.6	mmol/L	
Oximetry values			
sO_2	99.4	%	
↓ ctHb	93	g/L	[120 - 160
Hct_c	28.5	%	
FO_2Hb	97.4	%	[94.0 - 98.0
FCOHb	1.2	%	[0.5 - 1.5
FHHb	0.6	%	[-
FMetHb	0.8	%	[0.0 - 1.5
Electrolyte values			
cK^+	3.4	mmol/L	[3.4 - 4.5
↓ cNa^+	133	mmol/L	[136 - 146
↑ cCa^{2+}	1.30	mmol/L	[1.15 - 1.29
↑ cCl^-	109	mmol/L	[98 - 106
$Anion Gap_c$	16.5	mmol/L	
Metabolite values			
cGlu	4.0	mmol/L	[3.9 - 5.8

Boston rule: 8/5+1=2.6 kPa
RESPIRATORY ALKALOSIS

How low should pCO_2 be in metabolic acidosis?

$HCO_3^-/5 + 1$ kPa

Or

$1.5\ HCO_3^- + 8$ mmHg

(Winters 1963)

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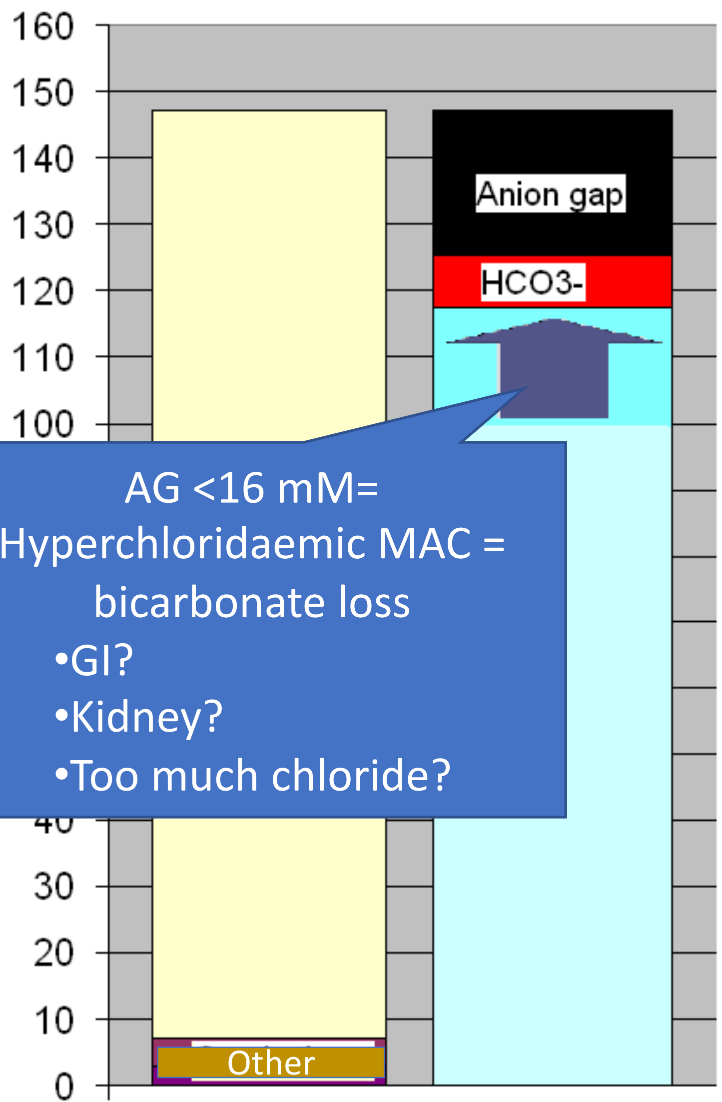
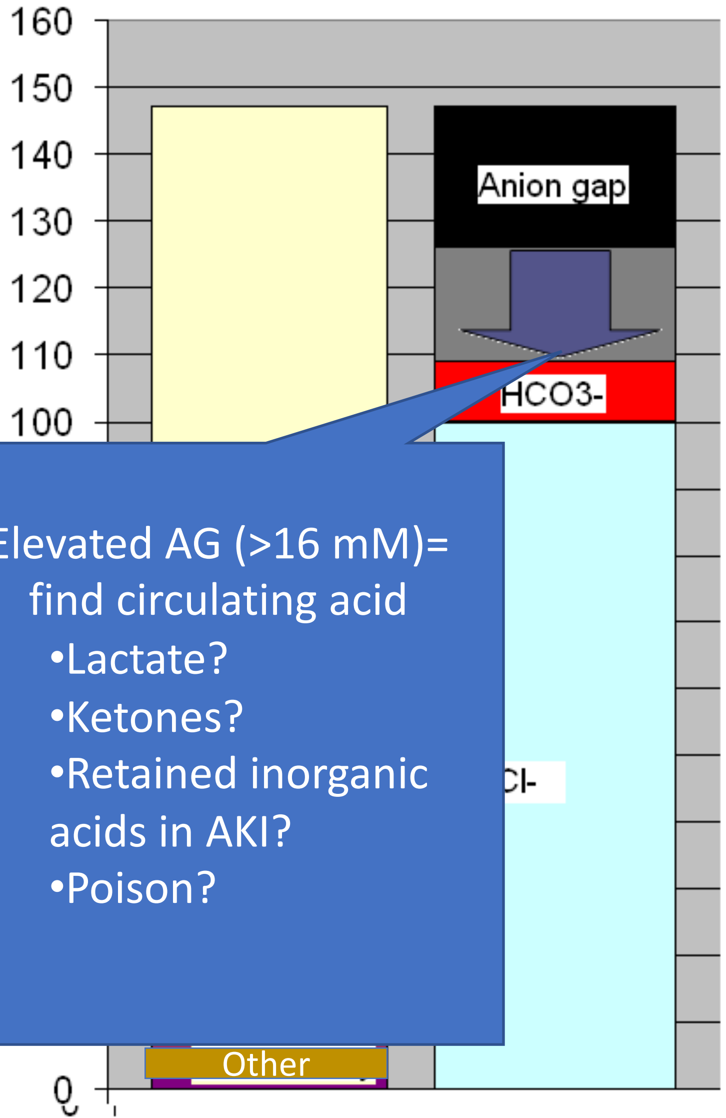
  - **Mixed disorders within one system**

Anion gap = electroneutrality sneaks in



AG <16 mM=
Hyperchloridaemic MAC =
bicarbonate loss
- GI?
- Kidney?
- Too much chloride?



Elevated AG (>16 mM)=
find circulating acid
- Lactate?
- Ketones?
- Retained inorganic acids in AKI?
- Poison?

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34-years-old, alcoholism, self-neglect, Now presents with after 3 days off legs. Vomiting, confused.

First blood gas in emergency room

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Alb 22 g/L

Albumin 22g/L

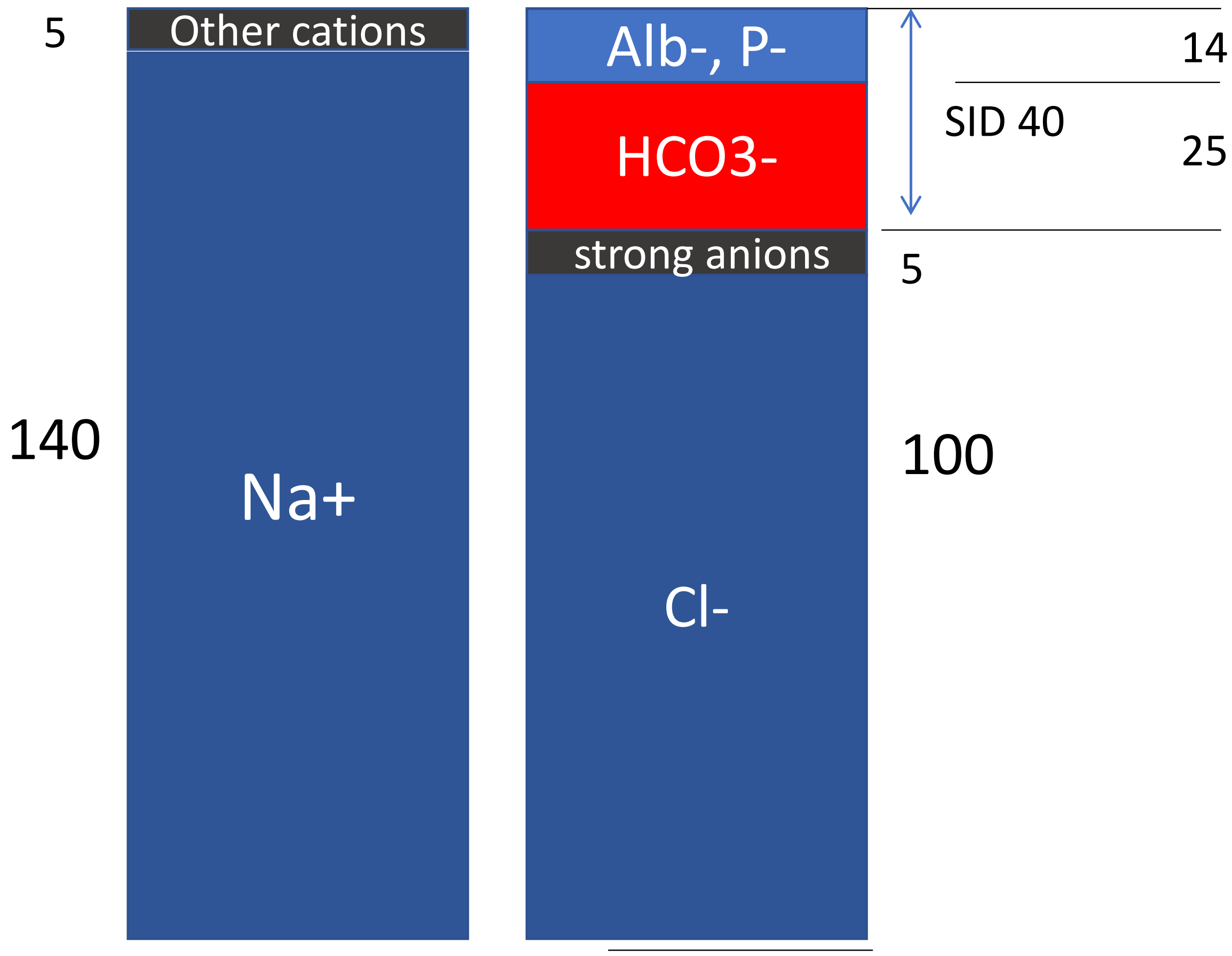
34-years-old, alcoholism, self-neglect, Now presents with after 3 days off legs. Vomiting, confused.

First blood gas in emergency room

Normal status of acid base status
Lactate 20 mM
Very low chloride

= lactic acidosis + hypochloridaemic alkalosis (due to vomiting?)

Principle of electroneutrality



Albumin 3mM of neg. charge per 10g/l

How can you possibly sell THIS to clinicians???

$$[H^+] \times [HCO_3^-] = K_C \times PCO_2$$

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

$$[H^+] \times [A^-] = K_A \times [H_A]$$

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

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

$$[SID] - [H^+] - [HCO_3^-] - [CO_3^{2-}] - [A^-] - [OH^-] = 0$$

«La République n'a pas besoin de chimistes»

M. Robespierre when announcing the death sentence order over Lavoisier

(8^{th} May, 1794)

Clinical applications

Brian M. Gilfix

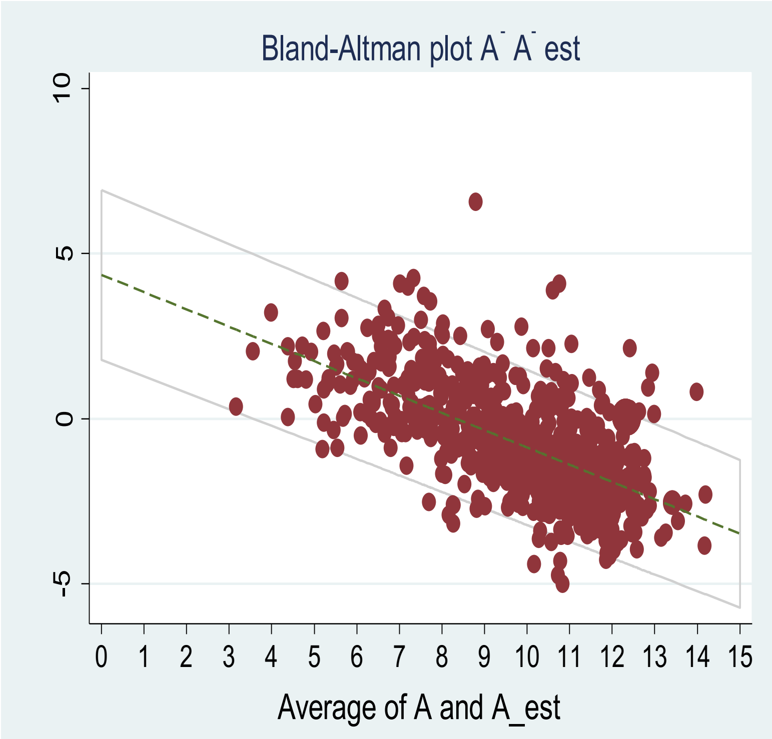
Vladimir Fencl

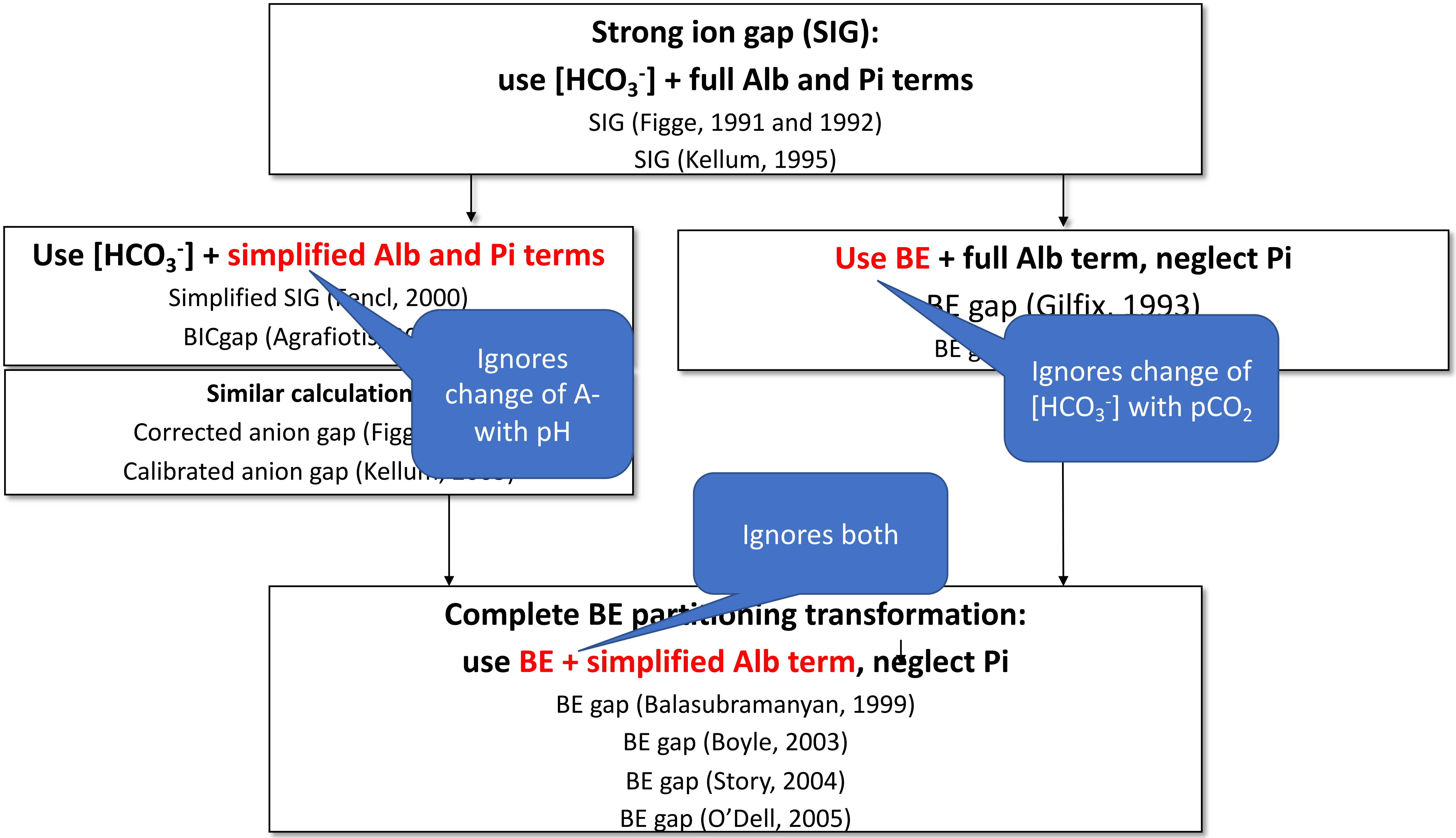
- SIDa $= \{[\mathrm{Na}^+] + [\mathrm{K}^+] + [\mathrm{Ca}^{2+}] + [\mathrm{Mg}^{2+}] - [\mathrm{Cl}^-]\}$
  - <42 mEq/L acidosis, >42 mEq/L alkalosis
- $A^- = \{Alb \times (0.123 \times pH - 0.631)\} - \{Pi \times (0.309 \times pH - 0.469)\}$
  - <14 mEq/L alkalosis, >14 mEq/L
- SIG = SIDa – A^- - $[\mathrm{HCO_3^-}]$
  - SIG>0 acidosis

This is still mathematically too complex for bedside use

Principles of simplifications

- SIDa:
  - Omission of $[K^+]$, $[Mg^{2+}]$ and $[Ca^{2+}]$
  - $[Na^+]$-$[Cl^-]$ as surrogate
- A^-
  - pH independent calculation of Alb and P charge
  - Omission of phosphates
- Detection of SIG
  - Ignoring $[HCO_3^-]_{act}$ is pCO_2 Using BE




Strong ion gap (SIG):
use [HCO3-] + full Alb and Pi terms
SIG (Figge, 1991 and 1992)
SIG (Kellum, 1995)
Use [HCO3-] + simplified Alb and Pi terms
Simplified SIG (Fencl, 2000)
BICgap (Agrafiotis
Similar calculation
Corrected anion gap (Figg
Calibrated anion gap (Kellum
Ignores change of A- with pH
Use BE + full Alb term, neglect Pi
BE gap (Gilfix, 1993)
Ignores change of [HCO3-] with pCO2
Ignores both
Complete BE partitioning transformation:
use BE + simplified Alb term, neglect Pi
BE gap (Balasubramanyan, 1999)
BE gap (Boyle, 2003)
BE gap (Story, 2004)
BE gap (O'Dell, 2005)

Handling of buffer anions	Name	Principal author (year)	Equation	Normal value
All buffer anions handled in a pH-dependent manner	Strong ion gap (SIG)	Figge (1992)[1,2]	$[XA^-] = \{[Na^+] + [K^+] + [Ca^{2+}] + [Mg^{2+}] - [Cl^-]\} - [HCO_3^-] - \{Alb\times(0.123\times pH - 0.631)\} - \{Pi\times(0.309\times pH - 0.469)\}$	~0
		Kellum (1995)[3]	$SIG = \{[Na^+] + [K^+] + [Ca^{2+}] + [Mg^{2+}] - [Cl^-] - [Lac^-] - [urate]\} - [HCO_3^-] - \{Alb\times(0.123\times pH - 0.631)\} - \{Pi\times(0.309\times pH - 0.469)\}$	0
Incomplete BE partitioning transformation	Base excess gap	Gilfix (1993)[9]	$[UA^-] = BE(B) - \{0.3\times([Na^+] - 140)\} - \left\{102 - [Cl^-]\times\frac{140}{[Na^+]}\right\} - \{(0.148\times pH - 0.818)\times(42 - Alb)\}$	
Complete BE partitioning transformation		Balasubramanyan (1999)[10]	$[UA^-] = BE(B) - \{0.3\times([Na^+] - 140)\} - \left\{102 - [Cl^-]\times\frac{140}{[Na^+]}\right\} - \{0.34\times(45 - Alb)\}$	0
		Boyle (2003)[11]	$[UA^-] = BE(Ecf) - \{[Na^+] + [K^+] - [Cl^-] - [Lac^-] - 42\} - \{0.25\times(40 - Alb)\}$	
		Story (2004)[12]	$[UA^-] = BE(Ecf) - \{[Na^+] - [Cl^-] - 38\} - \{0.25\times(42 - Alb)\}$	
A- simplification	Simplified SIG	Fencl (2000)[13]	$SIG = \{[Na^+] + [K^+] + [Ca^{2+}] + [Mg^{2+}] - [Cl^-]\} - [HCO_3^-] - \{0.28\times Alb\} - \{1.8\times Pi\}$	~ 0
	Bicarbonate gap	Agrafiotis (2018)[14]	$BIC_{gap} = \{[Na^+] + [K^+] - [Cl^-] + 6.5\} - [HCO_3^-] - (0.25\times Alb) - (2\times Pi)$	~ 0
	Corrected anion gap	Figge (1998)[15]	$AG_c = \{[Na^+] + [K^+] - [Cl^-]\} - [HCO_3^-] + 0.25\times(42 - Alb)$	<16 mmol/L

R^2 of unmeasured anion effect vs SIG				
	Full Alb and Pi term	Simplified Alb and Pi term	Combined simplification	
	$[HCO_3^-]$	$[HCO_3^-]$	BE(P)	BE(Ecf)
Full calculation	1.00	0.99	0.98	0.88
1) Rounding of coefficients	not applicable	0.98	0.98	0.89
2) Omission of [Ca2+]	0.99	0.97	0.99	0.89
3) Omission of [Mg2+]	0.98	0.96	0.96	0.86
4) Omission of [K+]	0.96	0.94	0.96	0.88
5) Omission of [Phos-]/Pi	0.93	0.94	0.88	0.76
Combination of 1-4	**0.91**	**0.88**	**0.92**	**0.86**
Combination of 1-5	0.88	0.89	0.86	0.76

area under ROC curve (to detect non-lactate SIG>6 mEq/l)				
	Full Alb and Pi term	Simplified Alb and Pi term		
	$[HCO_3^-]$	$[HCO_3^-]$	BE(P)	BE(Ecf)
Full calculation	1.000	0.996	0.995	0.961
1) Rounding of coefficients	not applicable	0.994	0.995	0.964
2) Omission of [Ca2+]	0.999	0.993	0.995	0.964
3) Omission of [Mg2+]	0.991	0.987	0.985	0.952
4) Omission of [K+]	0.987	0.979	0.986	0.962
5) Omission of [Phos-]/Pi	0.977	0.981	0.964	0.928
Combination of 1-4	**0.970**	**0.962**	**0.972**	**0.953**
Combination of 1-5	0.956	0.958	0.949	0.921

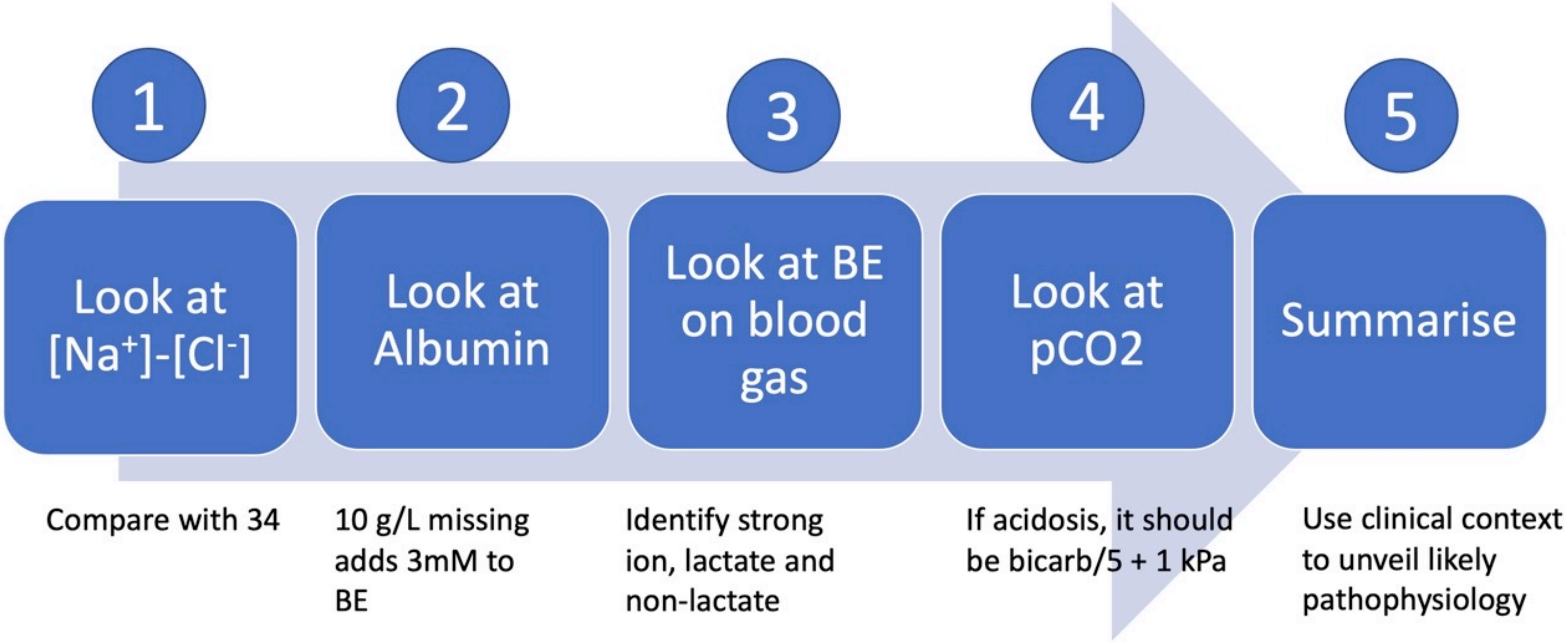
17 174 ICU patients with BG taken on admission

AmsterdamUMCdb

3985 ICU patients with full dataset to calculate SIG

(Krbec, Duska & Elbers 2023 manuscript in preparation)

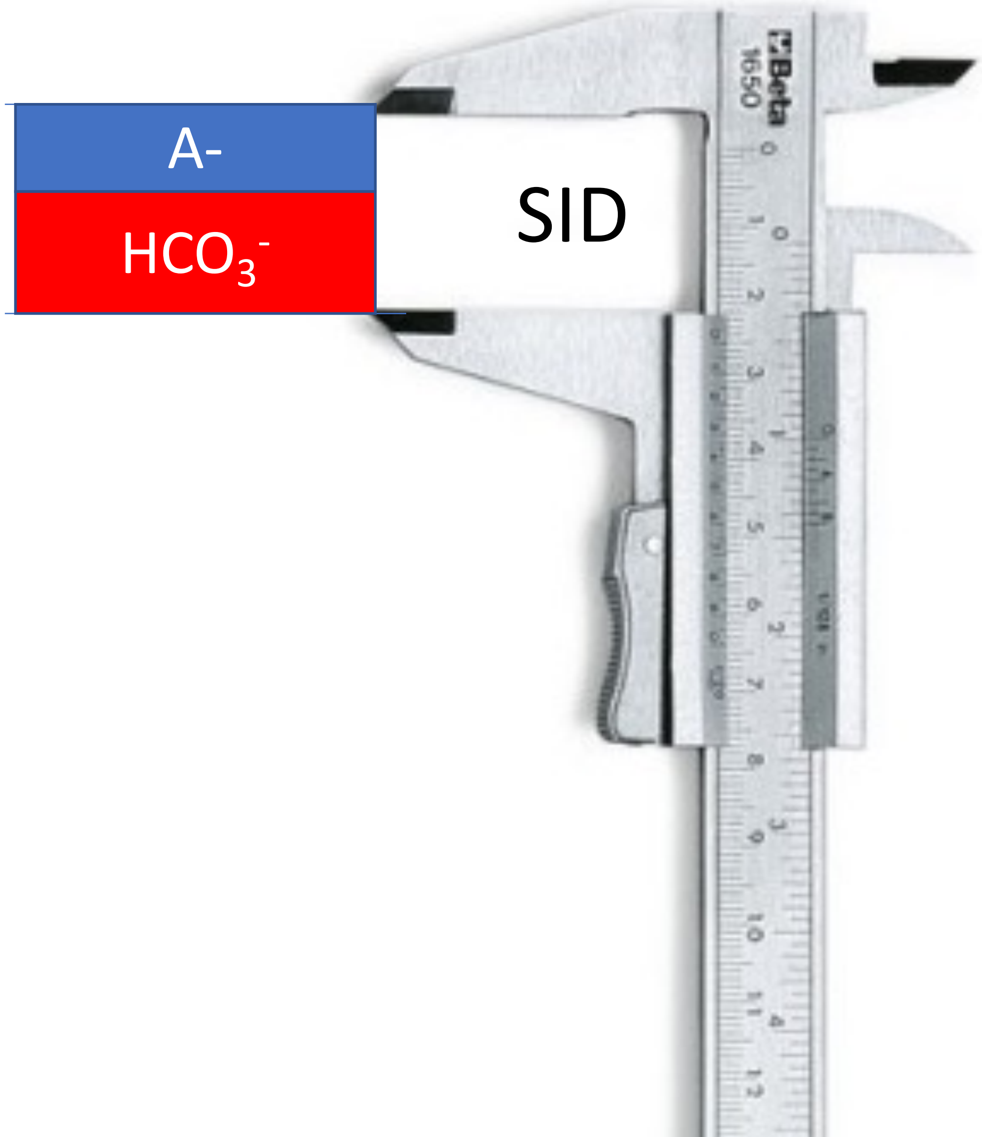
Validated approach to combined disorders



(BE partitioning method modified as per Story, BJA 2004)

Key concept

SID defines anion space shared by A^- a HCO_3^-



Electroneutrality used for diagnosis

- SID (approximated as $[Na^+]-[Cl^-] = 34$)
  - Low = acidosis
  - High = alkalosis
- Weak acids (each 10 g/L of albumin holds 3mM of negative charge)
  - Low = alkalosis
  - High = acidosis
- Strong ions

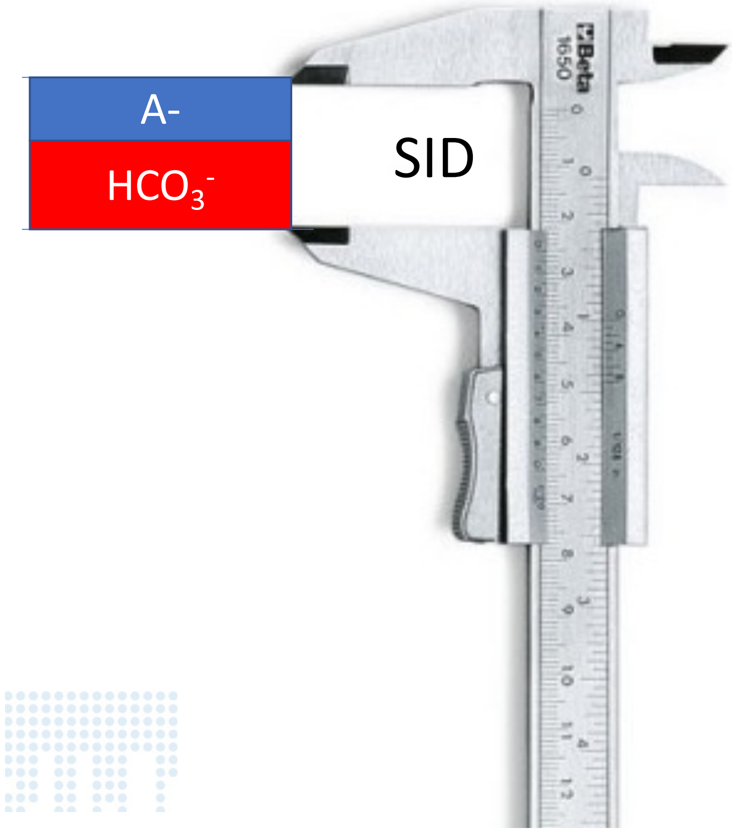
Note: There are 2 mechanismis how SID can change:

1. Na/Cl (e.g. hyperchloridaemia after normal saline)
2. Free water changes (e.g. concentration alkalosis in DI)

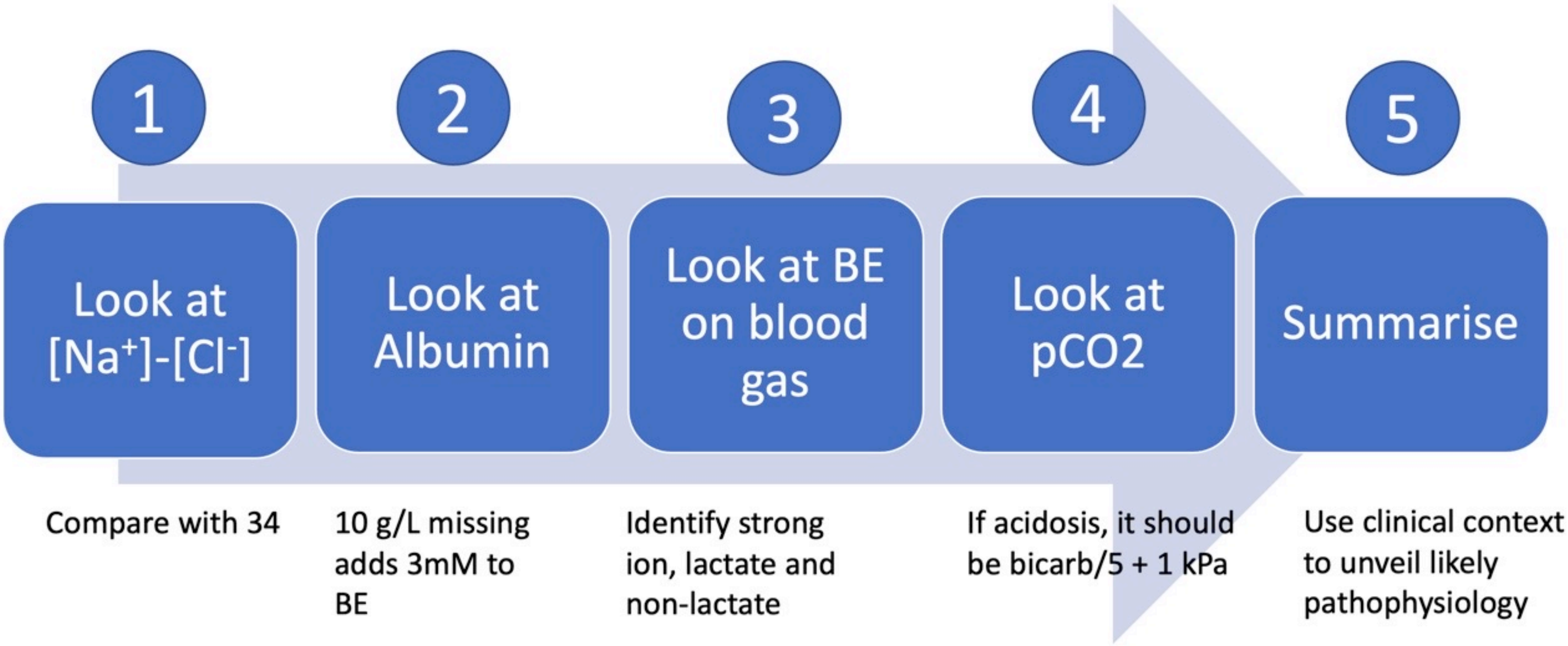
- Each disorder changes BE in predictable way, eg.
  - 1 mM decrease in Na-Cl = BE -1 mM
  - 1 mM increase in lactate or other strong acid = BE -1 mM
  - 10 g/L decrease in albumin = BE +3mM

- Concentrations of Na+, Cl-, albumin are known and predict certain BE. If real BG is lower, this means circulating unmeasured strong acids.

- This can all be done easily by using mental arithmetic only



Practical five-step approach



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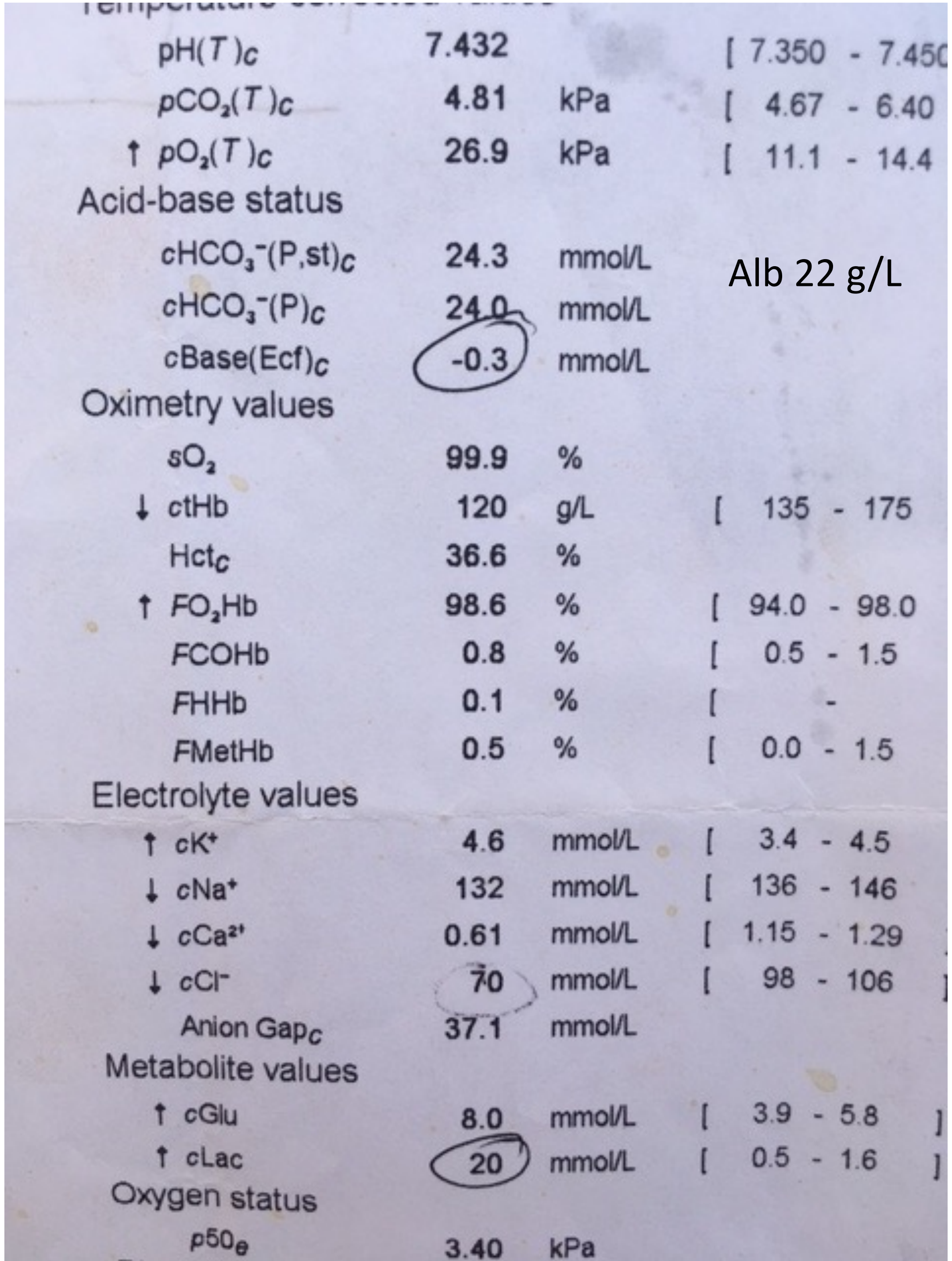

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↓ cNa⁺	132	mmol/L	[136 - 146
↓ cCa²⁺	0.61	mmol/L	[1.15 - 1.29
↓ cCl⁻	70	mmol/L	[98 - 106]
Anion Gapc	37.1	mmol/L	
Metabolite values			
↑ cGlu	8.0	mmol/L	[3.9 - 5.8]
↑ cLac	20	mmol/L	[0.5 - 1.6]
Oxygen status			
p50e	3.40	kPa	

Alb 22 g/L

34-years-old, alcoholism, self-neglect,
Now presents with after 3 days off legs,
Vomiting, confused.

Step 1: Na-Cl =62, corresponds to
BE = 62-34 – +28 mM

Step 2: Albumin 22 g/L,
corresponds to BE = +6 mM

Step 3: BE from step 1 and 2 combined should be +34, but it is 0, this means 34 of "unmeasured" anions.

Step 4: pCO2 is and should be normal
Step 5: Synthesis?

pH(T)c	7.432		[7.350 - 7.450
pCO₂(T)c	4.81	kPa	[4.67 - 6.40
↑ pO₂(T)c	26.9	kPa	[11.1 - 14.4
Acid-base status			
cHCO₃⁻(P,st)c	24.3	mmol/L	
cHCO₃⁻(P)c	24.0	mmol/L	
cBase(Ecf)c	-0.3	mmol/L	
Oximetry values			
sO₂	99.9	%	
↓ ctHb	120	g/L	[135 - 175
Hctc	36.6	%	
↑ FO₂Hb	98.6	%	[94.0 - 98.0
FCOHb	0.8	%	[0.5 - 1.5
FHHb	0.1	%	[-
FMetHb	0.5	%	[0.0 - 1.5
Electrolyte values			
↑ cK⁺	4.6	mmol/L	[3.4 - 4.5
↓ cNa⁺	132	mmol/L	[136 - 146
↓ cCa²⁺	0.61	mmol/L	[1.15 - 1.29
↓ cCl⁻	70	mmol/L	[98 - 106]
Anion Gapc	37.1	mmol/L	
Metabolite values			
↑ cGlu	8.0	mmol/L	[3.9 - 5.8]
↑ cLac	20	mmol/L	[0.5 - 1.6]
Oxygen status			
p50e	3.40	kPa	

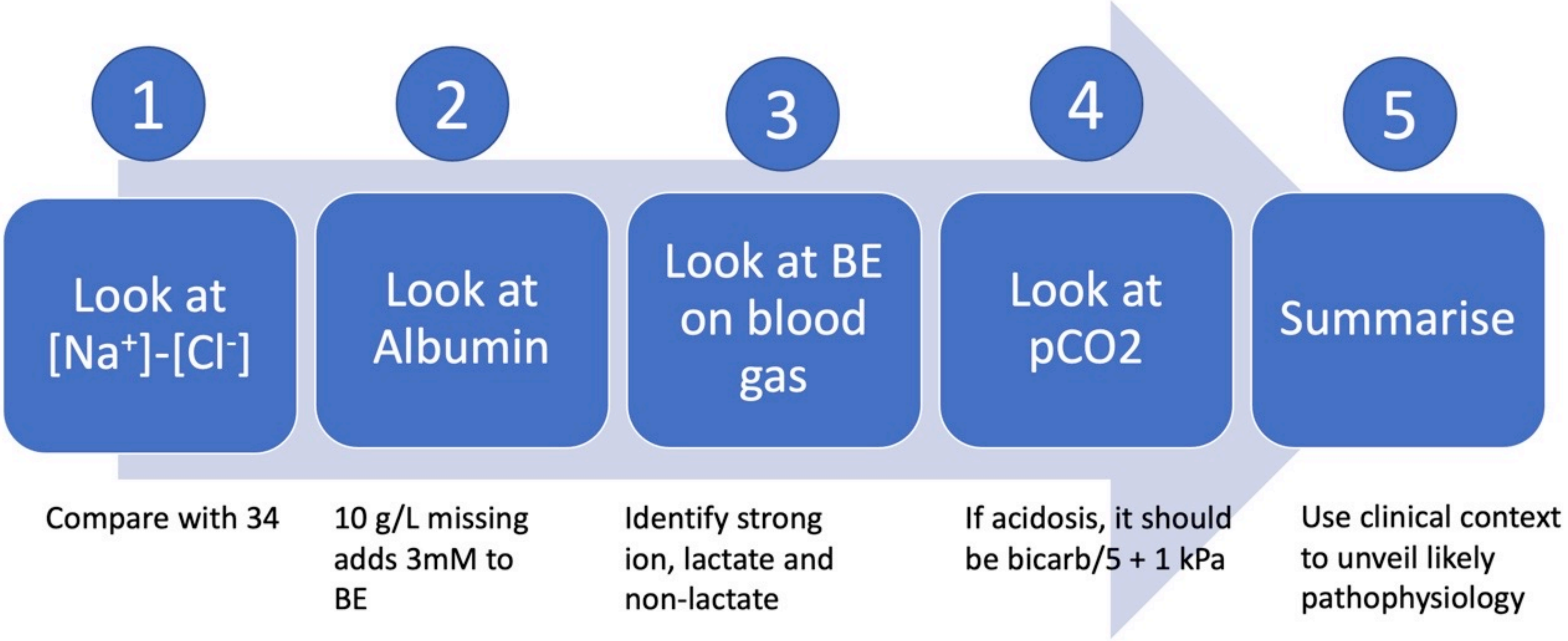
Alb 22 g/L

34-years-old, alcoholism, self-neglect,
Now presents with after 3 days off legs,
Vomiting, confused.

Hypochloridemic alkalosis (+28 mM):
due to ALD, vomiting
Hypoalbuminaemic alkalosis (+6mM)
Strong ion acidosis
- lactate (20mM)
- unknown (14 mM)-ketons?

No respiratory disorder

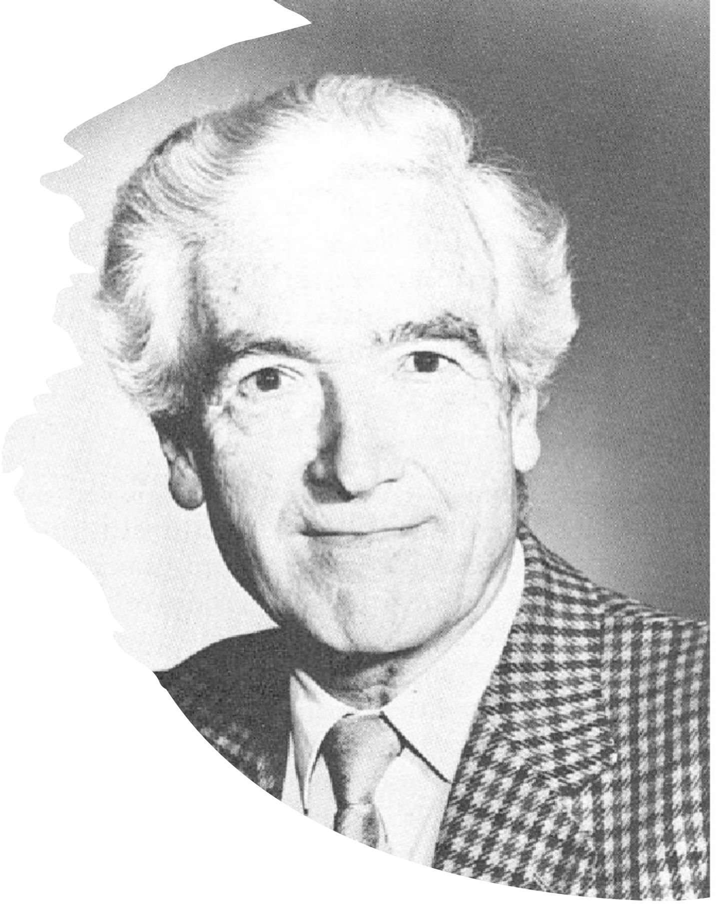
Five step approach



(BE partitioning method modified as per Story, BJA 2004)

Conclusions: Stewart or Astrup?

- Stewart and Astrup!
  - Classical, Bostonian and Stewart approaches are complementary, not contradictory
- Classic approach useful and good enough for most cases
  - Looks first at the final result and then try to find explanation
  - Good framework to understand concept of compensation
- Electroneutrality-based approach
  - Looks first at determinants of acid-base status and then the result
- Developed by geniuses, but useful for ordinary doctors



Thank you

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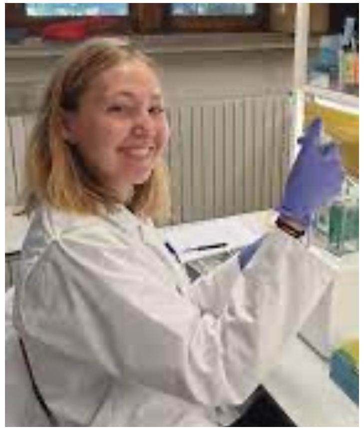

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Aged 34 years, bought on e-Bay