Acid-Base

Beyond the Basics

www.philippelefevre.com

- Acid-Base: Why should we care?

- Metabolic Acidosis
  - Osmolar Gap
  - Lactic Acidosis
  - Delta Gap
  - Albumin Correction
  - Pseudo Respiratory Alkalosis

- Sodium Bicarbonate

- Alpha-stat Vs pH-stat

- Trans-Atlantic Divide
  - Boston Rules
  - Copenhagen Rules

- Stewart's Strong Ion Theory

pH

Box Jellyfish or Canary?

Consequences of Severe Metabolic Acidosis

Cardiovascular

↓ Contractility & CO

↑ Incidence of Arrhythmia

↑ Pulmonary Vascular Resistance

↓ Hepatic and Renal Blood Flow

Centralisation of blood volume

Respiratory

↑ RR & Dyspnea

↑ Respiratory Muscle Fatigue

Metabolic

Insulin Resistance

Inhibition of Glycolysis

Reduced ATP Production

Hyperkalaemia

Haematological

Right shift of Hb O_2 curve

↓ Clotting Factor Function

Cerebral

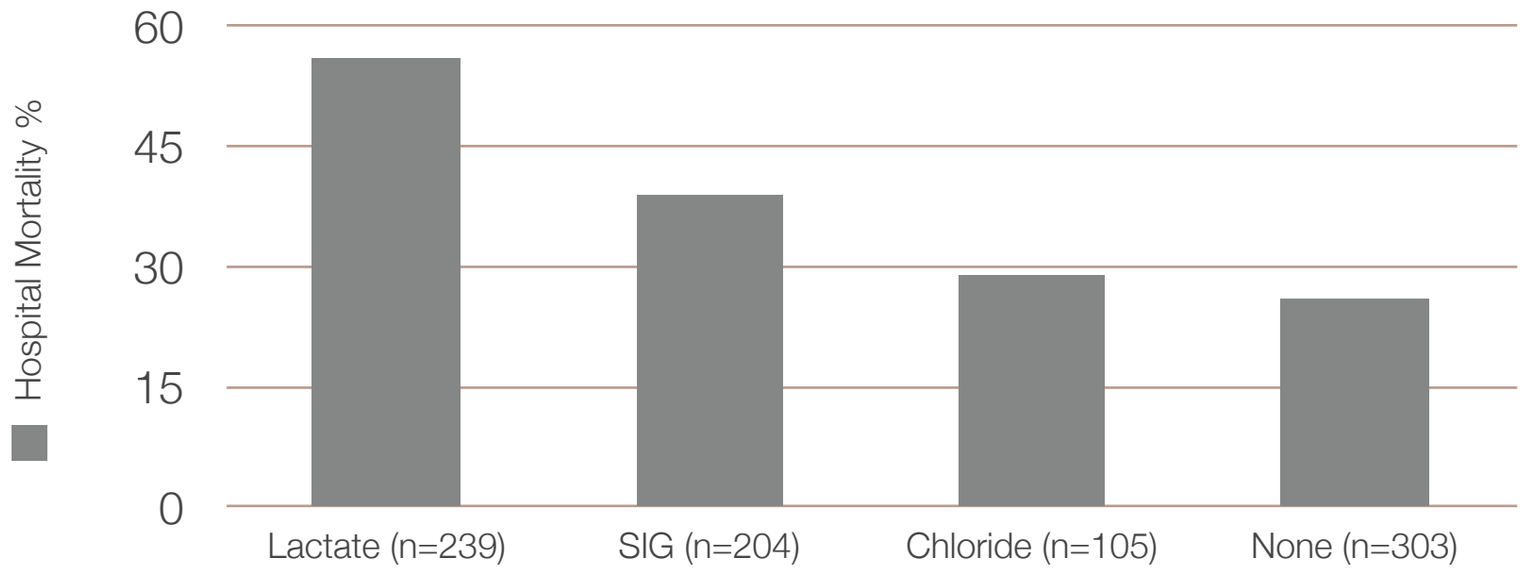
↑ Cerebral Blood Flow

Coma

Normal Anion Gap vs Raised Anion Gap prognosis

Normal Anion Gap vs Raised Anion Gap prognosis

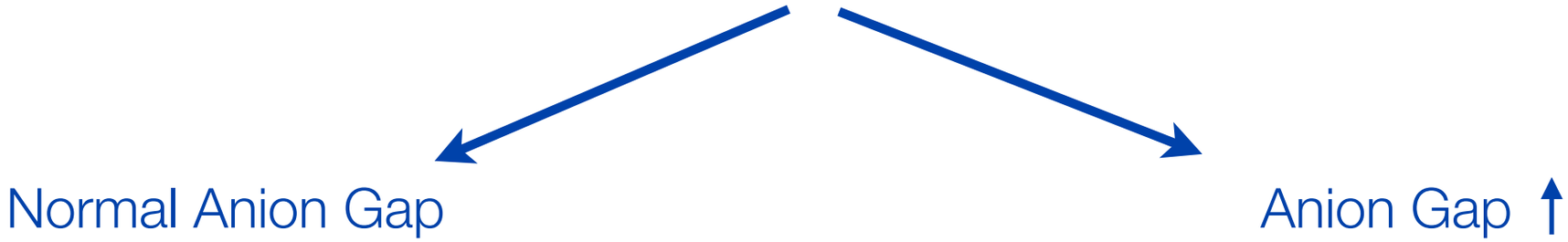
Kyle J Gunnerson1, Melissa Saul2, Shui He3 and John A Kellum, **Lactate versus non-lactate metabolic acidosis: a retrospective outcome evaluation of critically ill patients.** *Critical Care* 2006, 10:R22 (doi:10.1186/cc3987)



Observational, cohort study of 815 patients admitted to the ICUs of 4 Pittsburgh Hospitals

Metabolic Acidosis

Metabolic Acidosis



Metabolic Acidosis

Normal Anion Gap

Loss of high SID fluid

- Gastrointestinal
  - diarrhoea
  - iliostomy
  - uretosigmoidostomy
- Renal
  - acetazolamide
  - renal Tubular Acidosis
  - hyperparathyriodism
  - hypoaldersteronism

Addition of low SID fluid

- Normal Saline

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- Poisons
  - salicilate
  - methanol
  - ethanol Glycol

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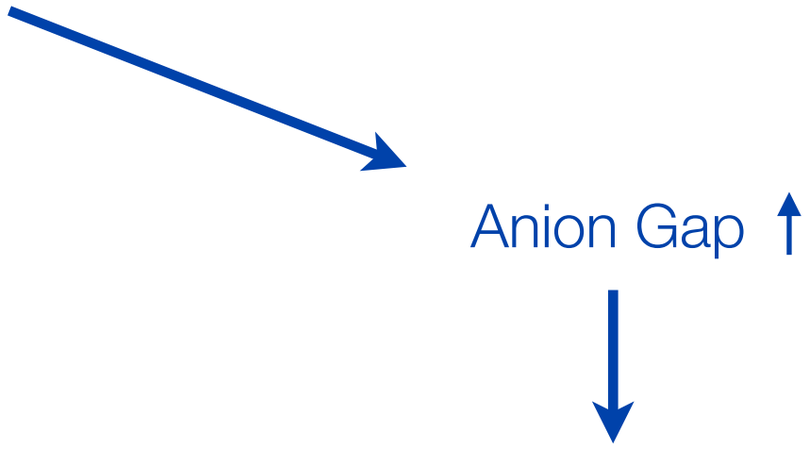

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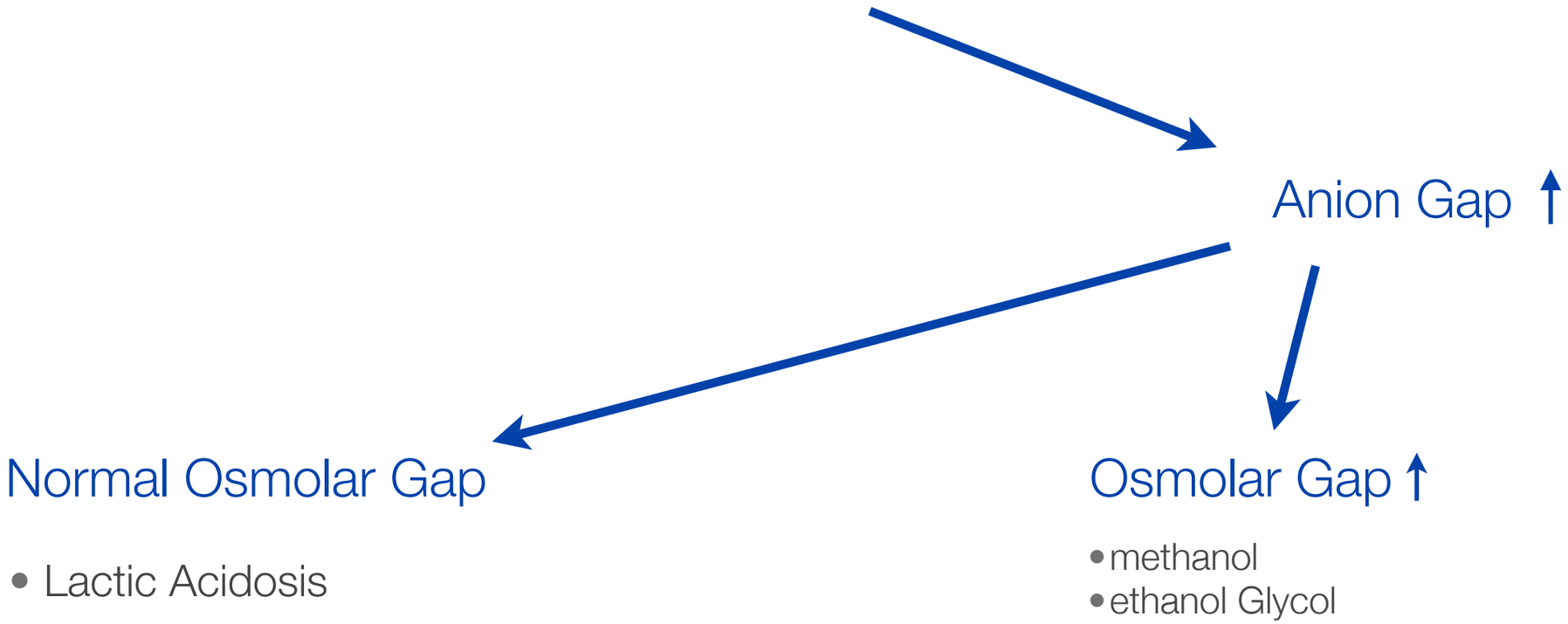


Osmolar Gap Poisonings

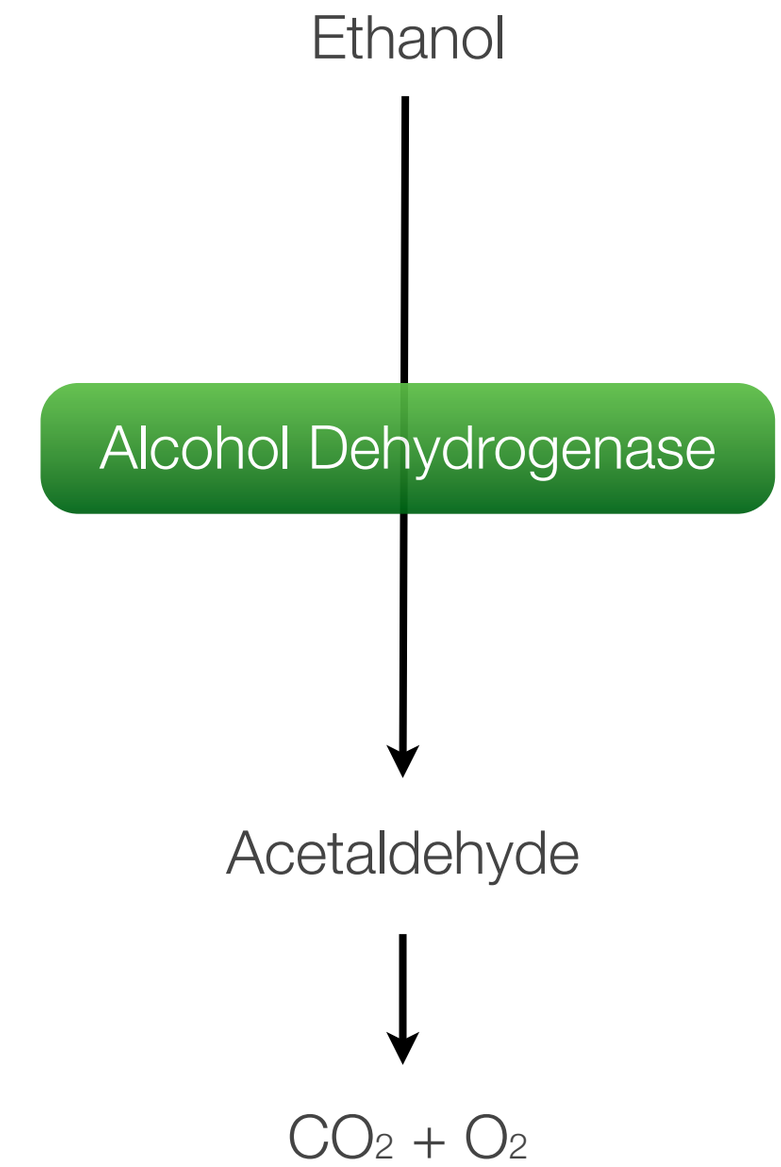
Methanol

- drowsiness, confusion & ataxia
- nausea, vomiting & abdominal pain
- blurred vision or changes in colour perception
- hypotension and cardiac arrest
- permanent blindness
- seizures, coma & death

Ethelene Glycol

- drowsiness, confusion & ataxia
- nausea, vomiting & abdominal pain
- hypertension
- ARDS
- acute tubular necrosis and renal failure - probably due to calcium oxalate deposition

Raised Osmolar Gap Acidosis



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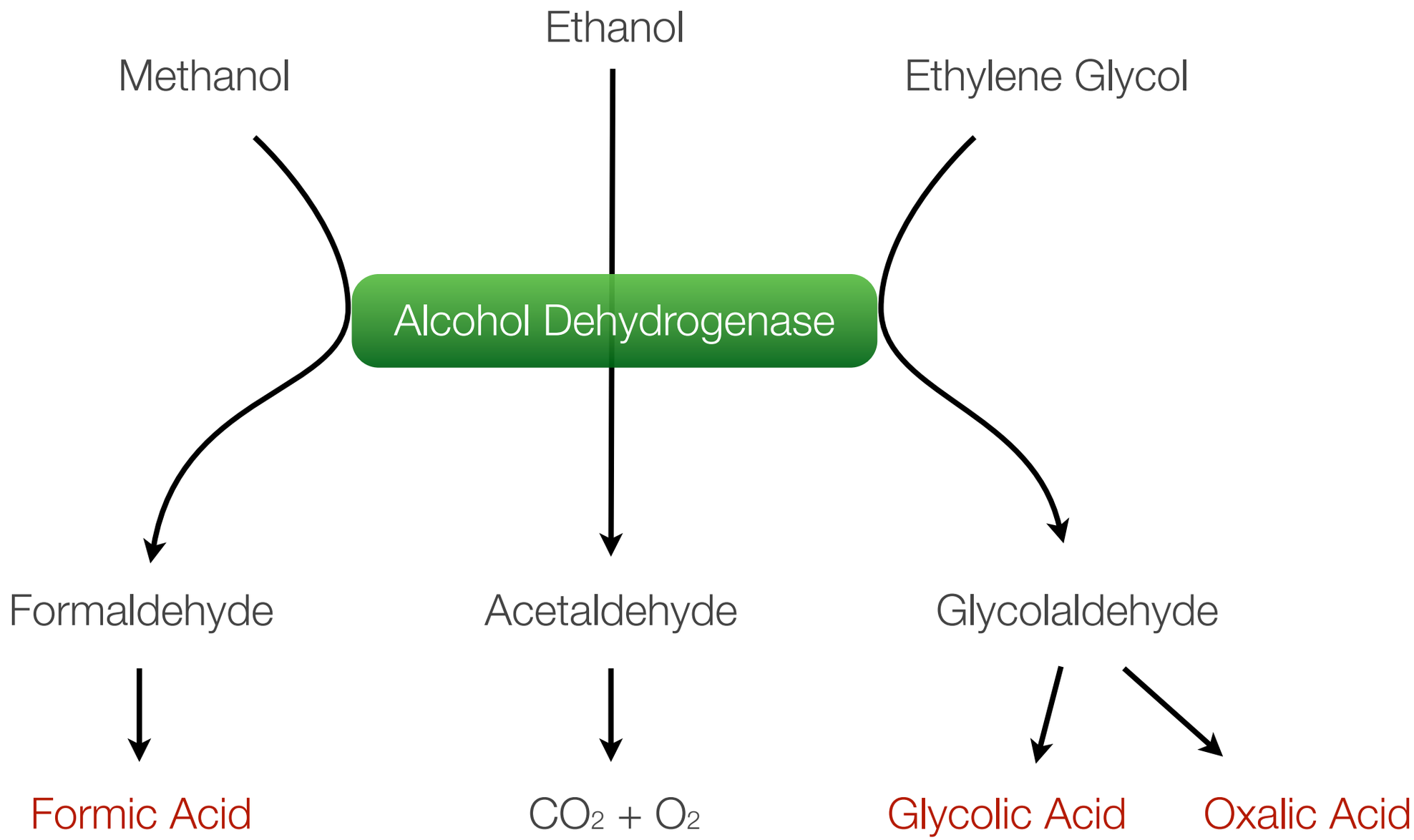

Treatment

- 100% Ethanol infusion - BSL↓ in children
- Fomepizole - occupies alcohol dehydrogenase without the side effects

Osmolar Gap

Osmolar Gap = Calculated Osmolarity - Measured Osmolarity

Normal less than 10

osmolarity = osmoles of solute per litre of solution - Calculated

osmolality = osmoles of solute per kilogram of solvent - Measured

osmole = an Avagadro's number of particles ($6.022 \times 10_{23}$) in solution

Measuring Osmolality

Colligative properties depend only on the ratio of the number of particles of solute to solvent in the solution, not the identity of the solute

- vapour pressure depression
- freezing point depression
- boiling point elevation
- osmotic pressure

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An osmole is the amount of a substance that yields, in ideal solution, that number of particles (Avogadro's number) that would depress the freezing point of the solvent by 1.86K

Calculating Osmolarity (properly)

$$\mathrm{Osm/L} = \sum_i \varphi_i \, n_i C_i$$

φ = osmotic coefficient - accounts for the degree of non-ideality of the solution.

n = number of particles into which the molecule dissociates

C = molar concentration of the solute

i = represents the identity of a particular solute

Estimating Osmolarity

Osmolarity = Cations + Anions + non-ionized Solutes

Estimating Osmolarity

Osmolarity = 2 Cations + ~~Anions~~ + non-ionized Solutes

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- ~~K~~
- ~~Ca~~
- ~~Mg~~

- glucose
- urea
- lipids

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Using the Osmolar Gap

Using the Osmolar Gap

- Time course

Osmolar Gap ↑ ⟶ Acidosis

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- Ethanol Cloaking

  2 Na + Glucose + Urea + Ethanol

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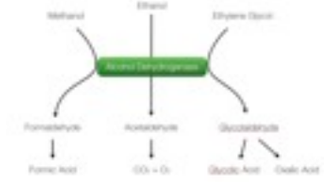

Osmolar Gap ↑ ⟶ Acidosis

- Ethanol Cloaking

2 Na + Glucose + Urea + Ethanol

Units

Divide mg/dl by 4.6 to find mmol/l
eg. An ethanol level of 0.05% is 50mg/dl, 50 / 4.6 = 10.9 mmols/l

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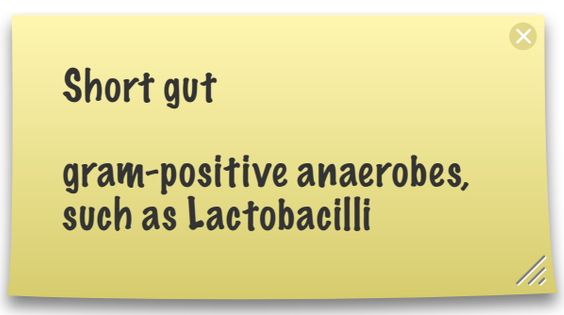
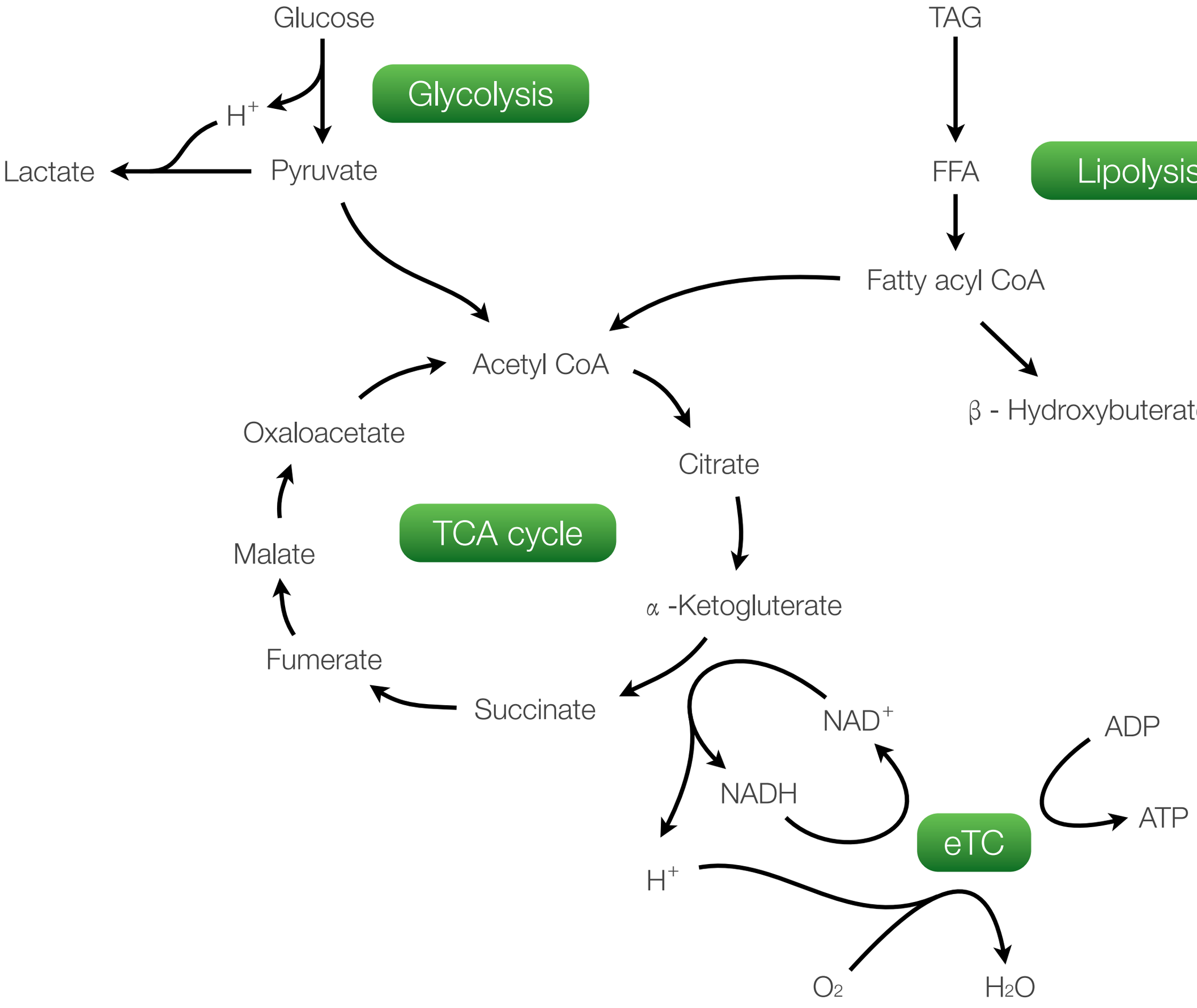
Lactic Acidosis

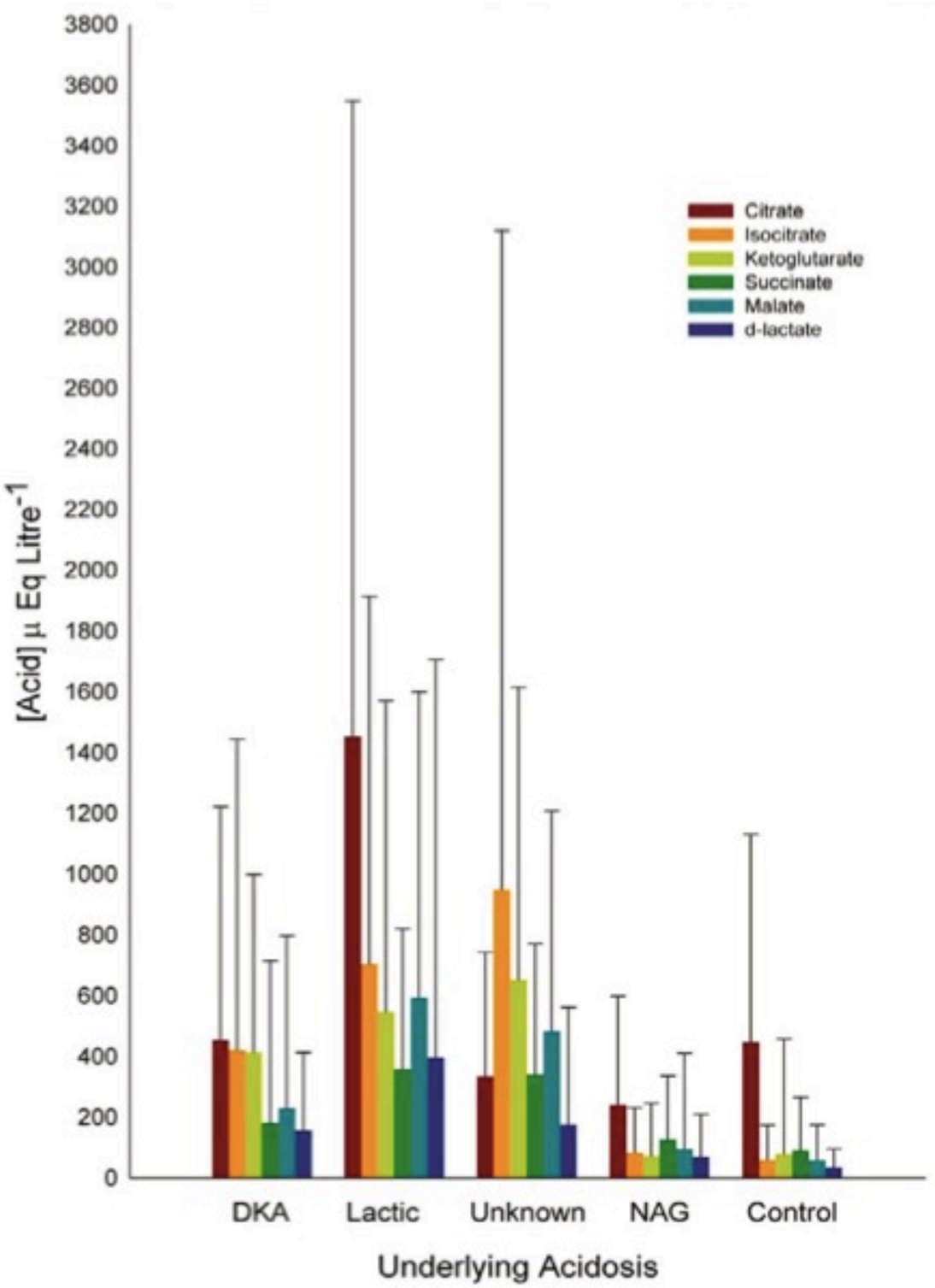
- Type A - increased production
  - Tissue hypoxia
  - β2 stimulation
  - insulin deficiency
- Type B - decreased metabolism
  - insulin deficiency
  - malignancies
  - rare enzyme defects
- Propofol Infusion Syndrome
- Metformin
- D-lactate - bowel fermentation




Glucose
Glycolysis
H+
Lactate
Pyruvate
TAG
FFA
Lipolysis
Fatty acyl CoA
Acetyl CoA
β - Hydroxybuterate
Oxaloacetate
Citrate
TCA cycle
Malate
α -Ketogluterate
Fumerate
Succinate
NAD+
NADH
ADP
ATP
eTC
H+
O2
H2O

Anions of the Raised Gap

- Lactic acidosis is so called for historical reasons
- A significant number of hypoxic patients have a near normal lactate
- Corrected anion gap or SID are better indicators of severity of tissue hypoxia
- DKA is not just about the ketoacids



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Metabolic Acidosis

Normal Anion Gap

Negative Urinary anion Gap

- Gastrointestinal
  - diarrhoea
  - iliostomy
  - uretosigmoidostomy

Positive Urinary anion Gap

- Renal
  - acetazolamide
  - renal Tubular Acidosis
  - hyperparathyriodism
  - hypoaldersteronism

Anion Gap ↑

Urinary Anion Gap

$$Urinary\ Anion\ Gap = Na^{+} + K^{+} - Cl^{-}$$

Gastrointestinal

- Compensated by increased renal excretion of NH_4^+

↓ Urinary anion gap (-ve)

Renal

- NAG renal acidosis is due to deduced relative NH_4^+ excretion

↑ Urinary anion gap (+ve)

Delta Ratio

$$\textit{Delta ratio} = \frac{\textit{Increase in anion gap}}{\textit{Decrease in bicarbonate}}$$

- Delta ratio greater than 2 strongly suggests a normal anion gap acidosis hiding behind a raised anion gap acidosis

Venous Blood Gases

- Good means of investigating Acid-Base balance
- Simple correction factors unless in circulatory failure

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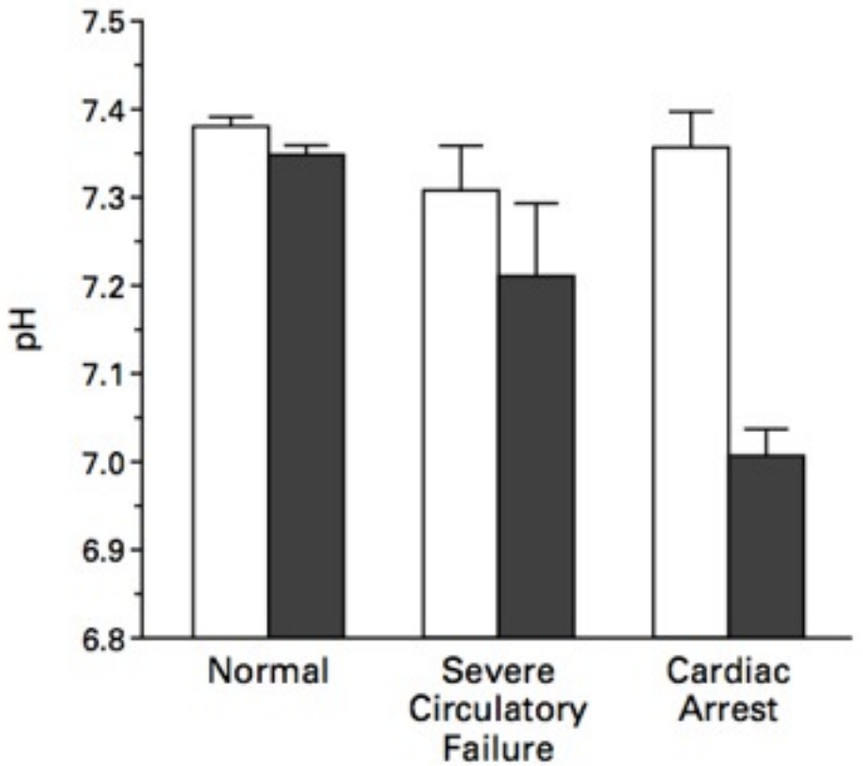
Pseudo-Respiratory Alkalosis



- 45 year old female nurse with nephrotic syndrome is brought to ED intoxicated

?

pH	7.44
P_{CO_2}	34
HCO_3	21
BE	0
Na	138
K	4
Cl	106
Albumin	13
Glucose	5.2
Urea	14.3
BAL	0.05
Osmolality	320

Osmolality
(50 / 4.6) = 10.9
(2 * 138) + 5.2 + 14 + 10.9 = 306.1

Anion Gap
138 + 4 - 106 - 21 = 15

Corrected Anion Gap
(42 - 13) = 27
15 + (27/3) = 24

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Raised Anion Gap Metabolic Acidosis

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Sodium Bicarbonate

Undesirable Effects

- hypernatraemia & hyperosmolality
- volume overload
- hypokalaemia
- left shift of the HbO_2 dissociation curve
- Increased lactate production
- CSF acidosis
- hypercapnia

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Legitimate Uses

- urine alkalisation
- life threatening hyperkalaemia

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Never give bicarb to a patient that can't blow off excess CO_2

Key Points

- pH derangement is a canary - treat the cause
- Correct AG for albumin or use the SIG
- Remember the osmols
- Consider a urinary anion gap for normal anion gap acidosis
- Beware of arterial gasses in circulatory failure

Alpha-stat Vs pH-stat

The Great Trans-Atlantic Acid-Base Debate

Mention the rules

Boston

(Schwarts and Relman)

Vs

Copenhagen

(Astrup and Siggaard-Anderson)

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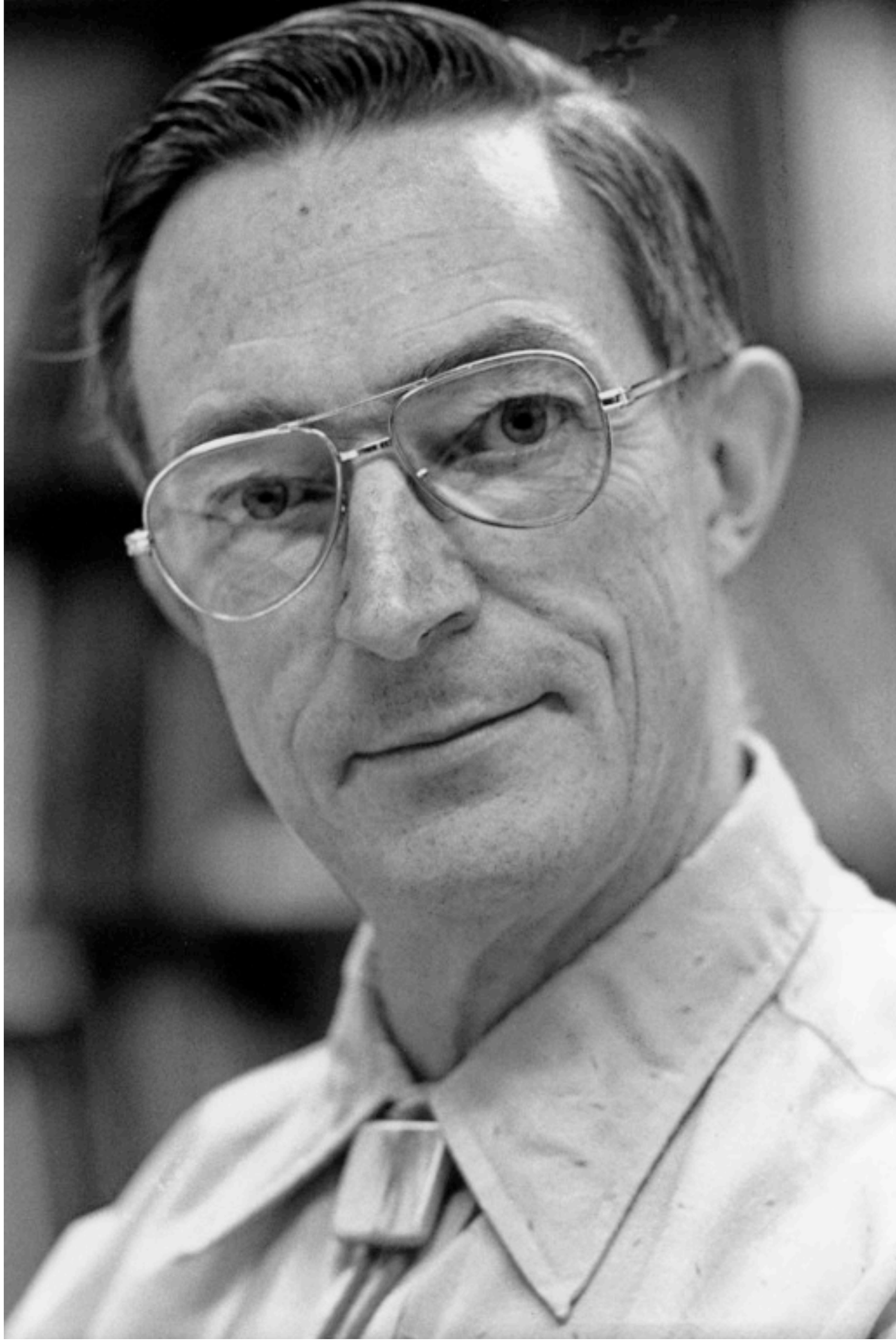
When will BE or Bicarb differ?

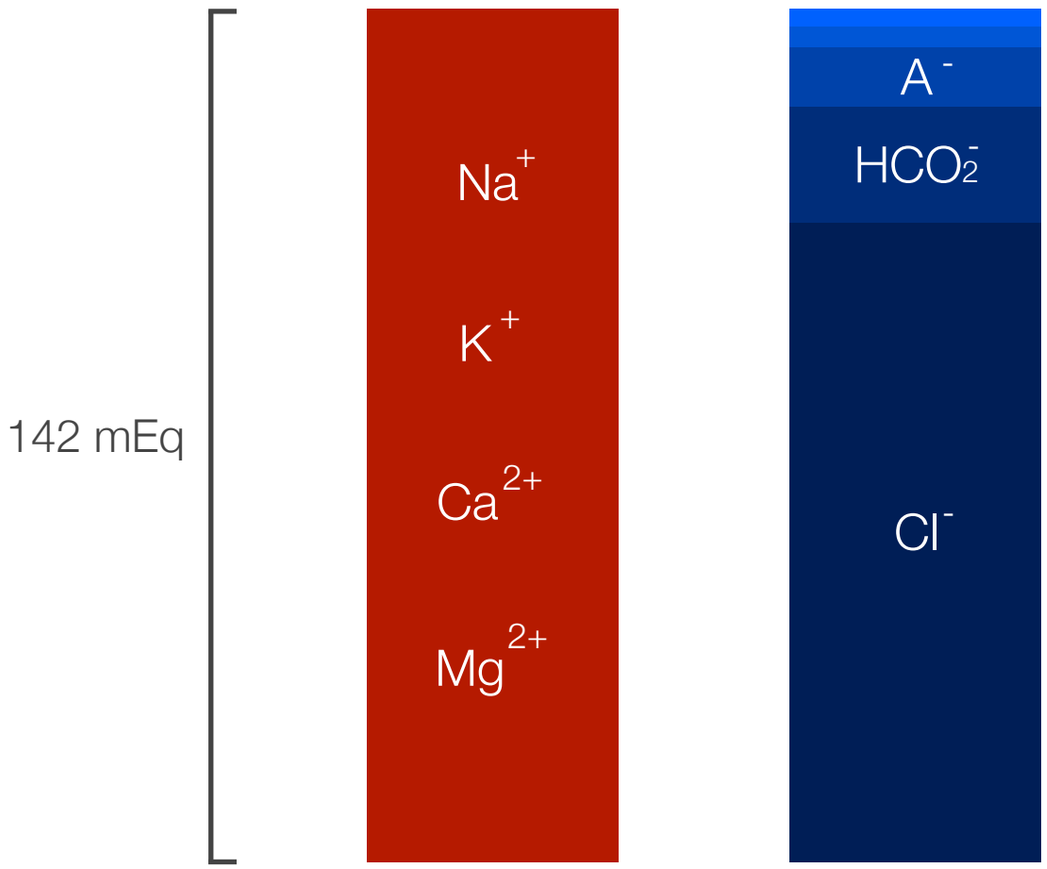
Peter Stewart (1921-1993)

- Intensely annoyed by bicarbonate
- Rather than just focus on a single indicator at the centre of acid base he went in search of quantitative picture of the whole
- Grand unifying theory of physiological acid-base



Strong Ions	Weak Ions
Na^{+}	HCO_3^{-}
K^{+}	CO_3^{2-}
Mg^{2+}	HPO_4^{-}
Ca^{2+}	Protein
Cl^{-}	
SO_4^{2-}	
Lactate	

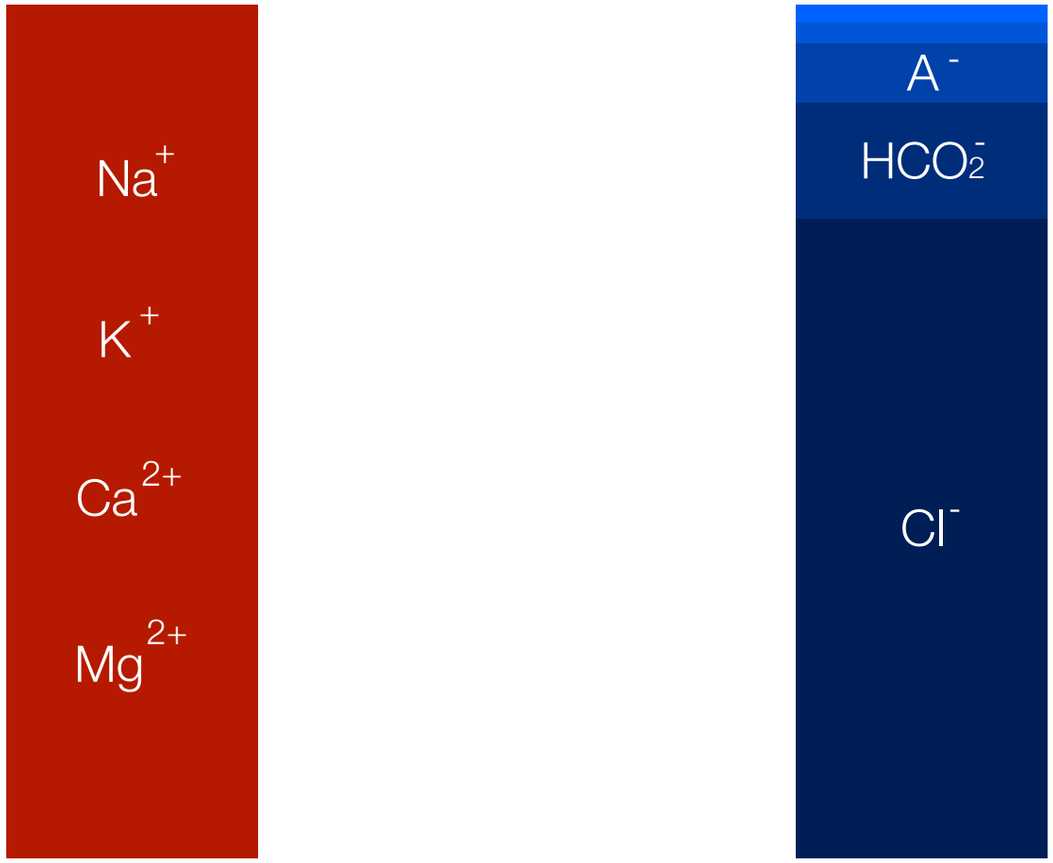
Strong Ion Difference



Gamblegram

1st principal - electrical neutrality

Strong Ion Difference



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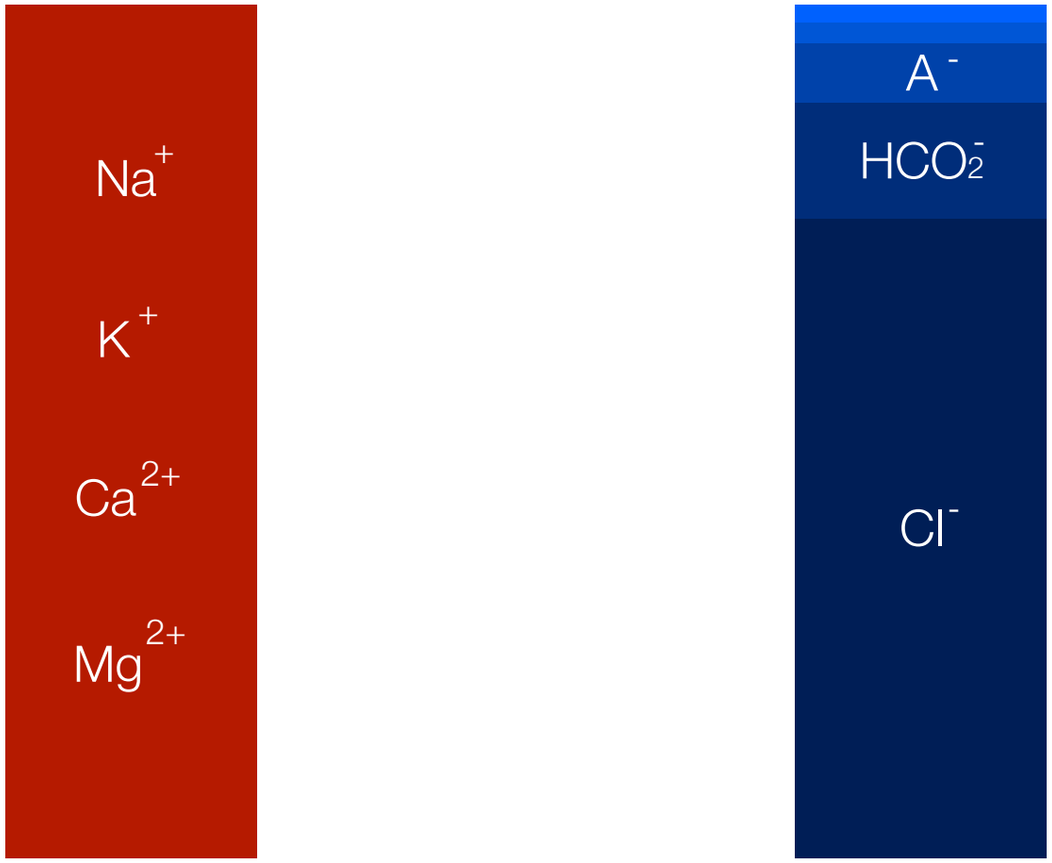

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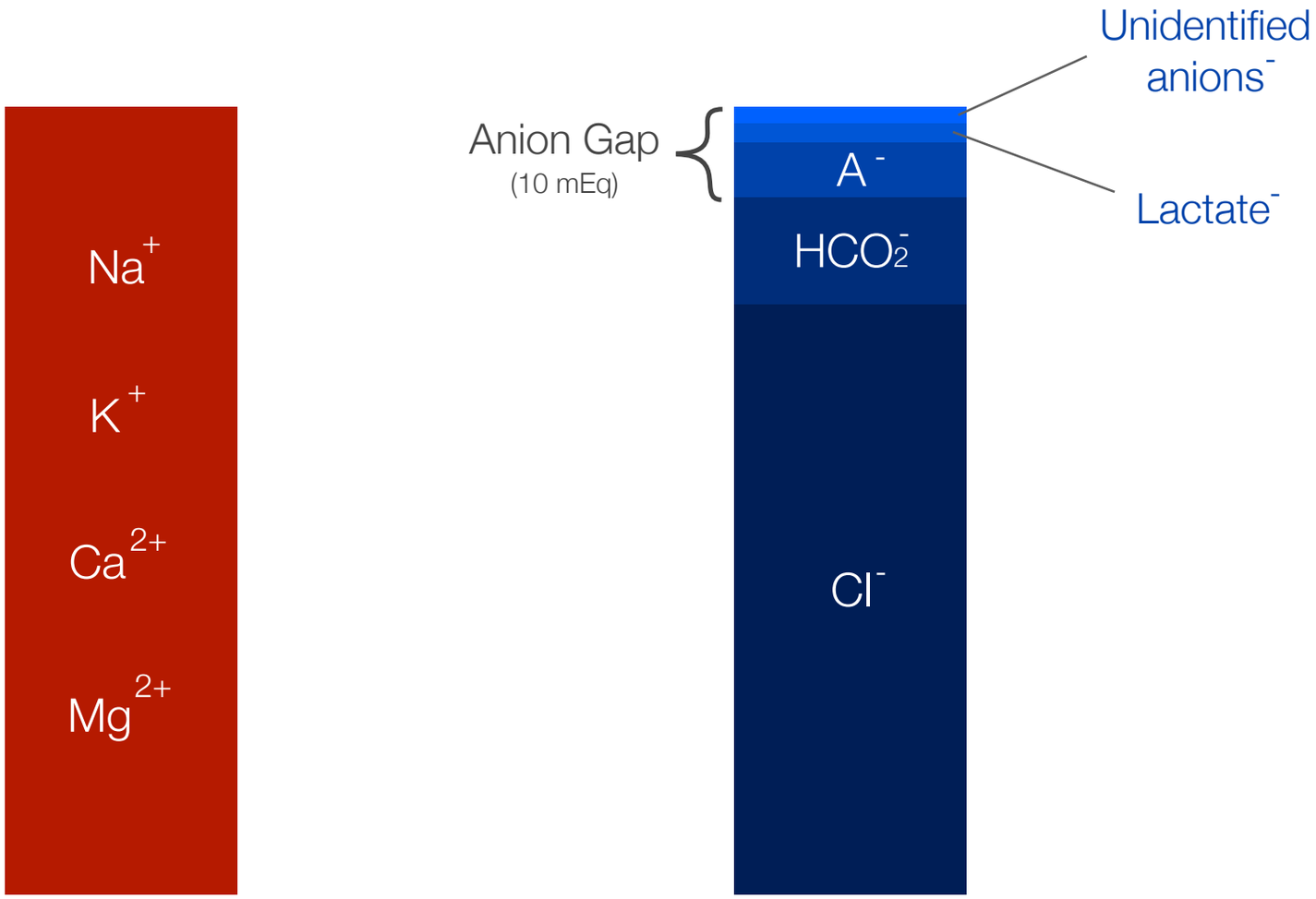

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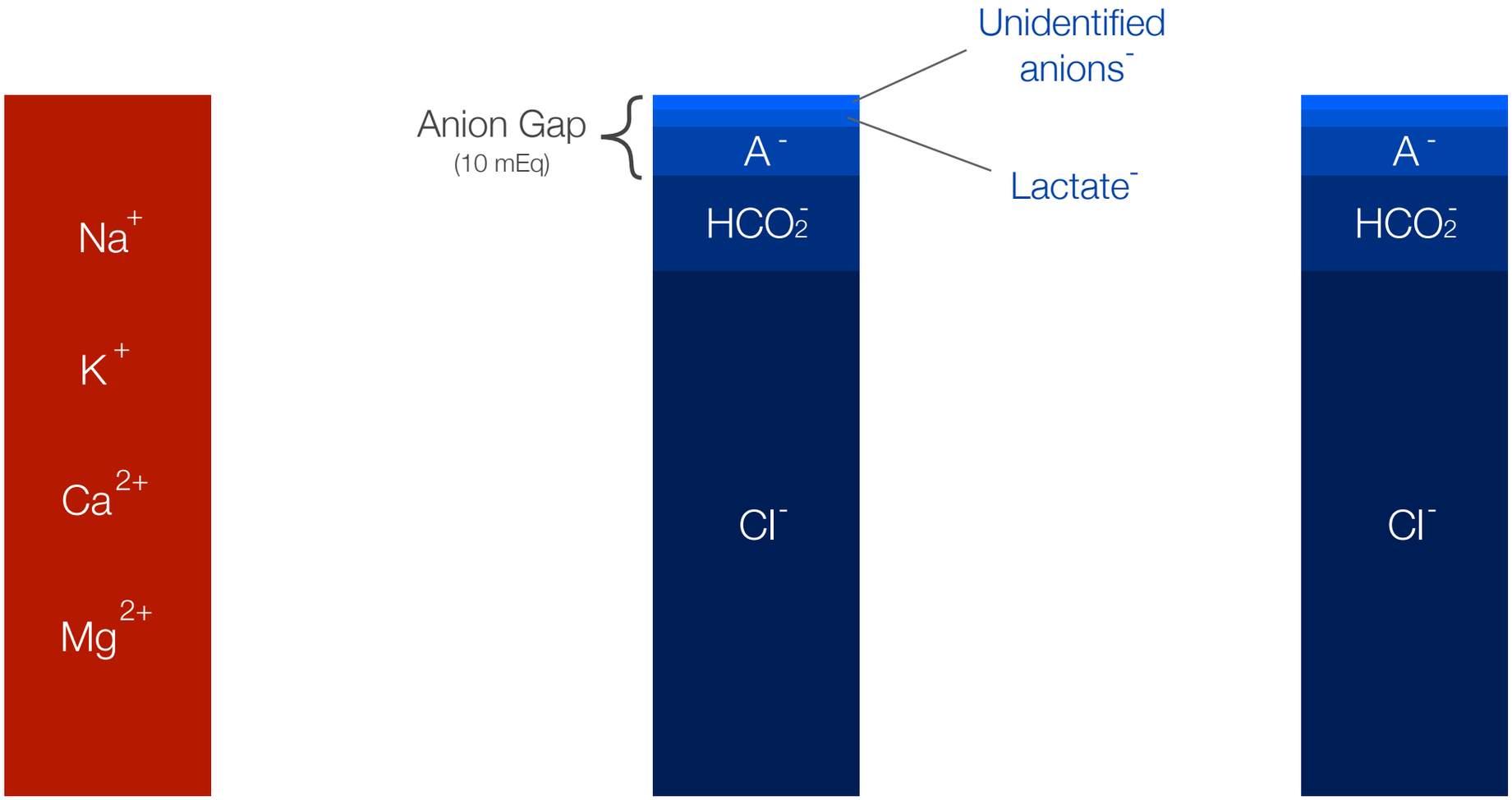

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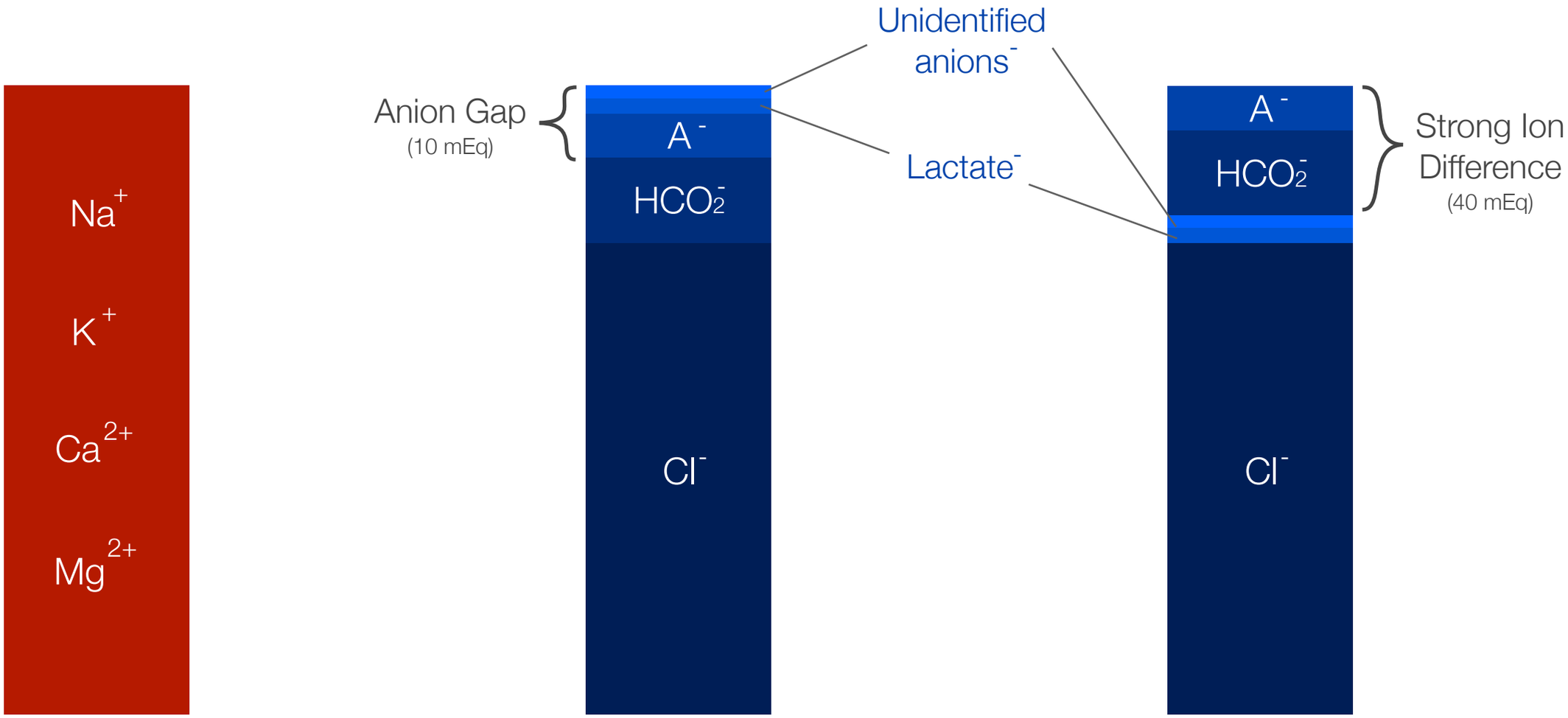
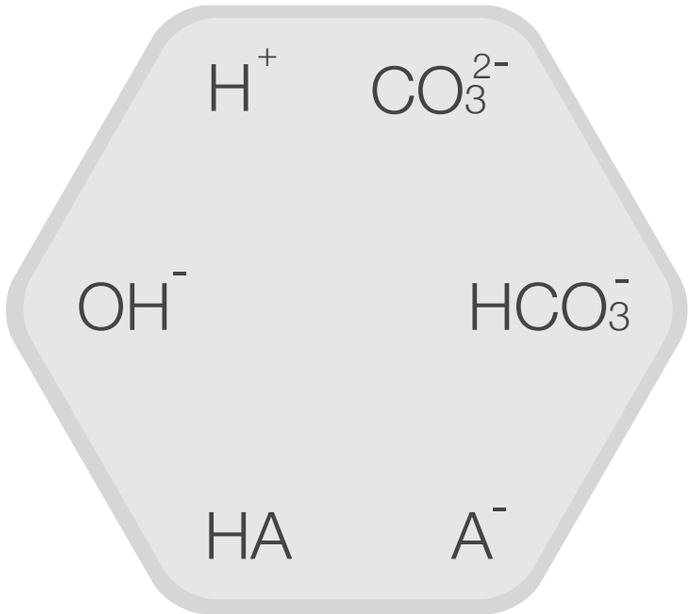


The Variables

Independent	Dependent	Constants
P_{CO_2}	H^+(pH)	Water dissociation (Kw)
Strong ion difference (SID)	OH^-	Weak acid dissociation Ka
Total weak acid (A_{Tot})	CO_3^{2-}	CO_2 Solubility (S_{CO_2})
	HCO_2^-	HCO_2^- equilibria K_1 & K_3
	Dissociated weak acid (A^-)	
	Undissociated weak acid (HA)	

The Variables



Second principal
dependant and independent

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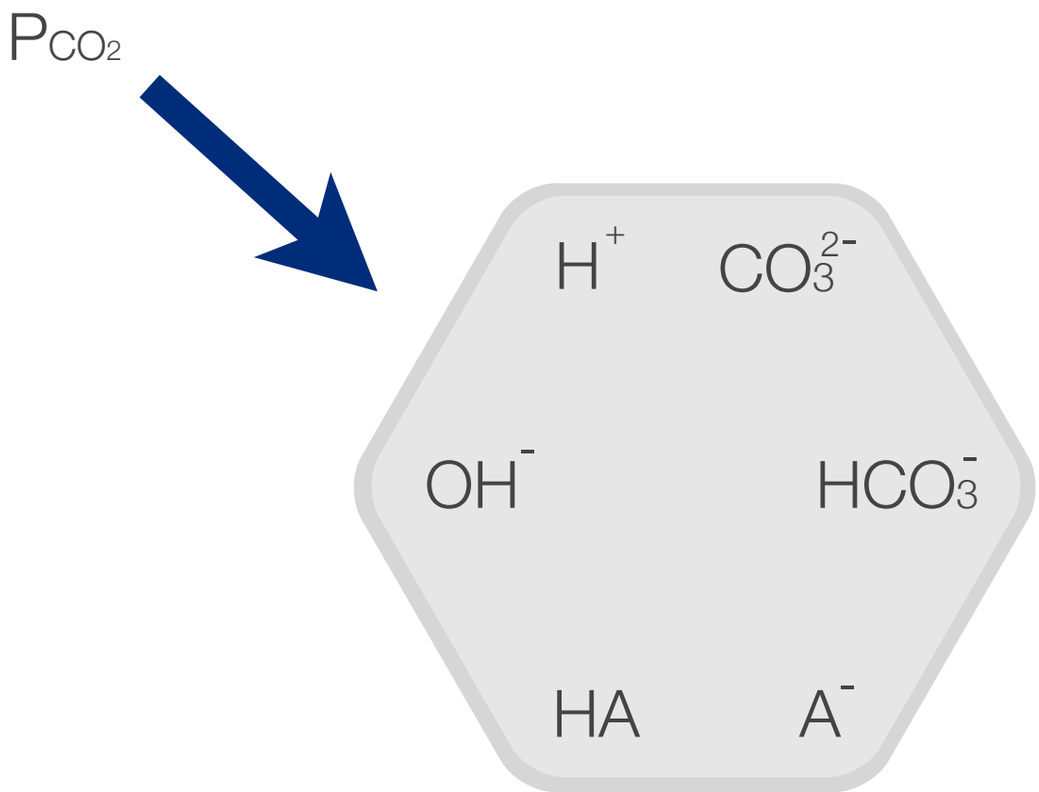

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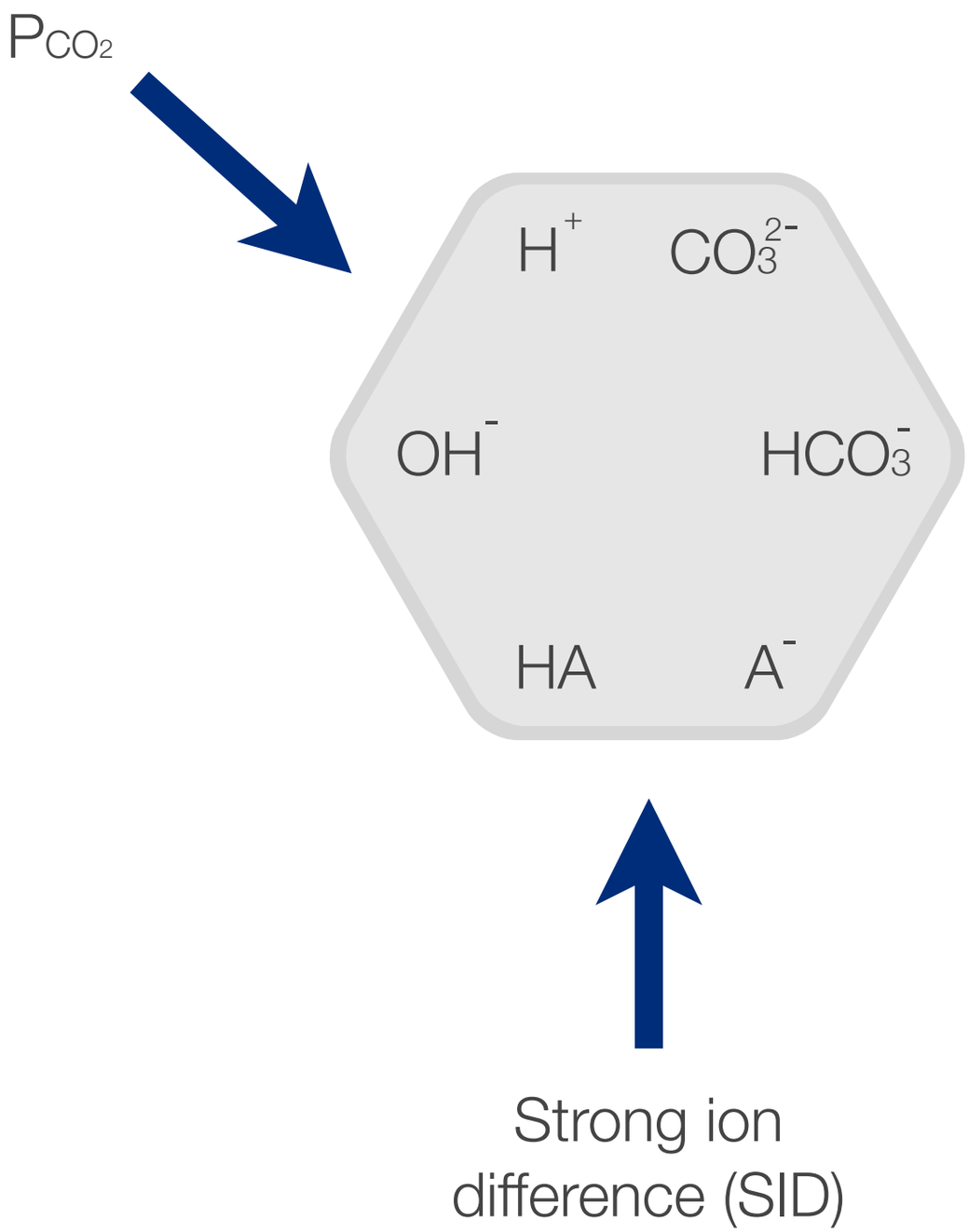

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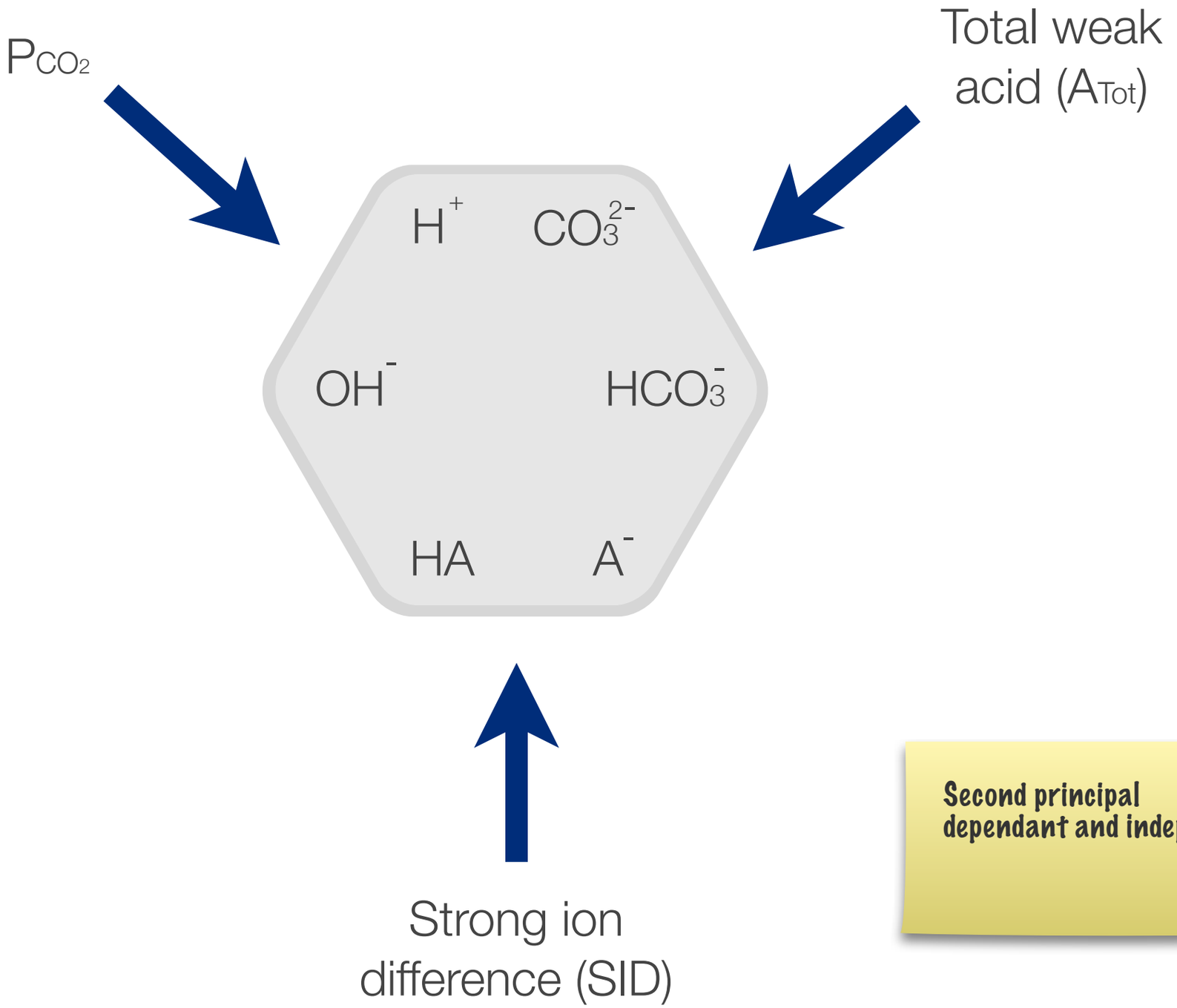

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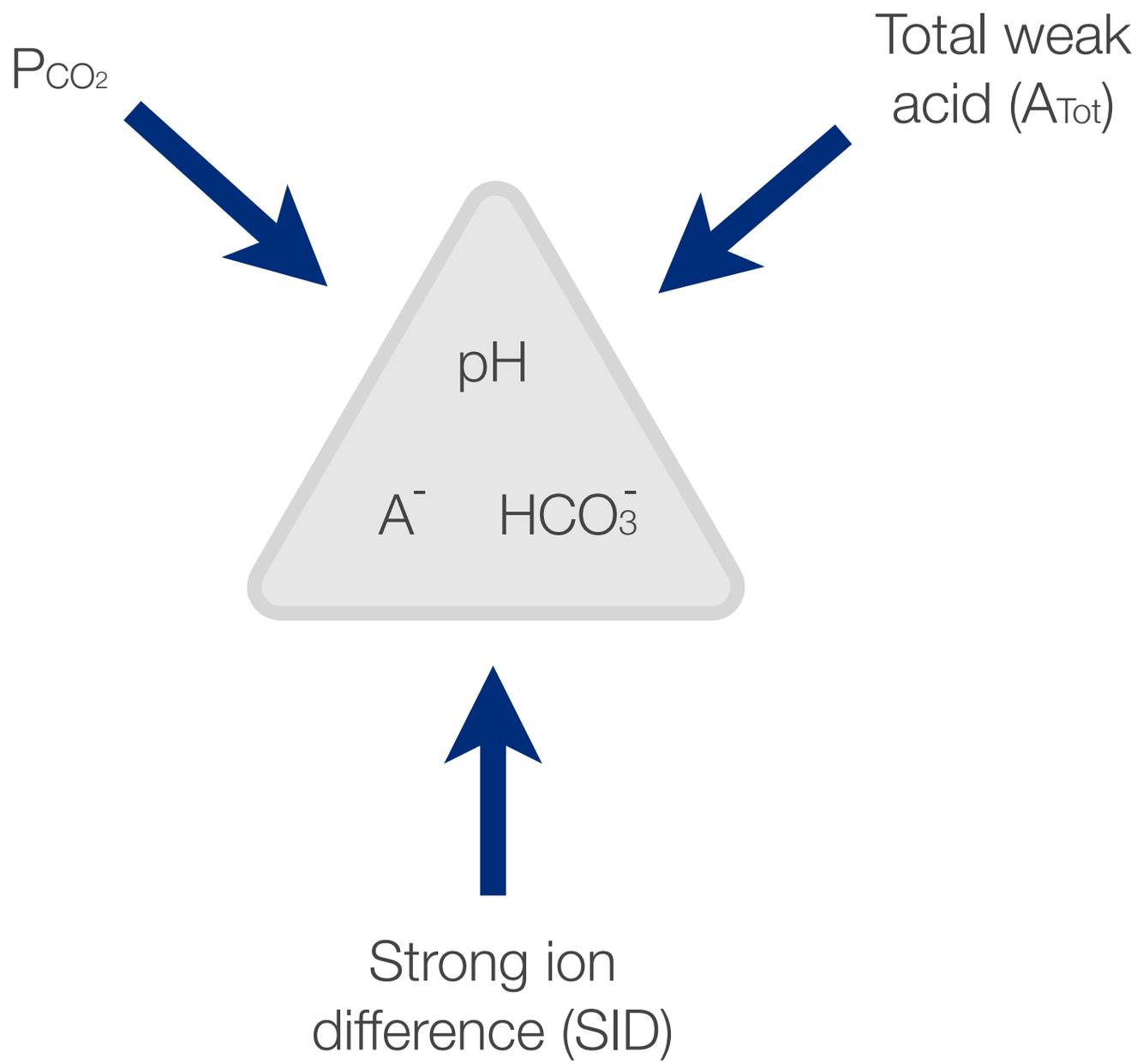

Stewart's Equations

Third principal
unified by pH

Stewart's Equations

1. Water Dissociation Equilibrium

$$H^{+} \;.\; OH \;=\; K_w$$

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$$H^{+} \cdot OH = K_w$$

2. Electrical Neutrality Equation

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

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$$A_{Tot} \;=\; H^+ + A^-$$

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$$H^+ \;.\; HCO_3^- \;=\; K_1 \;.\; S \;.\; P_{CO_2}$$

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$$H^+ \;.\; OH \;=\; K_w$$

2. Electrical Neutrality Equation

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

3. Weak Acid Dissociation Equilibrium

$$H^+ \;.\; A^- \;=\; K_a \;.\; HA$$

4. Conservation of Mass for 'A'

$$A_{Tot} \;=\; H^+ + A^-$$

5. Bicarbonate Ion Formation Equilibrium

$$H^+ \;.\; HCO_3^- \;=\; K_1 \;.\; S \;.\; P_{CO_2}$$

6. Carbonate Ion Formation Equilibrium

$$H^+ \;.\; CO_3^{2-} \;=\; K_3 \;.\; HCO_3^-$$

Stewart's Equations

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$$pH = pKi + \log \frac{SID - K_a \cdot (A_{Tot} / K_a) + 10^{-pH}}{S \cdot P_{CO_2}}$$

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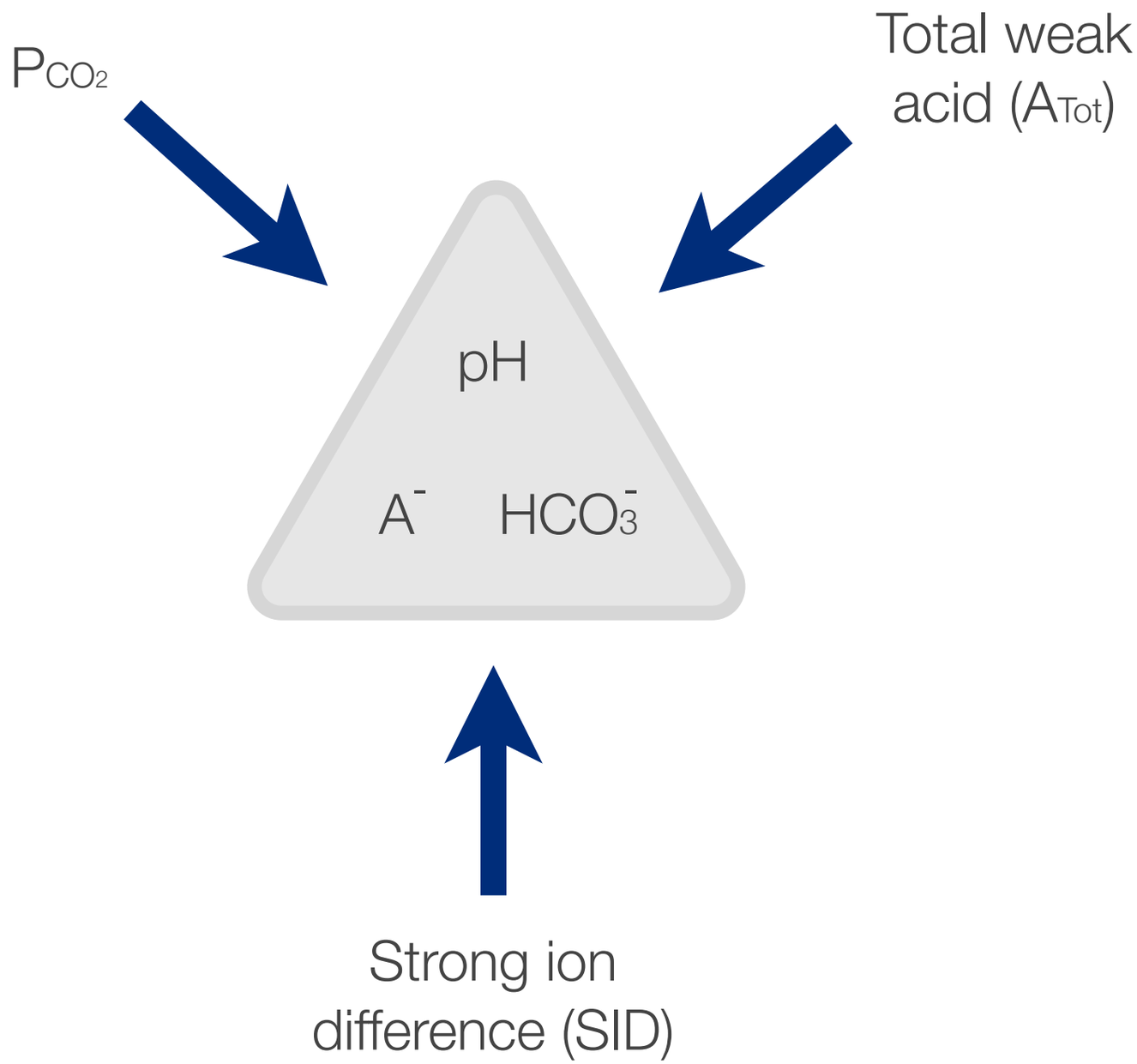
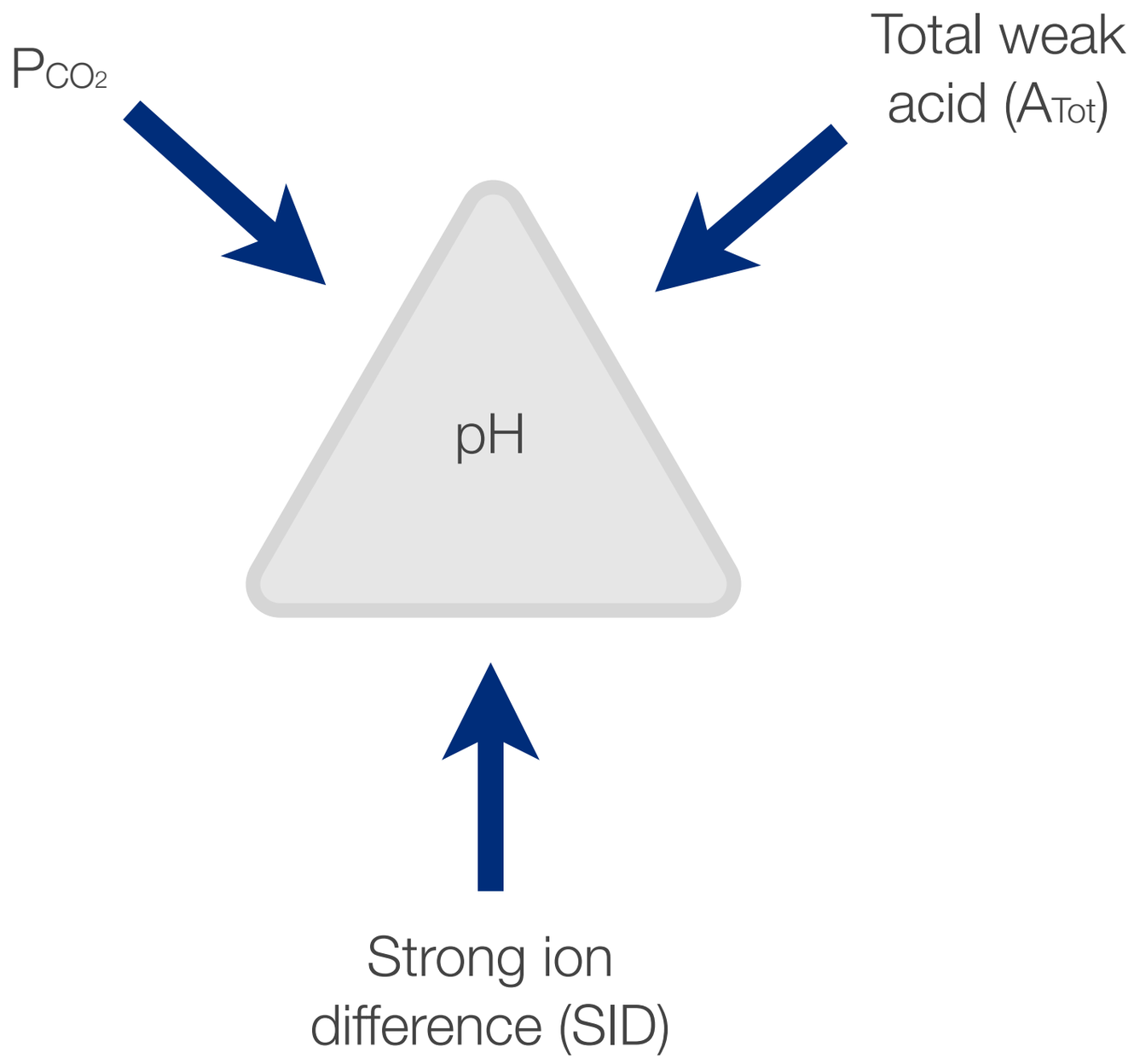
Henderson Hasselbach Equation

$$pH = pKi + Log \left\{ \frac{HCO_3}{S_{CO_2} \cdot PCO_2} \right\}$$

A New Clinical Approach



A New Clinical Approach



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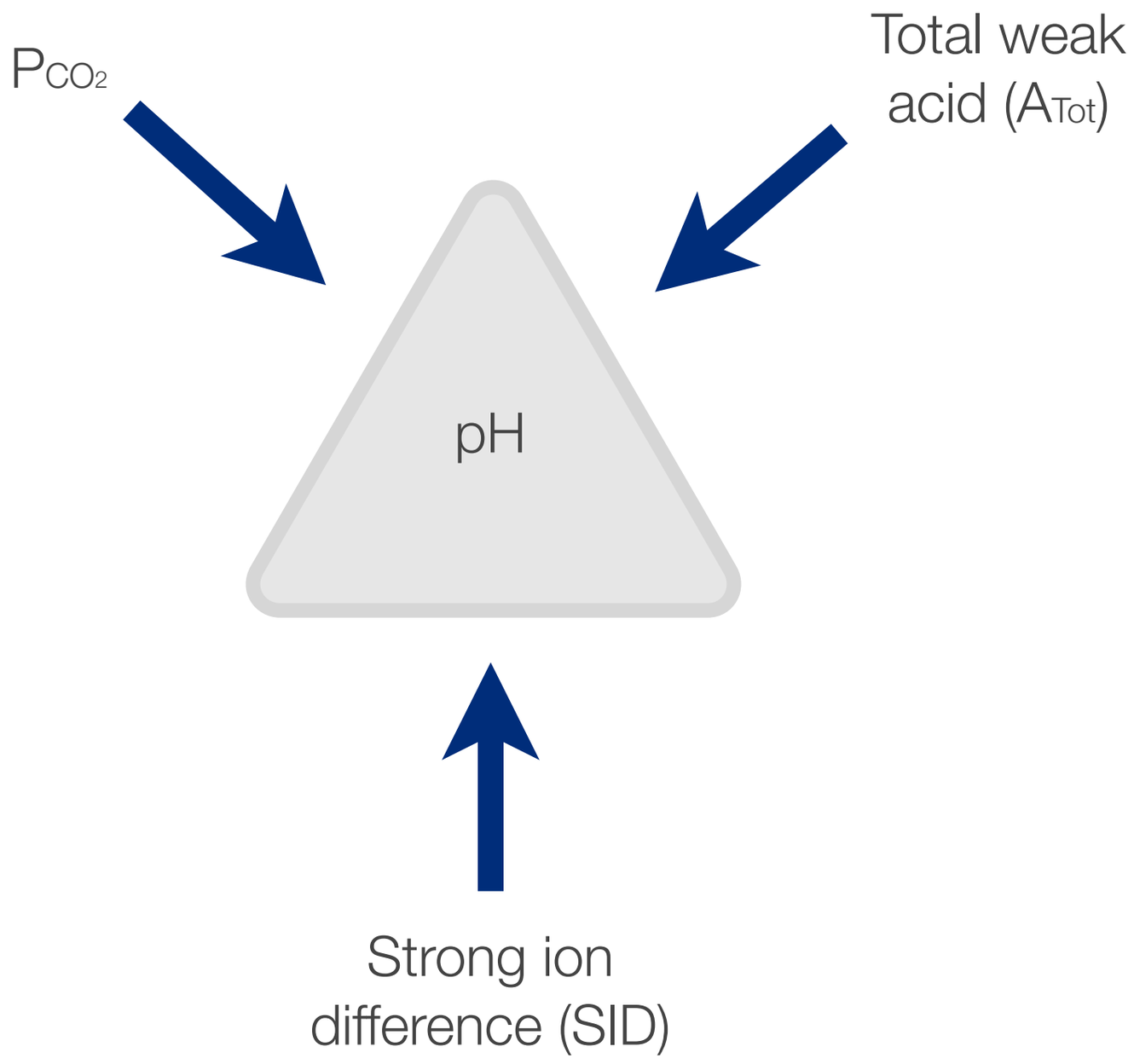

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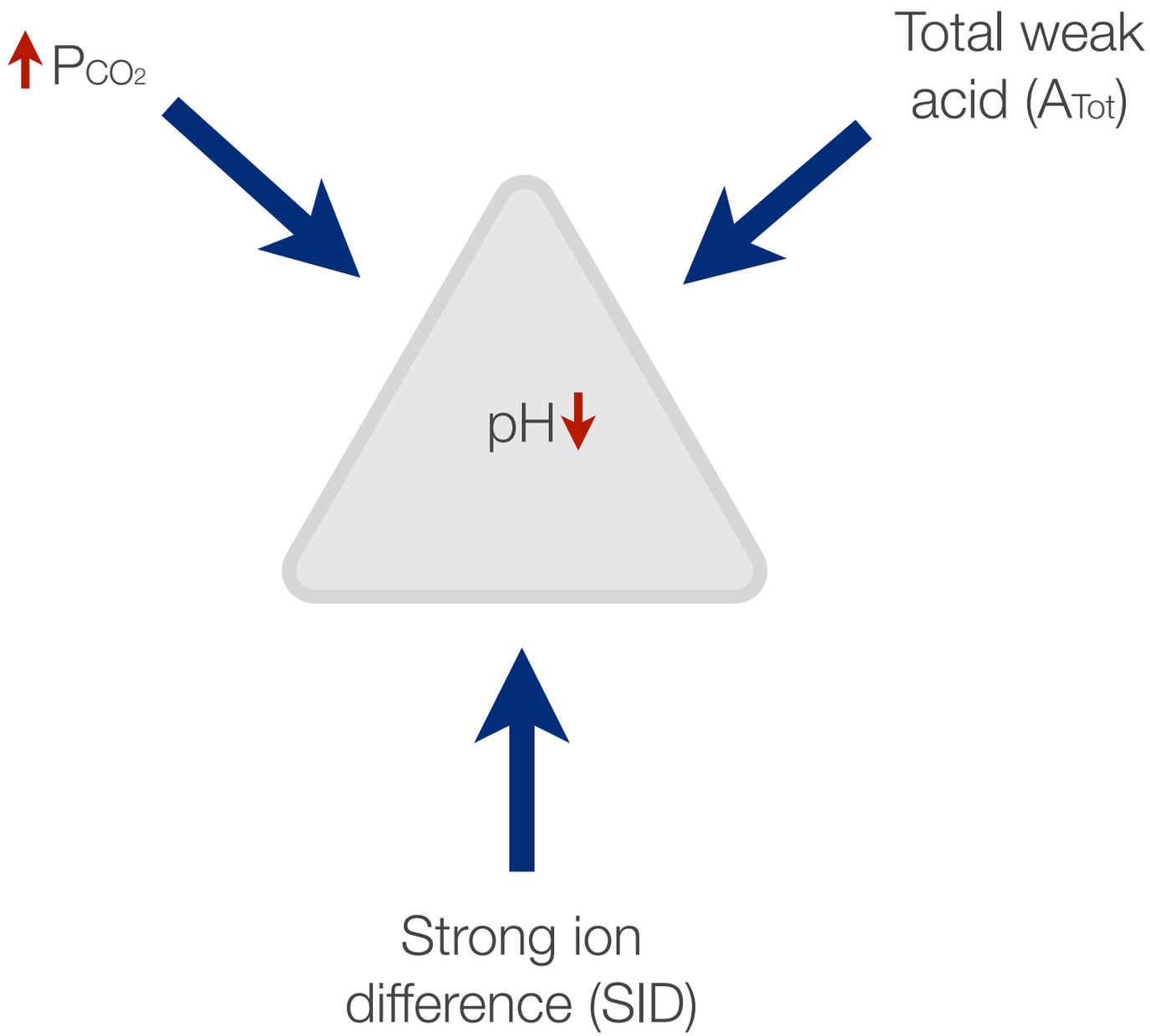

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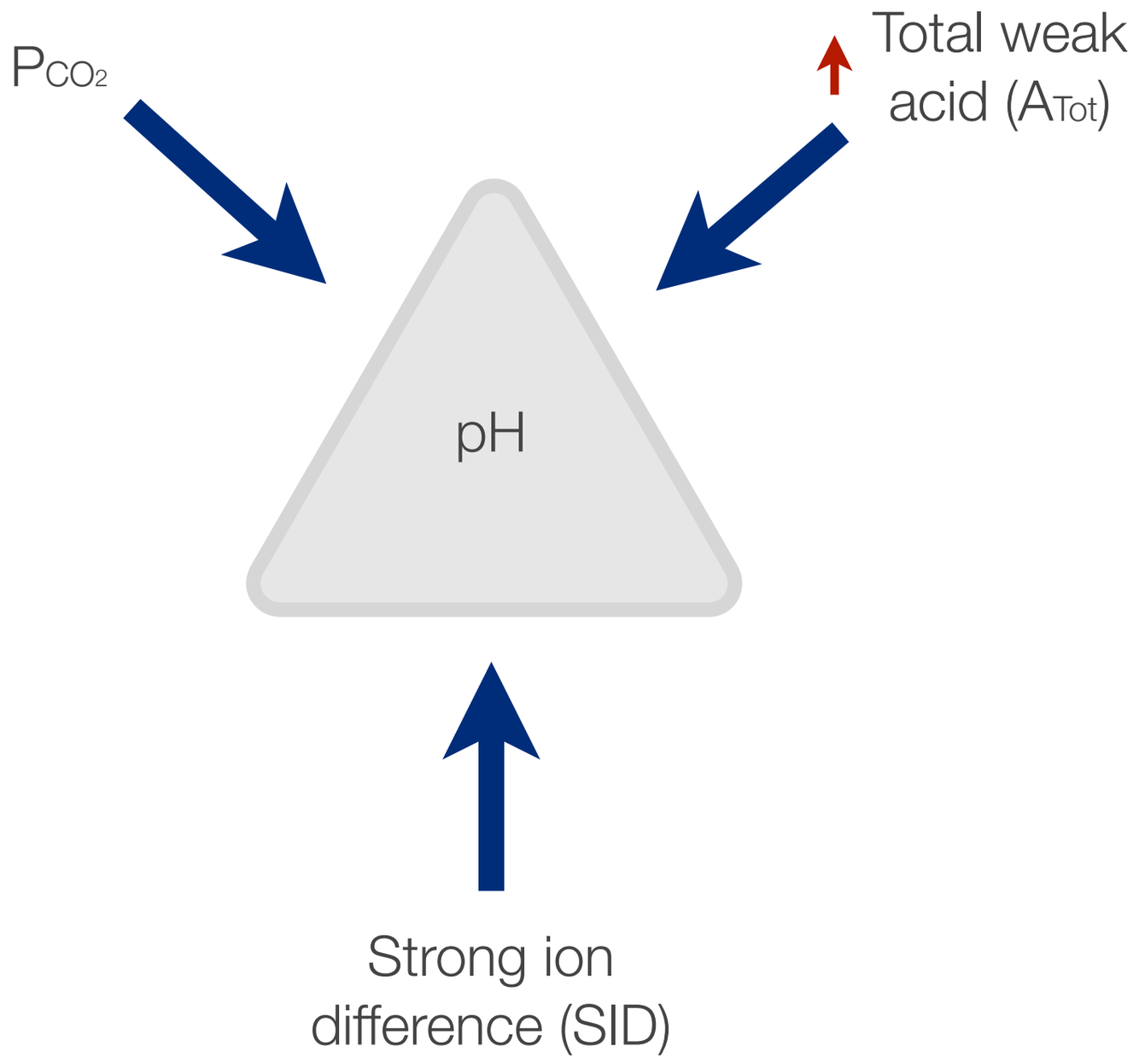

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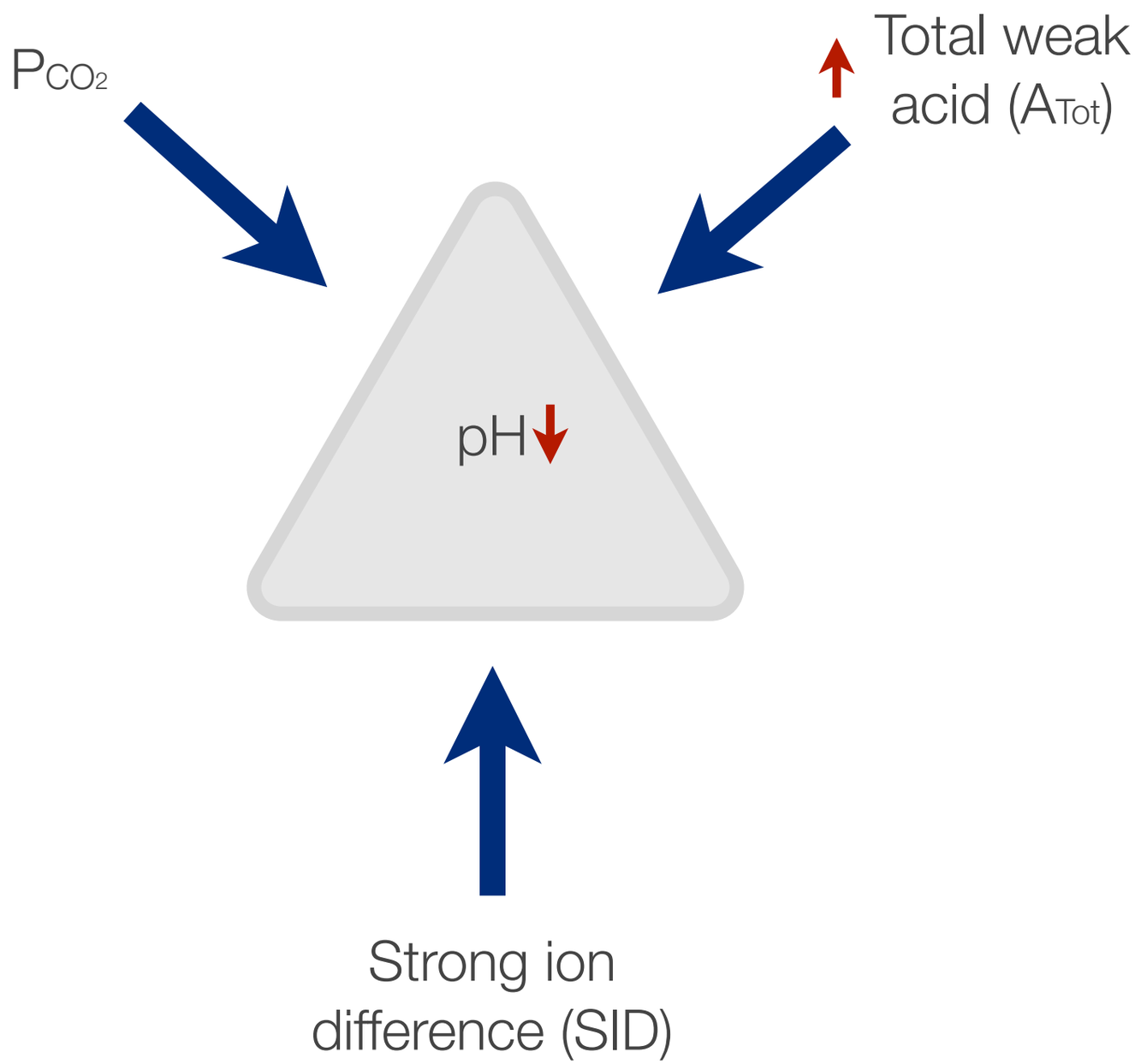

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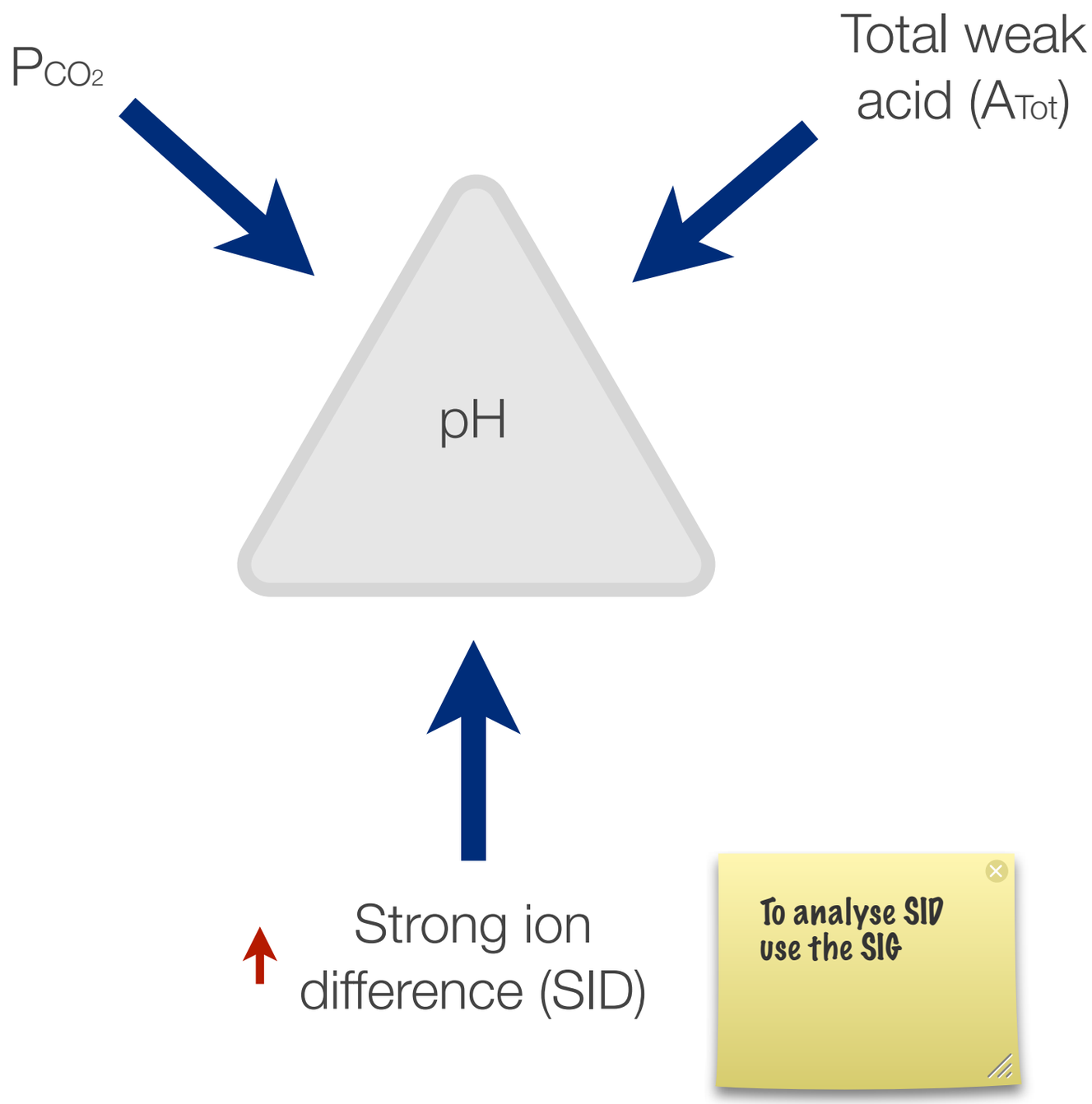

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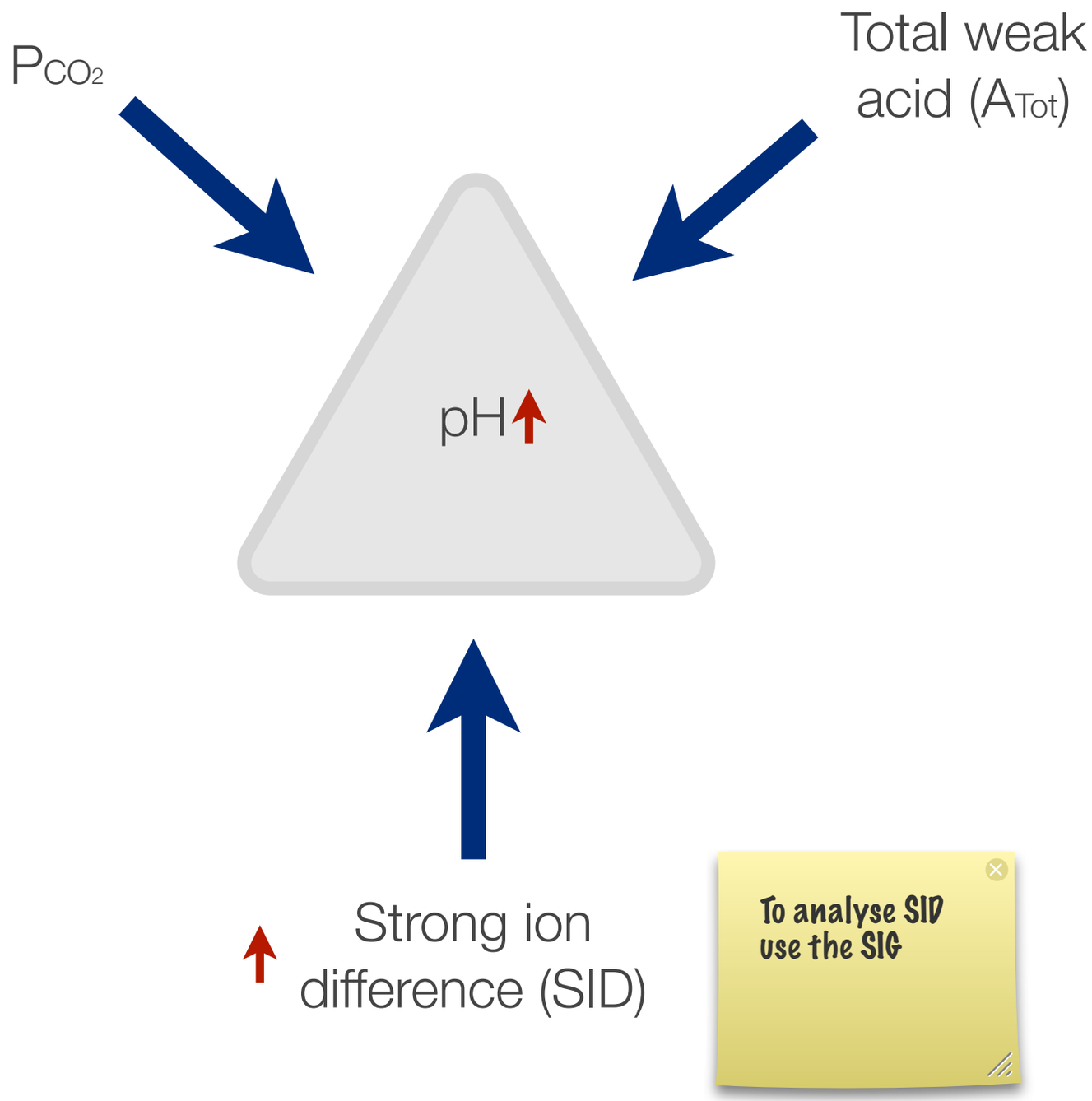

Strong Ion Gap

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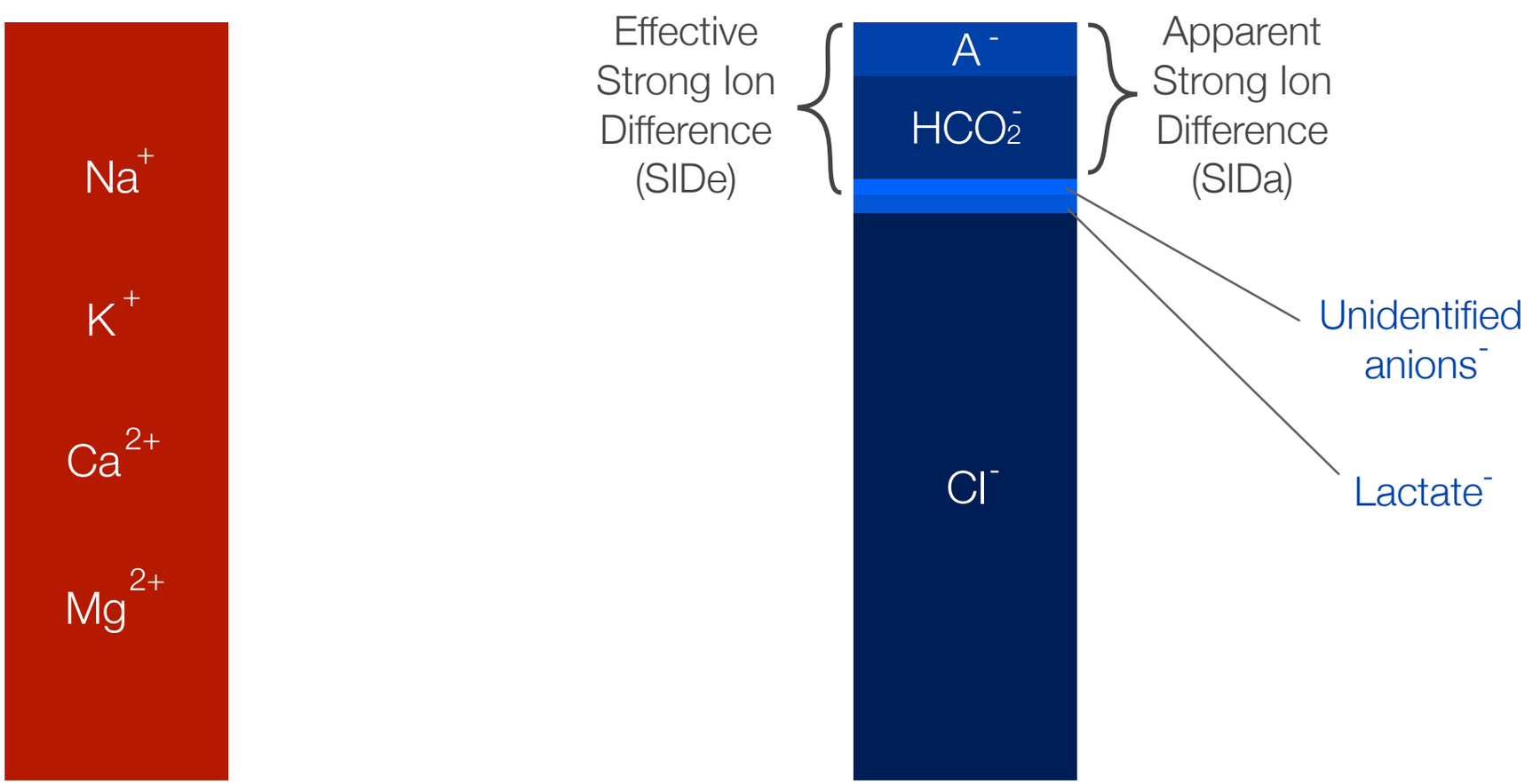

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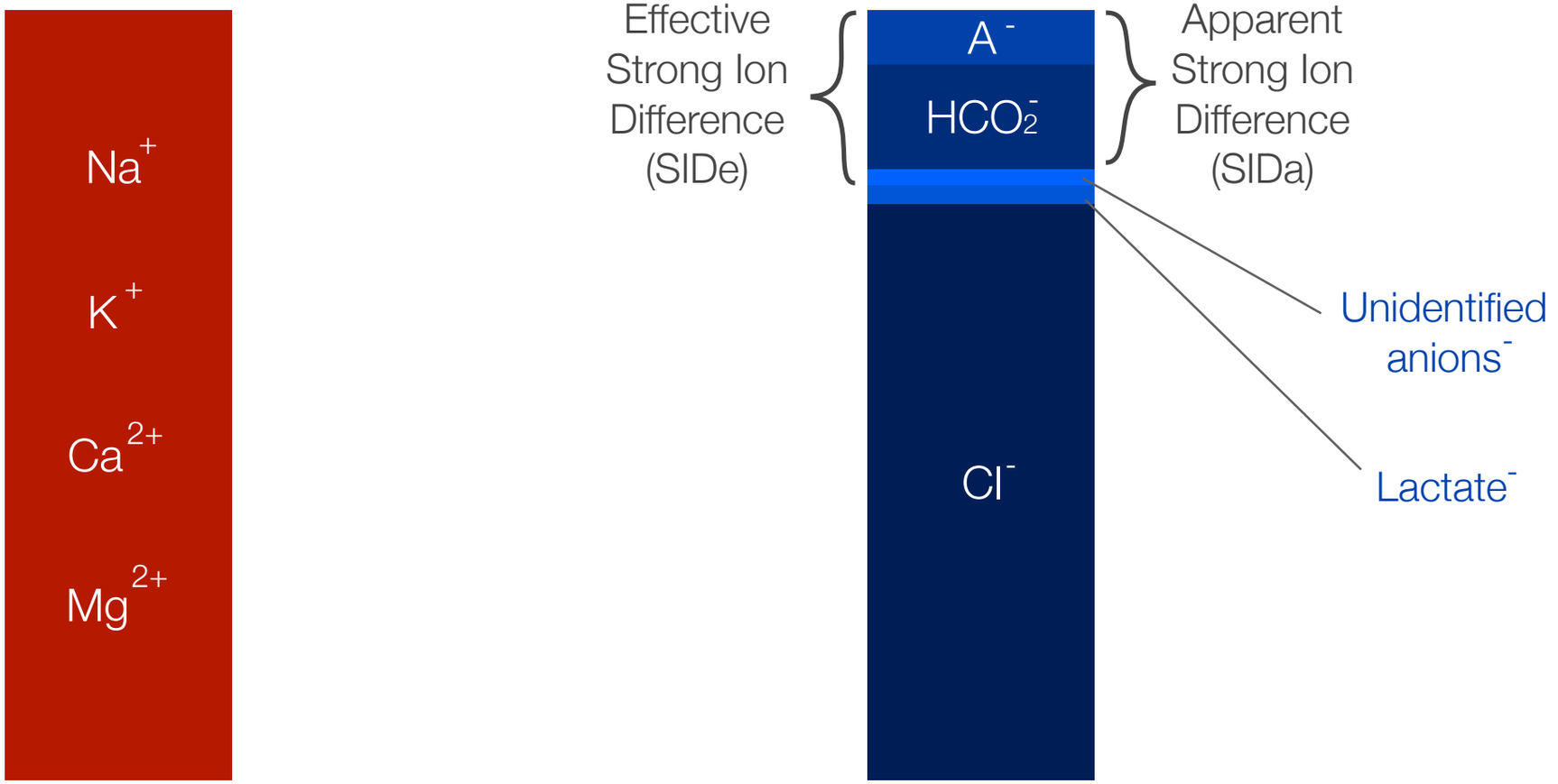
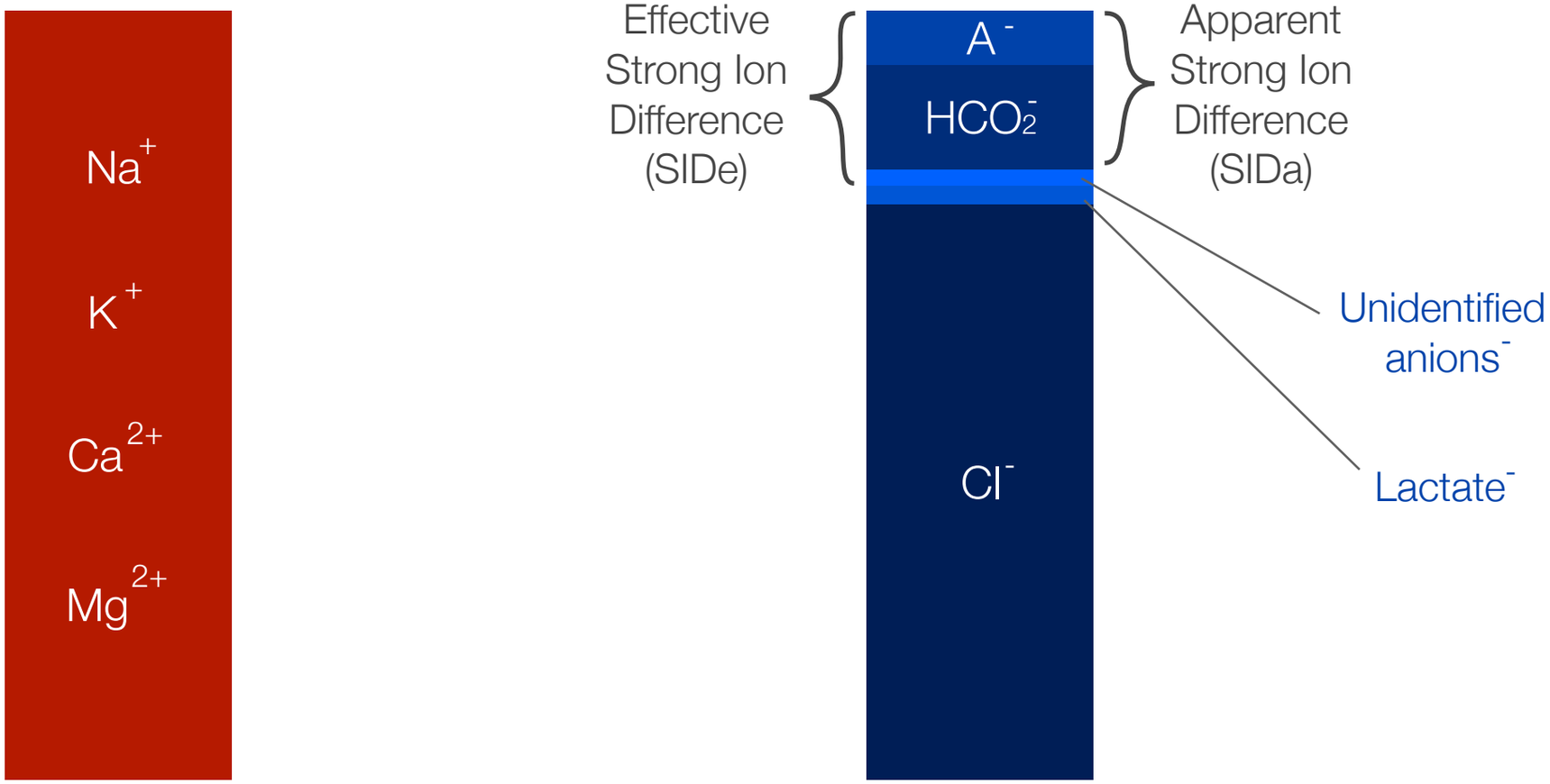


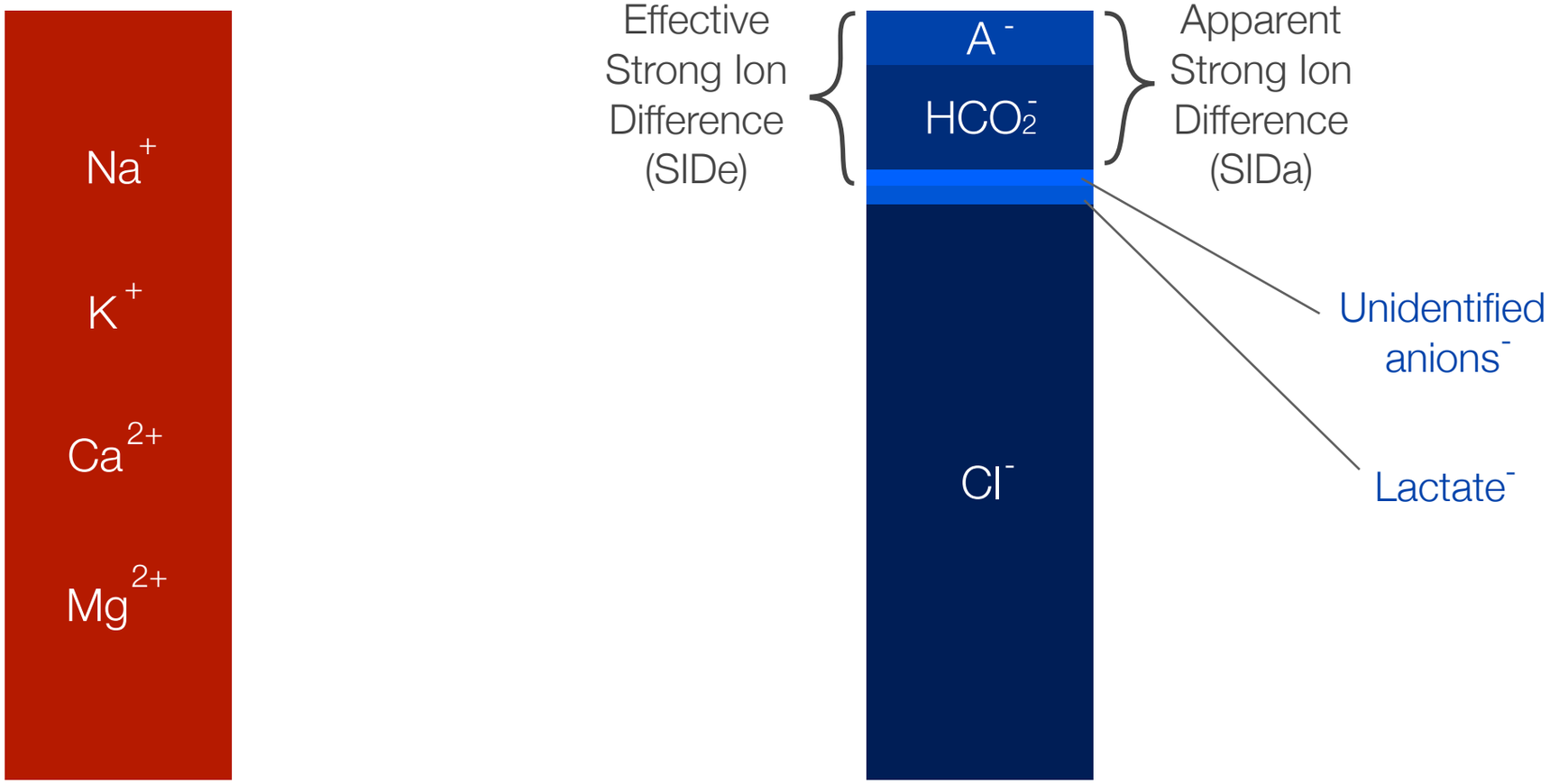
Figge



Apparent Strong Ion Difference

$$SIDa = Na + K + Mg + Ca - Cl - Lactate$$

Figge



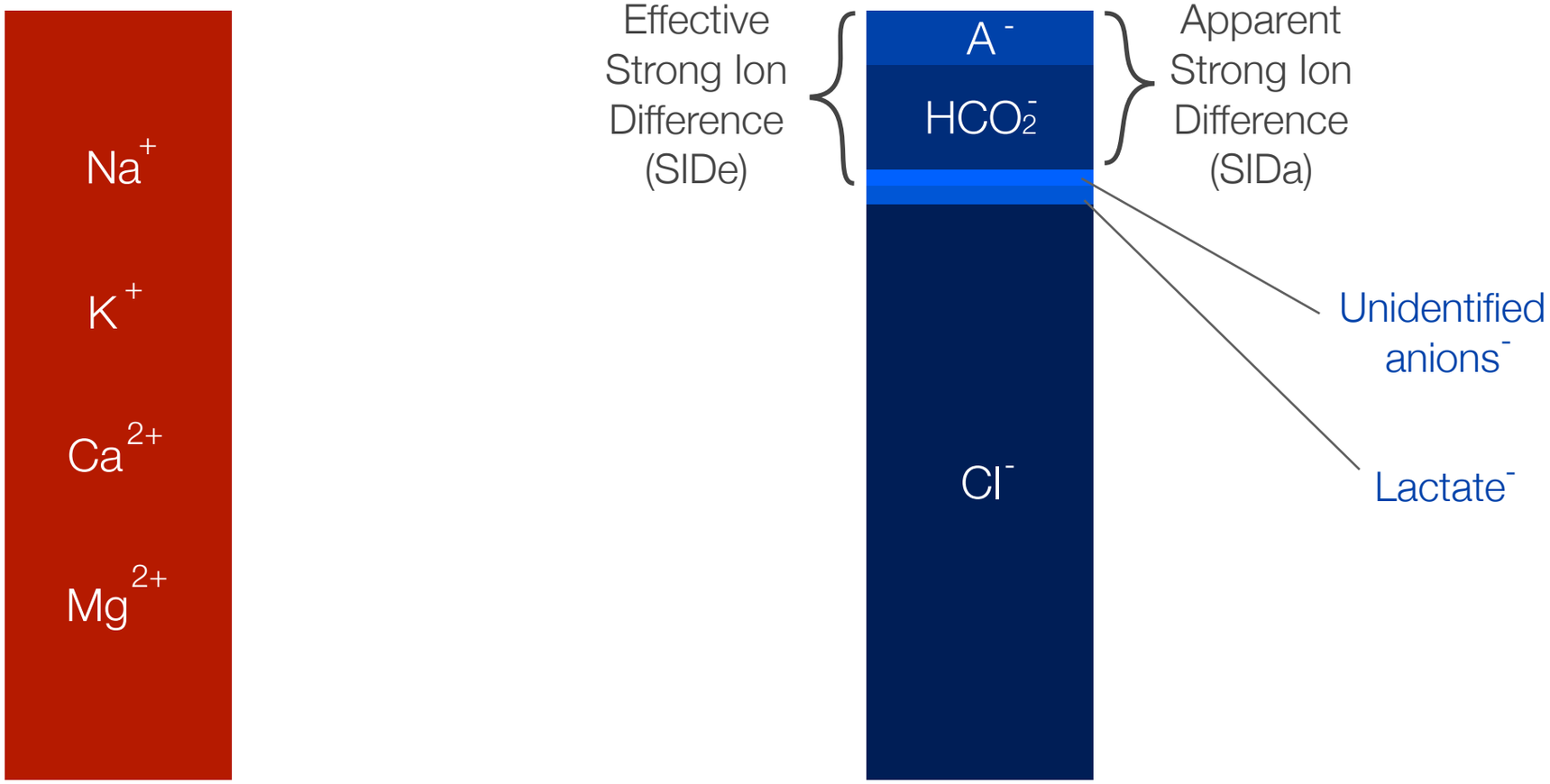
Apparent Strong Ion Difference

$$SIDa = Na + K + Mg + Ca - Cl - Lactate$$

Effective Strong Ion Difference

$$SIDe = (1000 \cdot 2.46_E10 \cdot P_{CO_2} / 10) + (Albumin \cdot 0.12 \cdot pH - 0.631) + (PO_4 \cdot (0.97 \cdot pH - 0.13)$$

Figge



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Strong Ion Gap

$$SIG = SIDa - SIDa$$

(Normal = 8 mEq)

Figge

Predictive Power

Predictive Power

- Kaplan et al.
- Yale, USA 1988 - 1997
- Trauma requiring vascular surgery
- n = 282,
  - 218 survivors
  - 64 mortalities
  - Compared as predictor of mortality
    - Strong Ion Gap
    - Corrected Anion Gap
    - Lactate
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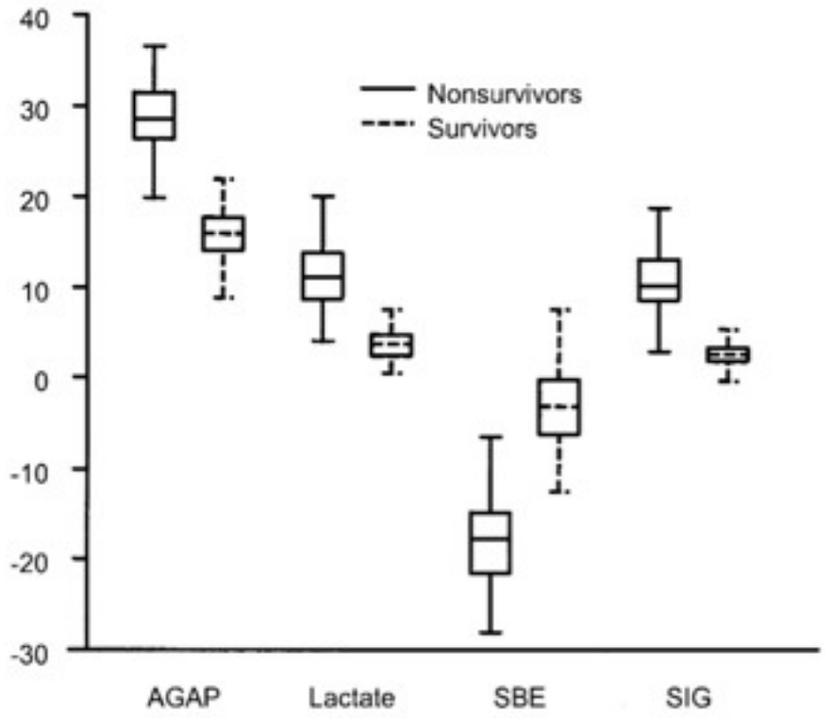

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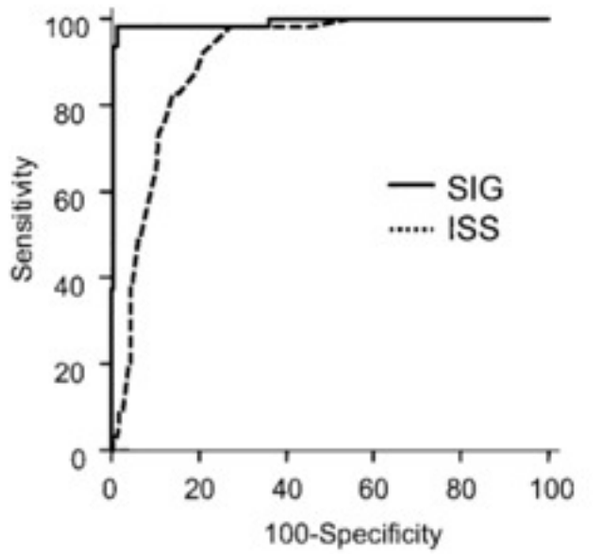
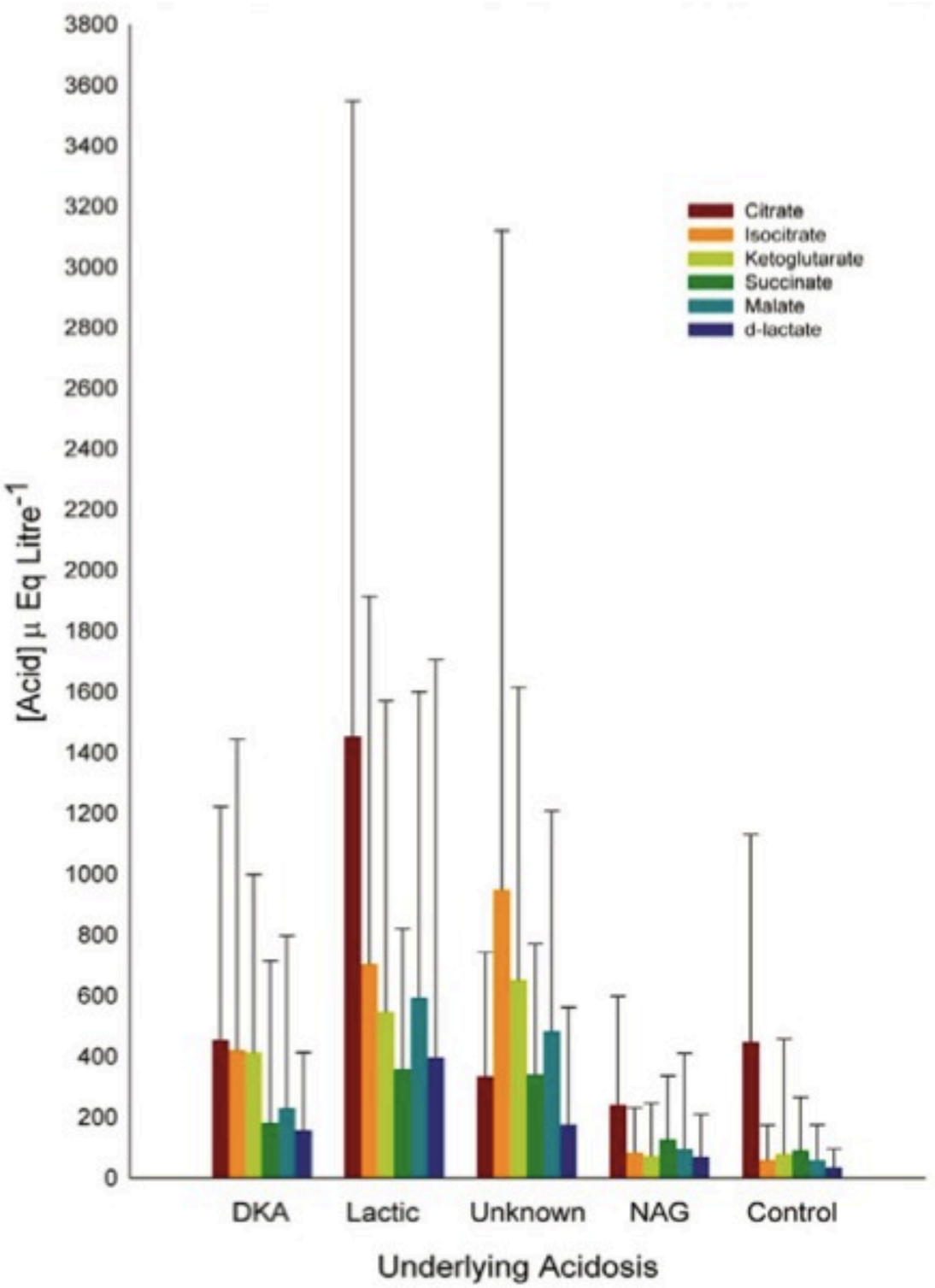


Element	Area	SE	95% CI
AG	0.994	0.007	0.976–0.999
ISS	0.905	0.026	0.865–0.0937
Lactate	0.981	0.012	0.957–0.993
pH	0.971	0.009	0.987–0.994
SBE	0.989	0.005	0.969–0.998
SIG	0.991	0.008	0.972–0.998

AG, anion gap; ISS, Injury Severity Score; SBE, standard base excess; SIG, strong ion gap.

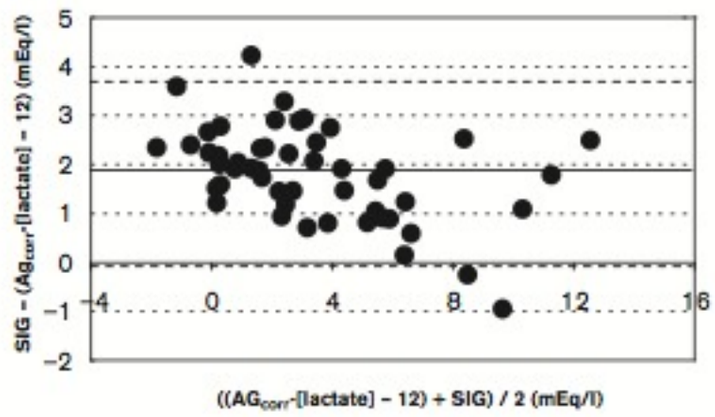
Anions of the Raised Gap

- Lactic acidosis is so called for historical reasons
- A significant number of hypoxic patients have a near normal lactate
- Corrected anion gap or SID are better indicators of severity of tissue hypoxia
- DKA is not just about the ketoacids



Stewart vs Tradition

- Moviat et al.
- Nijmegen, The Netherlands
- n = 50
- Consecutive ICU patients with SBE < 5
- Very close agreement between albumin corrected anion gap and strong ion gap



Bland–Altman analysis of the albumin-corrected anion gap minus lactate (AG_{corr}) and the strong ion gap (SIG) (bias, 1.81 and precision, 0.96).

- SIG is calculated from 9 measured values each with it's own measurement error.
- AG is calculated from 4.

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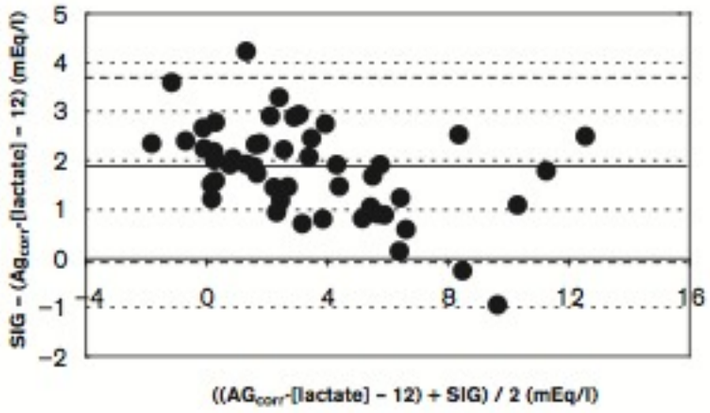
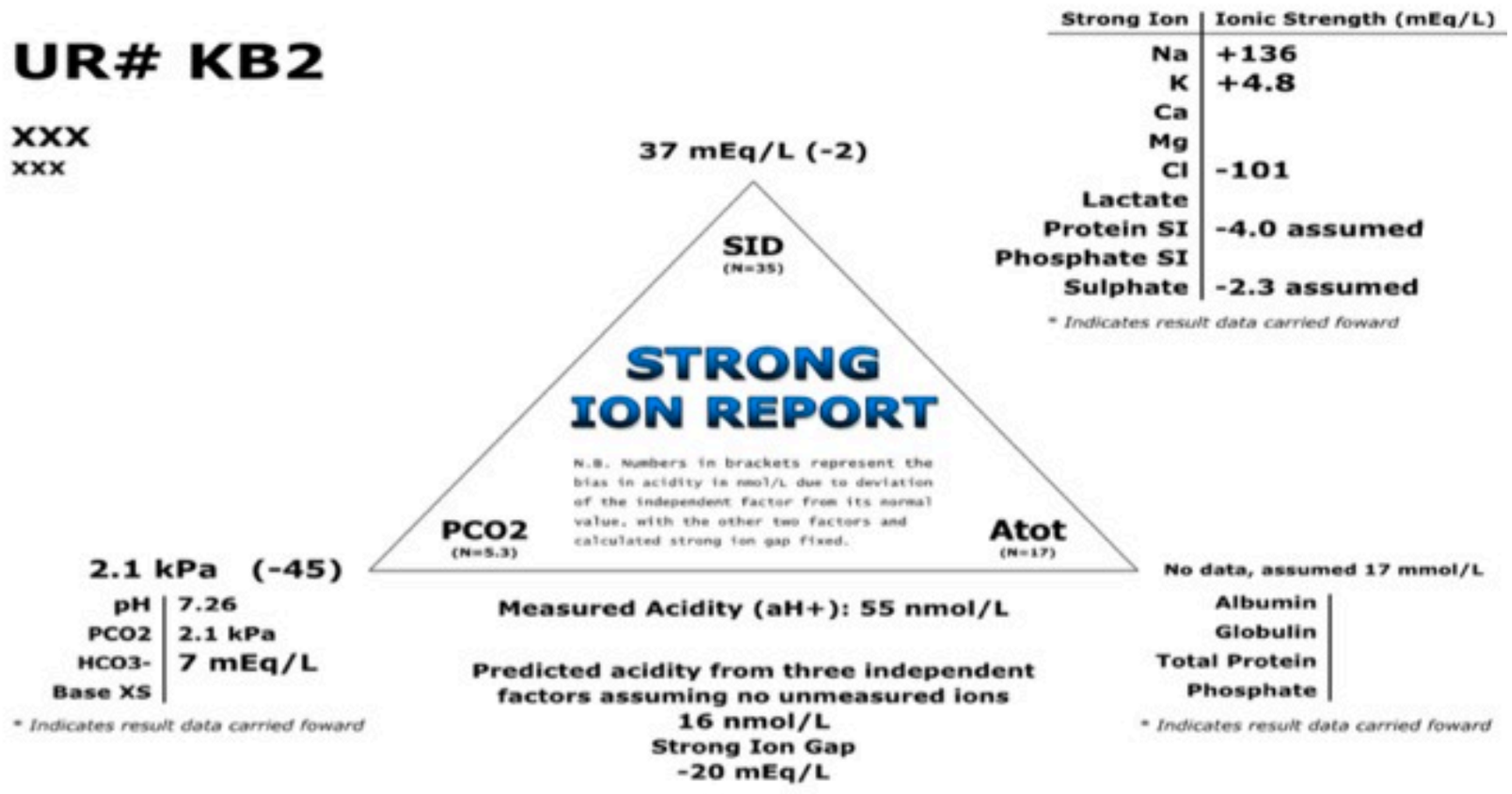


Bland–Altman analysis of the albumin-corrected anion gap minus lactate (AG_{corr}) and the strong ion gap (SIG) (bias, 1.81 and precision, 0.96).

Conclusion Multiple underlying mechanisms are present in most intensive care unit patients with a metabolic acidosis. These mechanisms are reliably determined by measuring the lactate-corrected and albumin-corrected anion gap. Calculation of the more time-consuming strong ion gap according to Stewart is therefore unnecessary.

- SIG is calculated from 9 measured values each with it's own measurement error.
- AG is calculated from 4.

Welcome to the 21st Century



Welcome to the 21st Century

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OVERALL SEVERE ACIDAEMIA FOR ARTERIAL BLOOD (55
nmol/L).  SEVERE RESPIRATORY ALKALOSIS BIASES
ACIDITY BY -45 nmol/L.  MEASURED STRONG ION
DIFFERENCE NORMAL. DEVIATION FROM 35mEq/L BIASES
ACIDITY BY -2 nmol/L.   .  LACTATE UNMEASURED.
LARGE NET CONCENTRATION OF UNMEASURED ANIONS (SIG
= -20 mEq/L).
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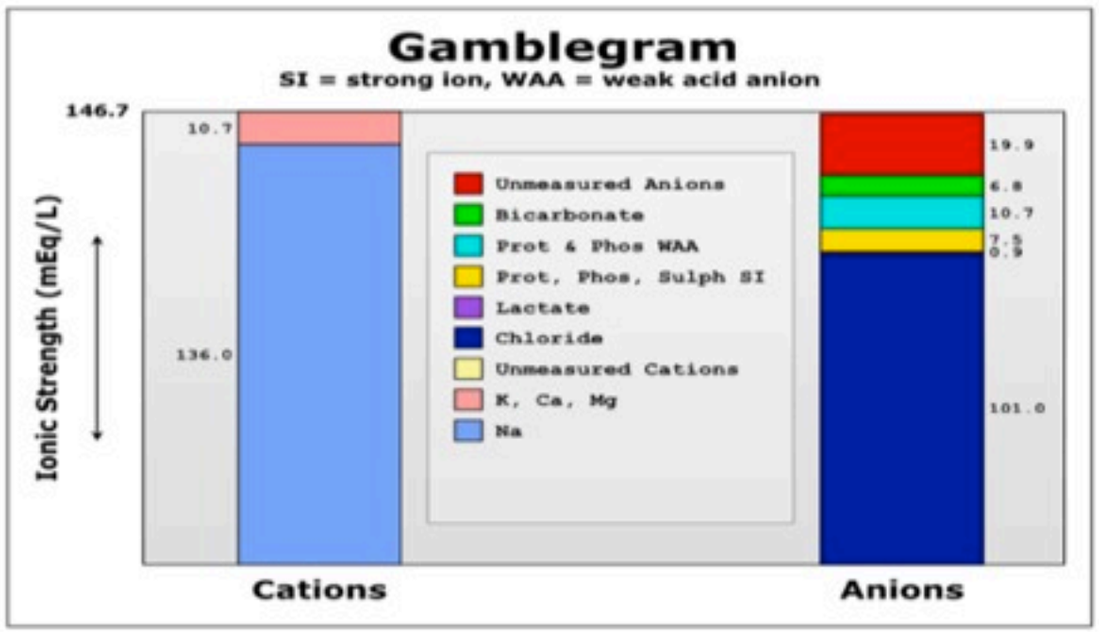

Questions

Key Points

- pH derangement is a canary - treat the cause
- Check the AG even if there is no apparent acid-base disturbance
- Correct AG for albumin or use the SIG
- Remember the osmols
- Consider a urinary anion gap for normal anion gap acidosis
- Beware of arterial gasses in circulatory failure
- Never give bicarb to a patient that can’t blow off excess CO_2