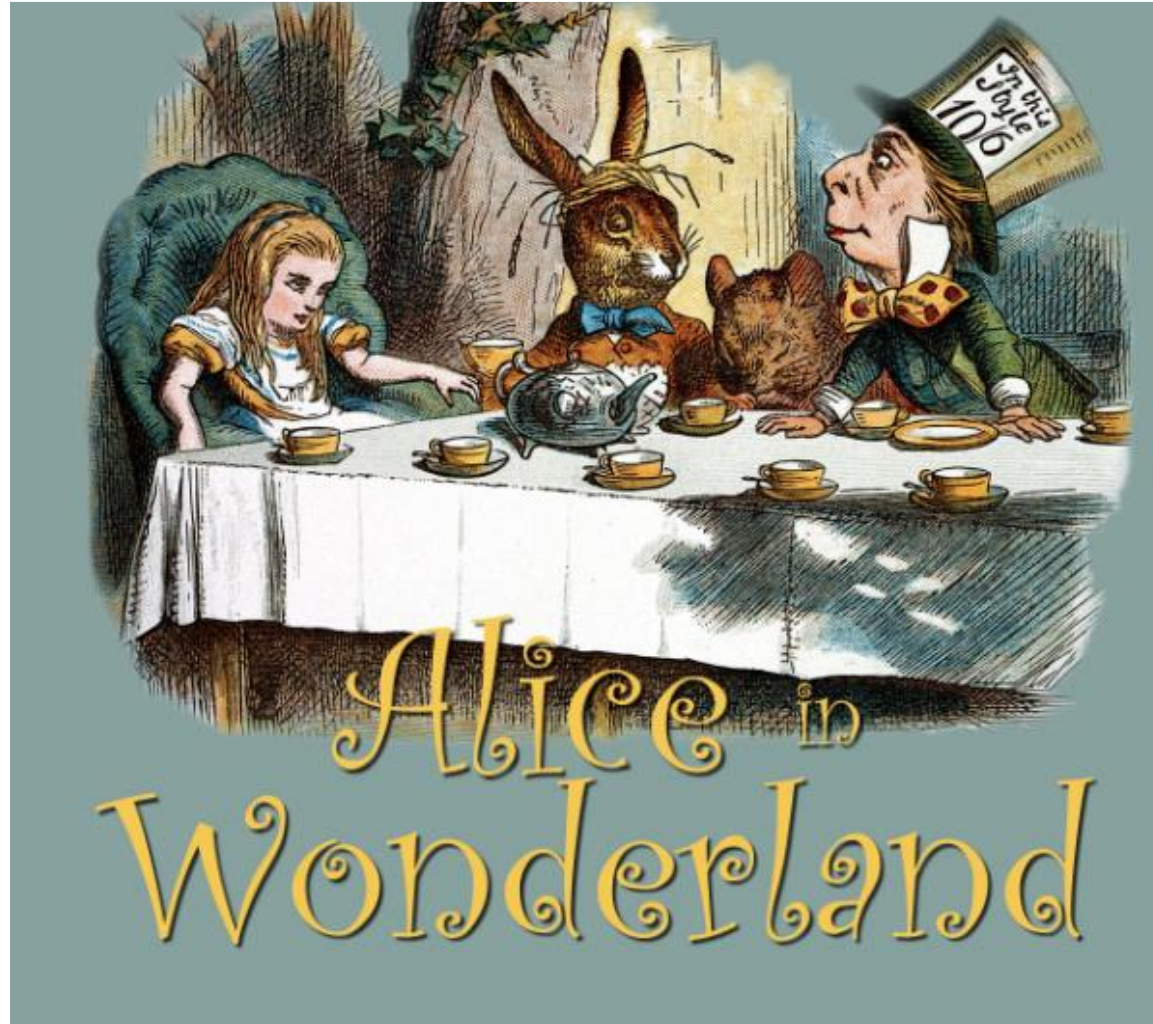


“Dear Alice, please put a stop to this pH nonsense! Let us inspect the world as it is.”



Can I change what you have been taught about acid-base balance?

My teaching aims are:

To demystify acid-base balance

To put hydrogen ion concentration (H^+ nmol/L) in the fore ground

To re-introduce the Henderson equation

To explain what is meant with base excess and base deficit

To reveal how these ideas arose



What does pH 7.4 really mean?

At a pH 7.4, the Hydrogen ion concentration is 40 nmol/L. What does this mean?

In plasma (or anything else) we measure quantities in gram-formula weight: mol/L, mmol/L, μ mol/L, nmol/L.

The intracellular H ion concentration is a bit higher at about 60 nmol/L

H⁺ ion concentration is expressed as pH (puissance hydrogen) or hydrogen strength

pH = log 1/H⁺ concentration

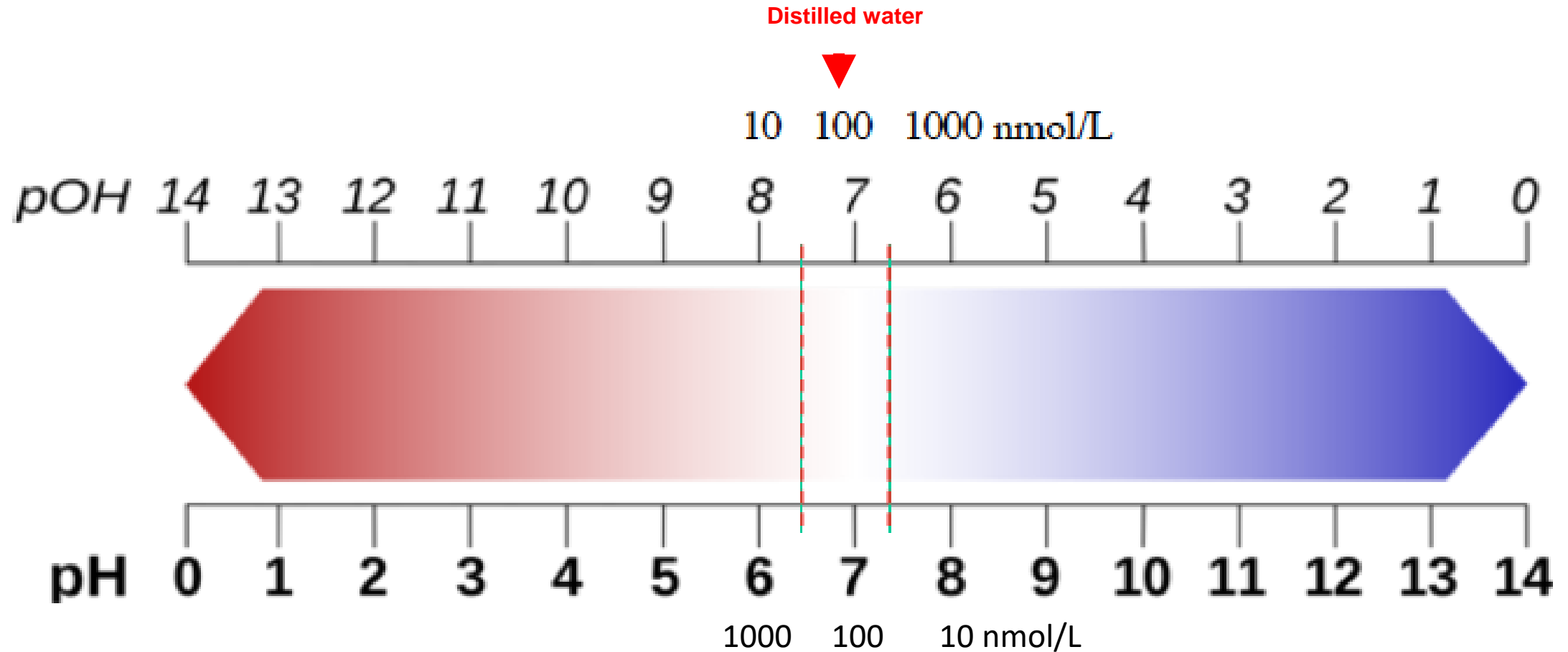
(Distilled) water has a pH of 7.00, or 1×10^{-7} M, or 0.000 000 1 M, or 100 nmol/L and also 100 nmol/L of OH⁻ ions.

Plasma has a normal pH of 7.4 or $1 \times 10^{-7.4}$, or 40 nmol/L

Why do we express H⁺ ions as a reciprocal of a logarithm?



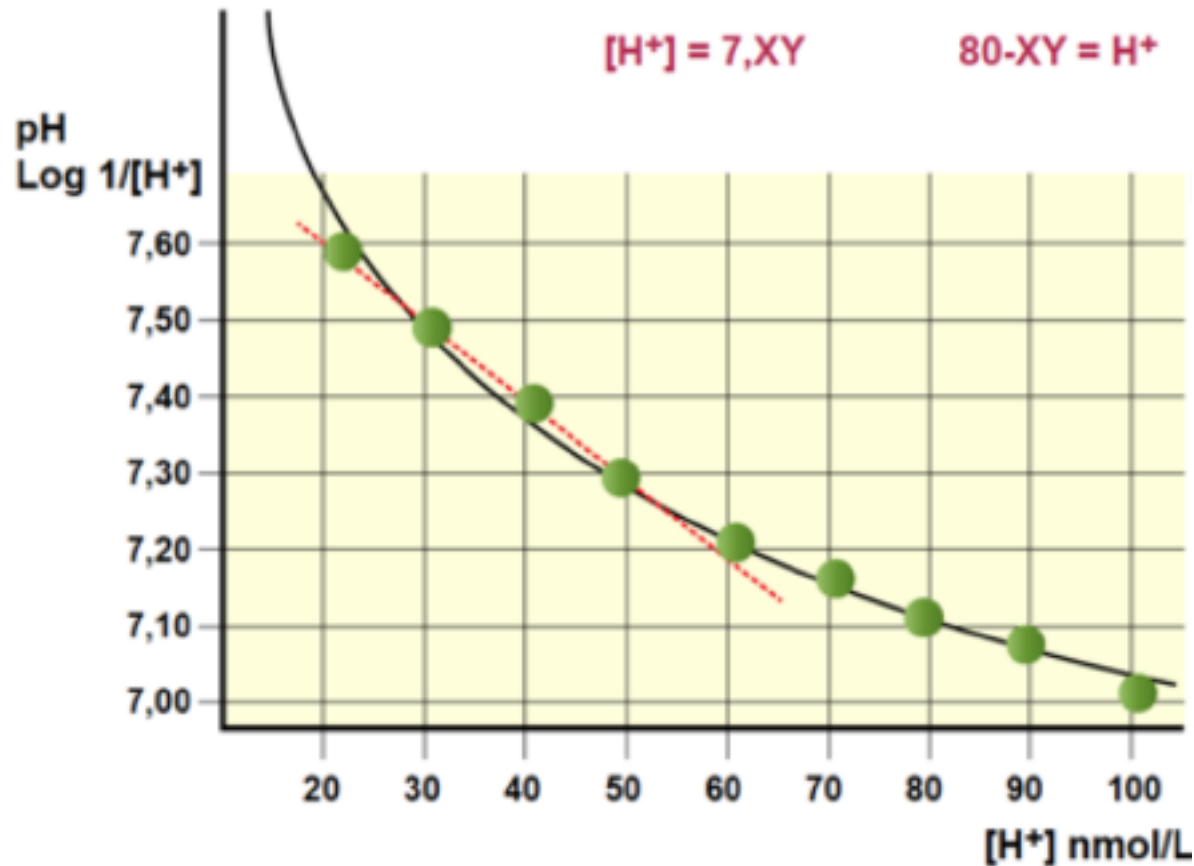
pH is great for physical chemists; however, we are only concerned about the white part here



We are solely concerned with the „pale“ area of this range

The area that concerns us is relatively “flat”.

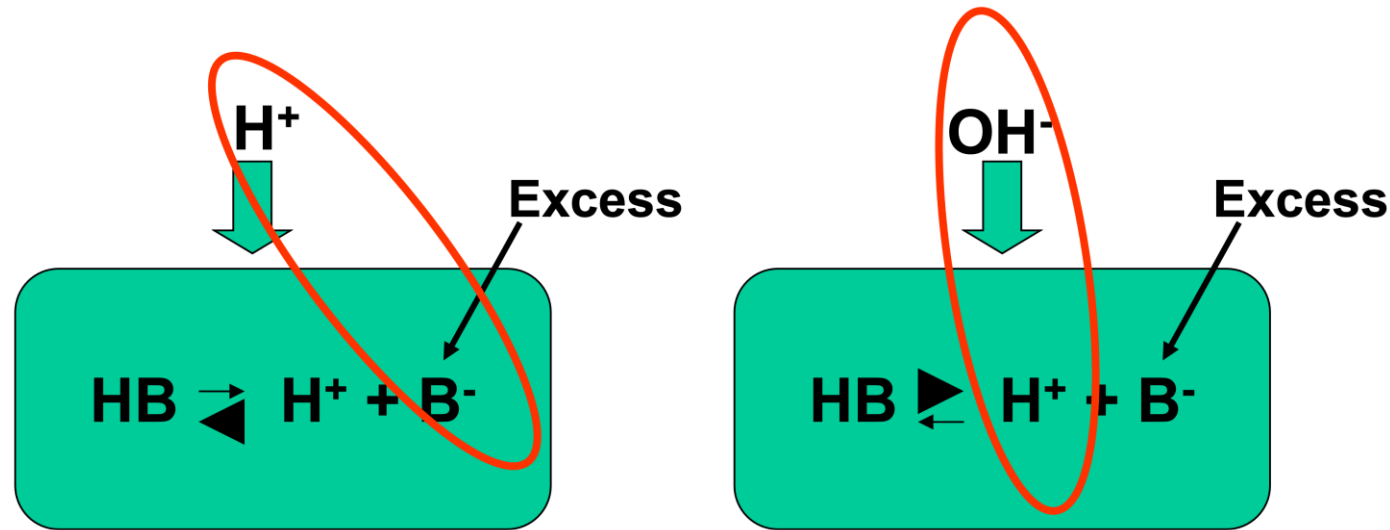
“PUISSANCE” HYDROGEN
Sorensen & Hasselbalch



So, we subtract the last two digits behind the decimal point to achieve the H ion concentration.

• 7.60 (pH)	20 [H] nmol/l	80-60=20	} Flat part of the curve
• 7.50	30	80-50=30	
• 7.40	40	80-40=40	
• 7.30	50	80-30=50	
• 7.20	60	80-20=60	
• 7.10	80	extrapolate from	
• 7.00	100	water = 100	
• 6.90	125	rare anyway	

Buffer systems consist of a weak acid and an excess of its conjugate base



There are lots of buffer systems

The $H_2CO_3 + HCO_3^-$ system represents about 60%

Hemoglobin makes up another 35%

They are all in equilibrium with each other

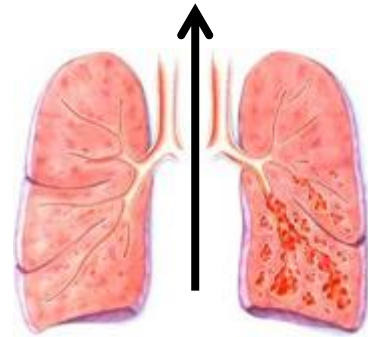
We measure the components of one

The HCO_3^- system is an „open“ system

We make PCO_2 and thereby HCO_3^-

The body can manipulate these components

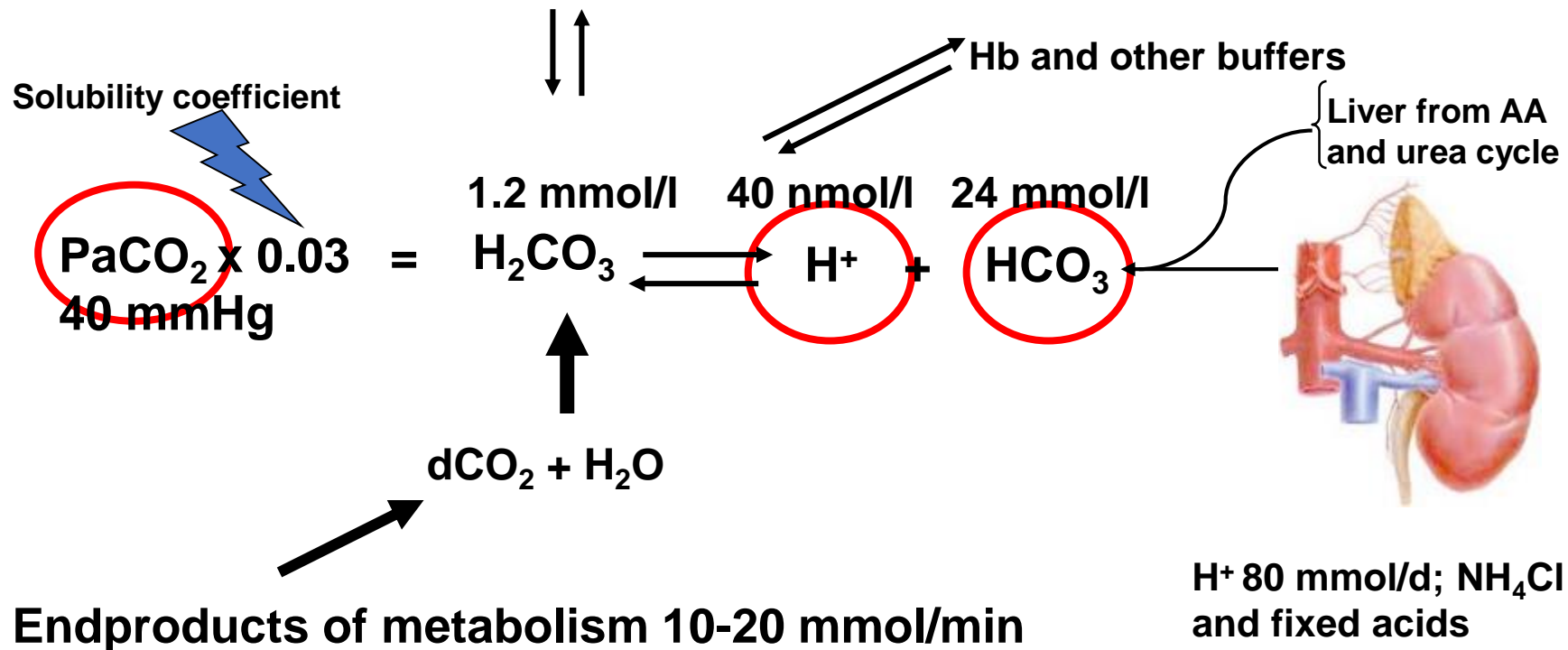
We make and eliminate our chief buffer system all the time



CO₂ is volatile (mostly)

Alveolar Capillaries

dCO₂ (PvCO₂ 45 mm Hg; PaCO₂ 40 mm Hg)



Lawrence Joseph Henderson (* 3. Juni 1878 in Lynn, MS, USA; † 10. Februar 1942 in Cambridge) was a US chemist and biologist.



Henderson wanted this:

$$H = \frac{24 \times p\text{CO}_2}{\text{HCO}_3}$$

$$[H] = K \frac{\text{H}_2\text{CO}_3}{\text{HCO}_3}$$

$$[H] = 24 \frac{(p\text{CO}_2)}{\text{HCO}_3} = \frac{24 \times 40}{24} = 40 \text{ nmol/l}$$

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



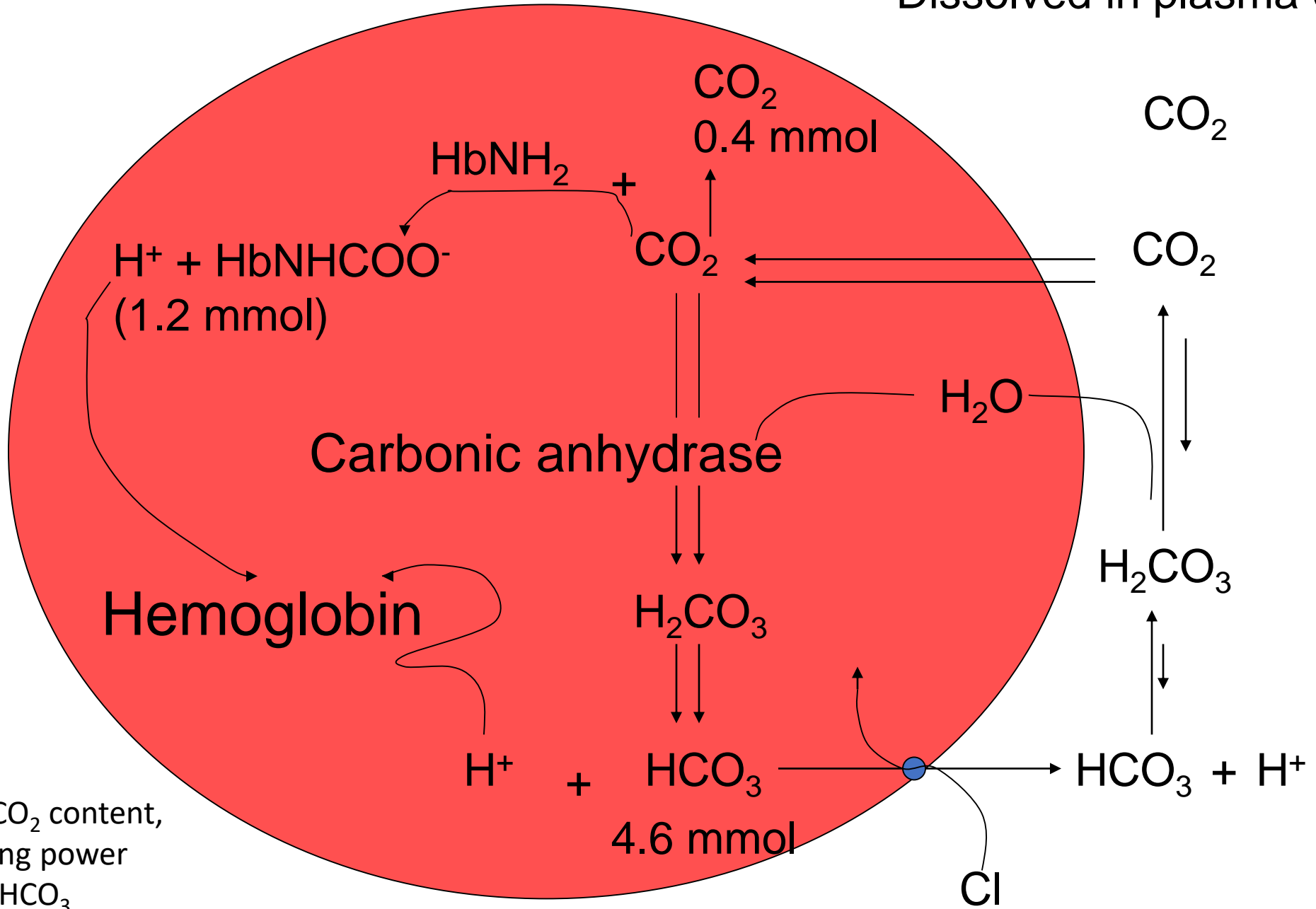
Henderson got this:

$$\text{pH} = 6.1 + \frac{\log \text{HCO}_3}{0.03 \times \text{PCO}_2}$$

Ever see your faculty calculate this on the wards???

Love those erythrocytes

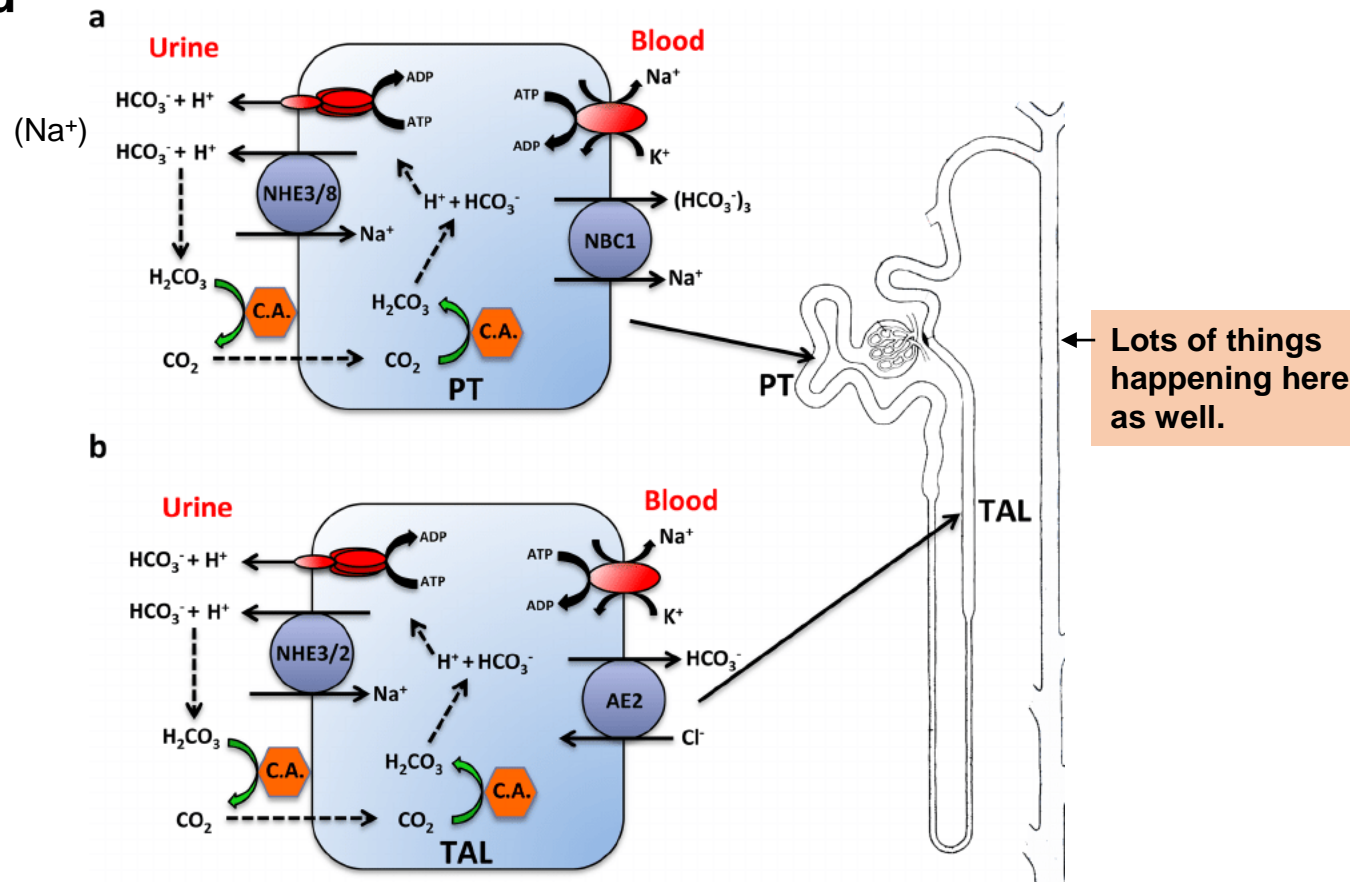
Dissolved in plasma 0.8 mmol/L



The total CO₂, CO₂ content, or CO₂ combining power are about 95% HCO₃⁻

The filtered bicarbonate is 100% reclaimed

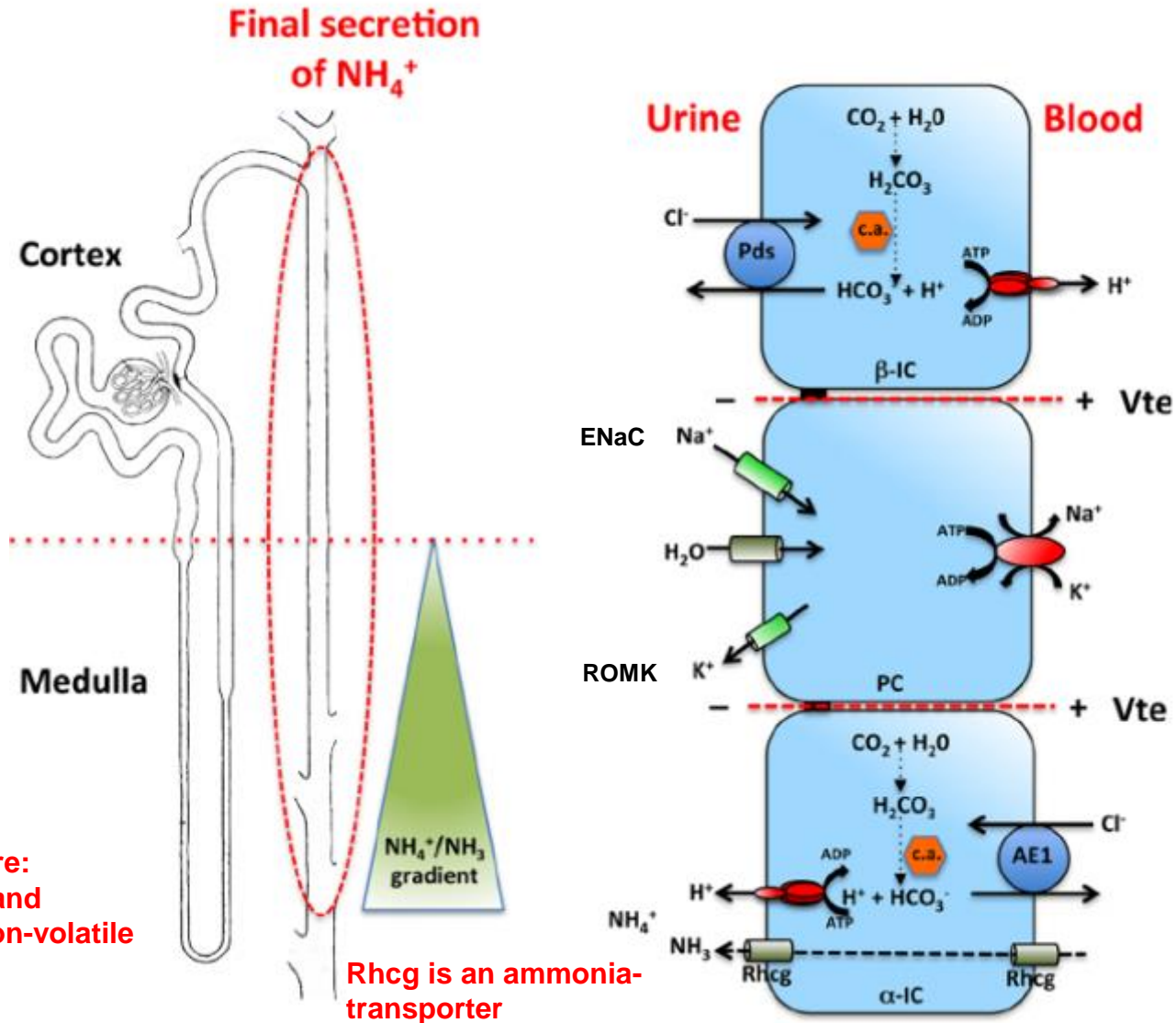
5000 mmol/day are filtered



C.A. = Carbonic anhydrase

Amount in urine is „0“, unless you are a rabbit

In the distal tubule, we excrete about 100 mmol H⁺ per day. We can raise this to 300 mmol/day if enough glutamine is made proximally



Excreted in urine are:
 NaHSO_4 , NaH_2PO_4 and
 NH_4Cl , i.e. „fixed, non-volatile
 acids.

Rhcg is an ammonia-
 transporter

In 1952, a polio epidemic struck Copenhagen

REVIEW ARTICLE

Diagnostic Use of Base Excess in Acid–Base Disorders

Kenrick Berend, Ph.D., M.D. 2018



Copenhagen 1952, the pH meter was not yet clinically available. Gas partial pressures could not yet be measured. Only total CO_2 could be assayed. This value consists of about 95% bicarbonate and the rest is H_2CO_3 or dissolved CO_2 . Since total CO_2 was always elevated, the clinicians thought the children had an alkalosis (high HCO_3). But actually a respiratory acidosis was the problem!

From where does this “excess” or “standard excess” come?

In Copenhagen, the clinicians organized a crisis staff. All health-care students were required to manually ventilate the children. The pH meter was introduced. The Van Slyke apparatus was obtained to measure PCO_2 . The iron lung did not provide enough alveolar ventilation.

The Danes could now measure PCO_2 and total CO_2 . But they wanted to know the entire (whole blood) buffer capacity.

So, in the blood samples, tonometry was done to restore the pH back to pH 7.4 (H^+ 40 nmol/L).

The mmol/L base or acid required was termed base excess (or negative base excess).

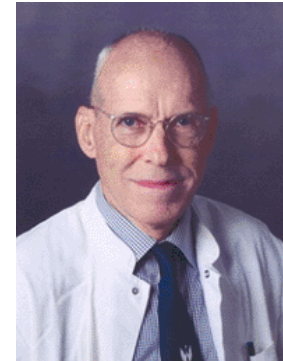
Since not all persons have a normal hemoglobin, the samples were all „standardized“ to a hemoglobin of 5 g/dL.

A transatlantic acid-base war ensued

Poul Bjørndahl Astrup was a Danish physiologist and laboratory chemist. Ole Siggaard-Andersen is a Danish clinical chemist. The two are largely responsible for the idea of base excess and standard base excess.



The great Danes



The Boston Brahmins (Pundits)



Arnold Seymour „Bud“ Relman was a US nephrologist. Jerome P. „Jerry“ Kassierer is a US nephrologist and previous editor of the New England Journal of Medicine.

The Europeans have stubbornly largely stuck with base excess

Condition	Paco ₂ or SBE Secondary Response
Acute respiratory acidosis (pH decreased, Paco ₂ increased, SBE = 0±2 mmol/liter)	SBE = 0±2 mmol/liter
Acute respiratory alkalosis (pH increased, Paco ₂ decreased, SBE = 0±2 mmol/liter)	SBE = 0±2 mmol/liter
Chronic respiratory acidosis (pH decreased, Paco ₂ increased, <u>SBE increased</u>)	SBE = 0.4 × (Paco ₂ - 40)
Chronic respiratory alkalosis (pH increased, Paco ₂ decreased, <u>SBE decreased</u>)	SBE = 0.4 × (Paco ₂ - 40)
Metabolic acidosis (pH decreased, Paco ₂ decreased, <u>SBE decreased</u>)	ΔPaco ₂ = SBE
Metabolic alkalosis (pH increased, Paco ₂ increased, <u>SBE increased</u>)	ΔPaco ₂ = 0.6 × SBE

Values calculated; responses based on empiricism.

I prefer the Boston Brahmins because it is easier (actually, it is pretty much the same)

Condition

Acute respiratory acidosis (pH decreased, Paco_2 increased, $\text{SBE} = 0 \pm 2$ mmol/liter)

Acute respiratory alkalosis (pH increased, Paco_2 decreased, $\text{SBE} = 0 \pm 2$ mmol/liter)

Chronic respiratory acidosis (pH decreased, Paco_2 increased, SBE increased)

Chronic respiratory alkalosis (pH increased, Paco_2 decreased, SBE decreased)

Metabolic acidosis (pH decreased, Paco_2 decreased, SBE decreased)

Metabolic alkalosis (pH increased, Paco_2 increased, SBE increased)

Paco_2 or HCO_3^- Secondary Response

Increase of 1 mmol/liter in HCO_3^- for each 10 mm Hg increase in Paco_2 above 40 mm Hg

Decrease of 2 mmol/liter in HCO_3^- for each 10 mm Hg decrease in Paco_2 below 40 mm Hg

Increase of 4–5 mmol/liter in HCO_3^- for each 10 mm Hg increase in Paco_2 above 40 mm Hg

Decrease of 4–5 mmol/liter in HCO_3^- for each 10 mm Hg decrease in Paco_2 below 40 mm Hg

Expected $\text{Paco}_2 = 1.5 \times [\text{HCO}_3^-] + 8 \pm 2$ mm Hg

Expected $\text{Paco}_2 = 0.7 \times ([\text{HCO}_3^-] - 24) + 40 \pm 2$ mm Hg

1 : 0.3

1 : 0.3

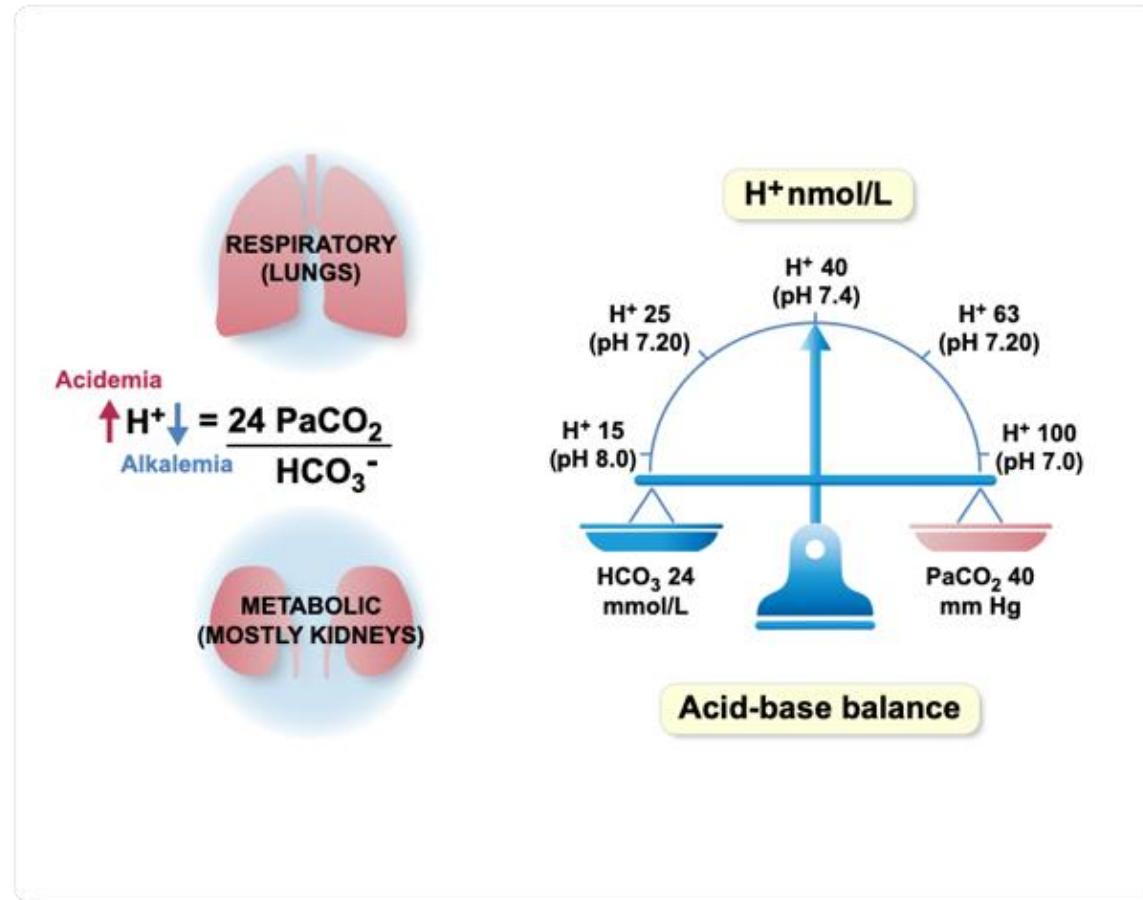
1 : 1.0

1 : 0.7

Values calculated; responses based on empiricism.

Introducing FCL's hydrogen ion tachometer

Base excess is defined as the amount of strong acid that must be added to each liter of fully oxygenated blood to return the pH to 7.40 at a temperature of 37°C and a PCO₂ of 40 mmHg (5.3 kPa), while a base deficit (ie. a negative base excess) is defined by the amount of strong base that must be added.



Four fundamental questions

1. Alkalemia or acidemia ($H^+ < 35 \text{ nmol/L}$ or $> 45 \text{ nmol/L}$)?
2. Metabolic or respiratory alkalosis or acidosis (these are syndromes)?
3. Has the compensation been established (metabolic or respiratory)?
4. Is the compensation appropriate (or is there another simultaneous disturbance)?

28-year-old man began feeling poorly about 2 weeks ago. He developed polyuria, polydipsia, lethargy, and weakness. In the ER, his temperature is 38° C, BP 90/50 mm Hg, HR 120/min, RR 30/min.

Creatinine 400 $\mu\text{mol/L}$, Urea 40 mmol/L , glucose 30 mmol/L
Na 137, K 4, Cl 105 (all mmol/L)

Urine dipstick – Ketones 4+

pH 6.97, PCO_2 18, PO_2 125 (all mm Hg) and the HCO_3 is 4 mmol/L

What is his H^+ concentration?

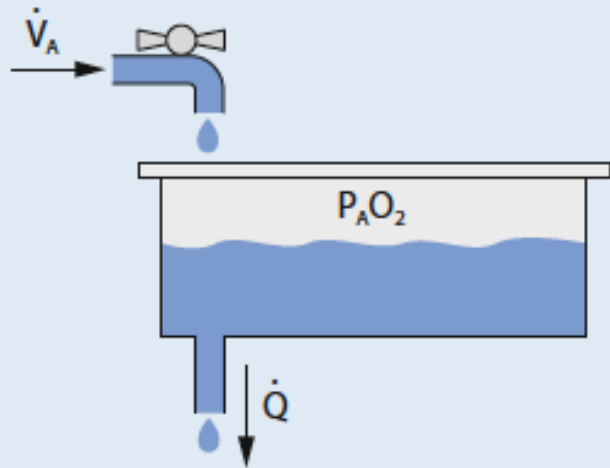
Why is the PO_2 so high on room air?

What here is life threatening?

What do you treat first?

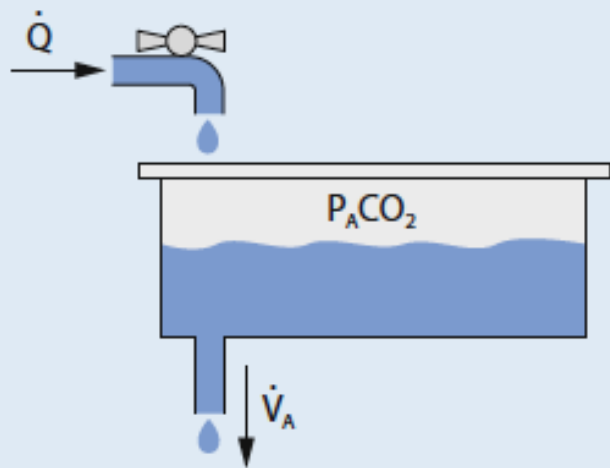
Alveolar ventilation is the “clearance” of PCO_2

Ventilation

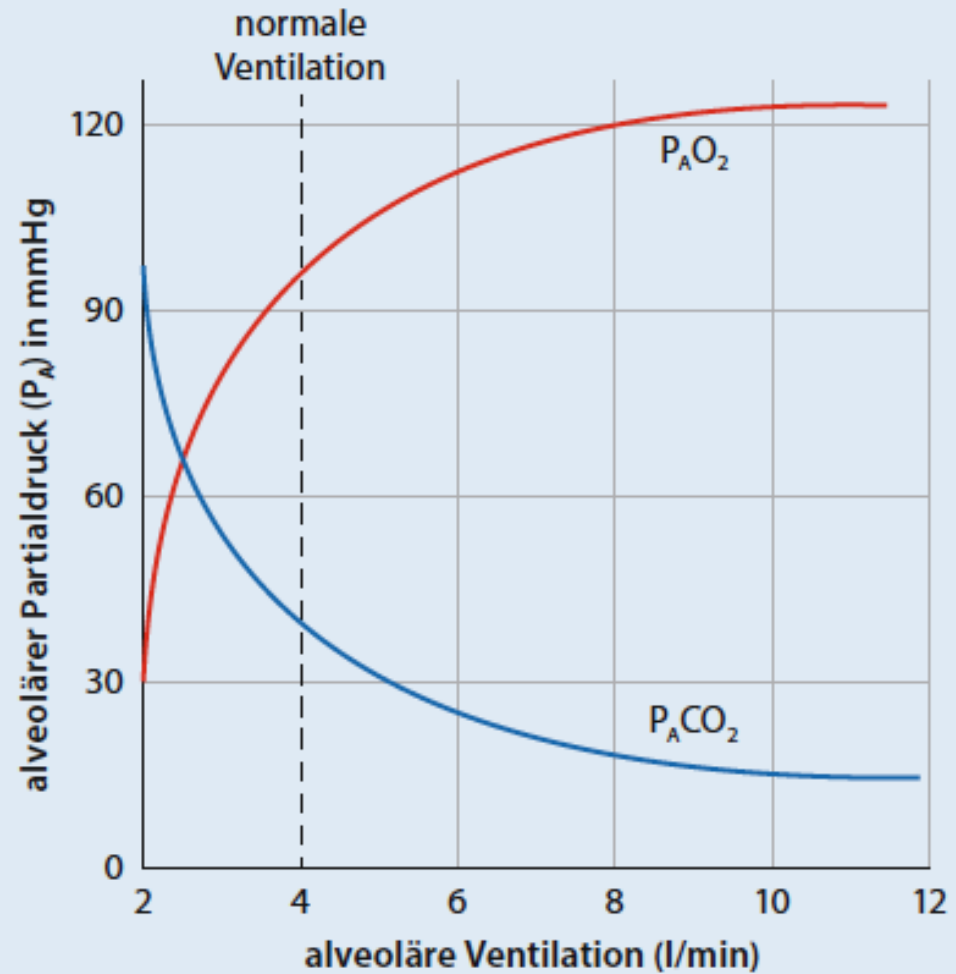


Perfusion

Perfusion



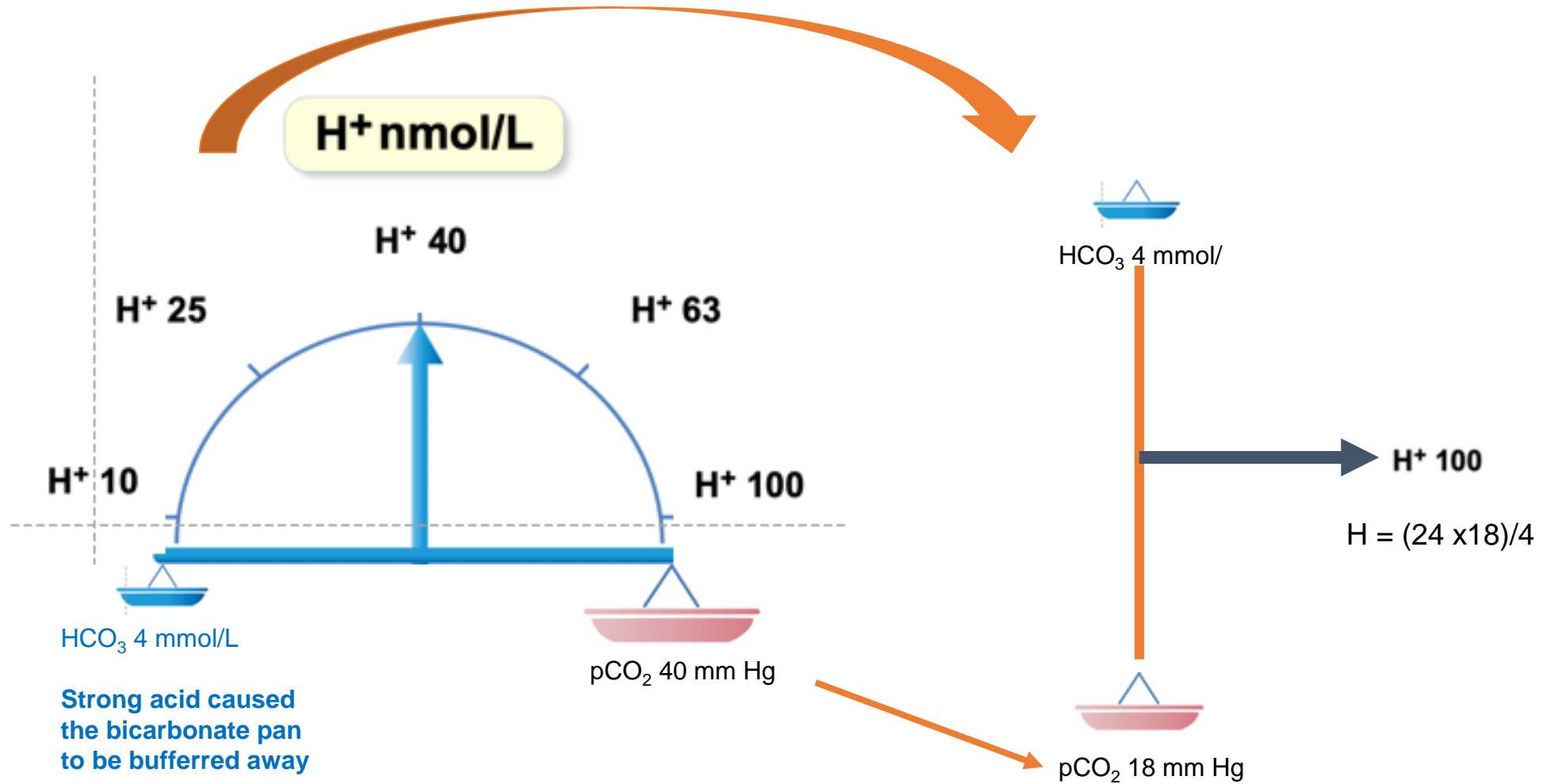
Ventilation



Clearance „in“

Clearance „out“

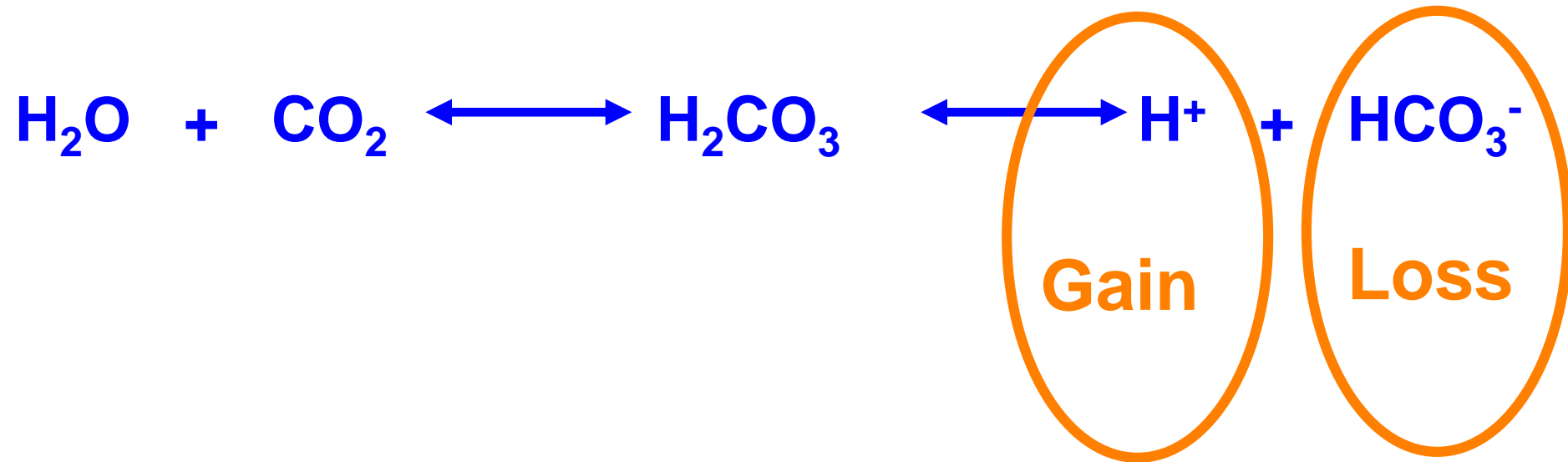
This metabolic acidosis due to gain of strong acid



To compensate, he decreased the size of the pCO₂ pan!

Bicarbonate decreased by 20 mmol/L, so we expect a compensation of 20 mm Hg. He did that very well!
Metabolic acidosis is compensated about 1:1.

Metabolic acidosis can be generated by two mechanisms – gain of acid or loss of bicarbonate.



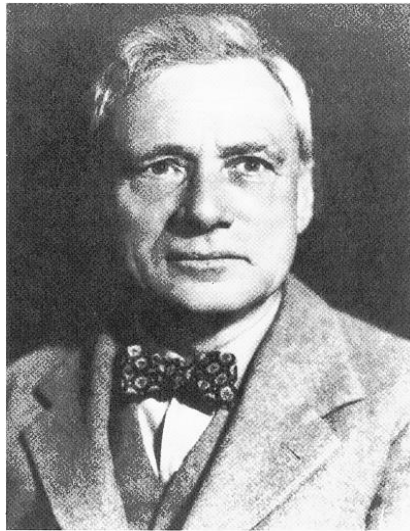
How can I very quickly distinguish between the two?

Gain of acid must include an anion (conjugate base)

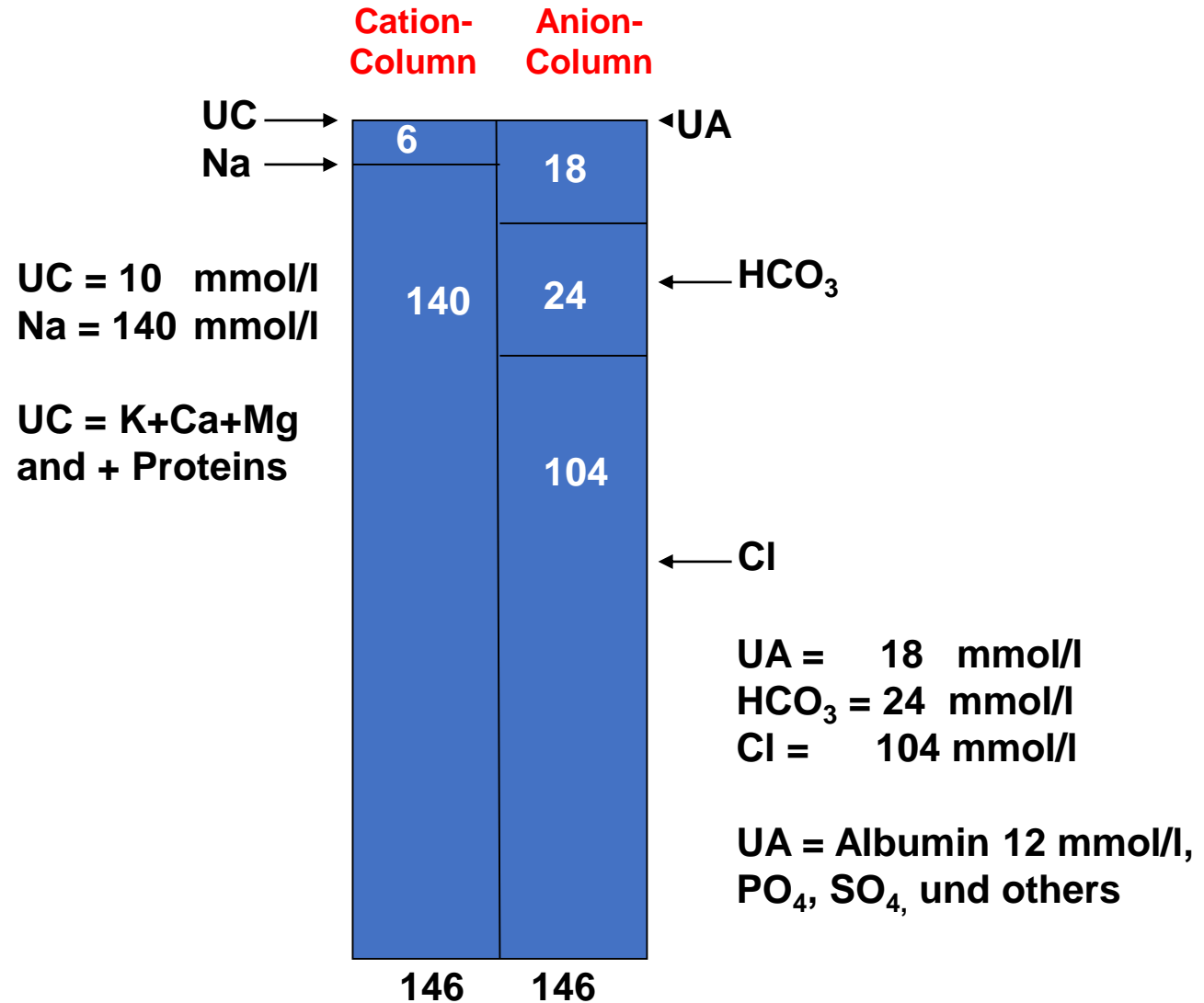
With the Gamble-Gram, we can tell the difference between addition of acid or loss of bicarbonate.

Unmeasured cations = UC

Unmeasured anions = UA



**James Lawder Gamble
(A Boston pediatrician)**



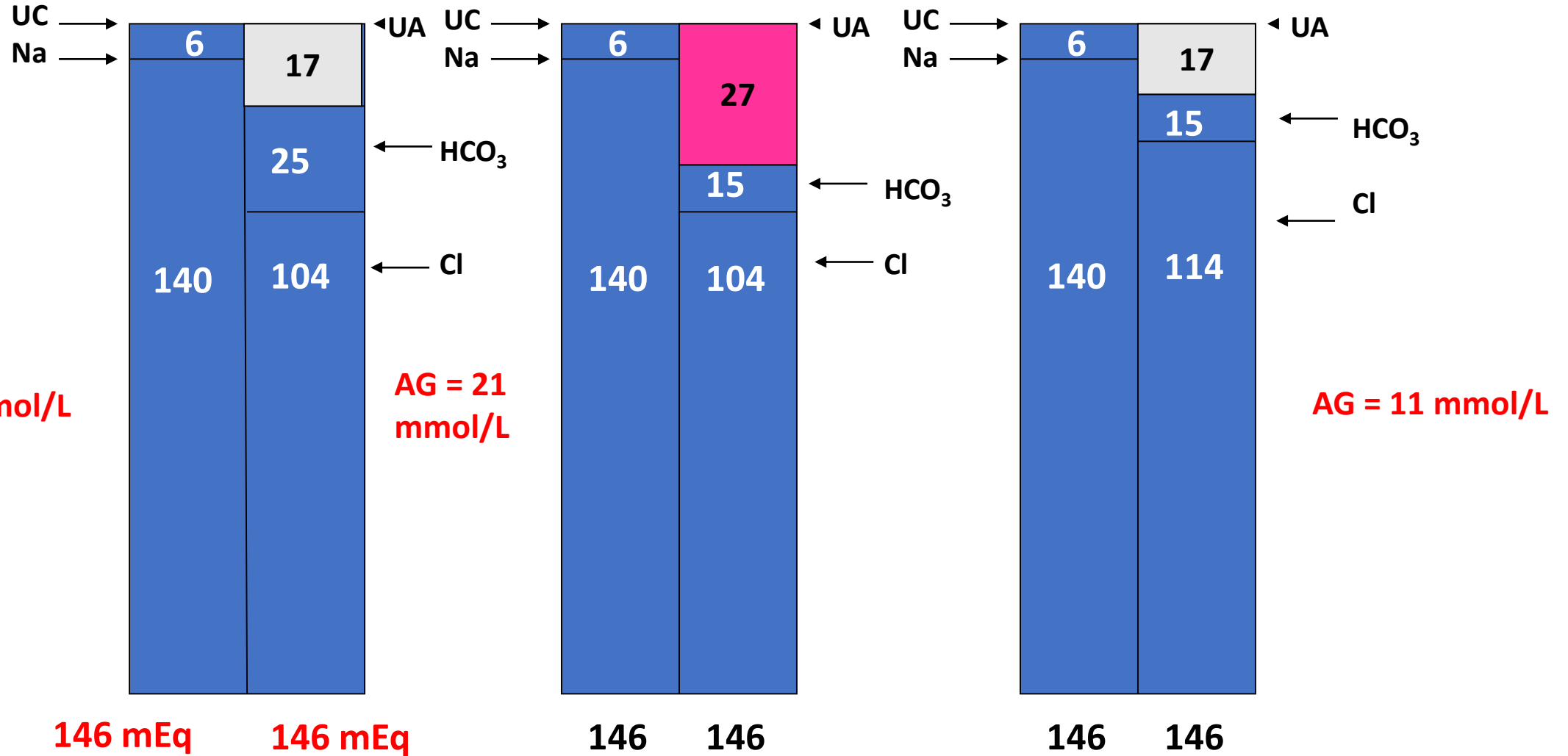
Which “Gamble”-gram fits our patient?

Metabolic acidosis with elevated or non elevated AG

Normal

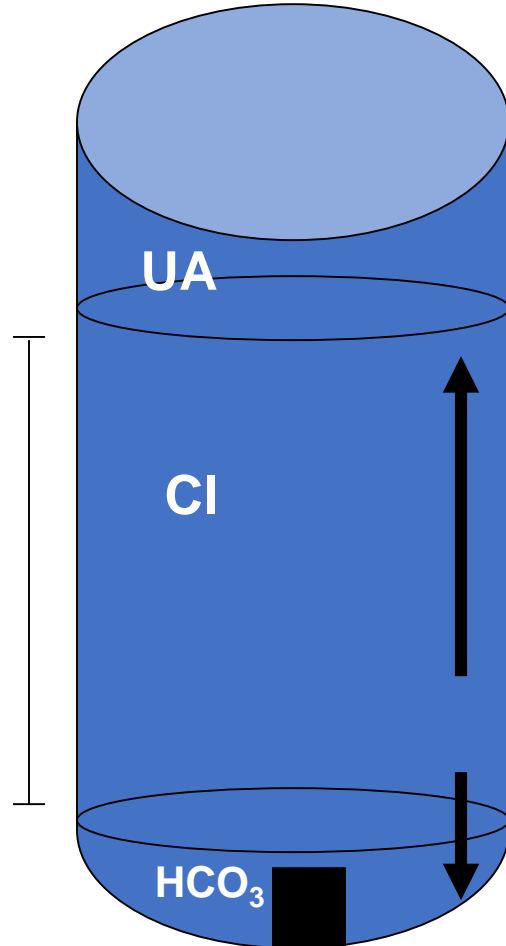
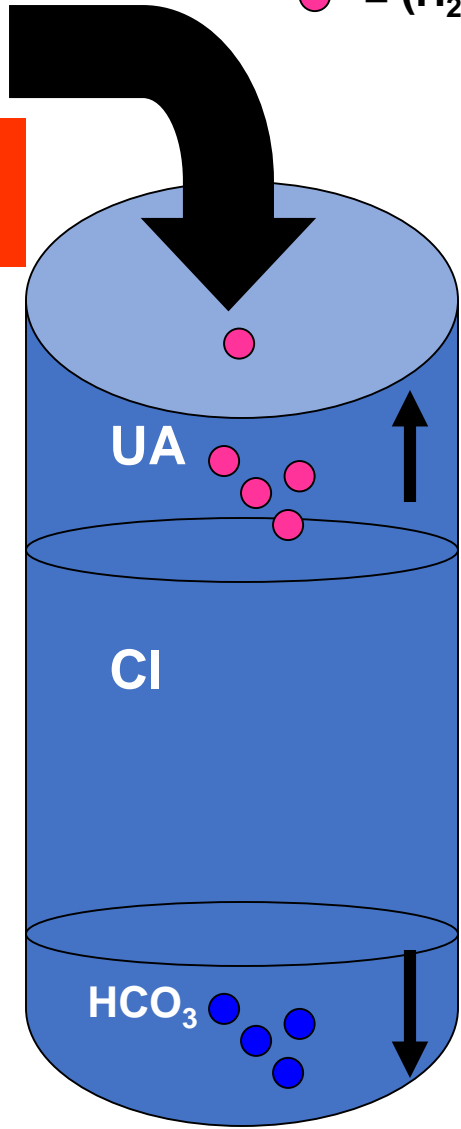
High AG

High Cl



● = (H₂) Sulfate balls

Strong acid
H₂SO₄



HCO₃
Losses
RTA
Diarrhea

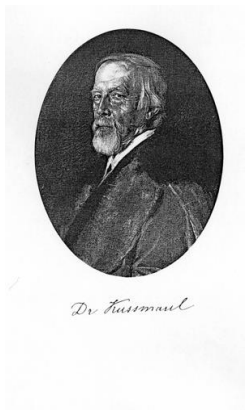


= Bicarbonate balls

Mneumonics – MUDPILES or German - KUSSMAUL



- Methanol, uremia, diabetic ketoacidosis (DKA), paraldehyde, phenformin (metformin), pyroglutamic acidosis (dicloxacillin), iron tablets, isoniazid, lactic acidosis, ethylene glycol, salicylates (English)



- Kussmaul: Ketoazidose, Urämie, Salizyl-Säure, Metanol, Äthylenglykol, (mehr) Urämie, Laktat (German)

How can we lose bicarbonate? (Check out the holes in the body)

- **Diarrhea**
- **Pancreatic-cutaneous fistulas**
- **Gall-bladder drainage**
- **Kidneys cannot reclaim bicarbonate (proximal RTA)**
- **Kidneys cannot excrete H⁺ ions (distal RTA)**
- **Kidneys cannot properly eliminate NH₄ (CKD)**

Two dialysis patients nearly drove me crazy (they have no kidneys)

49-year-old lady, renal failure, dialysis patient, no complaints.

She regularly comes in (3 x weekly) with: pH 7.2 ($H^+ > 60$ nmol/L), pCO_2 28 mm Hg, HCO_3 10 mmol/L. Na 132, Cl 95, and AG 27 (mmol/L).

She is doing fine (we are not). Lactate, ketones, and all poisons were not increased.

After each dialysis, all laboratory values were normal and she went home- a happy person.

56-year-old lady, renal failure, dialysis patient with no complaints comes into each treatment (3x weekly).

She regularly has pH 7.14 (H^+ about 90 nmol/L), PCO_2 27, HCO_3 9, Na 138, Cl 116, AG 13 (all mmol/L).

We were concerned, but she was not. Her AG was always normal.

After each dialysis, all laboratory values were normal and she went home- a happy person.

One patient had a regular „gain of hydrogen ions“; another had „loss of bicarbonate“

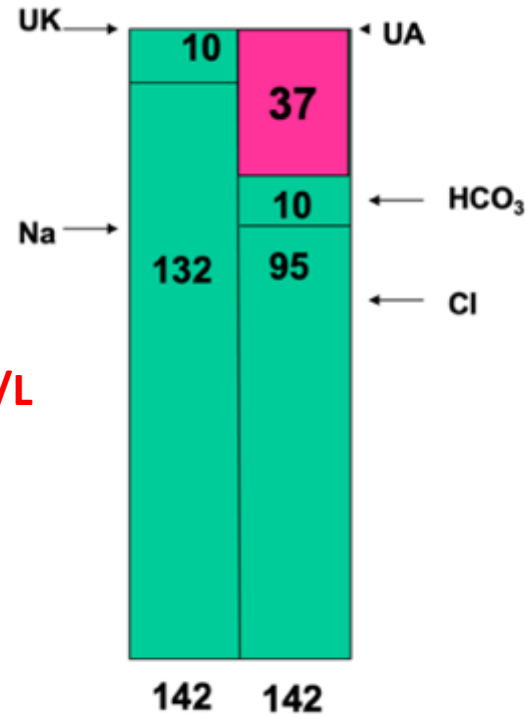
The acid had to come from someplace!



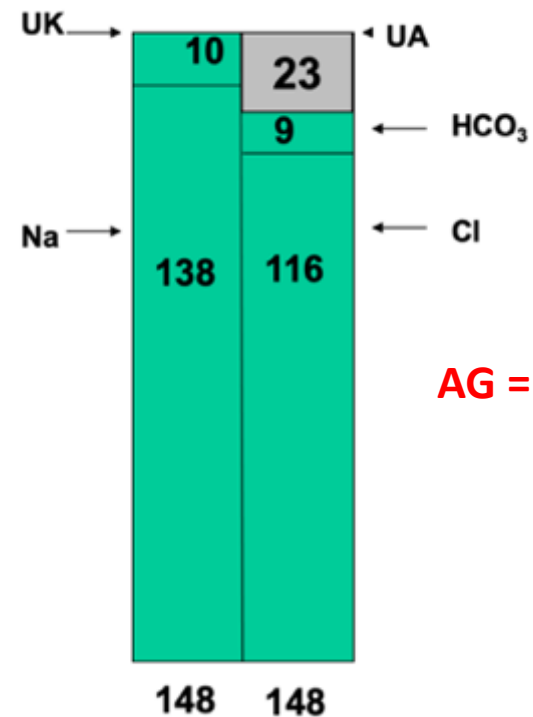
Contains tartaric acid (wine acid)



Contains NH_4Cl

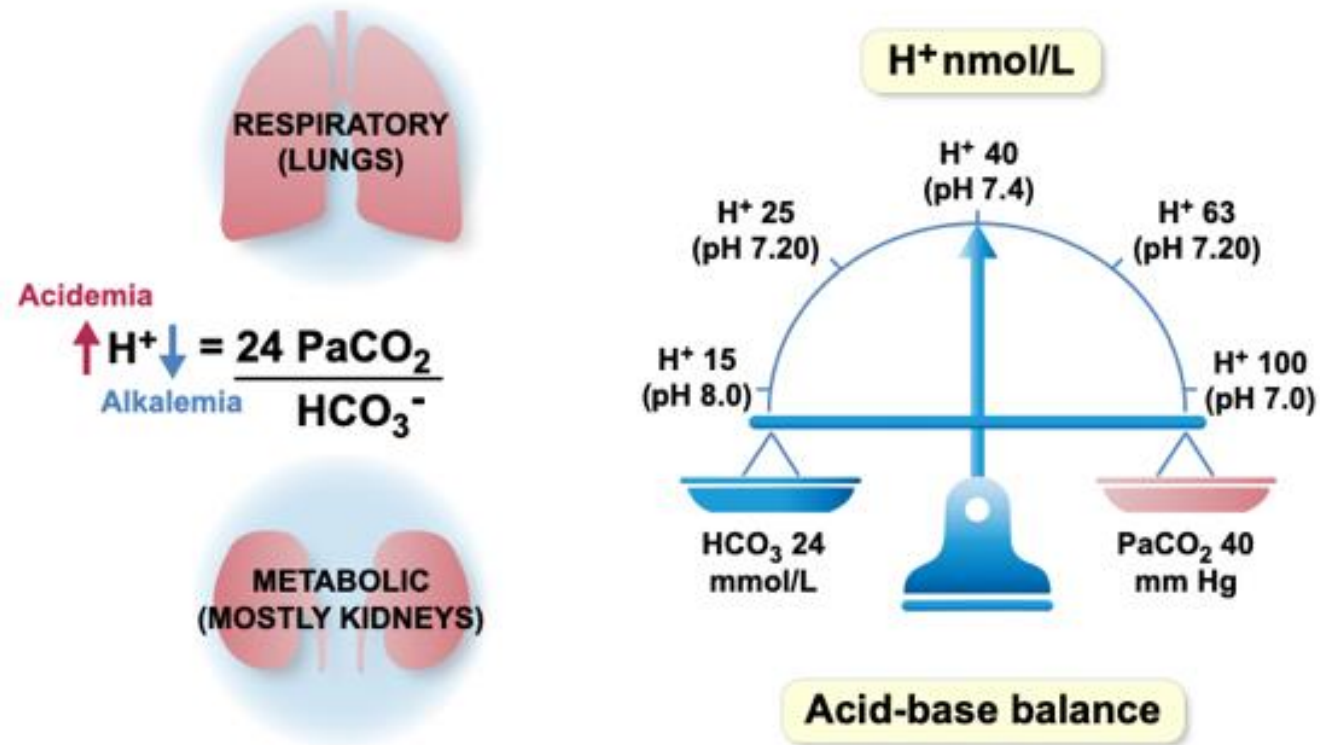


AG = 27 mmol/L



AG = 13 mmol/L

In metabolic alkalosis, we have a loss of H⁺ or a gain of HCO₃⁻



39-year-old patient admitted with weakness, vomiting, alcoholism and chronic pancreatitis (numerous times). He was oriented but somnolent. BP supine 140/80 and 85/60 (mm Hg) standing. Heart rate 110/min, respiratory rate 10/min.

Hb 13 g/dL, creatinine 272 $\mu\text{mol/L}$, Na 113, Cl 47, K 2.2, Ca 1.9 (all mmol/L).

pH 7.58 (H^+ about 20 nmol/L), PaO_2 65, PaCO_2 65 (all mm Hg) and HCO_3^- 65 mmol/L

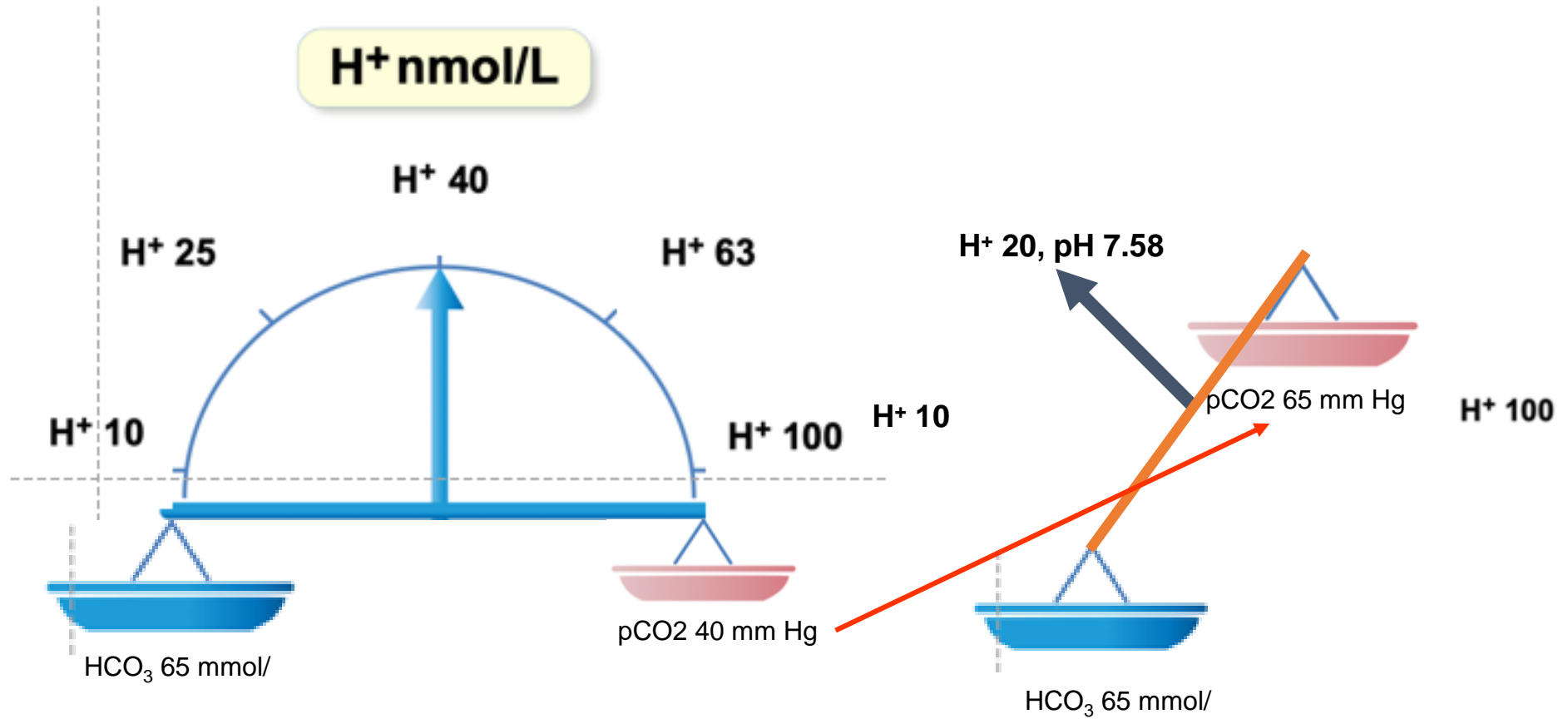
Chronic vomiting -> volume loss.

The loss comprises H^+ and Cl^-

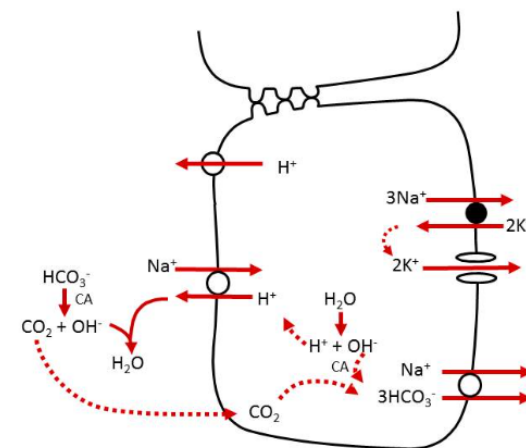
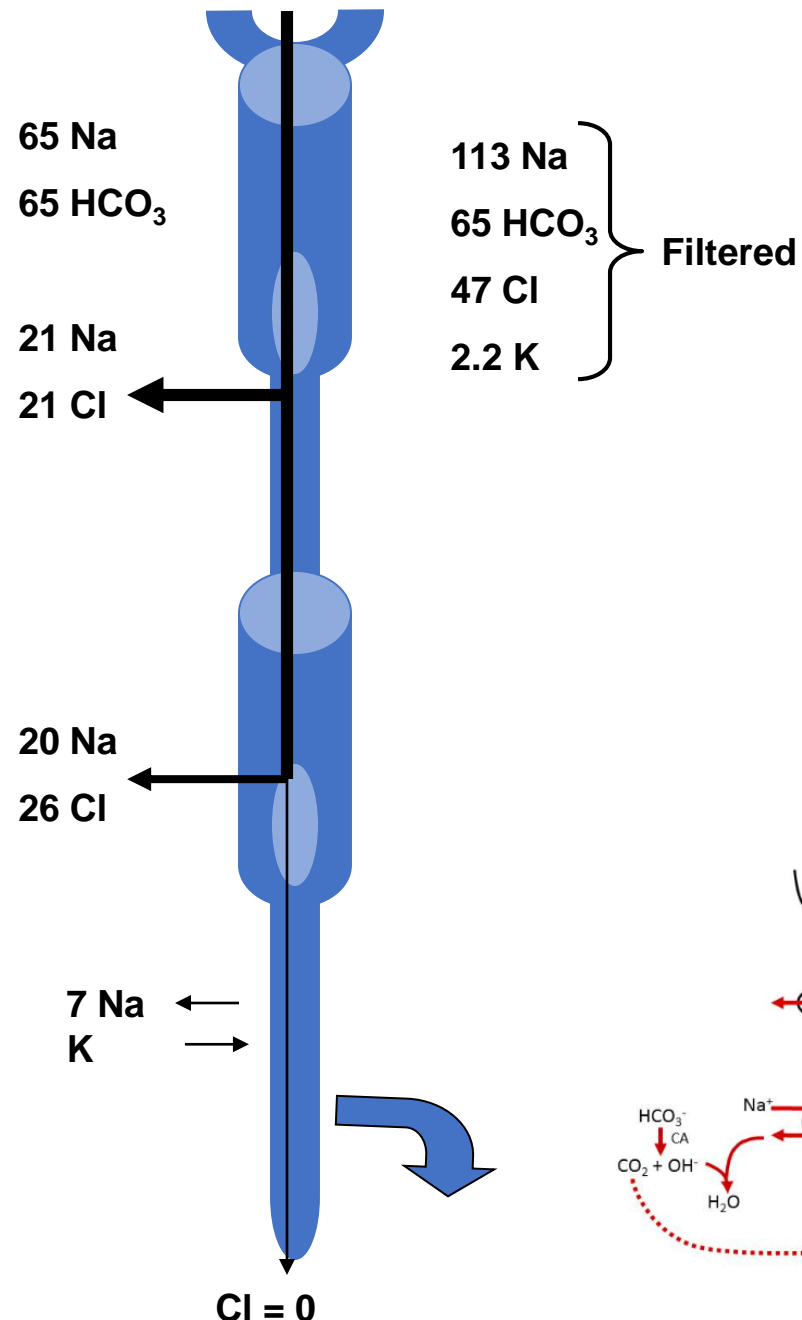
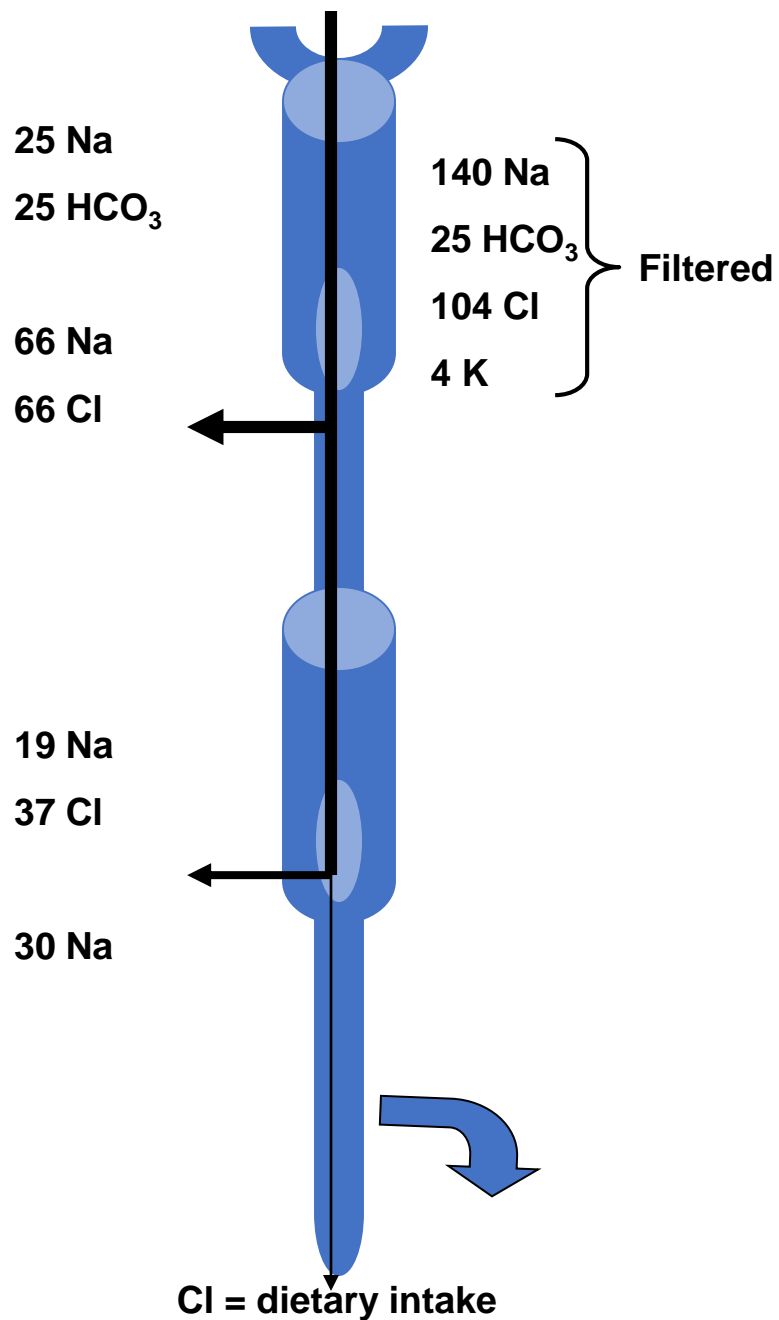
Renal failure (could be pre-renal)

Respiratory compensation (for this metabolic alkalosis) is perfect!

The poor man just vomited and vomited (some more)

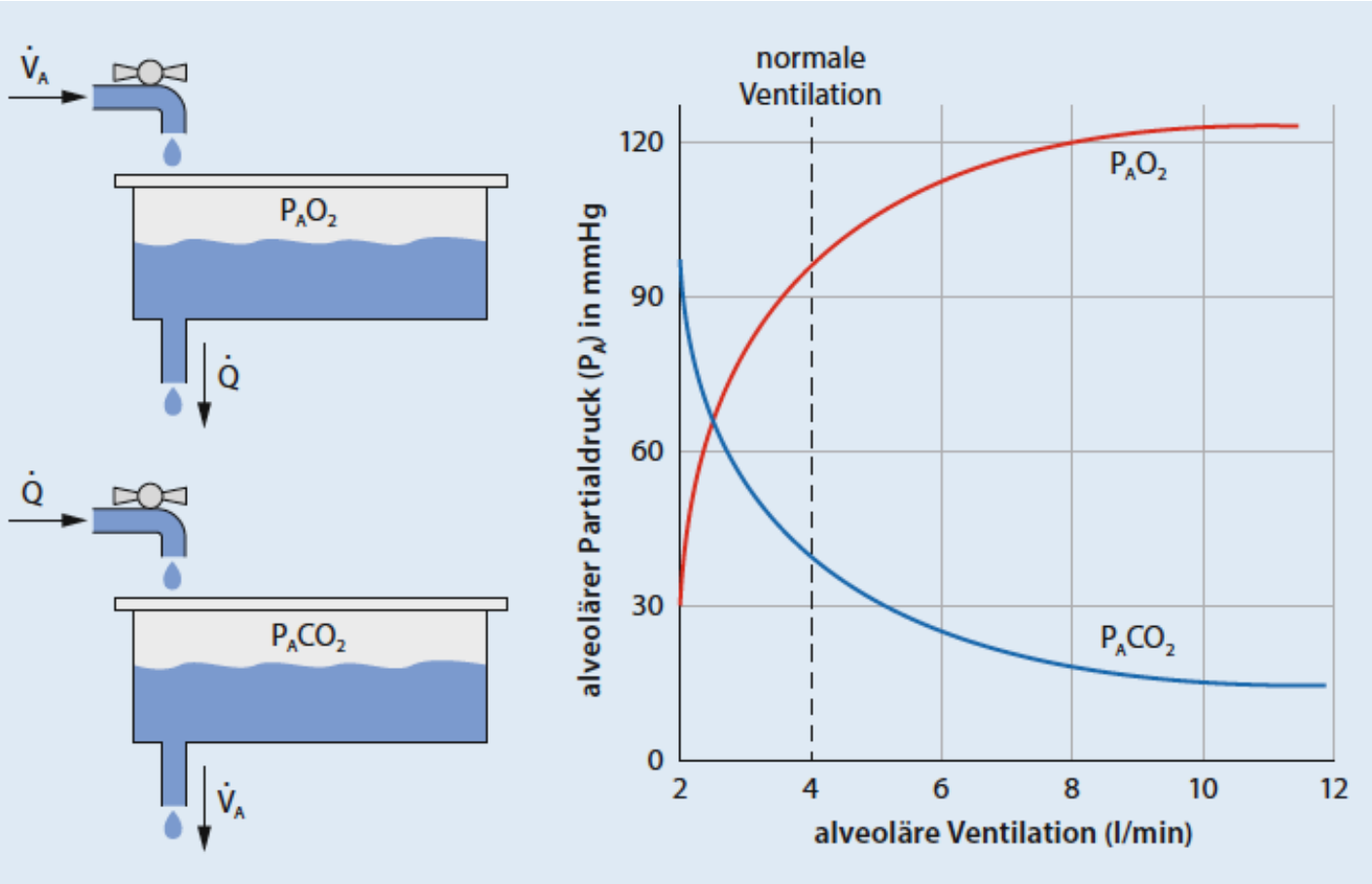


What choice do his kidneys have?



To deal with this problem, what do his lungs have to do? They must reduce V_a .

Ventilation



Clearance „in“

Perfusion

Perfusion

Clearance „out“

Ventilation

← To a pCO_2 of 65 mm Hg

The patient with vomiting, volume depletion, and hyponatremia, K 2.2 mmol/L and metabolic alkalosis (pH 7.58, HCO₃ 65 mmol/L)

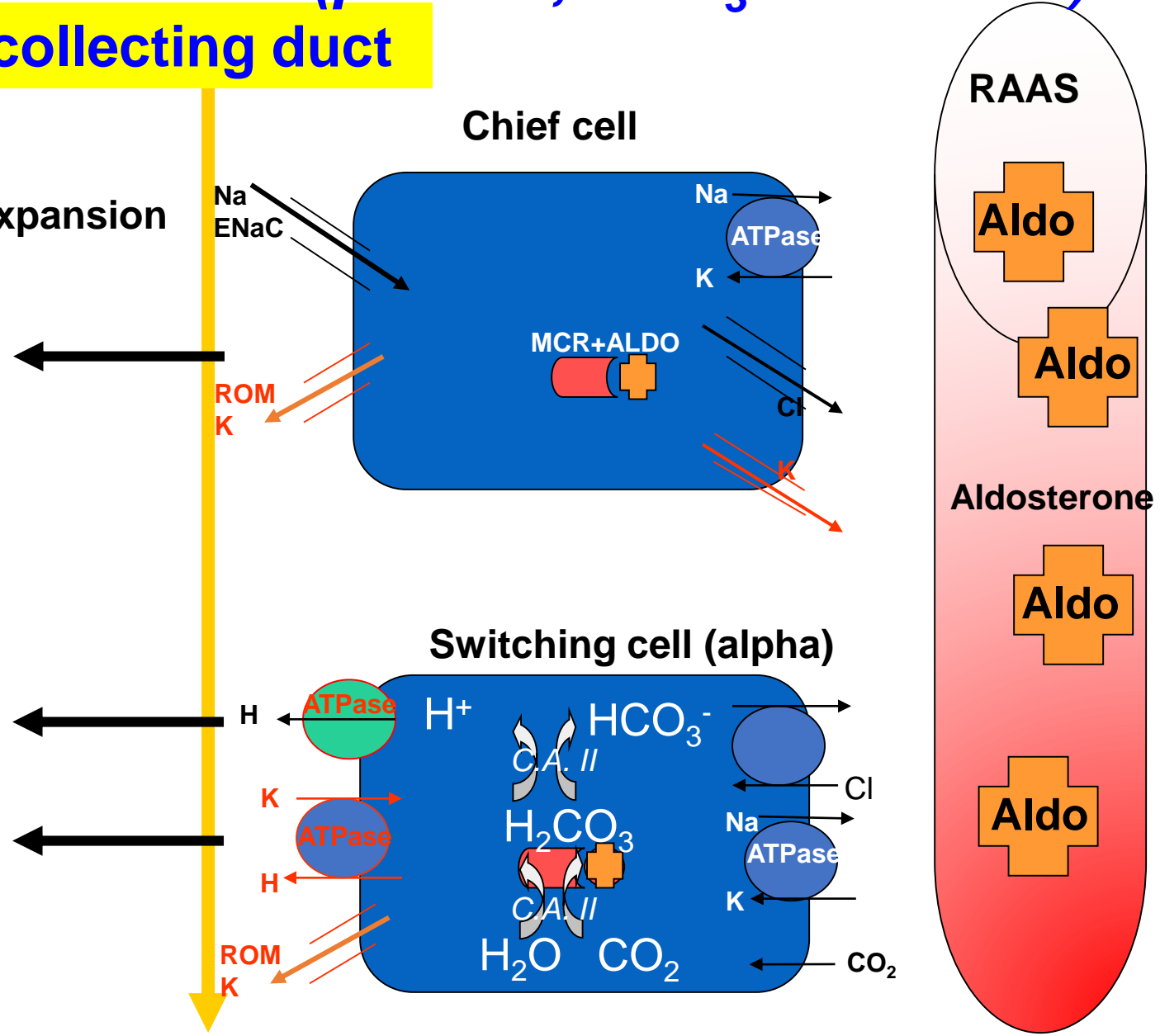
We are in the collecting duct

Na-Reabsorption for expansion (Shock!)

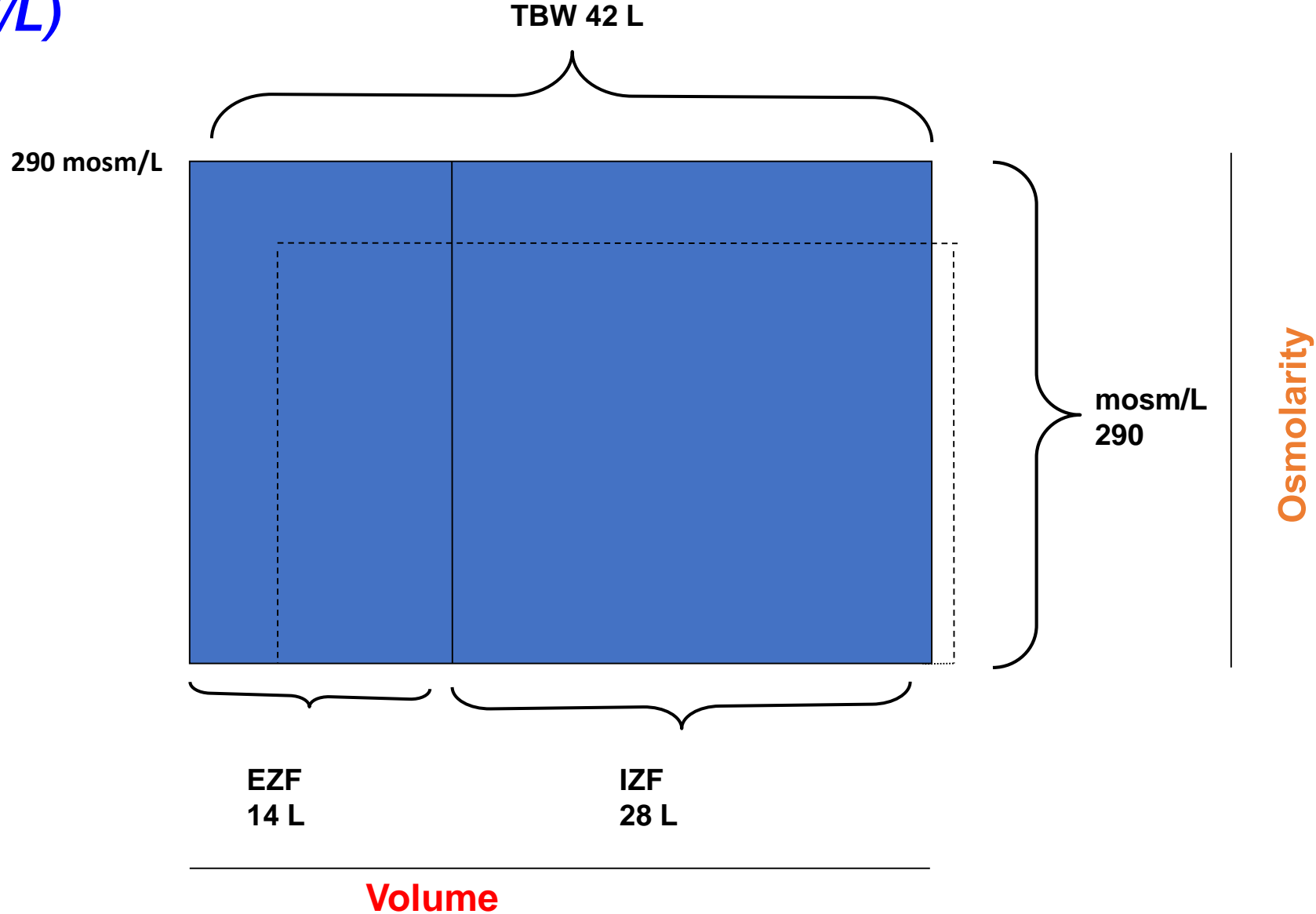
Hypokalemia

Metabolic alkalosis

Hypokalemia



The patient with vomiting, volume depletion, and hyponatremia, K 2.2, and metabolic alkalosis (pH 7.58, H⁺ 20 nmol/L, and HCO₃ 65 mmol/L)



This patient needs volume and chloride, ie. 0.9% NaCl (+ KCl)

Metabolic alkalosis is a bicarbonate problem. It can be (primarily) induced in two ways.

H⁺ ions can be lost from the body, in this case some conjugate base is lost also (namely chloride).

HCO₃ could be „introduced (gained)“ to the body. Some misguided persons actually „eat“ bicarbonate (baking soda).

HCO₃ can also be „gained“ over the kidney. This state-of-affairs is common with glucocorticoid excess (Cushing Syndrome) and in „aldosteronism“.

38-year-old woman with difficult to manage hypertension

150/90 mm Hg despite 3-medication classes

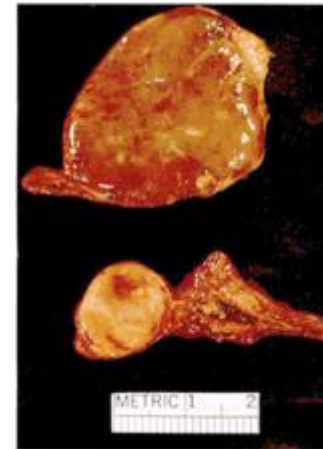
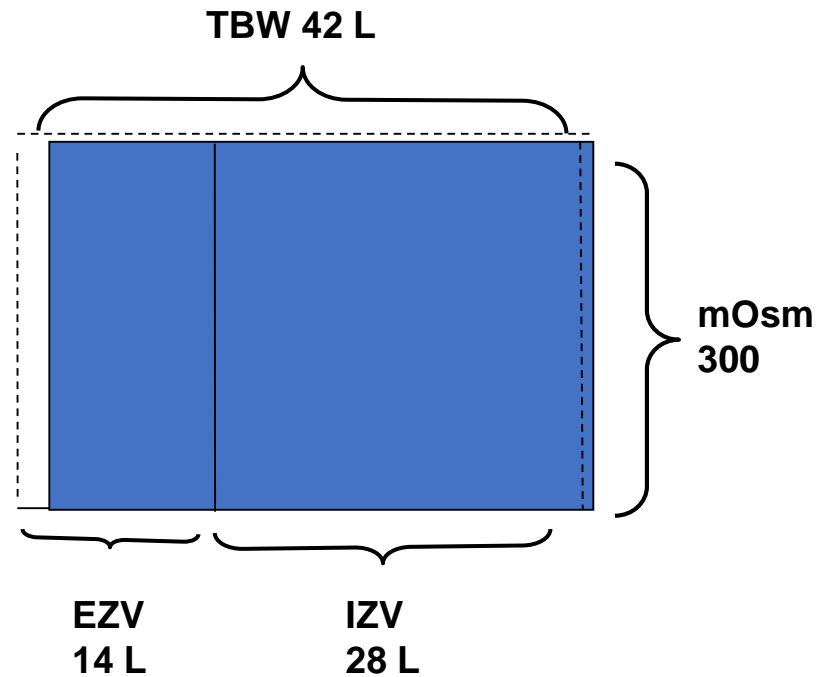
Family history was negative

24-h ABPM showed reduced night-time dipping

Blood work: Na 144, Cl 101, K 3.8, HCO₃ 34 (all mmol/L)

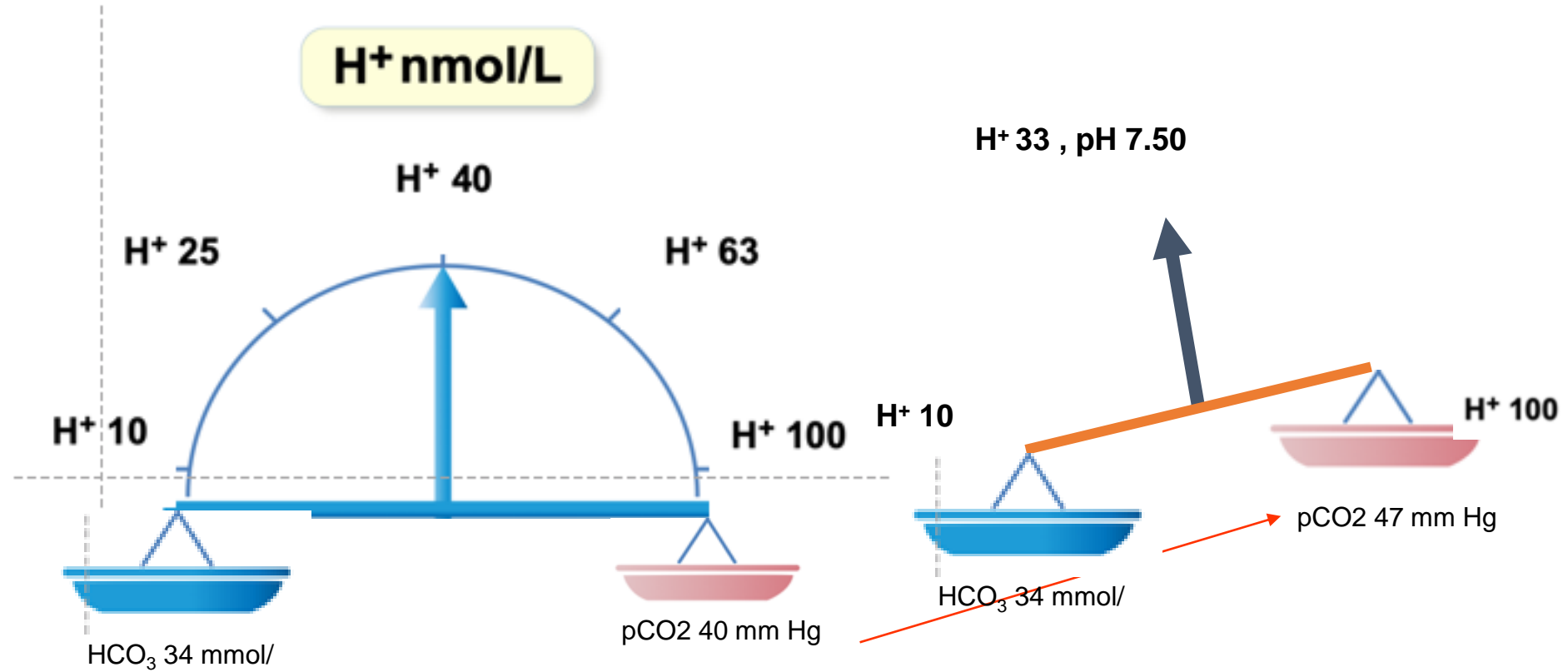
Urine Stick Protein +1

The patient had primary aldosteronism

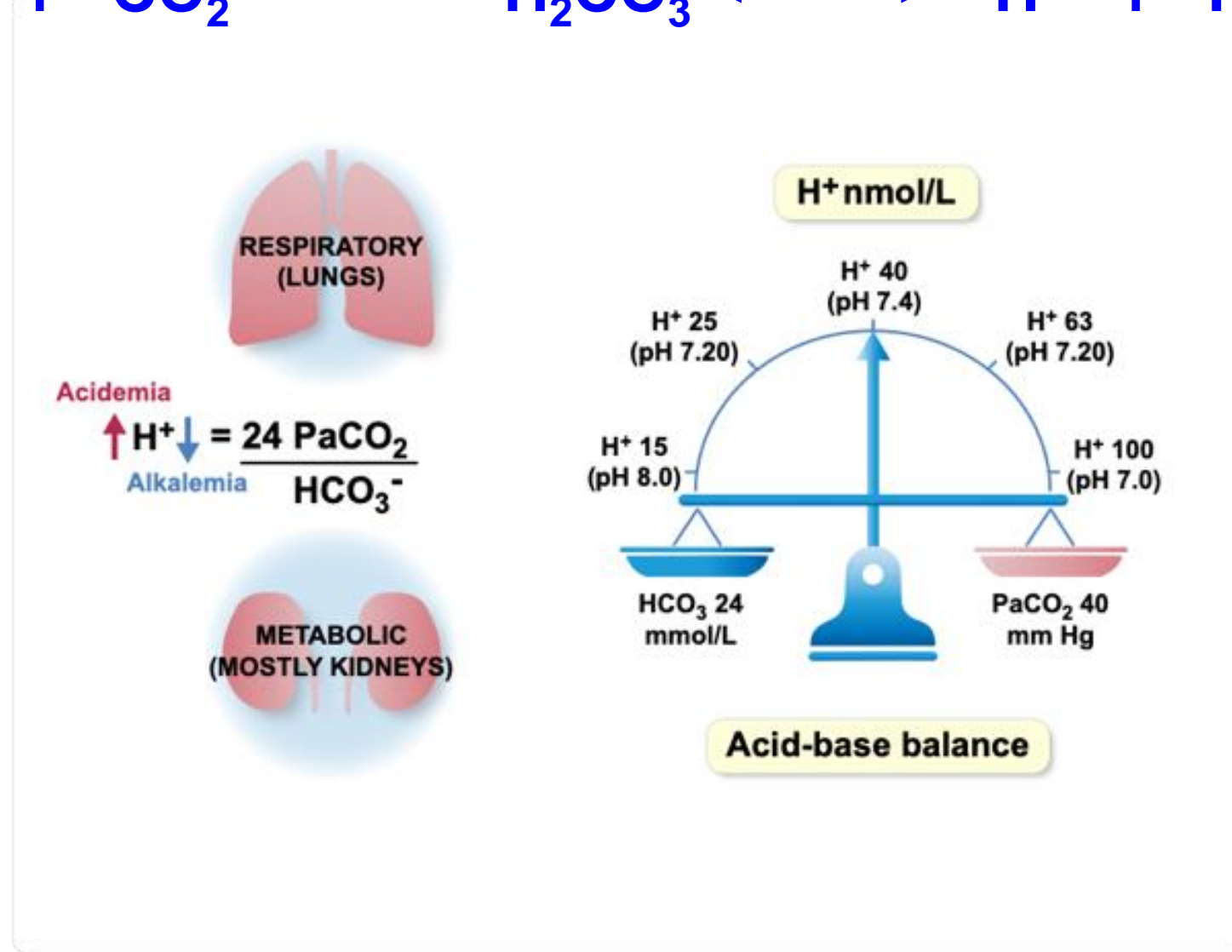


Aldosteronoma

The “driver” had nothing to do with volume depletion



Respiratory disturbances involve the PaCO_2 pan



The carbon dioxide clearance $PaCO_2$

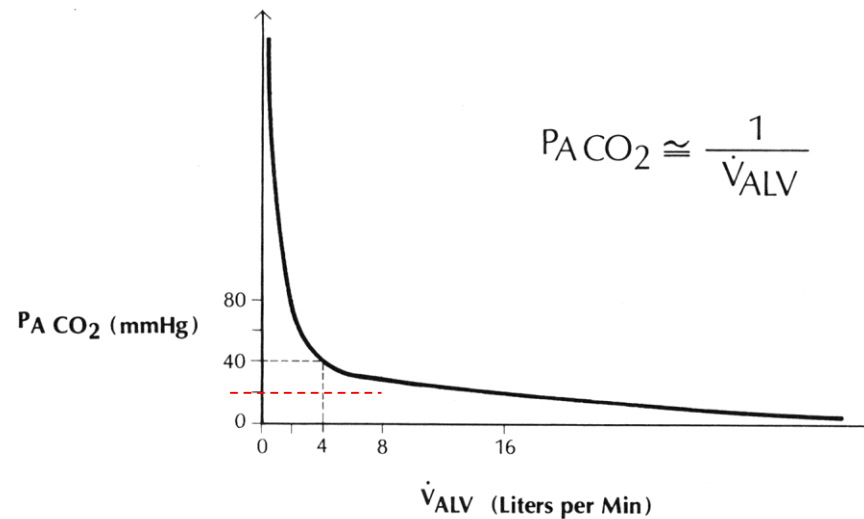
The respiratory component (H_2CO_3) is regulated by the lungs and measured as $PaCO_2$

The lungs excrete about 20,000 mmol CO_2 daily

The body of a 70 kg person contains about 110 L CO_2

The $PaCO_2$ is our key to alveolar ventilation

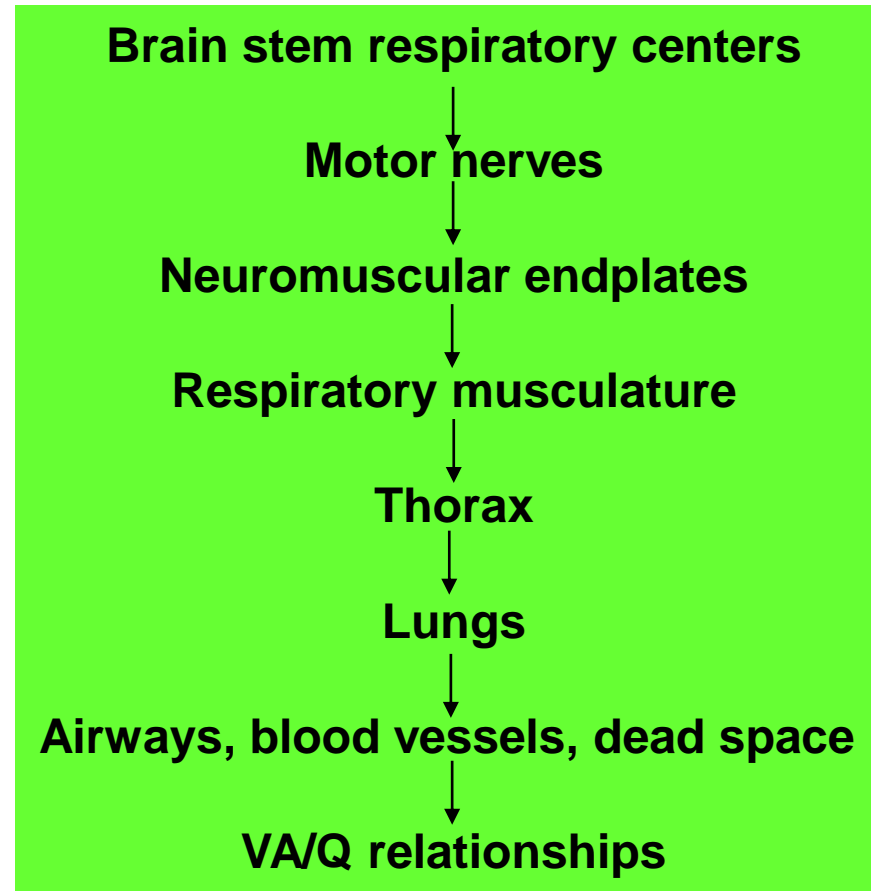
PCO_2 Clearance



$$Cl_{Cr} = \frac{UCr \times V}{SCr}$$


$$\dot{V}_{ALV} \approx \frac{gCO_2 \times V}{PCO_2}$$

Respiratory acidosis means alveolar hypoventilation - PaCO₂ retention



Alveolar hypoventilation, sleep apnea syndrome

Friday night 21:00, smoker with BMI 39, ICU is full, all other wards have no beds (the Bethlehem Syndrome)

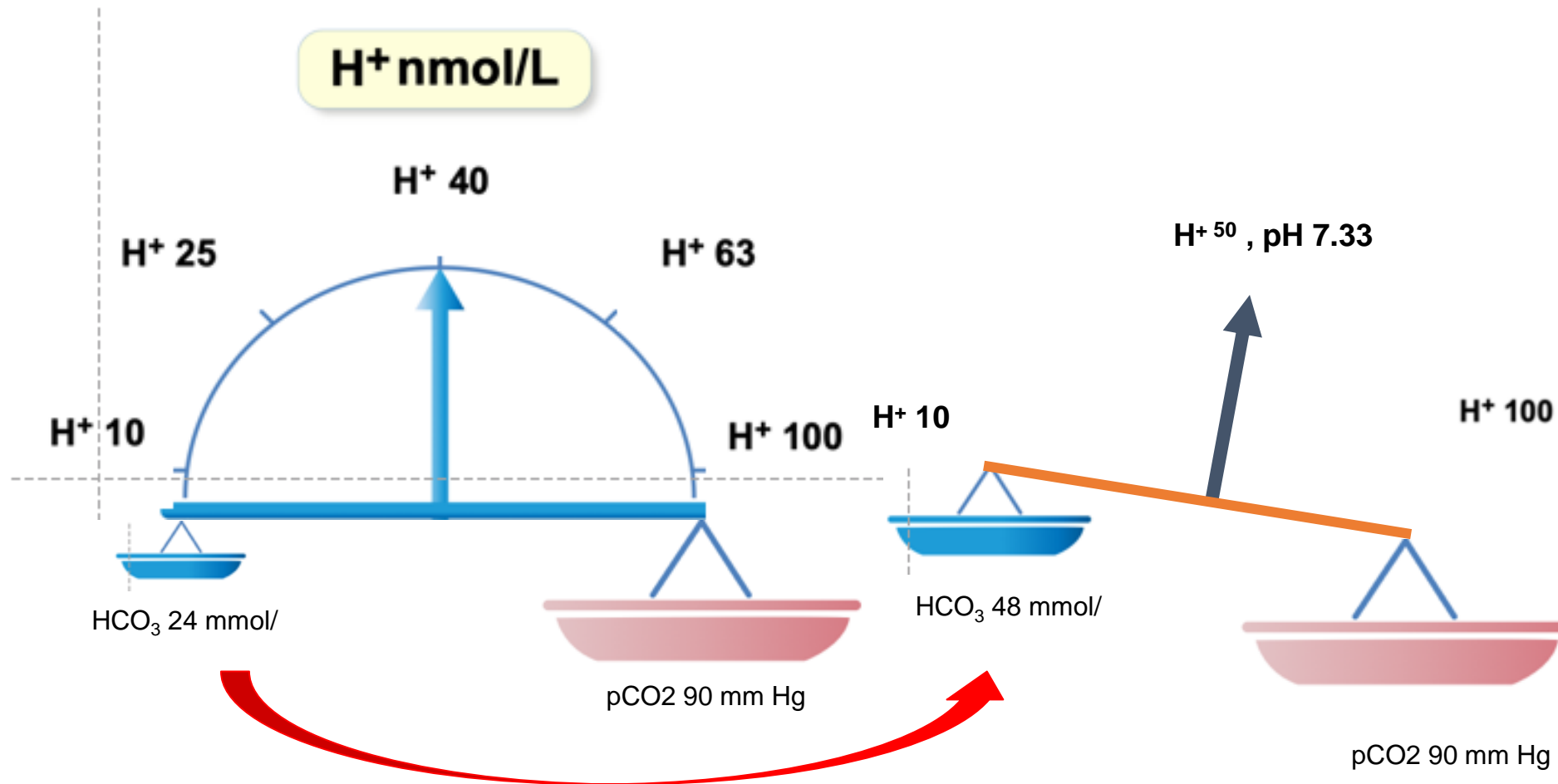


• pH	7,329
• pCO ₂	89,8 mm Hg
• pO ₂	32,4 mm Hg
• SO ₂	52,5%
• Hkt	54%
• Hb	18,8 mg/dl
• Na ⁺	138,1mmol/l
• K ⁺	4,17 mmol/l
• Cl ⁻	84,6 mmol/l
• Glu	7,2 mmol/l

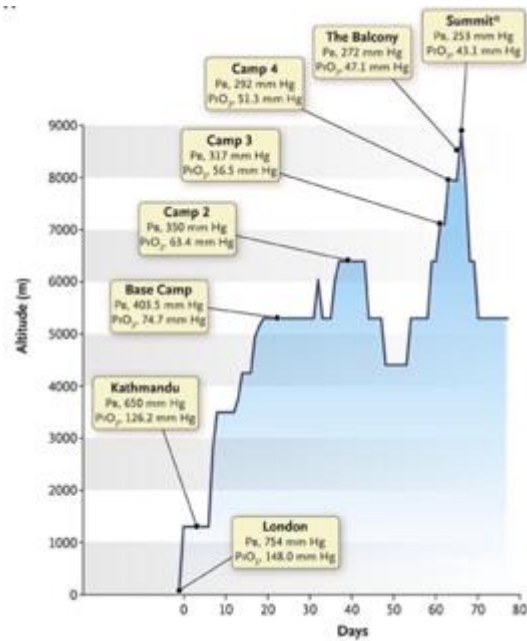
• BEecf	21,5 mmol/l
• BE	14,5 mmol/l
• SBC	36,9 mmol/l
• HCO ₃ ⁻	47,7 mmol/l
• TCO ₂	50,4 mmol/l
• A	44,6 mm Hg
• A-aDO ₂	12,3 mm Hg
• a/A	0,7
• An.Gap	10,0 mmol/l
• P50	27,9 mm Hg
• O ₂ Cap	24,2 ml/dl
• O ₂ Ct	12,8 ml/dl

Temperatur-abhängig

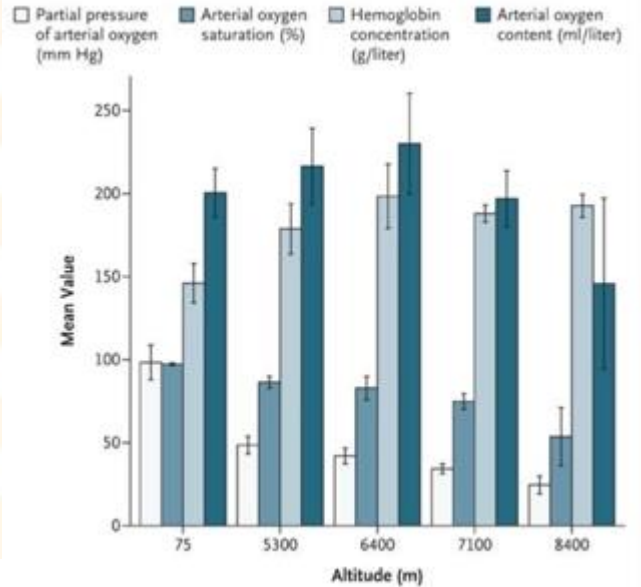
Today, we treat this problem with BiPAP



Blood gases on Mount Everest

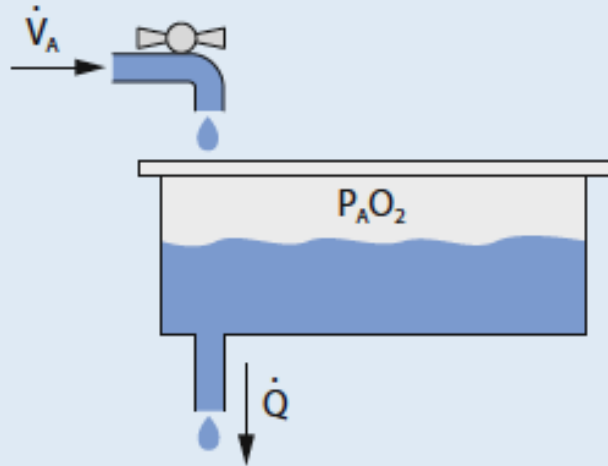


pH	7.55
PaO ₂ (mm Hg) †	29.5
PaCO ₂ (mm Hg) †	12.3
Bicarbonate (mmol/liter) ‡	10.5
Base excess of blood ‡	-6.3
Lactate concentration (mmol/liter)	2.0
SaO ₂ (%) ‡	68.1
Hemoglobin (g/dl) §	20.2
Respiratory exchange ratio ¶	0.81
PAO ₂ — mm Hg †**	32.4
Alveolar–arterial oxygen difference — mm Hg †	2.89



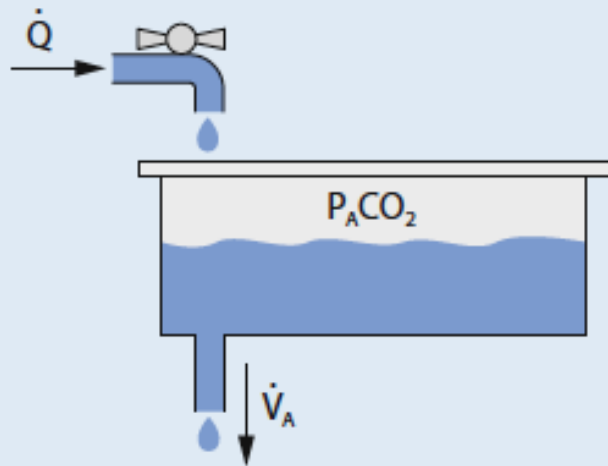
Alveolar ventilation is the “clearance” of PCO_2

Ventilation

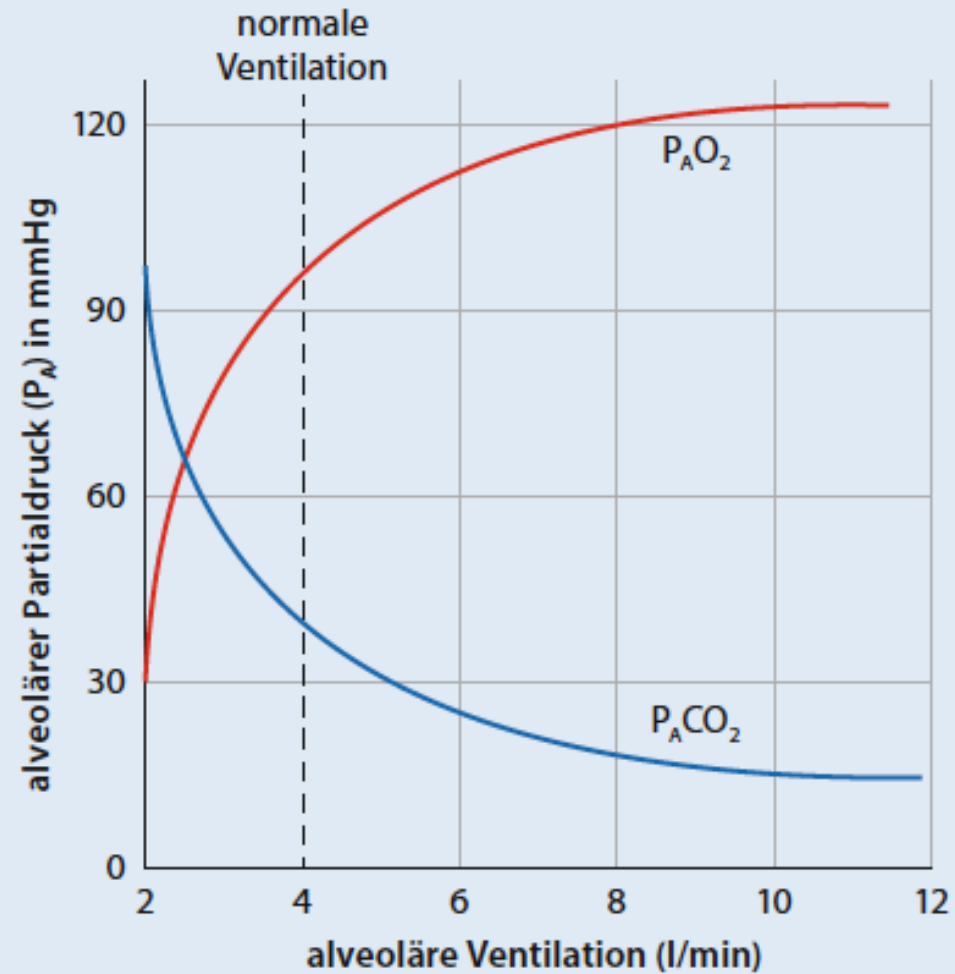


Perfusion

Perfusion



Ventilation

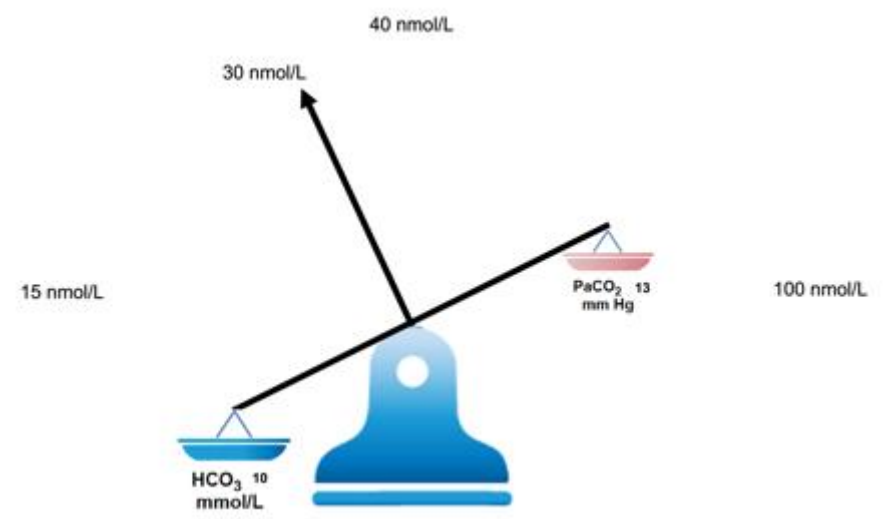
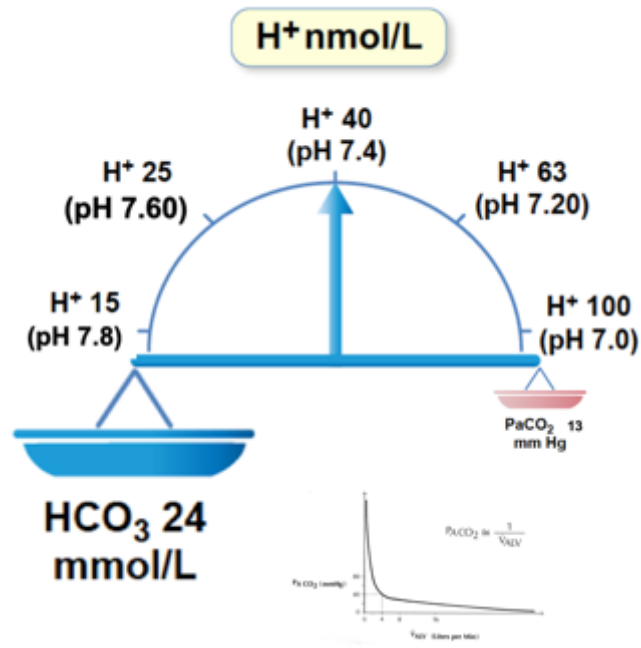


Clearance „in“

Clearance „out“

← To a pCO_2 of 12 mm Hg

Reduce $PaCO_2$ to 13 mm Hg and HCO_3^- to 10 mmol/L



pH	7.55
PaO ₂ (mm Hg) †	29.5
PaCO ₂ (mm Hg) †	12.3
Bicarbonate (mmol/liter) ‡	10.5

Patient found in snow

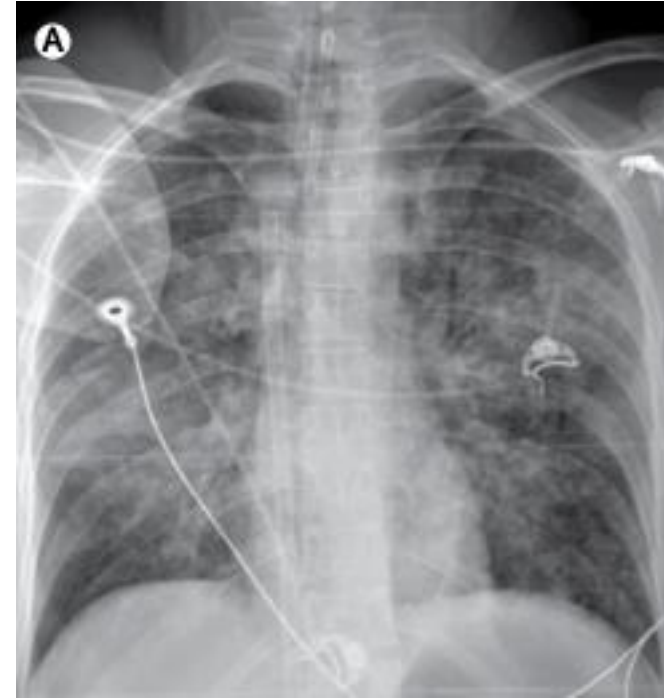
A 34-year-old woman who collapsed during a mountain trek in northern Spain was initially assessed at an emergency rescue centre. She was unresponsive, asystolic, and pulseless, had unreactive dilated pupils, and had a tympanic temperature of 18°

Temp 18° C
pH 6.81
H⁺ 160 nmol/L
PaCO₂ 84 mm Hg
HCO₃ 5.8 mmol/L
Lactate 10.3 mmol/L

Patient saved by heroes

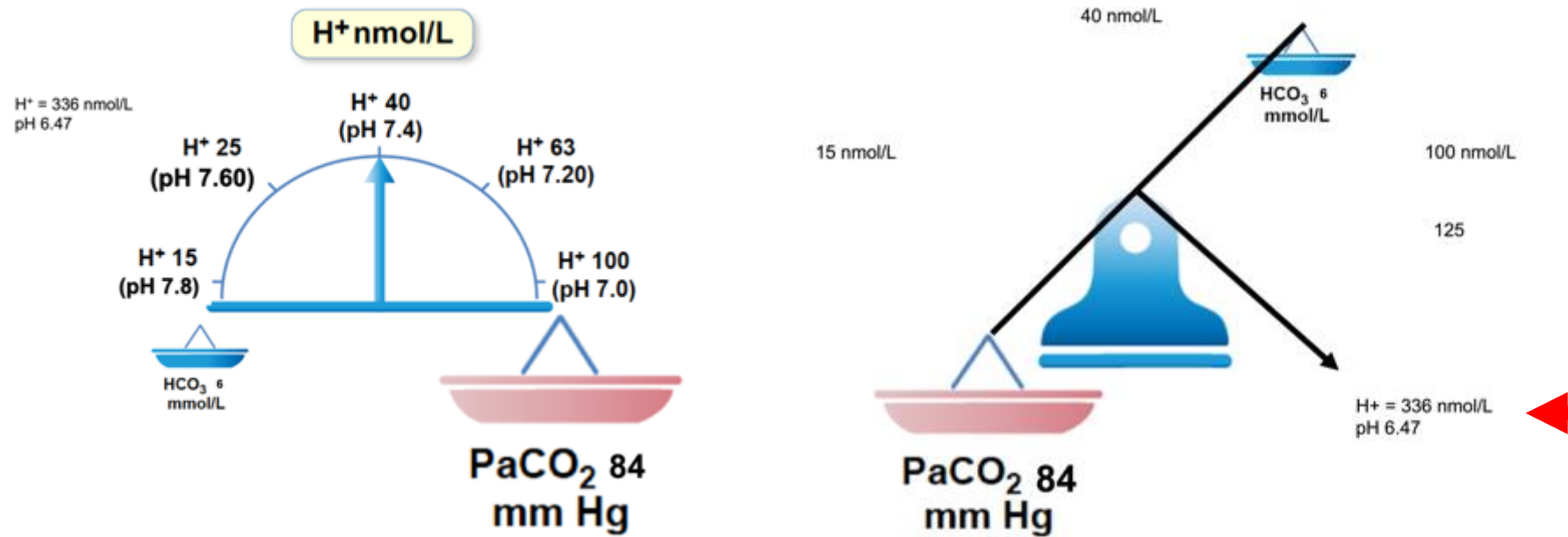


EKG at Temp 32° C



Lancet 2020

Check the numbers with Henderson's equation



	Hospital admission	ECMO start	2h	3h pre-DF	Day 1
pH	6.81	6.85	7.15	7.29	7.43
pCO ₂ (mmHg)	84	56	40	29	37
pO ₂ (mmHg)	-	361	330	109	107
HCO ₃ (mmHg)	5.8	6.8	13.9	13.9	25
BE (mmol/L)	-22	-23.3	-14	-11.5	+1
Lactate (mmol/L)	10.3	12.1	11.9	10.9	3.8
K (mmol/L)	4.4	-	3.8	3.4	3.7

And if you still cannot figure it out, here are some German tablets that may help.
Friedrich.luft@charite.de

When all else fails
buy these!

