Acid-Base Disturbances

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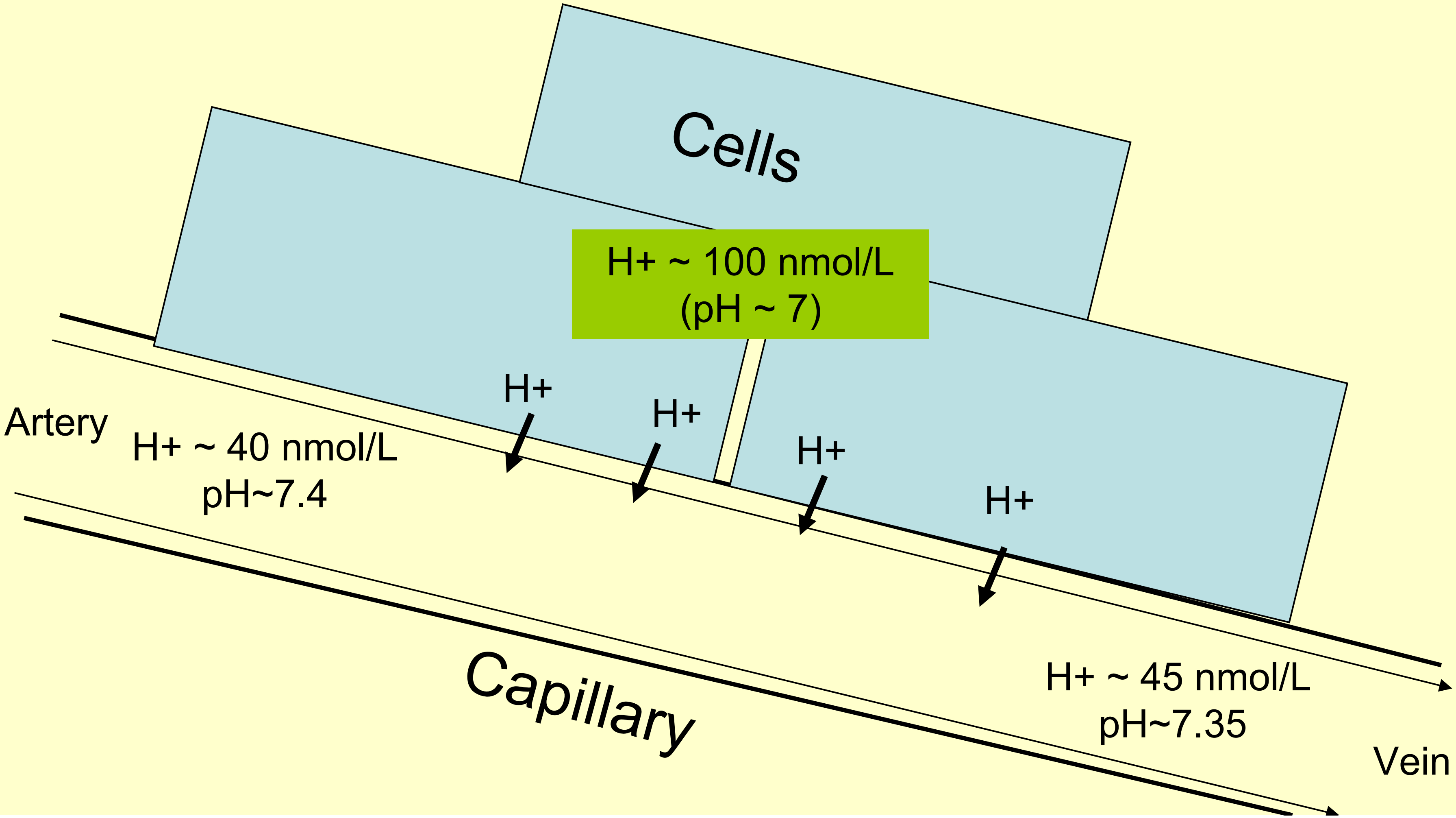
- Processes that alter the acid-base status of a patient
  - metabolic processes
  - respiratory processes
- Acidosis and alkalosis
- There can be (and often are) more than one of these processes simultaneously in a patient

Metabolic processes generate acid

Respiratory acids (volatile): CO2 (200 mL/min ~ 12000 mmols / day)
Metabolic acids (non-volatile): lactic-, pyruvic-, koto-acids (100 mmols/day)



Regulation of Acids

Principal regulators of acid-base balance

- Lungs
  - Control of pCO2 by respiratory function
- Kidney
  - Control of HCO3- concentration and acid (H^+) excretion by the kidney

Buffer systems

- Intracellular and extracellular buffers

Astrup and Siggard-Andersen approach to acid/base physiology
Traditional

- pCO_2 measurement (1952)
- measurement of pH at known pCO_2
- standard bicarbonate (1957)
- capillary microelectrode and the concept "Base-Excess" (1958)
- acid-base nomogram

Evaluation of the arterial blood gases and electrolytes

- <u>H^+ concentration</u>:
  - direct 36 - 44 nmol/L
  - indirect pH (- log H^+) 7.36 - 7.44
- <u>Partial pressure of CO_2</u> ($PaCO_2$): 36 - 44 mmHg
  4.8 – 5.8 kPa
- <u>Bicarbonates</u> (HCO_3^{--}):
  - <u>Standard</u> 24 ± 2 mmol/L
    - blood saturated with O_2, pCO_2 = 5.3 kPa (40 mmHg)
  - <u>Actual</u>: 24 ± 2 mmol/L
    - blood saturated with O_2, at actual pCO_2

What is measured and what is calculated?

- Hydrogen (H+) concentration / pH
- Carbon dioxide (CO2) partial pressure / concentration
- Bicarbonate ion (HCO3-) concentration

What is measured and what is calculated?

Measured (using electrode):

- pH
- CO2

Calculated:

- Bicarbonate ion (HCO3-) concentration

The important equation for acid-base evaluation?

Henderson-Hasselbalch equation (1916):

CO2 + H20 ↔ H2CO3 ↔ HCO3- + H+

$$pH = pKa + \log\left(\frac{[HCO_3^-]}{[CO_2]}\right).$$

- pKa = 6.1
- [CO2] = 0.3 x pCO_2

- **$[HCO_3^-] = 0.03 * pCO_2 * 10^{(pH - 6.1)}$**

Buffer base and base excess in acid/base physiology

- Traditional

Other calculated parameters to evaluate acid base balance

- **Buffer base (BB)** (Singer and Hastings 1948)**:**
  - sum of all weak bases under actual conditions
  - Bicarbonate (24)+ protein (15) + Hgb (9) mmol/L+ phosphate (1)
- **Normal buffer base (NBB):**
  - sum of all bases under standard conditions

Base excess

Base excess/deficit (BE/BD) (Siggaard-Andersen late 1950s)

- Amount of strong acid (in mmol/l) that must be added to the blood sample to return the sample to pH 7.40 under standard conditions (PCO2 ~ 5.3 kPa = 40 mmHg)
- Calculated acid or alkali required to return whole blood in vitro to a normal pH

- **HOWEVER:** plasma ***in vivo*** is in continuity with interstitial fluid that has less buffer capacity

Standard base excess/deficit (SBE/SBD)

- Calculated acid or alkali required to return anemic blood (Hgb 50g/L) in vitro to a normal pH under standard conditions

Interpretation of base excess (BE)

- Positive (Base Excess) > 2 mmol/L
  - Metabolic Alkalosis

- Negative (Base Deficit) < -2 mmol/L
  - Metabolic Acidosis

Boston six 'rules-of-thumb' to correct acid-base balance

Schwartz and Relman (instead of BE):

1. **The 1 for 10 Rule** for Acute Respiratory Acidosis
   - [HCO3] will increase by 1 mmol/L for every 10 mmHg elevation in pCO2 above 40 mmHg
   - **Expected [HCO3] = 24 + { (Actual pCO2 - 40) / 10}**
2. **The 4 for 10 Rule** for Chronic Respiratory Acidosis
   - [HCO3] will increase by 4 mmol/L for every 10 mmHg elevation in pCO2 above 40mmHg
   - **Expected [HCO3] = 24 + 4 { (Actual pCO2 - 40) / 10}**
3. **The 2 for 10** Rule for Acute Respiratory Alkalosis
   - [HCO3] will decrease by 2 mmol/l for every 10 mmHg decrease in pCO2 below 40 mmHg
   - **Expected [HCO3] = 24 - 2 { (40 - Actual pCO2) / 10 }**

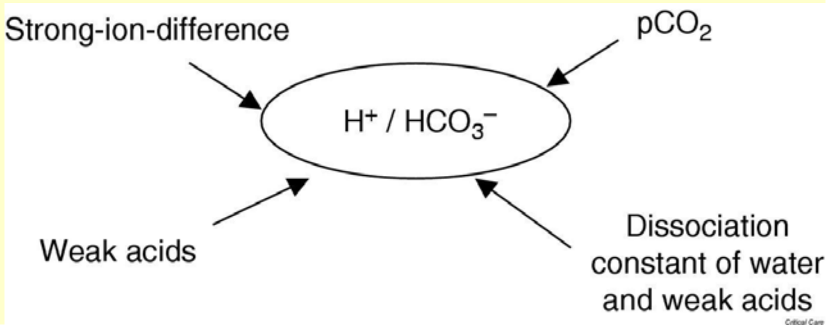
Boston six 'rules-of-thumb' to cerrect acid-base balance

4. **The 5 for 10 Rule** for a Chronic Respiratory Alkalosis
   - [HCO3] will decrease by 5 mmol/l for every 10 mmHg decrease in pCO2 below 40 mmHg.
   - **Expected [HCO3] = 24 - 5 { (40 - Actual pCO2) / 10 } (range: +/- 2)**
5. **The One & a Half plus 8 Rule** for a Metabolic Acidosis
   - The expected pCO2 (in mmHg) is calculated from the following formula:
   - **Expected pCO2 = 1.5 x [HCO3] + 8 (range: +/- 2)**
   - The limit of compensation is a pCO2 of about 10 mmHg
6. **The Point Seven plus Twenty Rule** for a Metabolic Alkalosis
   - The expected pCO2 (mmHg) is calculated from the following formula:
   - **Expected pCO2 = 0.7 [HCO3] + 20 (range: +/- 5)**

Stewarts strong ion theory

Stewarts strong ion theory

- Dr. Peter Stewart (1980s)
  - found the bicarbonate-centred approach confusing and inadequate to explain certain pathophysiological conditions



Stewarts strong ion theory

- **Three independent controlling variables:**
  - Partial pressure of carbon dioxide [paCO2]
  - Strong Ion Difference [SID] = [Na+] + [K+] + [Ca2+] + [MG2+] - [Cl-] - [Other Strong Anions]
  - Total weak non-volatile acids [ATOT] (albumin, proteins, phosphate)
- **Six dependent variables**
  - [H+], [OH-], [HCO3-], [CO3--2], [HA], [A-] (weak acids and ions)
  - Their concentration depend on concentration of other ions and molecules

Clinical Considerations

- **Respiratory changes:**
  - Changes of PaCO2 produce the expected alterations in [H+]
- **Metabolic (Non-Respiratory):**
  - Because bicarbonate is a dependent variable metabolic disturbances cannot be viewed as a consequence of bicarbonate concentration
  - The two possible sources of metabolic disturbances
    - Strong ion difference [SID]
    - Total weak non volatile acids [ATOT]

Clinical application of Steward approach

- **Explanation for**
  - metabolic alkalosis associated with decreased plasma albumin concentrations
  - hyperchloremic acidosis (dilutional acidosis after large infusion of normal saline)
  - the role of ammonia in acid–base homeostasis

Assessment of acid base disturbances

Traditional approach

Stepwise approach

- Determine primary disorder
- If metabolic acidosis calculate anion gap
- Check for compensatory response
  - if fully compensated = simple acid base disorder
  - if not sufficiently compensated = mixed acid base disorder
- Identify specific etiologies for acid base disorder
- Therapeutic decission

Respiratory processes

- Ventilation influences carbon dioxide
  - arterial blood level PaCO2 (38 - 42 mmHg)
- **Primary respiratory acidosis**
  - Low blood pH – Acidemia (pH<7.36)
  - high PaCO2
- **Primary respiratory alkalosis**
  - High blood pH – alkalemia (pH>7.44)
  - low PaCO2

Metabolic processes

- Primarily alter the bicarbonate (HCO_3^-) concentration in the blood
- **Primary metabolic acidosis**
  - Low blood pH – Acidemia (pH<7.36)
  - Low serum bicarbonate
- **Primary metabolic alkalosis**
  - High blood pH – alkalemia (pH>7.44)
  - High serum bicarbonate

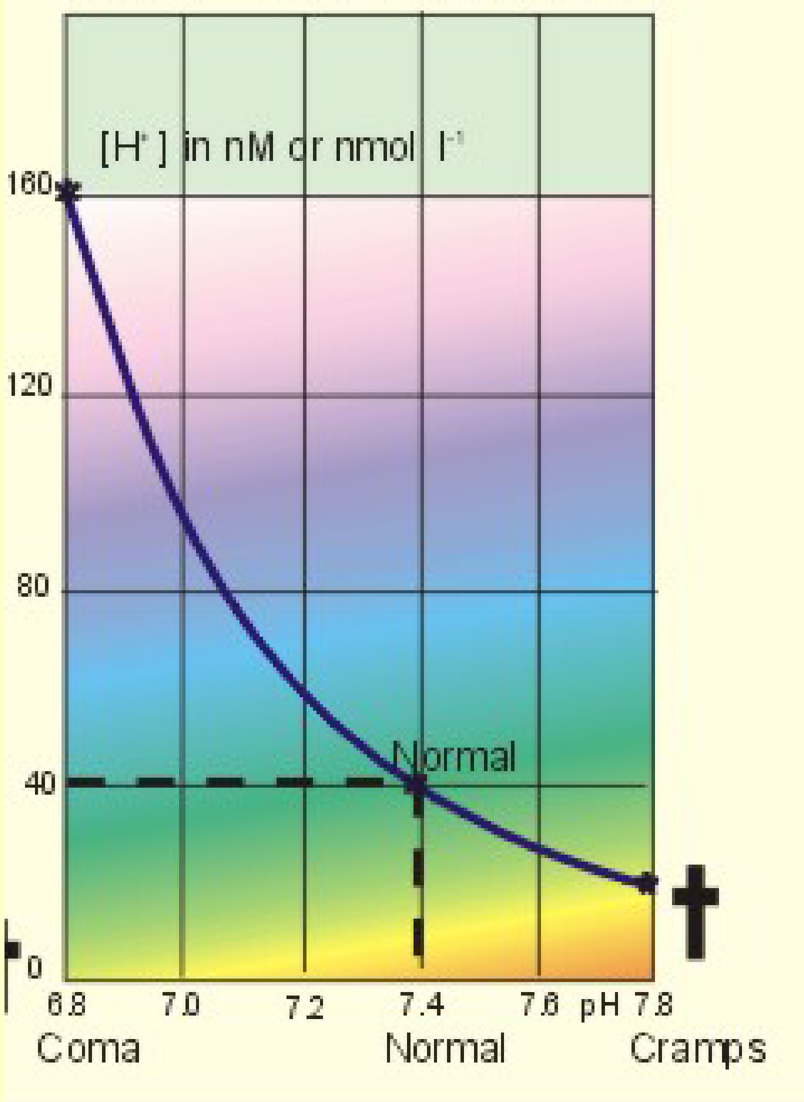
Combined disturbances of acid-base balance?

- Any combination except of
  - coexistence of respiratory acidosis with respiratory alkalosis

H+ concentration in blood

Life-threatening situations

- Above ~ 120 nmol/L (pH < 6.9)
- Below ~ 16 mnol/L (pH > 7.8)



Case report
Acid-base disturbances

A 42 year old diabetic female

A 42 year old diabetic female

- Has been on insulin since the age of 13
- Presents with a 4 day history of dysuria which has progressed to severe right flank pain
- Body temperature: 38.8 C
- WBC of 14 000 cells/μL
- disoriented

Electrolytes and ABG

• **Na+**	**135 mmol/L** (136-145)
• **K+**	**4.8 mmol/L** (3.5-5.0)
• **HCO3-**	**12 mmol/L** (22-26)
• **Cl-**	**99 mmol/L** (98-106)
• **pH**	**7.23** (7.38-7.42)
• **$PaCO_2$**	**25 mmHg** (36-44)
• **PaO_2**	**118 mmHg** (90-105)
• **BE**	**- 15.6 mmol/L** (-2 - +2)

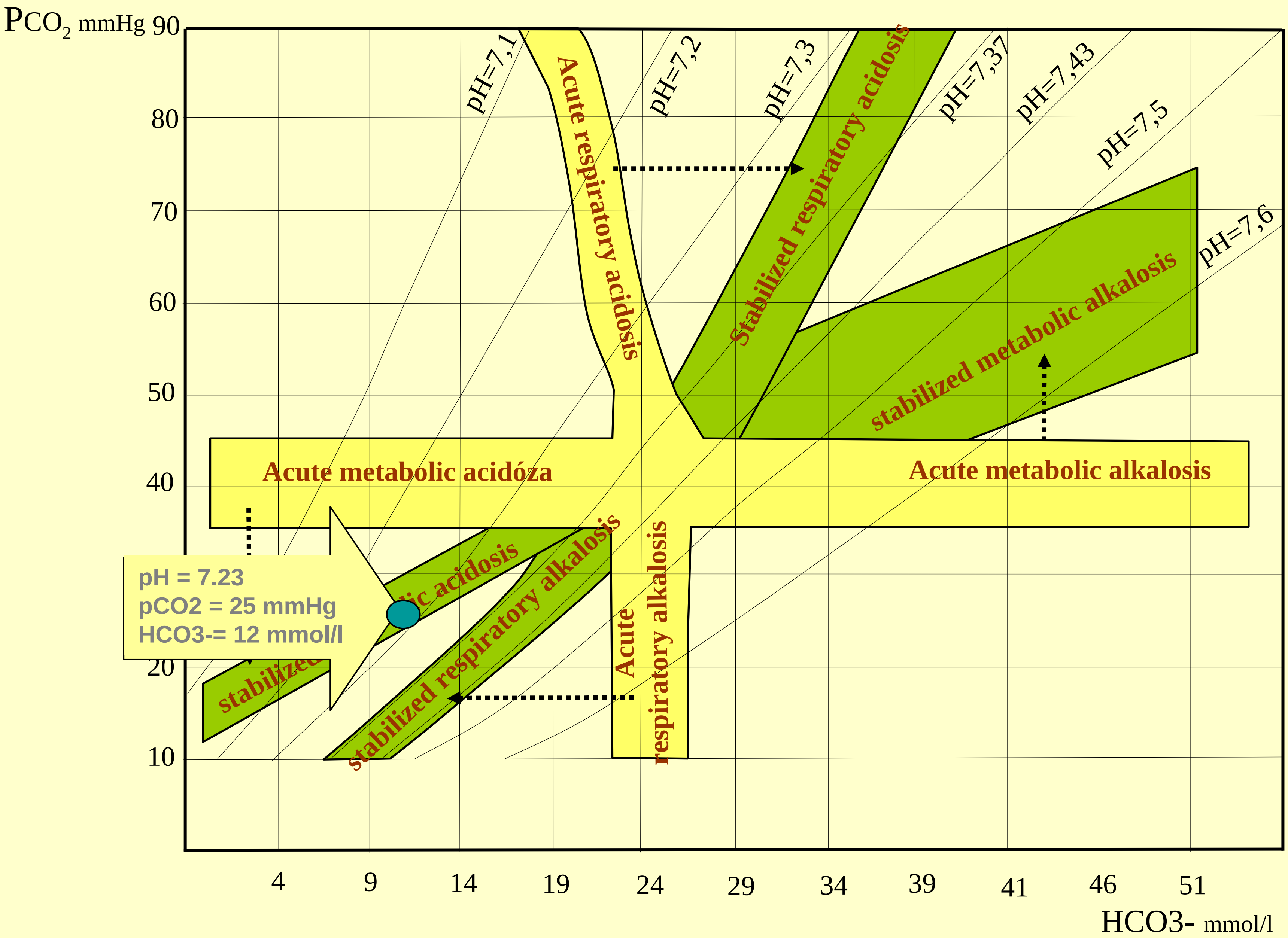
Diabetic F 42 year old

Is the acidemia primarily from a respiratory or metabolic process?

pH = 7.23 (7.38-7.42)

- $PaCO_2$ = 25 mmHg is low (< 36 mmHg)
  - respiratory system is not causing the acidosis
- **HCO_3^-** = 12 mmol/L (< 22 mmol/L)
- **BE** = -15.6 mmol/L (< -2 mmol/L)
  - **indicates a <u>metabolic acidosis</u>**

Diabetic F 42 year old



HCO3- 12 mmol/L ABG 7.23 / 25 / 118

Diabetic F 42 year old

Anion gap (AG)

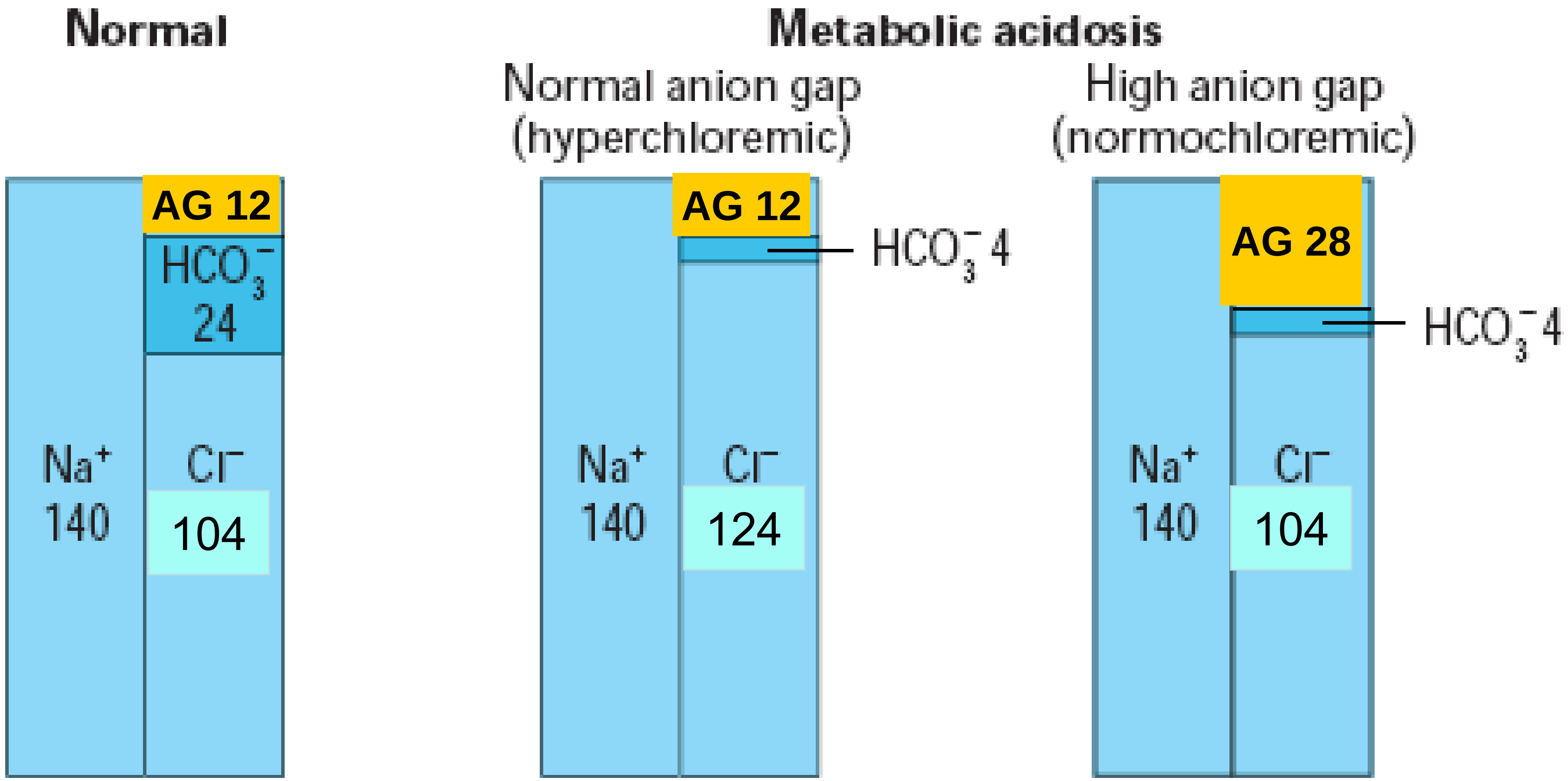
- The difference between the commonly measured serum cations (Na^+) and the measured serum anions (Cl^-, HCO_3^-).

- **Anion gap** = [Sodium] - ([Chloride] + [Bicarbonate])

- The normal anion gap **depends on the laboratory** set up (usually 12 ± 4)

- Alternatively
  - Anion gap = $([Na^+] + [K^+]) - ([Cl^-] + [HCO_3^-])$

Metabolic acidosis - anion gap



Is calculated as the difference between the Na+ concentration and the sum of Cl- and HCO3- concentrations.

Major Clinical Uses of the Anion Gap

- Help differentiate between causes of a **metabolic acidosis:**
  - **high anion gap** metabolic acidosis
  - **normal anion gap** metabolic acidosis
- To assist in assessing the biochemical severity of the acidosis and follow the response to treatment
- **Hypoalbuminaemia causes a low anion gap**

Normal anion-gap acidosis

- GI bicarbonate (HCO3-) losses (diarrhea, ileostomy, colostomy)
- Renal tubular acidosis (RTA)
- Interstitial renal disease
- Ingestion of ammonium chloride, chole-styramine, calcium chloride or magnesium chloride.
- Small bowel or biliary or pancreatic drainage or fistula

Increased anion-gap acidosis

- Ingestion of:
  - Methanol, ethanol, ethylene glycol, aspirin, paraldehyde, salicylates, cyanide
- Renal failure and uremia
- Lactic acidosis
- Alcoholic ketoacidosis or diabetic ketoacidosis

Is the metabolic acidosis associated with an increased anion gap?

- Na^+ 135 mmol/L; HCO_3^- 12 mmol/L; Cl^- 99 mmol/L
- 135 - [99 + 12] = 24 mmol/L
- AG is elevated (normal AG 12 ± 4 mmol/L)

Diabetic F 42 year old

Are there other metabolic processes present?

- For each mmol of anion gap above normal (12 mmol/L) the HCO3- decreases by 1 mmol/L
- **Patients AG = 24** (i.e. 12 mmol/L above normal)
- Corrected HCO3- for given AG
- = [HCO3-] + ([AG] - 12) = (12) + (24-12) = 24
- **Corrected HCO3- is normal** (24 ± 2 mmol/L)
  - **No other metabolic processes** are present

Diabetic F 42 year old

Respiratory system compensation of metabolic acidosis. The expected PaCO2

- Maximal compensation may take 12-24 hours
- The limit of compensation is a PaCO2 of about **10 mmHg**

Is the patient's respiratory system compensating adequately for the metabolic acidosis?

- **Expected PaCO2 = 1.5 x [HCO3-] + 8 ± 2**

- Patients expected $PaCO_2$ = 1.5 x 12 + 8 ± 2 = **24 to 28 mmHg**
- **The measured $PaCO_2$ = 25 mmHg**

- **Respiratory system is compensating adequately**

Diabetic F 42 year old

Acid-base disturbance summary
42 year old diabetic female

- **Metabolic acidosis**
- **Increased anion gap**
- **Compensatory respiratory response** (respiratory alkalosis)
- No other metabolic and/or respiratory acid-base balance disturbances are present

Case report
Acid-base disturbances

A 71 year old male with a history of increasing dyspnea, cough, and sputum production.

Case #3

- A 71 year old male, retired machinist, is admitted to the ICU with a history of increasing dyspnea, cough, and sputum production.
- He has a 120 pack-year smoking history, and quit 5 years ago
- On exam he is moving minimal air despite using his accessory muscles of respiration. He has acral cyanosis

CASE #3

Electrolytes and ABG

- Na+ 135 mmol/L (136-145)
- Cl- 93 mmol/L (98-106)
- HCO3- 30 mmol/L (22-26)
- pH 7.21 (7.38-7.42)
- PaCO2 75 mmHg (38-42)
- PaO2 41 mmHg (90-105)

- Na+ 135, Cl- 93, HCO3- 30, ABG 7.21 / 75 / 41

CASE #3

Differential diagnosis

•HCO_3^- 30 mmol/L, ABG 7.21 / 75 / 41

- Hypoventilation
  - High $PaCO_2$

- Hypoventilation due to COPD

CASE #3

Differential diagnosis
Is hypoventilation complicated by primary pulmonary defect??

•HCO3- 30 mmol/L, ABG 7.21 / 75 / 41

- Pneumonia and pulmonary embolism are two processes that are associated with an increased A-a gradient

- Pneumonia
- Pulmonary embolism

CASE #3

PA-a O2 gradient?

HCO3- 30mmol/L, ABG 7.21 / 75 / 41

- Calculated to be 147 - (1.25 x 75) – 41 = 12
- Expected 71/4 + 4 = < 21
- The oxygen is freely passing from the alveoli to the pulmonary capillaries
- Decrease in ventilation rather than a parenchymal process

CASE #3

Name the acid-base disturbance(s) present?

HCO_3^- 30mmol/L, ABG 7.21 / 75 / 41

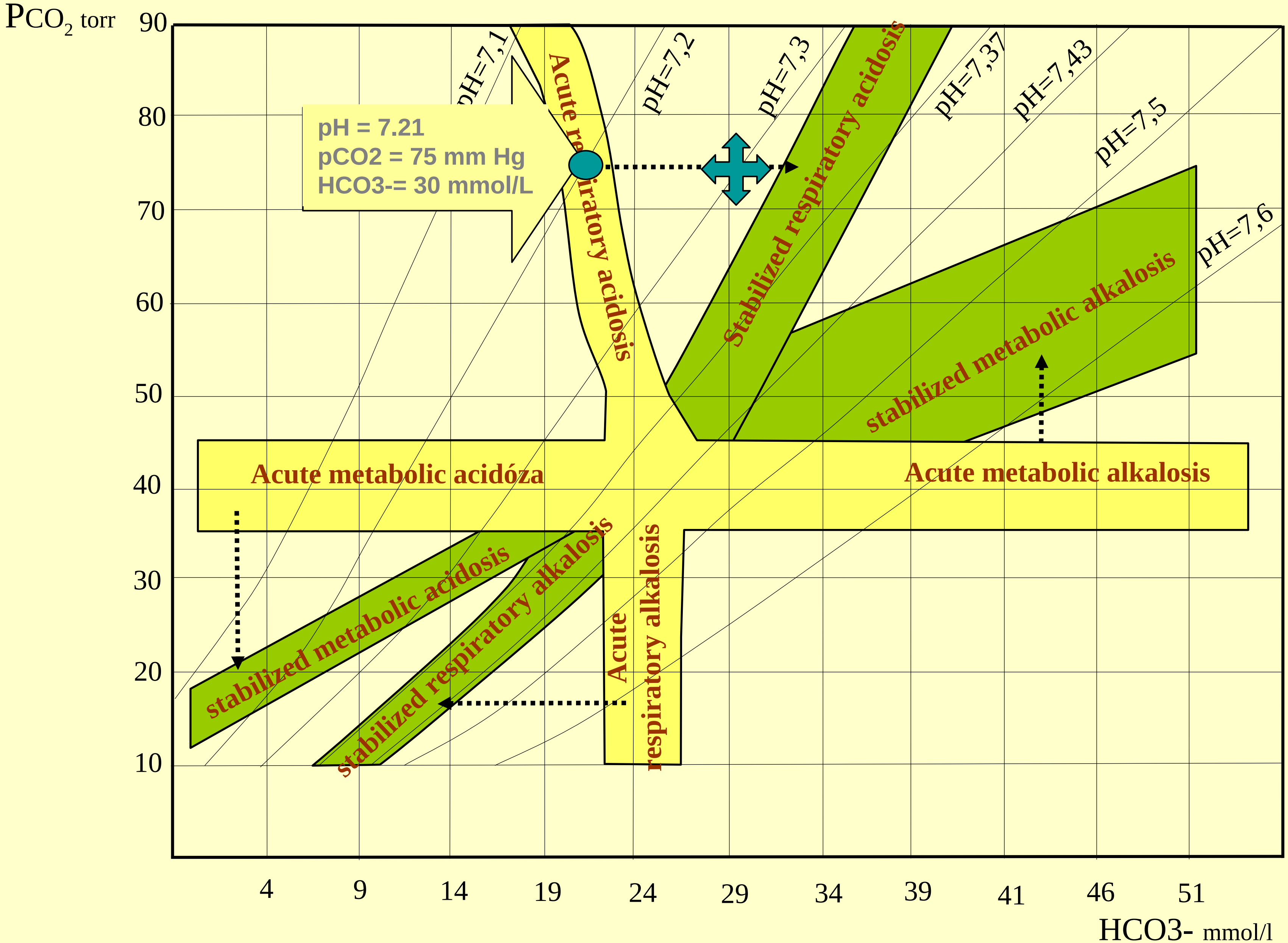
- Respiratory acidosis

Acute or chronic?

- Acute respiratory processes alter the pH by 0.08 for every 10 mm Hg the PCO2 changes.
    - If this process were an acute respiratory acidosis, his pH would change by (0.08)x(35/10)= 0.28 resulting in a pH of 7.12
- Chronic respiratory processes affect the pH by 0.03 for every 10 mm Hg of pCO2.
    - For a pCO2 of 75, the resulting pH would be 7.29

- The pH is between these two values sugesting ongoing compensation ()

CASE #3



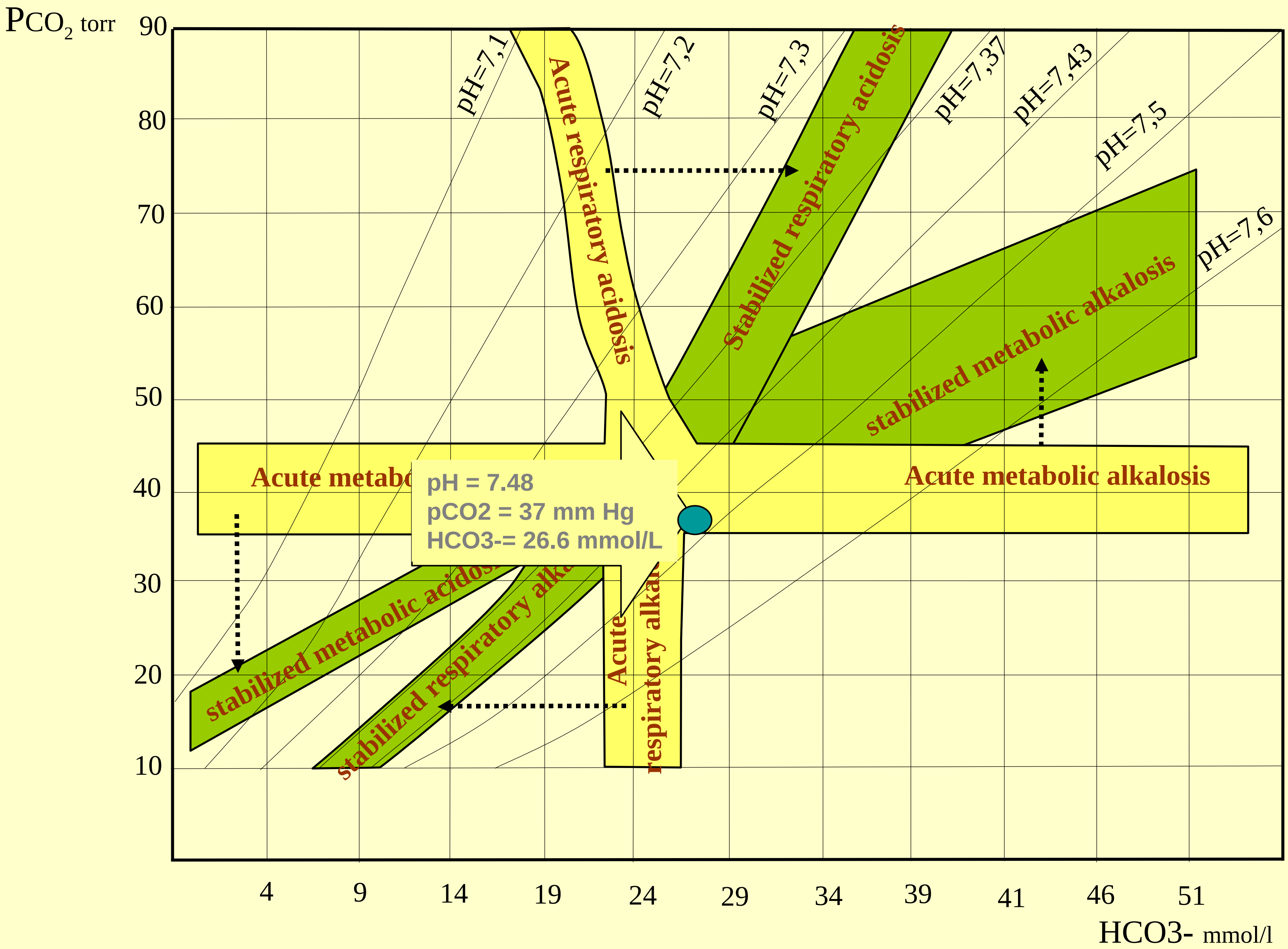
- ABG is 7.48 / 37 / 215

Patient is intubated and mechanically ventilated.

- During the intubation he vomits and aspirates. He is ventilated with an FiO2 of 50%, tidal volumes of 850cc, PEEP of 5, rate of 10

- ABG
  - pH 7.48
  - PaCO2 37 mmHg (35-45)
  - PaO2 215 mmHg (90-105)
  - HCO3- 26.6 mmol/L (22-26)

CASE #3



- ABG is 7.48 / 37 / 215

PA-a O2 gradient (< 20 torr)?

- ABG is 7.48 / 37 / 215
- patient is breathing 50% oxygen ($FiO_2 = 0.5$)
- alveolar gas equation
  $PA\text{-}aO_2 = \underline{FiO_2} \times (760-47) - 1.25\,(PaCO_2) - PaO_2$
- = (0.5)x(713) - 1.25 (37) - 215 = **95 mm Hg**
- markedly elevated A-a gradient
  - acute aspiration

CASE #3

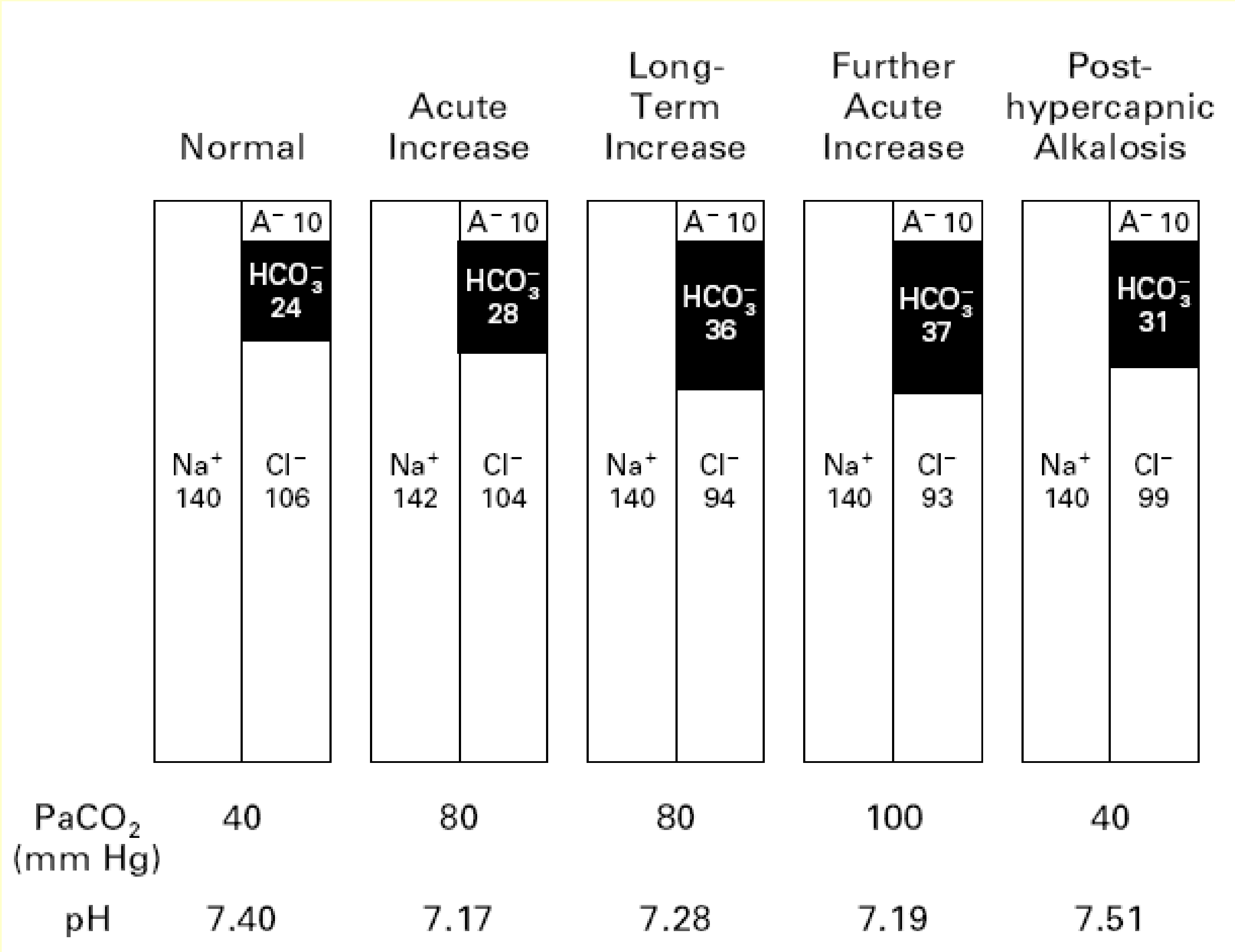
Why is this patient alkalemic with a normal PaCO2?

- Renal compensation (metabolic alkalosis)
- The respiratory problem is resolved with mechanical ventilation

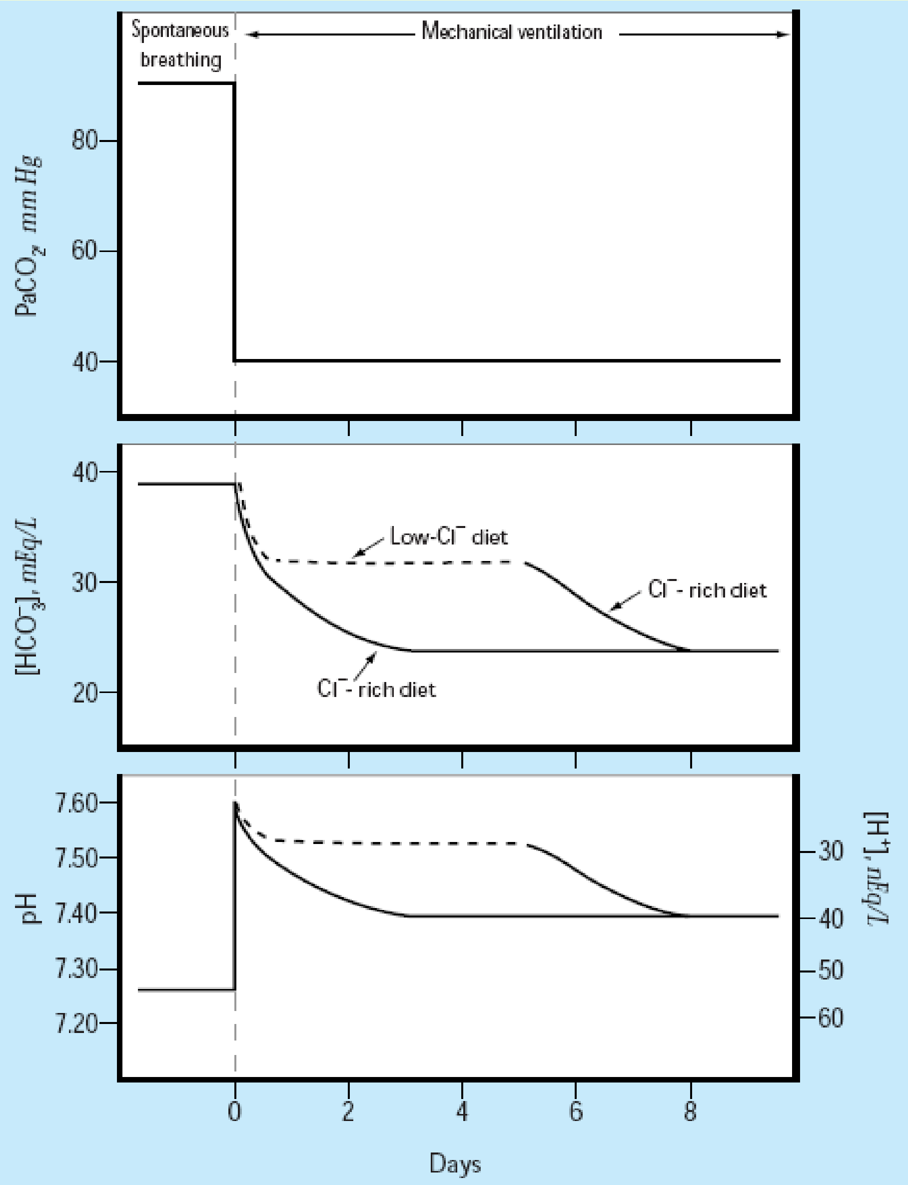
- The kidneys cannot react immediately to this ventilatory change, and the chronic metabolic alkalosis is unveiled

CASE #3

Changes in Acid-Base and Electrolyte Composition in Patients with Respiratory Acidosis



Posthypercapnic metabolic alkalosis



Chloride (Cl-) rich diet

- The excess bicarbonate is excreted by the kidneys over the next 2 to 3 days

Low-chloride (Cl-) diet

- sustains the hyperbicarbonatemia and perpetuates the posthypercapnic metabolic alkalosis.

Case report
Acid-base disturbances

M 23 year old with confusion

A 23 year old man presents with confusion

- A 23 year old man presents with confusion
- He has had diabetes since age 12, and has been suffering from an intestinal flu for the last 24 hours
- He has not been eating much, has vague stomach pain, stopped taking his insulin, and has been vomiting
- His blood glucose is high

Electrolytes and ABG

- **Na+** **130 mmol/L (136-145)**
- **Cl-** **80 mmol (98-106)**
- **HCO3-** **10 mmol/L (22-26)**
- **pH** **7.2 (7.38-7.42)**
- **$PaCO_2$** **25 mm Hg (38-42)**
- **PaO_2** **68 mm Hg (90-105)**
- **BE** **- 15.8 mmol/L**

M 23 year old with confusion

Interpretation of the ABG values

PaO_2 = 68 mm Hg

- Expected PaO_2 for a 22 year old man
  - PaO_2 = 100 – (1/3 x 22) ~ 93 mmHg
- **Patient is hypoxemic** for age

Is hypoxia caused by hypoventilation or primary pulmonary problem?

- **PaCO2**
  - **Hypoventilation = high PaCO2**
  - **Patients paCO2 = 25 mmHg (**
- The A-a 0_2 gradient (P_A-a0_2)
  - Hypoventilation = normal A-a 02 gradient
  - Primary pulmonary problem = PA-a02 increased

- $P_{AO2} = F_{iO2} \times (P_B - P_{H2O}) - P_{aCO2}/0.8$
- Expected A-a gradient < (Age/4) + 4

The A-a 0_2 gradient ($p_{A\text{-}a02}$)

$pA_{O2} = Fi_{O2} \times (P_B – P_{H20}) – Pa_{CO2}/R$

$\mathbf{P_{A\text{-}a02}} = PA_{O2} - Pa_{O2} = [150 – (1.25 \times 25)] – 68 =$ **51 mmHg**

Expected A-a gradient < (Age/4) + 4 = 23/4 + 4 = 9.75 mmHg

M 23 year old with confusion

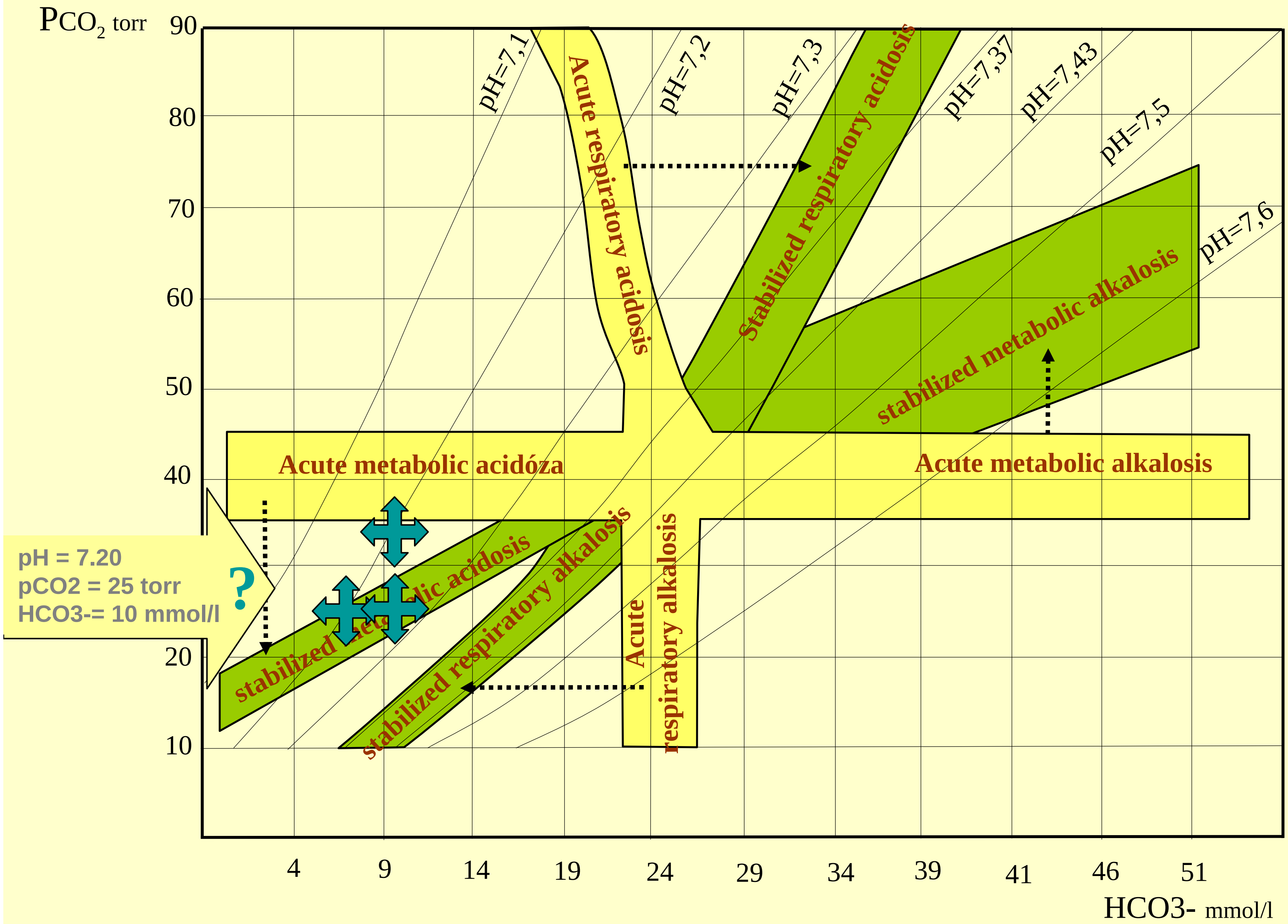
Primary lung problem

- Hypoventilation can be excluded
  - Low PaCO2
  - High PA-a02
- Hypoxia is related to primary lung defect
  - ? aspiration in the confusional state

Determine the acid-base abnormalities

- HCO_3^- =10 mmol/L, ABG = 7.20 / 25 / 68

- Respiratory or Metabolic disturbance?
- The $PaCO_2$ is low (< 40 mmHg)
  - respiratory system is not causing the acidosis
- The bicarbonate is low (< 24 mmol/L)
  - indicates a metabolic acidosis
- So the patient has a <u>metabolic acidosis</u>.



•HCO3- 10 mmol/L, ABG 7.20 / 25 / 68

Determine the acid-base abnormalities

- Na+ 130 mmol/L, Cl- 80 mmol, HCO3- 10mmol/L, ABG 7.20 / 25 / 68
- **Metabolic acidosis**

- **The anion gap (AG)**
  - AG = [Na+] - ([Cl-] + [HCO3-]) = 130-(80+10)= 130-90= 40 mmol/L
- The normal anion gap is 8-16 mmol/L
- Increased anion gap

M 23 year old with confusion

Metabolic acidosis with increased anion gap. Are there other metabolic disturbances?

Na+ 130, Cl- 80, HCO3- 10mmol/L, ABG 7.20 / 25 / 68

- For each mmol of anion gap above normal (12 mmol/L), the HCO3- decreases by 1 mmol/L)
- The anion gap is 40, which is 28 mmol/L above normal
- Corrected HCO3- for the anion gap = measured HCO3- + (AG-12) = (10) + (40-12) = **38 mmol/L**

M 23 year old with confusion

Metabolic acidosis with increased anion gap. Are there other metabolic disturbances?

- Corrected HCO_3^- for the anion gap = measured HCO_3^- + (AG-12) = (10) + (40-12) = **38 mmol/L**
- The corrected HCO_3^- is much higher than a normal HCO_3^- (24+/- 2)
  - suggesting there is a **metabolic alkalosis present**

Metabolic acidosis with an increased anion gap and a co-existing metabolic alkalosis.

M 23 year old with confusion

Is the respiratory system compensating for a metabolic acidosis?

Na+ 130 mmol/L, Cl- 80 mmol, HCO3- 10mmol/L, ABG 7.20 / 25 / 68

- Expected PaCO2 for the given bicarbonate
- **Expected PaCO2** = 1.5 (HCO3-) + 8 $\pm$ 2 = 1.5 (10) + 8 $\pm$ 2 = **23** $\pm$ **2**
- The measured $PaCO_2$ is within the expected range
  - **respiratory system is compensating appropriately**

M 23 year old with confusion

Summary

- Hypoxemia from a primary lung process
- Metabolic acidosis with an increased anion gap
- Coexisting metabolic alkalosis
- Compensatory respiratory alkalosis

End