Chapter 8
Arterial Blood Gas (ABG) Interpretation

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Abstract This chapter reviews the fundamentals in acid-base interpretation and the differential diagnosis for each acid-base pattern. We also discuss oxygen transfer physiology and pathophysiology with a final case based illustration of the topic.

Keywords Arterial blood gas (ABG) · Alkalosis · Acidosis · A-a gradient · Hypoxemia · Hypercapnea

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INTRODUCTION

- If you are given this ABG: pH (7.38); $PaCO_2$ (41 mmHg); PaO_2 (95 mmHg); HCO_3 (23 mmol/L); Na^+ (143 mg/dl); Cl^- (98 mg/dl), how would you interpret it?
- These values are all normal but the patient has significant acid base disturbances that may be fatal, if untreated. This chapter tries to introduce a simple approach to help solving any acid-base problem including the hidden ones, such as the one given above.
- The above ABG is discussed in case number 4, below.

DEFINITIONS [1]

- *Acidosis*: is a disturbance that lowers the extra-cellular fluid pH.
- *Alkalosis*: is a disturbance that raises the extra-cellular fluid pH.
- *Acidemia*: is a reduction of the extra-cellular fluid pH of the blood. Accordingly an acidemia may result from a combination of different types of acidosis or a combination of acidosis and alkalosis.
- *Alkalemia*: is an elevation of the extra-cellular fluid pH of the blood.
- *Base Excess (BE)*: is the amount of acid (+) or base (−) (in mEq/liter) required to restore the pH of a liter of blood to the normal range at a $PaCO_2$ of 40 mmHg. Table 8.1 shows the normal values of the ABG components.

Table 8.1 ABG normal values

pH	7.35–7.45
$PaCO_2$	35–45 mmHg
PaO_2	>80 mmHg
HCO_3	21–26 mmol/L (average: ~24)
BE	0 to −2 mmol/L
SaO_2	>95%
Anion Gap (AG)	10 ± 4 (average: ~12)
$P_{(A-a)}O_2$	<15

To convert from KPa (Kilo-Pascal) to mmHg, multiply by 7.5

HENDERSON EQUATION [2]

- This equation represents the relationship between the components of the ABG and may be written in different ways:
  - A simple way is:

$$\left[H^+\right] = K \times \frac{\left[H_2CO_3\right]}{\left[HCO_3\right]}, \quad \text{where} \quad K = 24$$

  - By substituting $PaCO_2$ for $[H_2CO_3]$ that is measured from ABG, the equation can be written in a more practical way [2]:

$$\left[H^+\right] = K \times \frac{PaCO_2}{\left[HCO_3\right]}, \quad \text{where} \quad K = 24$$

  - $[H^+]$ is the Hydrogen ion (proton) concentration, and it can be easily calculated from pH, see Table 8.2.
  - The rest of the variables can be acquired directly from the ABG.
- The purpose of this equation is:
  - To ensure that the ABG values are accurately recorded. Solving the equation should result in equalization of its two sides.
  - If one of the ABG values is missing, the equation can be solved to determine that missing value. Indeed this is usually done for ABG results. The pH and $PaCO_2$ are actually measured in the blood sample and the HCO_3 is calculated using this equation.

e.g.: pH 7.3 ($[H^+]$ = 50); $PaCO_2$ = 50 mmHg;
HCO_3 = unknown

  - By applying Henderson equation:

$$[H^+] = K \times (P_aCO_2/[HCO_3])$$

$$50 = 24 \times (50/[HCO_3])$$

Therefore: $[HCO_3] = 24$.

Table 8.2 Calculating $[H^+]$ from pH [2]

When pH is within: (7.30–7.50)

pH of 7.40 ↔ $[H^+]$ = 40 nmol/L

Then increasing or decreasing pH by 0.01 is equivalent to decreasing or increasing $[H^+]$ by 1 nmol/L, respectively (remember that $[H^+]$ changes in the opposite direction of pH; for instance: Acidosis decreases pH but increases $[H^+]$)

So if pH is 7.35, then $[H^+]$ will equal 40 + 5 = 45 nmol/L

When pH is outside the range 7.3–7.5, the following applies (Note, this technique can be applied when pH is within the above range too):

pH of 7.00 ↔ $[H^+]$ = 100 nmol/L

Then every increase or decrease of pH by 0.10 is equivalent to multiplying or dividing $[H^+]$ by 0.8

So if pH is 7.10, then $[H^+]$ will equal 100 × 0.8 = 80 nmol/L

If pH is 7.20, then $[H^+]$ will equal 100 × 0.8 × 0.8 = 64 nmol/L

If pH is 7.40, then $[H^+] = 100 \times 0.8^4 = 40$

If pH is 6.80, then $[H^+]$ = 100 / (0.8 × 0.8) = 156

If you don't want to bother yourself with these calculations, the following table can be of help:

pH	[H+]	pH	[H+]
7.00	100	7.35	45
7.05	89	7.40	40
7.10	79	7.45	35
7.15	71	7.50	32
7.20	63	7.55	28
7.25	56	7.60	25
7.30	50	7.65	22

METABOLIC ACIDOSIS

Causes

Metabolic acidosis can be classified into anion gap (AG) and non-anion gap (NAG) metabolic acidosis [3, 4]. The NAG metabolic acidosis is also called *hyperchloremic metabolic acidosis*, because it is associated with high serum chloride. Table 8.3 summarizes these causes.

TABLE 8.3 Causes of metabolic acidosis

Anion gap metabolic acidosis

Uremia

Ketoacidosis

Diabetes

Alcohol-induced

Starvation

Lactic acidosis

Toxin ingestion

Salicylates

Methanol

Ethylene glycol

Paraldehyde

Non-anion gap (hyperchloremic) metabolic acidosis

GI loss of HCO_3

Diarrhea

Ileostomy or colostomy

Uretero-segmoid fistula

Pancreatic fistula

Renal loss of HCO_3

Renal tubular acidosis

Proximal (type II)

Distal (types I and IV)

Carbonic anhydrase inhibitors / deficiency

Hypoaldosteronism, aldosterone inhibitors

Hyperkalemia

Renal tubular disease

Acute tubular necrosis (ATN)

Chronic tubulointerstitial disease

Iatrogenic

Ammonium chloride (NH4Cl)

Hydrochloric acid (HCl) therapy

Hyperalimentation (with TPN lacking citrate buffer)

Dilutional acidosis (caused by excessive isotonic saline infusion)

Approach to Metabolic Acidosis

- In both types of metabolic acidosis, the primary disturbance is a drop in bicarbonate. Because the respiratory system is fast in its compensation, there is a rapid drop in $PaCO_2$

Table 8.4 Approach to ABG interpretation

Determine whether the ABG data are accurate by quickly applying Henderson equation
Look at the pH and determine whether it is normal, acidemic or alkalemic
Determine the most likely primary disturbance (by looking at HCO_3 and $PaCO_2$ and determining which one is largely responsible)
If the primary disturbance is respiratory, determine whether it is acute or chronic
If the primary disturbance is metabolic, determine whether an appropriate respiratory compensation is present
Calculate the AG
Calculate the corrected HCO_3, if applicable

which should always accompany a pure metabolic acidosis (remember that $PaCO_2$ changes in the same direction as HCO_3 in a pure metabolic disturbance). Don't forget that normal bicarbonate doesn't exclude a metabolic disturbance as metabolic acidosis may coexist with metabolic alkalosis.

- We suggest using one of the many available protocols in interpreting the ABG. Table 8.4 summarizes a usefull one.
- The first step is to determine the type of disturbance (acidemia or alkalemia) by looking at the pH.
- Then determine the most likely primary disturbance. So, if a reduction in HCO_3 is the predominant abnormality in the setting of acidemia, then the primary disturbance is a metabolic acidosis.
- Determine the type of metabolic acidosis you are dealing with (AG or NAG) by calculating the AG [5]:

$$\mathbf{AG = Na^+ - (Cl^- + HCO_3^-)}$$

  - If normal (≤12), then this is a non-anion gap metabolic acidosis (NAGMA). Go to the next step.
  - If high (>12), then this is an anion gap metabolic acidosis (AGMA). In AGMA, you need to determine then whether another metabolic disturbance is present, by calculating the corrected HCO_3:

$$\mathbf{Corrected\ HCO_3 = \Delta G + measured\ HCO_3}; \text{ as } \mathbf{\Delta G = AG - 12}$$

(a) If the corrected HCO_3 is *within* the normal range of HCO_3 (21–26), then there is no other metabolic disturbance, so go to the next step.
(b) If the corrected HCO_3 is *higher* than the normal range, then there is an additional metabolic alkalosis (corrected HCO_3 is higher than it should)
(c) If the corrected HCO_3 is *lower* than the range, then there is an additional NAG metabolic acidosis (NAGMA)

- Determine whether there is a primary respiratory disturbance by initially looking at the $PaCO_2$
  - If $PaCO_2$ is normal or high (opposite direction to HCO_3), then there is a primary respiratory acidosis. Go to the next step.
  - If $PaCO_2$ is low (same direction as HCO_3), then calculate the expected $PaCO_2$ range [4, 6]:

$$\textbf{Expected } \mathbf{PaCO_2} \textbf{ Range} = \mathbf{1.5 \times HCO_3 + (8 \pm 2)}$$

(a) If the patient's $PaCO_2$ is *within* this range, then the patient has no respiratory disturbance (this is an appropriate compensation)
(b) If patient's $PaCO_2$ is *above* the range, then there is a primary respiratory acidosis (inadequate compensation).
(c) If patient's $PaCO_2$ is *below* the range, then there is a primary respiratory alkalosis (overcompensation). The lowest level $PaCO_2$ can reach as a compensation for metabolic acidosis is 10–12 mmHg [7].

- In non-anion gap metabolic acidosis, determine whether the cause is of renal or non-renal origin by calculating the urine anion gap (also called Urine Net Charge or UNC) [8]:

$$\textbf{Urine Gap} = \mathbf{(U_{Na} + U_K) - U_{Cl}}$$

  - If urine gap is *negative*, then the kidney is appropriately compensating by secreting H^+ in the form of ammonia (NH_4^+) which neutralizes this negative urine anion gap. An extra-renal cause of metabolic acidosis is the most likely.
  - If urine gap is *positive (or zero)*, then the kidneys are not secreting H^+ appropriately, indicating a renal cause of the metabolic acidosis (Renal tubular acidosis, RTA).
- These steps are summarized in Table 8.5.

Table 8.5 Approach to metabolic acidosis

Quickly apply the Henderson equation
Look at the pH (normal, acidemia or alkalemia).
If the reduction in HCO_3 is the predominant abnormality → primary metabolic acidosis
Calculate the AG ($AG = Na^+ - (Cl^- + HCO_3)$)
If normal (~ 12) → non-anion gap metabolic acidosis (NAGMA)
If high (>12) → anion gap metabolic acidosis (AGMA). Calculate the corrected HCO_3, (corrected $HCO_3 = \Delta G$ + measured HCO_3; as $\Delta G = AG - 12$):
– If within normal range of HOC_3 (21–26) → no other metabolic disturbance
– If >26 → primary metabolic alkalosis
– If <21 → primary non-anion gap metabolic acidosis
Look at $PaCO_2$:
If normal or high → primary respiratory acidosis. If in doubt, calculate expected $PaCO_2$ range
If low → calculate the (expected $PaCO_2$ range) which equals $1.5 \times HCO_3 + (8 \pm 2)$
– If the patient's $PaCO_2$ is within this range → no respiratory disturbance
– If patient's $PaCO_2$ is above the range → primary respiratory acidosis
– If patient's $PaCO_2$ is below the range → primary respiratory alkalosis
In NAGMA, calculate urine anion gap (Urine Gap = $(U_{Na} + U_K) - U_{Cl}$):
If negative → extra-renal cause of metabolic acidosis
If positive → a renal cause of the metabolic acidosis (RTA)

METABOLIC ALKALOSIS

Causes

- Are classified into *Cl^- responsive* and *Cl^- resistant alkaloses*, which are summarized in Table 8.6.

Approach to Metabolic Alkalosis

- Opposite to metabolic acidosis, metabolic alkalosis presents as a high HCO_3 which is compensated for by an increase in $PaCO_2$ [9, 10] (which rarely exceeds a level of 60 mmHg [7]). A normal or a low $PaCO_2$ indicates a respiratory alkalosis, in this setting.

Table 8.6 Causes of metabolic alkalosis

<u>Cl responsive:</u>
GI loss of H^+
Vomiting, nasogastric suctioning
Cl^- rich diarrhea
Villous adenoma
Renal loss of H^+
Diuretics
Hypovolemia
Post-hypercapnia
High-dose carbenicillin
<u>Cl resistant:</u>
Renal loss of H^+
Primary hyperaldosteronism
Increased corticosteroid activity
Primary hypercortisolism
Adrenocorticotropic hormone (ACTH) excess
Drug-induced
Licorice ingestion
Hypokalemia
Increased rinin activity (e.g. renin-secreting tumor)
Iatrogenic
Excessive $NaHCO_3$ infusion
Excessive citrate infusion (massive blood transfusion)
Excessive acetate infusion (hyperalimentation with acetate-containing TPN)
Excessive lactate infusion (Ringer's Lactate)
Milk–alkali syndrome

- Determine the type of disturbance (acidemia or alkalemia) by looking at the pH.
- Then determine the most likely primary disturbance. So if the increase in HCO_3 is the predominant abnormality rather than a decrease in $PaCO_2$, then the primary disturbance is metabolic alkalosis.
- Determine whether a primary metabolic acidosis is present as well by calculating AG:
  - If *normal* (~12), then there is no primary metabolic acidosis. Go to next step.
  - If *high* (>12), then there is an addition primary anion gap metabolic acidosis (AGMA).
- Determine whether there is a primary respiratory disturbance by initially looking at the $PaCO_2$

- If $PaCO_2$ is *normal* or low (opposite direction to HCO_3), then there is a primary respiratory alkalosis. Go to next step.
- If $PaCO_2$ is *high* (same direction as HCO_3), calculate the expected $PaCO_2$ range [11–13]:

$$\textbf{Expected } PaCO_2 \textbf{ Range} = 0.9 \times HCO_3 + (9 \text{ to } 16)$$

(a) If the patient's $PaCO_2$ is *within* this range, then the patient has no additional respiratory disturbance (this is an appropriate compensation).
(b) If patient's $PaCO_2$ is *above* the range, then there is a primary respiratory acidosis (overcompensation).
(c) If patient's $PaCO_2$ is *below* the range, then there is a primary respiratory alkalosis (inadequate compensation).

- Determine the type of metabolic alkalosis (Cl^- responsive or Cl^- resistant) by measuring the urinary Cl^- (U_{Cl}) [1]:
  - If U_{Cl} is <20 mmol/L, then this is Cl^- responsive (depleted) metabolic alkalosis. Think of it as the body is trying to conserve Cl^-.
  - If U_{Cl} is >20 mmol/L, then this is Cl^- resistant (expanded) metabolic alkalosis.
- Table 8.7 summarizes these steps.

TABLE 8.7 Approach to metabolic alkalosis

Quickly apply the Henderson equation
Look at the pH (normal, acidemia or alkalemia)
The increase in HCO_3 is the predominant abnormality → primary metabolic alkalosis
Calculate the AG ($AG = Na^+ - (Cl^- + HCO_3)$)
If normal (~12) → no primary metabolic acidosis
If high (>12) → primary anion gap metabolic acidosis (AGMA)
Look at $PaCO_2$:
If normal or low → primary respiratory alkalosis. If in doubt, calculate expected $PaCO_2$ range
If high → calculate the (expected $PaCO_2$ range = $0.9 \times HCO_3 + (9$ to $16)$):
– If patient's $PaCO_2$ is within this range → no respiratory disturbance
– If patient's $PaCO_2$ is above the range → primary respiratory acidosis
– If patient's $PaCO_2$ is below the range → primary respiratory alkalosis
Check the urinary Cl^- (U_{Cl}):
If <20 mmol/L → Cl^- responsive metabolic alkalosis
If >20 mmol/L → Cl^- resistant metabolic alkalosis

RESPIRATORY ACIDOSIS

Types of Respiratory Acidosis

- Because the body compensates slowly for a primary respiratory disturbance, the later is then classified into acute and chronic forms. The following will highlight these forms.
- In acute respiratory acidosis, for every 10 mmHg rise in $PaCO_2$ [14]:
  - pH drops by 0.08; that is:

$$pH = 0.08 \times \frac{PaCO_2 - 40}{10}$$

  - HCO_3 increases by 1 mmol/L; maximum level of HCO_3 is ~32 mmol/L.
- In chronic respiratory acidosis, for every 10 mmHg rise in $PaCO_2$ [15]:
  - pH drops by 0.03; that is:

$$pH = 0.03 \times \frac{PaCO_2 - 40}{10}$$

  - HCO_3 increases by 3 mmol/L; maximum level of HCO_3 is ~45 mmol/L.
- Tables 8.8 and 8.9 summarize the causes and steps of interpretation of respiratory acidosis, respectively.

Table 8.8 Causes of respiratory acidosis

Obstructive disorders
Upper airway obstruction
Foreign body
Laryngospasm
Obstructed endotracheal tube
Obstructive sleep apnea
Lower airway obstruction
Severe bronchospasm due to bronchial asthma or COPD
Restrictive disorders (see Table 1.7)
ILD
Chest wall restriction
Loss of air spaces (pleural effusion, pneumothorax)
Pleural disease

(continued)

Table 8.8 (continued)

Hypoventilation *Central (e.g. secondary to sedative and narcotic drugs)* *Obesity-hypoventilation syndrome* *Neuromuscular disease* (Table 5.1)
Parenchymal lung disease (like ARDS)
Increased CO_2 production *Fever, shivering* *Hypermetabolism,* *High carbohydrate diet*
Others *Inappropriate ventilator settings* *Compensatory*

Table 8.9 Approach to respiratory acidosis

Quickly apply the Henderson equation.
Look at the pH (normal, acidemia or alkalemia)
The increase in $PaCO_2$ is the predominant abnormality → primary respiratory acidosis
Determine whether acute or chronic
Acute: pH ↓ by 0.08 for every 10 mmHg ↑ in $PaCO_2$. HCO_3 ↑ by 1 mmol/L (max ~32)
Chronic: pH ↓ by 0.03 for every 10 mmHg ↑ in $PaCO_2$. HCO_3 ↑ by 3 mmol/L (max ~45)
Calculate the AG ($AG = Na^+ - (Cl^- + HCO_3)$)
If high (>12) → primary anion gap metabolic acidosis (AGMA)
If applicable, calculate the corrected HCO_3, as in metabolic acidosis
If normal (~ 12) → look at HCO_3
If ↓ or N → primary non-anion gap metabolic acidosis
If ↑ → look at HCO_3 and determine the type of respiratory acidosis: (HCO_3 ↑ by 1 (acute) <u>OR</u> 3 (chronic) for each 10 mmol/L ↑ in $PaCO_2$)
If within the expected → no primary metabolic disturbance
If lower → non-anion gap metabolic acidosis
If higher → metabolic alkalosis

RESPIRATORY ALKALOSIS

Types of Respiratory Alkalosis

- In acute respiratory alkalosis, for every 10 mmHg drop in $PaCO_2$ [16]:
  - pH rises by 0.08; that is:

$$pH = 0.08 \times \frac{40 - PaCO_2}{10}$$

  - HCO_3 drops by 2 mmol/L.
- In chronic respiratory alkalosis, for every 10 mmHg drop in $PaCO_2$ [17, 18]:
  - pH increases by 0.03; that is:

$$pH = 0.03 \times \frac{40 - PaCO_2}{10}$$

  - HCO_3 drops by 5–7 mmol/L.
- Tables 8.10 and 8.11 summarize the causes and steps of interpretation of respiratory alkalosis, respectively.

Table 8.10 Causes of respiratory alkalosis

Increased hypoxemic drive
Right-to-left shunt
High altitude
Pulmonary disease
Pulmonary embolism (leading to dyspnea then hyperventilation)
Pulmonary interstitial edema (leading to dyspnea then hyperventilation)
Stimulation of respiratory center
Anxiety, pain, psychogenic
Liver failure with encephalopathy
Fever, Sepsis, infection
Respiratory stimulants (e.g. salicylates, progesterone)
Pregnancy
Others
Inappropriate ventilator settings
Compensatory

Table 8.11 Approach to respiratory alkalosis

Quickly apply the Henderson equation
Look at the pH (normal, acidemia or alkalemia)
The drop in $PaCO_2$ is the predominant abnormality → primary respiratory alkalosis
Determine whether acute or chronic
Acute: pH ↑ by 0.08 (and HCO_3 ↓ by 2 mmol/L) for every 10 mmHg ↓ in $PaCO_2$
Chronic: pH ↑ by 0.03 (and HCO_3 ↓ by 5–7 mmol/L) for every 10 mmHg ↓ in $PaCO_2$
Calculate the AG (AG = $Na^+ - (Cl^- + HCO_3)$)
If high (>12) → primary anion gap metabolic acidosis (AGMA)
If applicable, calculate the corrected HCO_3, as in metabolic acidosis
If normal (~ 12) → look at HCO_3
If ↑ or N → primary metabolic alkalosis
If ↓ → look at HCO_3 and determine the type of respiratory alkalosis (HCO_3 ↓ by 2 (acute) OR 5–7 (chronic) for each 10 mmol/L ↓ in $PaCO_2$)
If within the expected → no primary metabolic disturbance
If lower → non-anion gap metabolic acidosis
If higher → metabolic alkalosis

EFFECT OF A LOW ALBUMIN LEVEL ON AG

- Because albumin is one of the unmeasured anions in the blood, a drop in its level (e.g. secondary to a critical illness or liver disease) will influence the AG level. In this case, the calculated AG should be adjusted for albumin:

$$\textbf{Adjusted AG} = \textbf{Calculated AG} + [2.5 \times (4.5 - \textbf{alb in g/dl})]$$

- If this adjustment is ignored with a low albumin, the calculated anion gap will be underestimated and a significant AGMA may be missed.

ACID BASE NOMOGRAM

- The nomogram shown in Figure 8.1 is one of many acid-base nomograms developed to assisst in solving difficult acid base disturbances and involves plotting pH, HCO_3 and $PaCO_2$ [19]. These are commonly referred to as Flenley's acid base nomograms.

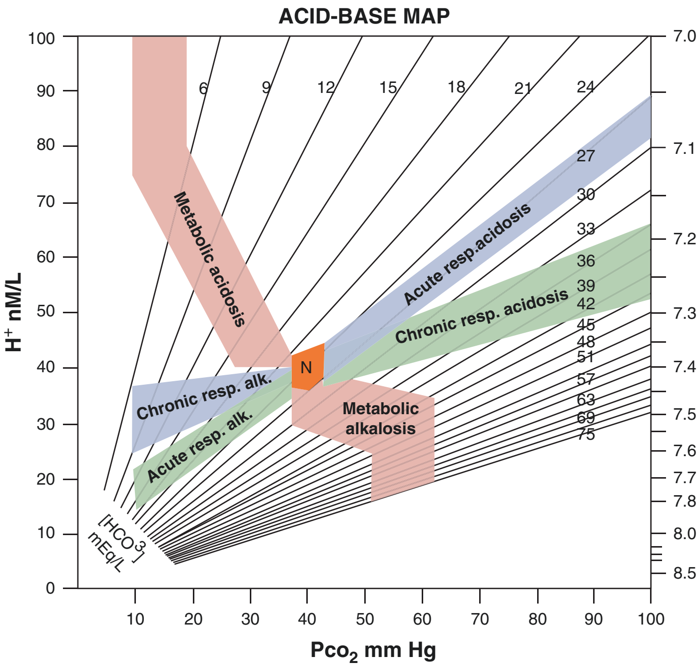

FIGURE 8.1 An acid–base nomogram, used to interpret ABG by directly plotting HCO_3, $PaCO_2$, and pH (With permission from Goldberg et al. [20])

THE ALVEOLAR—ARTERIAL (A-a) GRADIENT AND ALVEOLAR GAS EQUATION [21]

Alveolar Gas Equation

- This equation allows us to estimate the O_2 tension in the alveoli (P_AO_2):

$$P_AO_2 = P_IO_2 - \frac{P_aCO_2}{RQ}; \quad \text{where} \quad P_IO_2 = F_IO_2\left(P_{atm} - P_{H_2O}\right)$$

- To understand this equation it is good to go through certain definitions:
  - $\boldsymbol{P_{atm}O_2}$: is the atmospheric O_2 tension or partial pressure of O_2. It is calculated by multiplying the atmospheric pres-

sure (760 mmHg at sea level) by the percentage of O_2 in the atmosphere (21%):

$$P_{atm}O_2 = 0.21 \times P_{atm} = 0.21 \times 760 = 160 \text{ mmHg}, \textit{(at sea level)}$$

– ***P_IO_2***: is the O_2 tension of inspired air. Because the inspired air contains water vapor, it doesn't equal $P_{atm}O_2$. The water vapor tension (P_{H2O}) should then be extracted from the atmospheric pressure before applying the above equation:

$$P_IO_2 = F_IO_2 \times (P_{atm} - P_{H2O}) = 0.21 \times (760-47) = 0.21 \times 713 = 150 \text{ mmHg}$$

(if breathing room air, at sea level)

– ***P_AO_2***: the alveolar O_2 tension. CO_2 diffuses from the circulation into the alveoli and hence reduces the P_AO_2. Accordingly, P_ACO_2 has to be subtracted from P_IO_2 to get P_AO_2. P_aCO_2 can be substituted for P_ACO_2 (when taking the Respiratory Quotient (RQ) into consideration, which is assumed to be 0.8 while at rest):

$$P_AO_2 = P_IO_2 - \frac{P_aCO_2}{RQ}; \quad \text{as} \quad RQ = 0.8$$

$$= 150 - \frac{P_aCO_2}{0.8} \quad \text{OR} \quad 150 - \left(P_aCO_2 \times 1.25\right)$$

$$= 150 - (40 \times 1.25) = 100 \text{ mmHg}$$

(if breathing room air, at see level)

– ***PaO_2***: is the arterial O_2 tension that is measured in the ABG.
– ***F_IO_2***: is the *Fractional Inspired O_2*, i.e. the percentage of O_2 in the inspired air. If breathing room air at sea level, it equals 0.21. This value changes if the patient is breathing through a nasal cannula or a face mask.
– ***RQ***: is the *Respiratory Quotient* and represents the amount of CO_2 produced for a given amount of O_2 consumed by our bodies. It equals 0.8 at rest, in a normal individual (because we produce 0.8 mole of CO_2 for each mole of O_2 we consume while at rest). The RQ increases with exercise however. Next chapter discusses this in more detail.

A-a Gradient ($P_{(A\text{-}a)}O_2$)

- It is the difference between the alveolar and the arterial O_2 tension. Its calculation is now easy; see Figure 8.2:

$$P_{(A-a)}O_2 = P_AO_2 - P_aO_2; \quad \text{where} \quad P_AO_2 = P_IO_2 - \frac{P_aCO_2}{RQ}$$

$$\text{OR} \quad P_{(A-a)}O_2 = \left[P_IO_2 - \frac{P_aCO_2}{RQ}\right] - P_aO_2$$

- If at see level and breathing room air (F_IO_2 of 0.21), then the equation can be simply written as follows:

$$P_{(A-a)}O_2 = \left[150 - \frac{P_aCO_2}{0.8}\right] - P_aO_2$$

$$\text{OR} \quad P_{(A-a)}O_2 = [150 - (1.25 \times P_aCO_2)] - P_aO_2$$

- $P_{(A\text{-}a)}O_2$ is normally ≤ 15 mmHg and increases with age. Different formulas are used to determine the normal $P_{(A\text{-}a)}O_2$ in relation to age, the following is a popular one [20]:

$$\text{Normal } P_{(A\text{-}a)}O_2 = 2.5 + (0.21 \times \text{age in years})$$

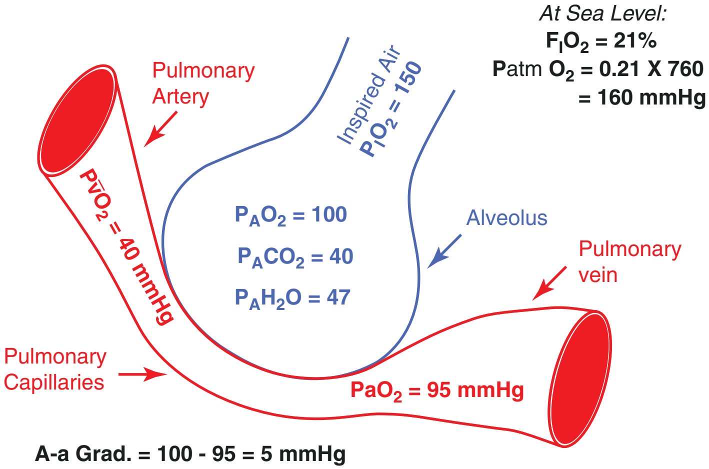

FIGURE 8.2 This diagram summarizes the alveolar gas principles. Breathing RA at sea level in a normal person

MECHANISMS OF HYPOXEMIA [21]

These mechanisms can be classified into hypoxemia with a wide A-a gradient and hypoxemia with a normal A-a gradient:

- Hypoxemia with a wide A-a gradient ($P_{(A\text{-}a)}O_2 > 15$)
  - Shunting, like intra-cardiac shunts or pulmonary AV malformation.
  - VQ mismatch, as in atelectasis
  - Decreased mixed venous O_2 tension $\left(P\bar{v}O_2\right)$.
  - Diffusion limitation (reduced gas tranfer) (seen in severe ILD).
- Hypoxemia with a normal A-a gradient ($P_{(A\text{-}a)}O_2 \leq 15$)
  - Low inspired O_2 (↓ F_IO_2), as in case of high altitude.
  - Hypoventilation, as in *obesity hypoventilation syndrome*.
    (a) Hypoventilation causes primarily hypercapnia because of impaired washout of CO_2. As the alveolar CO_2 equals the arterial CO_2, both PaCO2 and P_ACO_2 will be equally elevated.
    (b) Hypoventilation causes hypoxemia, as well, if the patient is breathing room air. In this case, the degree of hypoxemia can be predicted from the level of $PaCO_2$ using the alveolar gas equation. In general, if P_aCO_2 increases by 20 mmHg, P_AO_2 drops by 25 mmHg, even if the lungs are normal; Figure 8.3.

TYPES OF RESPIRATORY FAILURE [21]

- *Type I respiratory failure* (hypoxemic respiratory failure) is characterized by hypoxia and defined as an isolated reduction of PaO_2 to <60 mmHg (the point at which the SaO_2 drops steeply as shown in the O_2 dissociation curve); Figure 8.4. This type of respiratory failure is associated with an increased A-a gradient.
- *Type II respiratory failure* (ventilatory failure) is characterized by hypoxia and hypercapnia and defined as a $PaCO_2$ of >50 mmHg. The A-a gradient is normal.

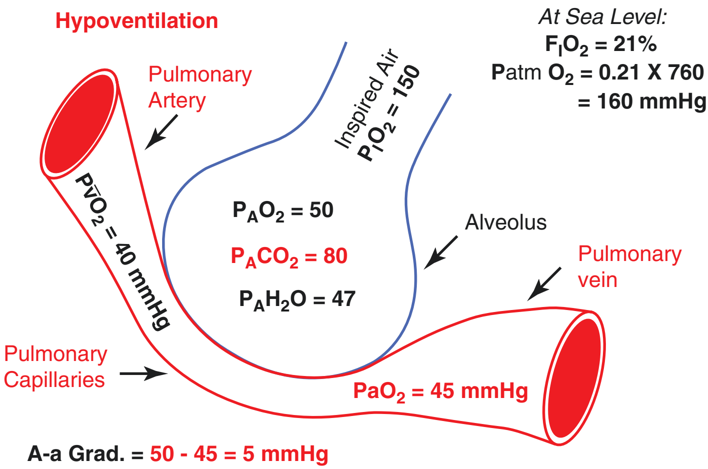

FIGURE 8.3 Effects of hypoventilation on alveolar and arterial O_2 and CO_2 tension: This patient is breathing room air at sea level and has a normal A – a gradient but still has a severe hypoxemia (P_aO_2 of 45). The reason for this hypoxemia is the elevated P_ACO_2 (secondary to hypoventilation). The P_ACO_2 has increased by 40 mmHg resulting in a reduction in P_AO_2 by 50 mmHg, which resulted in this degree of hypoxemia: $P_AO_2 = 150 - (1.25 \times 80) = 150–100 = 50$ mmHg

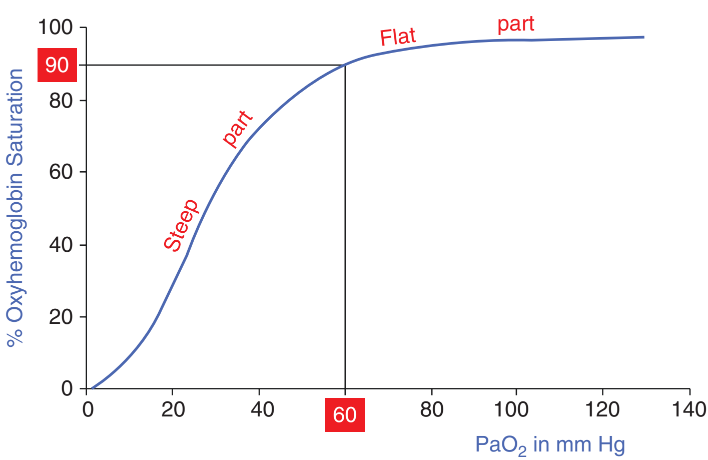

FIGURE 8.4 O_2 dissociation curve: when P_aO_2 > 60 mmHg, SaO_2 changes slightly with any given change in P_aO_2. When P_aO_2 < 60 mmHg, SaO_2 changes significantly with any given change in P_aO_2

ILLUSTRATIVE CASES

Case 1

- *A 63-year-old man presents with generalized malaise. His ABG shows: pH (7.32); $PaCO_2$ (24); HCO_3 (12); Na^+ (135); K^- (5.4); Cl^- (101). What type of acid base disturbance does this patient have?*
- Interpretation:
  – Applying the Henderson equation:

    $$[H^+] = K \times (PaCO_2/ [HCO_3]) \leftrightarrow 48 = 24 \times (24/12) = 48$$

  – So, the equation proves that the values are accurate.
  – pH is ↓, so this is an acidemia.
  – The predominant abnormality is the ↓ HCO_3 → so this is primary metabolic acidosis.
  – By calculating the AG = $Na^+ - (Cl^- + HCO_3) = 22$ (↑). It is >12 → so this is an ***anion gap metabolic acidosis*** (AGMA).
  – Corrected HCO_3 = ΔG + measured HCO_3 (as ΔG = AG – 12 = 10).
    = 10 + 12 = 22; it is within the normal range of HCO_3 (21–26), so there is no other metabolic disturbance.
  – $PaCO_2$: is low, so we should calculate the expected $PaCO_2$ range:
  – Expected $PaCO_2$ Range = $1.5 \times HCO_3 + (8 \pm 2)$= 24–28; the patient's $PaCO_2$ lies within this range, so there is no primary respiratory disturbance.
  – Conclusion: This patient has a pure anion gap metabolic acidosis. This patient was found to have a creatinine of 500 mg/dl and so the unmeasured anions producing the gap were related to renal failure.

Case 2

- *Interpret the following ABG: pH (7.11); $PaCO_2$ (16); HCO_3 (5); Na^+ (133); Cl^- (118).*
- Interpretation:
  – Applying Henderson equation indicates accurate results.
  – ↓ pH → so this is an acidemia.
  – ↓ HCO_3 → so this is a primary metabolic acidosis.

  - AG = $Na^+ - (Cl^- + HCO_3) = 10$ (normal) → so this is a ***non-anion gap metabolic acidosis*** (NAGMA).
  - Expected $PaCO_2$ Range = $1.5 \times HCO_3 + (8 \pm 2) = 13.5$–$17.5$ → the patient's $PaCO_2$ lies within this range, so there is no primary respiratory disturbance.
  - Conclusion: the patient has a simple non-anion gap metabolic acidosis. This patient is a 74-year-old very anxious lady who presented with severe gastroenteritis (diarrhea).

Case 3

- *Interpret the following ABG: pH (6.88); $PaCO_2$ (40); HCO_3 (7); Na^+ (135); Cl^- (118).*
- Interpretation:
  - Applying Henderson equation indicates accurate results.
  - ↓ pH → so this is acidemia.
  - ↓ HCO_3 → so this is primary metabolic acidosis.
  - AG = $Na^+ - (Cl^- + HCO_3) = 10$ (normal) → so this is a ***non-anion gap metabolic acidosis*** (NAGMA).
  - $PaCO_2$ is normal (it should be low in the face of a very low pH) → so, there is a ***primary respiratory acidosis***. Although unnecessary, you can still apply the Expected $PaCO_2$ Range = $1.5 \times HCO_3 + (8 \pm 2) = 16.5$–$20.5$ → the patient's $PaCO_2$ is higher than this range so there is primary respiratory acidosis.
  - Conclusion: A combined non-anion gap metabolic acidosis and respiratory acidosis. This is the same patient described in case 2 after she was sedated with a benzodiazepine that suppressed her respiratory centre. Sedation can be harmful in elderly patients.

Case 4

- *A 23-year-old man presented with generalized malaise and vomiting. His ABG showed: pH (7.38); $PaCO_2$ (41);PaO_2 (95); HCO_3 (23); Na^+ (143); Cl^- (98). What type of acid base disturbance this patient has?*
- Interpretation:
  - Applying Henderson equation indicates accurate results.
  - Normal pH → so no acidemia or alkalemia.
  - Normal HCO_3 → so no obvious metabolic abnormality.

- AG = Na^+ – (Cl^- + HCO_3) = 22 (↑) → so there is an ***anion gap metabolic acidosis***.
- Corrected HCO_3 = ΔG + measured HCO_3 (ΔG = 22–12 = 10). = 10 + 23 = 33; So, the corrected HCO_3 = 33 → it is higher the normal range of HCO_3 (21–26) → so there is an additional ***metabolic alkalosis***.
- $PaCO_2$ is normal (so does the pH and HCO_3, so this is appropriate. If in doubt, apply expected $PaCO_2$ range).
- Expected $PaCO_2$ Range = 1.5 × HCO_3 + (8 ± 2) = 41–45 → the patient's $PaCO_2$ (41) lies within this range → so, there is no primary respiratory disturbance.
- Conclusion: Although this ABG looked normal, a combined disturbance is present, anion gap metabolic acidosis and metabolic alkalosis. This patient was found to have a blood sugar of 28 mmol/L and he had ketones in the urine. He had diabetic ketoacidosis causing his AGMA and vomiting caused his metabolic alkalosis.

Case 5

- *Interpret this ABG: pH (7.55); $PaCO_2$ (49); HCO_3 (42); Na^+ (148); Cl^- (84).*
- Interpretation:
  - Applying Henderson equation indicates accurate results.
  - ↑ pH → so there is an alkalemia.
  - ↑ HCO_3 → so there is a ***metabolic alkalosis***.
  - AG = Na^+ – (Cl^- + HCO_3) = 22 (↑) → so there is an ***anion gap metabolic acidosis***.
  - ↑ $PaCO_2$ (same direction as HCO_3) → Expected $PaCO_2$ Range = 0.9 × HCO_3 + (9-to-16) = 47–54 → the patient's $PaCO_2$ (49) lies within this range → so, there is no primary respiratory disturbance.
  - Conclusion: a combined anion gap metabolic acidosis and metabolic alkalosis with an alkalemic pH.

Case 6

- *A 58-year-old man (heavy smoker) admitted to the ICU with sepsis. He is not intubated yet but has an NG tube. His ABG* *showed: pH (6.88); $PaCO_2$ (40); HCO_3 (7); Na^+ (142); Cl^- (100). What type of acid base disturbance does this patient have?*

- Interpretation:
  - Applying the Henderson equation indicates accurate results.
  - ↓ pH → so this is an acidemia.
  - ↓ HCO_3 → so this is a ***primary metabolic acidosis***.
  - AG = $Na^+ - (Cl^- + HCO_3)$ = 35 (↑) → so this is an ***anion gap metabolic acidosis***.
  - Corrected HCO_3 = 30; it is higher than the normal range of HCO_3 (21–26), so there is an additional ***primary metabolic alkalosis***.
  - $PaCO_2$ is normal (it should be low) → there is a ***primary respiratory acidosis***.
  - Conclusion: A combined anion gap metabolic acidosis, metabolic alkalosis and respiratory acidosis. This patient's metabolic acidosis is most likely related to sepsis. His respiratory acidosis is likely due to respiratory failure (COPD) and the metabolic alkalosis due to gastric suction.

Case 7

- *Interpret the following ABG: pH (7.55); $PaCO_2$ (44); HCO_3 (45); Na^+ (144); Cl^- (112).*
- Interpretation:
  - Applying Henderson equation:

    $$[H^+] = K \times (PaCO_2/ [HCO_3]) \leftrightarrow 28 \neq 24 \times (44/45) = 21$$

    So, the equation indicates that the values are incorrect. Repeat ABG sampling is advised or check with the lab to ensure accurate calculation of HCO_3 and recording of results.

Case 8

- *A 68-year-old man known to have COPD presented to the emergency department with increasing cough. His ABG showed: pH (7.34); $PaCO_2$ (60); PaO_2 (60); HCO_3 (31); AG (11). What is the* *acid base disturbance? What is the A-a gradient provided that the patient was on room air, at sea level?*.

- Interpretation:
  - Applying Henderson equation indicates accurate results.
  - pH is slightly low indicating a mild acidemia.
  - ↑ $PaCO_2$, so this is a ***primary respiratory acidosis***.
  - Metabolic compensation indicates a chronic respiratory acidosis: $PaCO_2$ increased by 20 mmHg which corresponds to a drop in pH by ~ 0.6 (0.3/10 mmHg of $PaCO_2$) and an increase in HCO_3 by ~ 6 (3/10 mmHg of $PaCO_2$).
  - AG is normal and HCO_3 is adequately increased, therefore no metabolic disturbances.
  - The A-a gradient = $(150 - PaCO_2 \times 1.25) - PaO_2 = 11$ (normal)
  - Conclusion: Chronic primary respiratory acidosis related to COPD.

Case 9

- *The patient in case 8 became drowsy and unresponsive 4 hours after presentation. A repeated ABG showed: pH (7.15); $PaCO_2$ (96); PaO_2 (169) HCO_3 (33); AG (10).*
- Interpretation:
  - Applying Henderson equation indicates accurate results.
  - ↓ pH → acidemia.
  - ↑ $PaCO_2$ → so this is ***primary respiratory acidosis***.
  - Metabolic compensation indicates an acute respiratory acidosis in addition to the chronic respiratory acidosis.
  - AG is normal and HCO_3 is adequately increased, therefore no metabolic disturbances.
  - Conclusion: Acute primary respiratory acidosis and a chronic respiratory acidosis. This COPD patient was given a high flow O_2 (indicated by the high PaO_2) unnecessarily resulting in CO_2 elevation (the pathophysiology behind this is multifactorial) and severe acute respiratory acidosis. The acute increase in $PaCO_2$ resulted in mental deterioration and unresponsiveness.

Case 10

- *The patient in the previous case was intubated and mechanically ventilated to protect his airways. A repeat ABG showed: pH (7.55); $PaCO_2$ (39); PaO_2 (198); HCO_3 (33); AG (10).*
- Interpretation:
  - Applying the Henderson equation indicates accurate results.
  - ↑ pH, therefore alkalemia.
  - The elevated HCO_3 indicates a metabolic alkalosis resulting from overcorrecting the chronic respiratory acidosis. The elevated HCO_3 was primarily a compensatory mechanism for the respiratory acidosis. The resulting metabolic alkalosis is sometimes called "*post-hypercapnic metabolic alkalosis*". The ventilator should have been set to target a normal pH rather than a normal HCO_3.

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