

Neonatal blood gas: read it right, step by step

Sample quality, compensation rules, neonatal anion gap, Winters's formula and oxygenation indices.



REFERENCES

1. Travers C, Ambalavanan N. Blood gases: technical aspects and interpretation. In: Keszler M, Gautham KS, eds. *Goldsmith's Assisted Ventilation of the Neonate*. 7th ed. Elsevier; 2022. Ch. 10, p. 94–110.
2. Mathew B, Lakshminrusimha S. Noninvasive monitoring of gas exchange. In: *Goldsmith's Assisted Ventilation of the Neonate*. 7th ed. Elsevier; 2022. Ch. 11.
3. Albert MS, Dell RB, Winters RW. Quantitative displacement of acid-base equilibrium in metabolic acidosis. *Ann Intern Med*. 1967;66:312–22.
4. Adrogué HJ, Madias NE. Secondary responses to altered acid-base status: the rules of engagement. *J Am Soc Nephrol*. 2010;21:920–3.
5. Berend K, de Vries AP, Gans RO. Physiological approach to assessment of acid-base disturbances. *N Engl J Med*. 2014;371:1434–45.
6. Lorenz JM, Kleinman LI, Markarian K, et al. Serum anion gap in the differential diagnosis of metabolic acidosis in critically ill newborns. *J Pediatr*. 1999;135:751–5.
7. Kraut JA, Madias NE. Serum anion gap: its uses and limitations in clinical medicine. *Clin J Am Soc Nephrol*. 2007;2:162–74.
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9. Kliegman RM, St Geme JW III, Blum NJ, et al. *Nelson Textbook of Pediatrics*. 22nd ed. Elsevier; 2025.
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Six steps, every gas

Arterial blood gas remains the gold standard for oxygenation and ventilation in sick neonates, but only if it is read in order.

STEP 0

Trust the sample?

Air bubbles, dilution, delay, capillary site, HbF, temperature.

STEP 1

pH

Acidemia or alkalemia?

STEP 2

PaCO_2 + expected pH

Is the pH fully explained by the CO_2 ?

STEP 3

HCO_3^- / BE / lactate

Metabolic component and its origin.

STEP 4

Expected compensation

Winters's, alkalosis rule, respiratory acidosis rule.

STEP 5

Anion gap + oxygenation

Neonatal AG range; CaO_2 , OI, OSI, AaDO_2 .

A gas that is very different from the previous one is either **a major change in the patient** or **a measurement error**. Never interpret it without the clinical picture.

Errors happen **before** the analyzer

Pre analytical errors (collection and handling) are the ones clinicians meet most often.

Problem	Effect on the result
Air bubbles	PaCO ₂ falls. PaO ₂ moves toward ~150 mmHg (rises if it was below, falls if above). Even a butterfly set exposes enough air.
Dilution with IV fluid	PaCO ₂ falls and base deficit rises, with almost no pH change: mimics metabolic acidosis + respiratory alkalosis .
Lipid emulsion · dry heparin	No relevant effect.
Processing delay	Cells keep consuming O ₂ . PaO ₂ /SaO ₂ stable up to 30 min (room temp or iced); PaCO ₂ rises after 20 min, not clinically significant.
Lactate	Run within 15 min , or it rises in the syringe.

Expel every air bubble before the sample goes into the analyzer.

Three traps that are unique to the NICU

1 • Arterialized capillary sample

- Simultaneous UAC vs. warmed heel: a **poor predictor** of arterial pH, PaCO₂ and PaO₂.
- Most useful in chronically ventilated infants, to track **large changes** in pH and PaCO₂.
- Never titrate FiO₂ on a capillary PaO₂.

2 • Fetal hemoglobin and the reported SaO₂

- Most analyzers **calculate** SaO₂ from PaO₂ assuming adult hemoglobin.
- With high HbF (left-shifted curve) the calculated saturation is **falsely low**.
- Need the real value? Use **co-oximetry**.

3 • Temperature (therapeutic hypothermia)

- Analyzers report at 37 °C; cooled infants are at 33.5 – 34.5 °C.
- The 37 °C result may not reflect the patient's true status, and there is no consensus on correction.
- Some centers report **both** corrected and uncorrected values.

pH first: which side are we on?

7.35 – 7.45

Normal pH

 $\text{HCO}_3^- : \text{CO}_2 = 20 : 1$

Carbonic acid–bicarbonate buffer

- Across the whole pH range compatible with life (6.9–7.6), $[\text{H}^+]$ varies by **less than 0.13 mmol/L**: control is extremely tight.
- Compensation (a "secondary response") brings the pH **toward** normal but usually does not fully correct or overcorrect it.
- **Respiratory** response: starts almost immediately and acts within minutes.
- **Renal** response: starts in 6–12 h and takes **3–5 days**.

Primary disorder	pH	Primary change
Respiratory acidosis	↓	PaCO_2 ↑
Respiratory alkalosis	↑	PaCO_2 ↓
Metabolic acidosis	↓	HCO_3^- ↓ (BE more negative)
Metabolic alkalosis	↑	HCO_3^- ↑

A "normal" pH with abnormal PaCO_2 and HCO_3^- is a **mixed disorder** until proven otherwise.

Does the CO₂ explain the pH?

Normal PaCO₂: 35 - 45 mmHg. An acute change in PaCO₂ moves the pH by a predictable amount.

Hypercarbia: expected pH = 7.40 - (PaCO₂ - 40) × 0.006

Hypocarbia: expected pH = 7.40 + (40 - PaCO₂) × 0.01

Example: PaCO₂ 55 mmHg → 15 × 0.006 = 0.09 → expected pH **7.31**.
If the measured pH differs by **more than ± 0.03**, a **metabolic disorder must be present**.

- Alveolar ventilation = RR × (V_T - dead space). Dead space can reach **20% of V_T** in intubated ELBW infants.
- This check works without looking at HCO₃⁻ or BE.

Base excess and lactate: **know their limits**

Base excess / base deficit

- Amount of acid or base needed to return pH to 7.4 at normal PaCO₂.
- Derived from **nomograms**: values **differ between analyzer manufacturers**.
- HCO₃⁻ on the gas report is **calculated**, not measured.

Lactate

- Term infants: usually **< 2.0 mmol/L** (use local reference values).
- Arterial, venous and capillary values correlate well. Run within 15 min.
- The highest lactate in the first hours predicts **moderate to severe HIE** after intrapartum asphyxia.
- Separates **acid production** (poor O₂ delivery) from **bicarbonate loss** (e.g. renal tubular acidosis).

Winters's formula: is ventilation keeping up?

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$$\text{Expected pCO}_2 = (1.5 \times \text{HCO}_3^-) + 8 \quad (\pm 2) \text{ mmHg}$$

Example: HCO_3^- 12 → expected pCO₂ **26** (24–28 mmHg)

- Measured pCO₂ **above** the range → coexisting **respiratory acidosis**.
- Measured pCO₂ **below** the range → coexisting **respiratory alkalosis**.
- In a ventilated neonate, the "respiratory response" is **your ventilator settings**.

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Winters' formula - Expected PCO2 compensation in metabolic acidosis

HCO₃ (mEq/L)
12

26 mmHg
Expected PCO₂: expected partial pressure of carbon diox...

24 mmHg - 28 mmHg
Expected PCO₂ range

Interpretation of the result

Compare the calculated PCO₂ with the patient's PCO₂ obtained from blood gas analysis as follows:

- Patient's PCO₂ is higher than the calculated (expected) PCO₂: the patient has an associated respiratory acidosis (hypoventilation).
- Equal values (within a ±2 range): respiratory compensation is adequate. This is a pure metabolic acidosis.
- Patient's PCO₂ is lower than the calculated (expected) PCO₂: the patient has an associated respiratory alkalosis (hyperventilation).

Note: formula used: $\text{PCO}_2 = (1.5 \times [\text{HCO}_3^-]) + 8$. (range ± 2)

Anion gap: use the neonatal range

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$$AG = Na^+ - (Cl^- + HCO_3^-)$$

Without potassium · mEq/L

AG (mEq/L)	Reading
4 – 12	Normal neonatal range (8 ± 4)
> 12	Elevated
> 16	In metabolic acidosis, suggests lactic acidosis

- Between 8 and 16, the AG **does not differentiate** the causes.
- Range from critically ill newborns in week 1. It **varies with the analyzer**.

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Anion gap

Σ FORMULA

AG = Na⁺ – (Cl[–] + HCO₃[–])

Na⁺ (mEq/L)

Na⁺ in mEq/L, from 100 to 200

Cl[–] (mEq/L)

Cl[–] in mEq/L, from 50 to 150

HCO₃[–] (mEq/L)

HCO₃[–] in mEq/L, from 1 to 60

Albumin-corrected anion gap

>

Notes

The calculation does not include potassium. The neonatal range comes from critically ill neonates in the first week of life (Lorenz 1999) and varies with the analyzer. In metabolic acidosis, an AG above 16 suggests lactic acidosis; between 8 and 16, it does not differentiate the causes (Lorenz 1999).

Na⁺, Cl[–] and HCO₃[–]: 1 mEq/L = 1 mmol/L.

Reference

- Kraut JA, Madias NE. Serum anion gap: its uses and limitations in clinical medicine. Clin J Am Soc Nephrol 2007;2:162-74.
- Lorenz JM, Kleinman LI, Markarian K, Oliver M, Fernandez J. Serum anion gap in the differential diagnosis of metabolic acidosis in critically ill newborns. J Pediatr 1999;135:751-5.

Metabolic alkalosis: often iatrogenic

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Expected $p\text{CO}_2$ =
 $20 + 0.7 \times (\text{HCO}_3^-) (\pm 5)$
 mmHg

Example: HCO_3^- 34 → expected $p\text{CO}_2$ **43.8**
 (38.8 – 48.8 mmHg)

Neonatal causes

- Compensated chronic respiratory acidosis with PaCO_2 **lowered too fast**.
- Chronic diuretics (hypochloremia); gastric losses.
- Excess acetate in PN; citrate after exchange transfusion.

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Expected $p\text{CO}_2$ in metabolic alkalosis

Σ FORMULA

Rule 1 (Oh's): $p\text{CO}_2 = 0.9 \times \text{HCO}_3^- + 9 (\pm 2)$ mmHg

Rule 2 (Boston): $p\text{CO}_2 = 0.7 \times \text{HCO}_3^- + 20 (\pm 5)$ mmHg

Rule 3 (Adrogué and Madias; Harriet Lane): $p\text{CO}_2 = 40 + 0.7 \times (\text{HCO}_3^- - 24)$ mmHg

HCO_3^- (mEq/L)

34

HCO_3^- in mEq/L, from 15 to 60

39.60 mmHg (37.60 to 41.60)

Expected $p\text{CO}_2$, rule 1: $0.9 \times \text{HCO}_3^- + 9$

43.80 mmHg (38.80 to 48.80)

Expected $p\text{CO}_2$, rule 2: $0.7 \times \text{HCO}_3^- + 20$

47.00 mmHg

Expected $p\text{CO}_2$, rule 3: $40 + 0.7 \times (\text{HCO}_3^- - 24)$

Notes

The three rules were derived from studies in adults (and partly in dogs) and differ from one another by about 3 to 11 mmHg, depending on HCO_3^- ; Berend 2014 notes that the respiratory response in metabolic alkalosis is difficult to predict. The range of rule 1 is Morgan's (Oh's); the range of rule 2 is Brandis's.

Classically, appropriate respiratory compensation does

Respiratory acidosis: acute or chronic?

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Phase	Expected HCO_3^- rise
Acute	+1 mEq/L per 10 mmHg rise in pCO_2
Chronic > 2 – 5 days	$\approx +4$ (3.5 – 5) mEq/L per 10 mmHg rise in pCO_2

Example: infant with BPD, pCO_2 60 mmHg for weeks → expected $\text{HCO}_3^- \approx 24 + 2 \times (3.5-4) = 31-32$ mEq/L.

- HCO_3^- lower than expected → added metabolic acidosis.
- HCO_3^- higher than expected → added metabolic alkalosis (e.g. diuretics).

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Acid-base balance

METABOLIC ACIDOSIS

Winters' formula >

Anion gap >

Albumin-corrected anion gap >

METABOLIC ALKALOSIS

Expected pCO_2 in metabolic alkalosis >

RESPIRATORY ACIDOSIS

Expected metabolic compensation

Acute phase

+ 1 mEq/L of HCO_3^- for every 10 mmHg rise in pCO_2

Chronic phase

about + 4 (3.5 to 5) mEq/L of HCO_3^- for every 10 mmHg rise in pCO_2

Chronic: 2 to 5 days (Berend 2014).

Reference

- Winters' formula: Albert MS, Dell RB, Winters RW. Quantitative displacement of acid-base equilibrium in metabolic acidosis. Ann Intern Med 1967;66:312-22.
- Respiratory acidosis: Adrogué HJ, Madias NE. Secondary responses to altered acid-base status: the rules of engagement. J Am Soc Nephrol 2010;21:920-3.
- Respiratory acidosis: The Harriet Lane Handbook. 23rd ed. Elsevier; 2023. Table 11.14.
- Respiratory acidosis: Berend K, de Vries AP, Gans RO. Physiological approach to assessment of acid-base disturbances. N Engl J Med 2014;371:1434-45. Table 1.

Sodium bicarbonate: rarely, and slowly

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Not for routine use. **No longer recommended in CPR.** May be harmful in hypoxia with metabolic acidosis: treat the cause and restore O₂ delivery.

$$\text{HCO}_3^- \text{ (mEq)} = \text{base deficit} \times \text{weight (kg)} \times 0.3$$

- 8.4% (1 mEq/mL) diluted 1:1 with sterile water → 0.5 mEq/mL.
- Infuse slowly, preferably over **30–60 min.**
- Generates CO₂: caution in mixed acidosis unless minute ventilation rises.

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Bicarbonate deficit

Weight (kg)

2

Target HCO₃⁻ (mEq/L)

24

Patient's current HCO₃⁻ (mEq/L)

15

Patient's blood gas value

5.4 mEq

Bicarbonate deficit · ΔHCO₃⁻ 9 mEq/L

The app converts this dose to mL of 8.4% bicarbonate in the Medications section:

Sodium bicarbonate (metabolic acidosis)

Note: HCO₃⁻ required (mEq) = (target HCO₃⁻ – current HCO₃⁻) × 0.3 × weight (kg). For bicarbonate, 1 mEq = 1 mmol (monovalent ion), which is why both values coincide.

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Medicines

Sodium bicarbonate

Metabolic acidosis (calculation based on base deficit)

Calculate the HCO_3^- deficit

I already have the HCO_3^- deficit

8.4%

mEq/L

mg/dl

Weight (kg)

2

HCO_3^- deficit (mEq/L)

5.4

Sodium bicarbonate

I already have the HCO_3^- deficit - 8.4%

Dose	3.24mEq
Dose	3.24mL
Dilution	
Dilute the dose in mL with SWFI	3.24mL
Final concentration after dilution	0.5mEq/mL
Total volume to be administered	6.48mL
Infusion time (at 1 mEq/kg/h)	1h38min
Pump rate (0.5 mEq/mL solution)	4mL/h

OXYGENATION

PaO₂ is **not** oxygen content

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$$\text{CaO}_2 = (\text{Hb} \times 1.34 \times \text{SaO}_2) + (\text{PaO}_2 \times 0.0031)$$

Example: Hb 15, SaO₂ 95%, PaO₂ 60 → **19.3 mL/dL**, of which only 0.2 is dissolved.

- Hemoglobin carries almost all the O₂: raising PaO₂ adds very little.
- HbF shifts the curve to the **left**: higher SaO₂ at the same PaO₂. Transfusion of adult Hb shifts it back.
- O₂ delivery also depends on cardiac output (120–150 mL/kg/min).

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Arterial Oxygen Content - CaO2

Σ FORMULA

CaO2 = (Hb × 1.34 × SaO2) + (PaO2 × 0.0031)

Hb (g/dL)

SaO2

Values between 0 and 1.0, where 1 equals 100%.

PaO2 (mmHg)

Reference values

Normal: 18 – 20 mL/dL. Reference venous content is 13 to 16 mL/dL, and the arteriovenous difference 4 to 5.5 mL/dL.

Source: Knobel.

Reference

- Elias Knobel, Adalberto Stape, Eduardo Juan Troster, Alice D'Agostini Deutsch - Terapia Intensiva: Pediatría e Neonatología - Atheneu, p. 851 e 853 — formula and normal range.
- Ashok P. Sarnaik, Shekhar T. Venkataraman, Bradley A. Kuch - Mechanical Ventilation in Neonates and Children: A Pathophysiology-Based Management Approach - Springer (2022), p. 26 — formula.



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Arterial Oxygen Content - CaO2

Σ FORMULA

$$\text{CaO}_2 = (\text{Hb} \times 1.34 \times \text{SaO}_2) + (\text{PaO}_2 \times 0.0031)$$

Hb (g/dL)

15

SaO2

0.95

Values between 0 and 1.0, where 1 equals 100%.

PaO2 (mmHg)

60

19.28 mL/dL

Arterial oxygen content

Normal (18 – 20 mL/dL)

CaO2 between 18 and 20 mL/dL: the total amount of oxygen carried in arterial blood is within the expected range.

Reference values

Normal: 18 – 20 mL/dL. Reference venous content is 13 to 16 mL/dL, and the arteriovenous difference 4 to 5.5 mL/dL.

Source: Knobel.

Reference

- Elias Knobel, Adalberto Stape, Eduardo Juan Trost, Alice D'Agostini Deutsch - Terapia Intensiva: Pediatria e



OI and OSI: severity, with or without a gas

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$$OI = FiO_2 \times 100 \times MAP \div PaO_2$$

$$OSI = FiO_2 \times 100 \times MAP \div SpO_2$$

Predictal $SpO_2 \cdot OI \approx 2 \times OSI$ (SpO_2 70–99%)

Example: MAP 12, FiO_2 0.6, SpO_2 90% → OSI 8 → OI ≈ 16

OI	Published cutoffs
> 15	Severe respiratory compromise
> 25	Consider ECMO
≥ 40	Historically ~80% mortality; ECMO criterion

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Índice de Saturação de Oxigênio - OSI

Σ FÓRMULA

OSI = (MAP × FiO2 × 100) ÷ SpO2

Calcular a Pressão Média de Via Aérea >

Sobre o OSI

O Índice de Saturação de Oxigênio é uma versão não invasiva do Índice de Oxigenação (OI).

MAP (cmH2O)

FiO2

Valores entre 0,21 e 1,00, onde 1,00 equivale a 100% e 0,40, a 40%, por exemplo.

SpO2 (%)

Insira um valor inteiro entre 1 e 100, como 94 para uma saturação de 94%.

Ver Índice de Oxigenação (IO) >

Referência

- Textbook of Pediatrics - 22nd Edition - Elsevier, p. 616
- Formula e definição PARDS 2.0.
- Keszler (editor), K. Suresh Gautham (editor) - Smith's Assisted Ventilation of the Neonate - 7th Edition - Elsevier (2022), p. 116 — relação com o Índice de Oxigenação.



Oxygen Saturation Index - OSI

Σ FORMULA

$$OSI = (MAP \times FiO2 \times 100) \div SpO2$$

Calculate Mean Airway Pressure



About OSI

The Oxygen Saturation Index is a non-invasive version of the Oxygenation Index (OI).

MAP (cmH2O)

12

FiO2

0.6

Values between 0.21 and 1.00, where 1.00 equals 100% and 0.40 equals 40%, for example.

SpO2 (%)

90

Enter a whole number between 1 and 100, such as 94 for a saturation of 94%.

8

Oxygen saturation index

Diagnostic threshold reached (5 – 12)

OSI of 5 or more reaches the diagnostic threshold of the PARDS 2.0 definition on invasive ventilation. Below 12, severity is classified as mild to moderate.



A-a gradient: compare at the same FiO_2

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$$\text{AaDO}_2 = [(713 \times \text{FiO}_2) - (\text{PaCO}_2 \div 0.8)] - \text{PaO}_2$$

mmHg

Example: FiO_2 0.6, PaCO_2 50, PaO_2 60 →
 $\text{AaDO}_2 \approx 305 \text{ mmHg}$

- Newborn normal: < 50 mmHg. In room air, 20–40 mmHg may persist for days.
- AaDO_2 rises unpredictably as FiO_2 increases: to follow the trend, compare measurements at the same FiO_2 .
- Hypoxemia is most often V/Q mismatch or shunt (PPHN, atelectasis).

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Alveolar-Arterial Oxygen Difference - AaDO2

Σ FORMULA

$$\text{AaDO}_2 = [(713 \times \text{FiO}_2) - (\text{PaCO}_2 \div 0.8)] - \text{PaO}_2$$

About AaDO2

It assesses lung efficiency through the difference between the alveolar pressure and the arterial pressure of oxygen.

Condition for the calculation

This equation is used for bedside calculation assuming barometric pressure at sea level.

FiO2

Values between 0.21 and 1.00, where 0.21 equals 21% and 1.00 equals 100%.

PaCO2 (mmHg)

PaO2 (mmHg)

Reference

- Martin Keszler (editor), K. Suresh Gautham (editor) - Goldsmith's Assisted Ventilation of the Neonate - 7th Edition - Elsevier (2022), p. 26 e 581 — alveolar gas equation; p. 355 (Box 28.1) — ECMO criterion.
- Ashok P. Sarnaik, Shekhar T. Venkataraman, Bradley A. Kuch - Mechanical Ventilation in Neonates and Children: A Pathophysiology-Based Management Approach - Springer (2022), p. 57 — normal range



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Alveolar-Arterial Oxygen Difference - AaDO₂

Σ FORMULA

$$\text{AaDO}_2 = [(713 \times \text{FiO}_2) - (\text{PaCO}_2 \div 0.8)] - \text{PaO}_2$$

About AaDO₂

It assesses lung efficiency through the difference between the alveolar pressure and the arterial pressure of oxygen.

Condition for the calculation

This equation is used for bedside calculation assuming barometric pressure at sea level.

FiO₂

0.6

Values between 0.21 and 1.00, where 0.21 equals 21% and 1.00 equals 100%.

PaCO₂ (mmHg)

50

PaO₂ (mmHg)

60

305.3 mmHg

Alveolar-arterial oxygen difference

Above the neonatal normal (≥ 50 mmHg)

Above the newborn normal range, which is below 50 mmHg. The references do not define severity grades in this range, because AaDO₂ rises unpredictably as FiO₂ increases. To track progression, compare measurements taken at the same FiO₂.

Meaning of elevated values

An elevated gradient indicates impaired gas exchange. Possible causes include venous admixture from intrapulmonary shunt, as in atelectasis, or intracardiac shunt; ventilation-perfusion (V/Q) mismatch; and

28-week preterm, day 3, conventional ventilation

Arterial sample from the UAC, no bubbles, run immediately.

pH
7.22

PaCO₂
58

HCO₃⁻
23

Na⁺
138

Cl⁻
106

Lactate
1.4

Step 1 · pH

7.22 → acidemia.

Step 2 · Does the CO₂ explain it?

Expected pH = $7.40 - (58 - 40) \times 0.006 = 7.29$.

Measured 7.22 is **0.07 lower** (beyond ± 0.03) → a **metabolic acidosis is also present**.

Putting it together

Step 4 · Expected compensation

Acute respiratory acidosis: HCO_3^- should rise ~ 1 per 10 mmHg $\rightarrow$ expected ≈ 25.8 .

Measured 23 is **lower** $\rightarrow$ confirms the added metabolic acidosis.

Step 5 · Anion gap

$138 - (106 + 23) = 9 \text{ mEq/L}$ $\rightarrow$ within the neonatal range (4–12): **normal-AG** acidosis. Lactate 1.4 is normal.

Conclusion

Mixed acidosis: acute respiratory + normal-AG metabolic.

Review ventilation (V_T , rate, dead space) and look for **bicarbonate loss**, which is common in very preterm kidneys. Consider acetate in PN before thinking of bicarbonate.

Giving bicarbonate here would generate more CO_2 in an infant who already cannot clear it.

SAVE FOR YOUR NEXT SHIFT

Bedside checklist

- 0 · Trust the sample: bubbles, dilution, delay, capillary, HbF, temperature.
- 1 · pH: acidemia or alkalemia?
- 2 · PaCO₂: does the expected pH match within ± 0.03 ?
- 3 · HCO₃⁻, BE and lactate: same analyzer, same method.
- 4 · Expected compensation: Winters's, alkalosis rule, acute vs. chronic.
- 5 · Neonatal anion gap (4–12) and oxygenation: CaO₂, OI/OSI, AaDO₂.

NeoFast puts these formulas at the bedside, in seconds, with neonatal ranges and references on every screen.

