Acid-Base Chemistry

Acid-base state

If pH<7.35 → acidaemia, or if >7.45 → alkalaemia

Primary acid-base disturbance

Primary disorder	Init change	Compensation	Expected level of compensation
Metabolic Acidosis	↓ HCO_3^-	↓ PCO_2	PCO_2= (1.5 × [HCO_3^-]) + 8 ± 2 or PCO_2= 40 – 1.2 × (24-[HCO_3^-])
			PCO_2= last 2 digits of pH (7.40-7.10)
Metabolic Alkalosis	↑ HCO_3^-	↑ PCO_2	PCO_2= (0.7 × [HCO_3^-]) + 20 ± 5 or PCO_2= 40 + 0.7 × ([HCO_3^-]-24)
			PCO_2= last 2 digits of pH (7.40-7.60)
Respiratory Acidosis	↑ PCO_2	↑ HCO_3^-	Acute: [HCO_3^-] = 24 + (PCO_2 - 40)/10 × 1
			Chronic: [HCO_3^-] = 24 + (PCO_2 - 40)/10 × 4
Respiratory Alkalosis	↓ PCO_2	↓ HCO_3^-	Acute: [HCO_3^-] = 24 + (PCO_2 - 40)/10 × 2
			Chronic: [HCO_3^-] = 24 + (PCO_2 - 40)/10 × 5

Metabolic acidosis:

- If measured $PaCO_2$>expected $PaCO_2$, then respiratory acidosis also.
- Calc anion gap: AG = [Na^+] + [K^+] – [Cl^-] – [HCO_3^-] or [Na^+] – [Cl^-] – [HCO_3^-]
    - Normal Range: 12-20 mmol/L (or without [K^+]: 8-16 mmol/L).
    - As few other cations (Ca^{2+}, Mg^{2+}), AG is mainly unmeasured anions: plasma proteins (mostly albumin), PO_4^-, and SO_4^{2-}. Correct for low albumin by 0.25 x (40-[Alb]).

High Anion Gap + Metabolic Acidosis	Normal Anion Gap + Metabolic Acidosis
Carbon monoxide, cyanide	**H**yperalimentation (TPN)
Alcoholic ketoacidosis	**A**mmonium Cl, Acetazolamide & other CAI
Toluene	**R**enal tubular acidosis, renal failure
Methanol	**D**iarrhoea & cholestyramine
Uremia	**U**reteroenteric or pancreaticoduodenal fistula
Diabetic ketoacidosis	**P**ost-hyperventilation
Paraldehyde, propylene glycol, paracetamol	**S**pironolactone, hypoaldosteronism
Isoniazid, iron	• Normal anion gap usually from hyperchloraemic compensation for loss of HCO_3^- • Check: Urinary AG = [Na^+] + [K^+] – [Cl^-] if negative: likely GIT cause, else renal
Lactic acidosis **A** – Hypoperfusion: sepsis, shock **B1** – Systemic disease: e.g. DM, RF, liver dz **B2** - Drugs - metformin, CO, Fe, CN, INH, EtOH **B3** – Inborn errors of metabolism	
Ethylene glycol	
Salicylates, starvation	

- Calc Delta ratio: Δ↑AG / Δ↓HCO_3^- = (AG – 16) / (24 - HCO_3^-) or (AG – 12) / (24 - HCO_3^-) alternatively use the Delta (bicarbonate) gap: Δ↑AG - Δ↓HCO_3^-

Delta Ratio	Delta Gap	Implication – be wary of over-interpretation
< 0.4	<< -6	Hyperchloraemic Normal AG Metabolic acidosis
0.4 – 0.8	< -6	High AG Metabolic Acidosis + Normal AG Metabolic Acidosis
1 - 2	-6 to 6	Pure High AG Metabolic Acidosis (DKA tends to be ~1 as ketones lost in urine)
> 2	> 6	High AG Metabolic Acidosis + Metabolic Alkalosis or Comp Resp Acidosis (Both ↑HCO_3^-)

- Osmolar gap = Measured osmolarity – {2*([Na]+[K])+[Ur]+[glu]}: >10 in toxic alcohol OD

Causes: (see above)

- HAG: RF, lactic acidosis, ketoacidosis, ingestions.
- NAG: GIT HCO_3^- loss (diarrhoea, ureteral diversion), renal HCO_3^- loss (RTA, early RF, carbonic anhydrase inhibitors, aldosterone inhibitors), Cl- admin, post-hyperventilation

Metabolic alkalosis

- If measured $PaCO_2$>expected $PaCO_2$, then respiratory acidosis present also.

Causes:

- <u>Saline responsive/↓ECF/hypoCl^-</u> - U_{Cl-}<10mmol/L: vomiting, excessive diarrhea (laxative abuse, villous adenoma), prev diuretics, CF, post-hypercapnia, burns.
- <u>Saline resistant/Norm or↑ECF/hypoK^+</u> – U_{Cl-}>20mmol/L: ↑aldosterone (1° & 2°), Cushings, diuretics, RF/RAS, licorice, Barrter's & Gitelman syndromes, severe hypoK^+
- <u>Unclassified</u> – Milk-alkali, massive txf, $NaHCO_3$ intake, severe hypoalbuminaemia.
- If a high Anion Gap (& hypoK^+): Penicillin, carbenicillin are possible causes.

Respiratory acidosis

Causes:

- <u>Hypoventilation</u>: airway obs, ↓resp drive (sedating drugs, CNS depression), pulm dz (pneumonia, acute on COAD, APO, PTX, ARDS, aspiration), neuromusc dz (myaethenia gravis, Guillain-Barre, muscle relaxants, snake venom, myopathies), chest wall dz (flail chest, splinting) , ↓IPPV
- ↑<u>CO_2 Production:</u> malignant hyperthermia, endoscopy (insufflation of CO_2), rebreathing

Respiratory alkalosis

Causes:

- <u>Hyperventilation:</u> hypoxaemia (high altitude, anaemia, PE, lung infection, APO, asthma), anxiety, hypermetabolic/toxic states (thyrotoxicosis, sepsis, pregnancy), drugs (salicylates, pressor,T4), CNS (↑ICP, liver encephalopathy), hypoNa, ↑IPPV.

Compensation:

- Chronic respiratory alkalosis is only type that completely compensates.
- $PaCO_2$ can only compensate in range ~10-60mmHg
- HCO_3^- can only compensate for chronic respiratory acidosis in range 18-45mmol/L

Causes of a low anion gap

- Relatively rare.
  - **C**ations (e.g. Lithium, Ca^{2+}, Mg^{2+})
  - **L**ow albumin
  - **I**odine (falsely measured as Cl-)
  - **M**ultiple myeloma (i.e. paraprotein cations)
  - **B**romide (falsely measured as Cl-)

PaO2 and A-a Gradient

- *Minimum PaO_2 for age:* PaO_2 = 104.2 - (0.27*age) or PaO_2~100-age/3
- A-a O_2 Gradient = [(FiO_2) * (Atmospheric Pressure - H_2O Pressure) - ($PaCO_2$/RQ)] - PaO_2
  - RQ=Respiratory quotient= 0.8 on RA, 1.0 on 100% O_2
  - Atmospheric Pressure=760mmHg & H_2O Pressure=47mmHg at sea level.
- On air @ sea level: A-a Gradient=150-1.25*$PaCO_2$ - PaO_2
  - Normally 5-20 OR (Age/4) + 4 OR (Age/3)-3 mmHg
- The 5 Causes of Hypoxemia, #1-3 have an elevated A-a Gradient:
  1. V/Q Mismatch (e.g. PNA, CHF, PE ,ARDS, atelectasis, etc)
  2. Shunt (e.g. PFO, ASD, pulmonary AVMs)
  3. Alveolar Hypoventilation (e.g. interstitial lung dz, environmental lung dz, PCP PNA)
  4. Hypoventilation (e.g. COPD, CNS dz, neuromuscular dz, etc)
  5. Low PiO_2 (e.g. low FiO_2, and high altitude (low PO_2))