METABOLIC ACIDOSIS

Defined as an acidaemia created by a primary increase in H^+ or a reduction in $[HCO_3^-]$

Acutely compensated for by *hyperventilation.*
Chronically, renal absorption of HCO_3^- takes place.

AETIOLOGY:

Three main mechanisms can cause metabolic acidosis;

1. Increased production of acids
2. Decreased excretion of acids
3. Loss of alkali.

Practically, the causes are divided into those with either an *elevated or normal anion gap.*

THE ANION GAP

- Normal AG = 12 (±3)

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

Increased Anion Gap Metabolic Acidosis	
M	Methanol (formic acid), metformin
U	Uraemia (including aminoglycosides)
R	Renal failure (Uric acid)
K	Ketoacidosis (alcohol, diabetes (acute), starvation)
L	Lactic acidosis
E	Ethanol
S	Salicylates
E	Ethylene glycol (glycolic acid)
P	Paraldehyde, propylene glycol
T	Toluene
I	Iron, isoniazid
C	Cyanide and carbon monoxide

Normal Anion Gap Metabolic Acidosis	
U	Ureteric diversion
S	Small bowel fistula
E	Extra chloride (ED resuscitation) or HCl ingestion
D	DKA (resolving)
C	Carbonic anhydrase inhibitors
A	Addisons (Type 4 RTA)
R	Renal tubular acidosis types 1, 2, and 4
P	Pancreatic fistula

THE DELTA GAP

$$\Delta G = (\text{calculated AG} - 12) - (24 - \text{measured } HCO_3^-)$$

ΔG > +6 = metabolic alkalosis or respiratory acidosis

ΔG < -6 = a mixed disorder (greater loss of HCO_3^-).

WINTER's FORMULA

$$PCO_2 = (1.5 \times [HCO_3^-] + 8) \pm 2$$

Allows us to predict the degree of respiratory compensation.

THE OSMOLAR GAP

Calculated Osmolality (mOsmol/kg) = 2 x [Sodium mmol/L] + [urea mmol/L] + [glucose mmol/L] + [ethanol mmol/L]

Osmolar Gap = Measured Osmolality – Calculated Osmolality

Differential Diagnosis of elevated OG (ME DIE)

M	Methanol
E	Ethylene glycol
D	Diuretics (osmotic agents like mannitol)
I	Isopropyl alcohol
E	Ethanol

ELEVATED ANION GAP:

Carbon monoxide / Cyanide Poisoning

- These are cellular toxins
- Associated with exposure to smoke from fires.
    - Interfere w/ cellular respiration at cytochrome level.
    - Anaerobic metabolism ensues --> organic acidaemia.

Alcoholic Ketoacidosis

- Results from abrupt termination of EtOH intake after significant or lengthy exposure.
- Associated with & compounded by malnutrition & dehydration
- AG usually 30-35.
- May have multiple acid-base disturbances
    - Respiratory alkalosis (EtOH withdrawal)
    - Metabolic alkalosis (vomiting)
- Treatment includes;
    - Hydration w/ 5% dextrose & normal saline
    - Carbohydrate & fluid replacement
    - *Insulin is contraindicated.*

Toluene Inhalation

- Used as a solvent, now abused for its euphoric effect.
- Produces HAGMA, complicated by distal renal tubular damage.
    - Mix of NAGMA & HAGMA
- Treatment is supportive & aimed at electrolyte & fluid replacement.

Methanol, Ethylene Glycol & Paraldehyde

- Methanol --> Formaldehyde (metabolite) --> Formic acid.

- Ethylene Glycol --> oxalates, aldehydes & lactic acid
    - (oxalates result in significant anion gaps & increased mortality).

- Paraldehyde (rare).
    - Formation of acetic and chloracetic acids.

Treatment is aimed at preventing metabolism to toxic metabolites using;
- Fomepizole
- Ethanol
- Haemodialysis

Uraemia

- Failure to excrete acids from kidneys including;
    - NH_4^+
    - HSO_4^+
    - HPO_4^{2-}

- In chronic RF --> HAGMA is common
- In acute RF --> usually a NAGMA (due to hyperchloraemia).

Diabetic Ketoacidosis

- A triad of hyperglycaemia, ketonaemia & acidaemia.
- Caused by any condition that reduces insulin availability or increases glucagon.
- Lipolysis --> fatty acid breakdown --> formation of ketoacids.
- Simplified treatment includes; fluid replacement, insulin replacement and electrolyte correction.
- Identify and treat the underlying precipitant.

Isoniazid & Iron Toxicity

- Isoniazid is a common treatment for TB.
    - Ingestions of >40-60 mg/kg = risk of seizures and profound HAGMA
    - Treatment = pyridoxine & haemodialysis
- Iron ingestion results in mitochondrial poisoning & uncoupled oxidative phosphorylation.
    - MA = phase I of toxicity (within 6 hours of ingestion).
    - Phase III = impending hepatic failure & shock.
    - Treatment = early recognition & administration of deferoxamine.

Lactic Acidosis

- A product of anaerobic metabolism, acidosis occurs when an imbalance exists between production and subsequent conversion in liver / kidney.
- A marker of hypoperfusion & ongoing shock.
    - Also elevated with many medications including;
        - Metformin (particularly post IV contrast or with renal failure)
        - Nucleoside analogue reverse transcriptase inhibitors (HIV therapy).

Salicylates

- *First phase* of toxicity = inducing **respiratory alkalosis** by direct stimulation on respiratory centre; increasing minute ventilation.
- *Second phase* of toxicity = **paradoxical aciduria** with continued respiratory alkalosis.
- *Third phase* of toxicity = marked dehydration, hypokalaemia & **progressive metabolic acidosis*.***
- Treatment is supportive with GIT contamination if possible. Serum & urine alkalinisation may enhance elimination & minimise toxicity.

NORMAL ANION GAP:

Metabolic acidosis with a normal AG is caused by either an excessive loss of HCO_3^- or an inability to excrete H^+.

Any condition causing excessive loss of intestinal fluid *distal to the stomach* can cause a NAGMA.

- Primarily a HCO_3^- wasting condition.
- 95% of cases result from diarrhoea.

Renal tubular acidosis:

- Type I = unable to secrete H^+ at distal tubule
- Type 2 = impaired HCO_3^- reabsorption at proximal tubule.

PHYSIOLOGIC COMPENSATION.

Response to acidaemia utilises four buffering systems;

1. extracellular bicarbonate / carbonic acid
2. intracellular blood protein systems
3. renal compensation (H^+ excreted & HCO_3^- reabsorbed)
4. respiratory compensation (increased H^+ at medulla chemoreceptors).

When pH is 7.1 or less, minute ventilation can reach 30 L/min = *Kussmaul's respiration.*

The kidneys secrete H+; as $NH4^+$ and $H2PO4^-$.

MANAGEMENT.

Primary efforts should be directed at restoring homeostatic mechanisms, treating the patient & using laboratory markers only as a guide. This usually involves identification and correction of the underlying cause / precipitant.

Most patients with metabolic acidosis do not require aggressive attempts at pH manipulation.

Therapy with sodium bicarbonate has some inherent complications, and rapid replacement can result in paradoxical CNS intracellular acidosis, impaired oxygen delivery, hypokalemia, hypocalcemia, “overshoot” alkalosis, hypernatraemia, volume overload, and hyperosmolality.