Metabolic Acidosis

See also separate Lactic Acidosis and Arterial Blood Gases - Indications and Interpretations articles.

Description

Metabolic acidosis is defined as an arterial blood pH <7.35 with plasma bicarbonate <22 mmol/L. Respiratory compensation occurs normally immediately, unless there is respiratory pathology. Pure metabolic acidosis is a term used to describe when there is not another primary acid-base derangement - ie there is not a mixed acid-base disorder. Compensation may be partial (very early in time course, limited by other acid-base derangements, or the acidosis exceeds the maximum compensation possible) or full.

The Winter formula can be helpful here - the formula allows calculation of the expected compensating pCO₂:

\[
pCO_2 = (1.5 \times [HCO_3^-]) + 8 \pm 2
\]

If the measured pCO₂ is >expected pCO₂ then additional respiratory acidosis may also be present.

It is important to remember that metabolic acidosis is not a diagnosis; rather, it is a metabolic derangement that indicates underlying disease(s) as a cause. Determination of the underlying cause is the key to correcting the acidosis and administering appropriate therapy[1].

Epidemiology

It is relatively common, particularly among acutely unwell/critical care patients. There are no reliable figures for its overall incidence or prevalence in the population at large.

Causes of metabolic acidosis

There are many causes. They can be classified according to their pathophysiological origin, as below. The table is not exhaustive but lists those that are most common or clinically important to detect.

<table>
<thead>
<tr>
<th>Increased acid load</th>
<th>Excessive loss of gastrointestinal bicarbonate</th>
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<tbody>
<tr>
<td>Any cause of lactic acidosis - eg, heart failure, drugs or toxins, inborn errors of</td>
<td>Diarrhoea</td>
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<tr>
<td>metabolism</td>
<td>Fistulae of pancreas, biliary tree or intestine</td>
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<td>Ketoacidosis due to diabetes, starvation or alcohol excess</td>
<td>Urinary-gastrointestinal diversion surgery</td>
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<td>Parenteral or hyperalimentary nutrition</td>
<td>Cholestyramine</td>
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<td>Poisoning with substances that generate acid or prevent its excretion - eg:</td>
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<tr>
<td>Methanol</td>
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<td>Salicylate</td>
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<td>Ethylene glycol</td>
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<td>Paraldehyde</td>
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<td>Iron</td>
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<td>Sulfur</td>
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<td>Toluene</td>
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<td>Biguanides</td>
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<td>Isoniazid</td>
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<td>Ammonium chloride</td>
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<td>Ciclosporin</td>
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<tr>
<td>Excessive loss of gastrointestinal bicarbonate</td>
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<tr>
<td>Impaired excretion of dietary acid load</td>
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<tr>
<td>Renal failure leading to impaired NH4+ production</td>
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<tr>
<td>Hyponatremiaism in type 4 renal tubular acidosis (RTA)</td>
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<td>Impaired excretion of H+ in type 1 (distal) RTA</td>
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<tr>
<td>Excessive loss of renal bicarbonate</td>
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<tr>
<td>Type 2 (proximal) RTA</td>
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<tr>
<td>Acetazolamide or other carbonic anhydrase inhibitors</td>
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Presentation

History
There are no specific symptoms of metabolic acidosis as such. Those that occur are due to the effects of the metabolic derangement on the body, or may give clues to the underlying cause. Patients may notice a subjective sensation of dyspnoea caused by stimulation of the respiratory centre in an attempt to ‘blow off’ CO$_2$ and increase blood pH. Nausea, vomiting and anorexia are frequently present, particularly in children. Metabolic acidosis occurring in children is very rarely due to an inborn error of metabolism (conditions such as moderately severe gastroenteritis being more common).

The following points should be covered in the history in an attempt to identify the underlying cause:

- Family history of any similar episodes of illness (may indicate inborn error of metabolism).
- Family or personal history of diabetes.
- Symptoms of undiagnosed diabetes - eg, polyuria, polydipsia or weight loss.
- Symptoms of renal failure such as nocturia, polyuria, oliguria, pruritus and anorexia.
- Recent history of urinary problems such as nephrolithiasis may indicate RTA.
- Recent history of severe or prolonged diarrhoea.
- Recent nutritional status.
- Alcohol intake.
- Any history of deliberate or accidental ingestion of potentially toxic materials or medicines.
- Occupational/DIY exposure to fumes or solvents.
- Visual disturbances such as dimming, photophobia, scotomata or blindness may indicate methanol poisoning. Blurred vision may occur with salicylate poisoning.
- Tinnitus or vertigo may occur with salicylate poisoning.
- Ask about any chest pain, palpitations, dyspnoea or oedema indicating possible cardiovascular causes for lactic acidosis.
- Recent history of confusion, headache or visual changes may indicate poisoning, particularly with methanol or ethylene glycol.

**Examination**

- Lethargy, stupor and progression to a state of coma may occur, particularly in cases of poisoning. An intoxicated-appearing patient who has no smell of alcoholic drink on their breath may have ingested ethylene glycol.
- Check vital signs, as hypotension may occur due to myocardial suppression in severe acidaemia. Tachypnoea is likely to be present.
- In undiagnosed renal failure there may be dryness of mouth, eyes and skin, scratch marks on skin, pallor, drowsiness and fetor.
- To detect diabetic ketoacidosis look for evidence of dehydration and smell the patient’s breath to detect the presence of ketones (which give off a musty/fruity odour akin to pear drops or nail polish remover).
- Look for signs of congestive cardiac failure that may be caused by the acidosis itself, or suggest lactic acidosis as a cause, due to generalised hypoperfusion.
- Listen for a pericardial rub which may indicate acute renal failure as the cause.
- The presence of tachypnoea without any history of pre-existing cardiorespiratory disease to account for it should strongly suggest metabolic acidosis as the cause of the illness.
- Kussmaul’s respiration may be noted where there is deep, slowly rhythmic breathing that increases the minute tidal volume.
- Children with chronic metabolic acidosis may have growth restriction and show signs of rickets.
- Neurological examination may reveal cranial nerve palsies in the case of ethylene glycol poisoning.
- Retinal oedema may be noted on fundoscopy in cases of methanol ingestion.

**Differential diagnosis**

The combination of clinical features of illness and arterial blood gas/plasma bicarbonate results indicate the presence of a metabolic acidosis. Determination of its underlying cause, as outlined in the investigation section below, is crucial to try to optimally treat and correct the acidosis. As such there is no differential diagnosis, rather a list of possible underlying causes to be refuted/confirmed as its cause. See the table above for a list of potential causes.

**Investigations**

- The first indication of an acidic problem may be the presence of a low serum bicarbonate on routine U&E testing. This in itself is not enough to confirm an acidosis. The presence of metabolic compensation of respiratory alkalosis, or a laboratory error could account for a low plasma bicarbonate. Arterial blood gases or venous blood gases must be checked to determine the arterial blood pH and confirm the diminution of bicarbonate. pH and pCO$_2$ values must be interpreted carefully and a judgement made as to whether this is a pure metabolic acidosis or a mixed acid-base disorder. The base excess or base deficit is usually given as a part of the blood gas result and allows a determination of the overall severity of the acidosis, particularly where respiratory compensation complicates the picture.
- U&Es help to determine the cause of the acidosis by allowing the calculation of the anion gap (AG) as below:

\[
AG = ([Na\ mmol/L] + [K\ mmol/L]) - ([HCO_3\ mmol/L] + [Cl\ mmol/L])
\]

- The normal range: 10-20 mmol/L.
- Some laboratories will exclude [K+] in which case the normal range is: 8-16 mmol/L.
- Check locally for reference ranges in your laboratory.
• It is a measure of the unmeasurable anions not routinely detected by analyser machines. Where the AG is elevated it indicates the presence of an organic acid causing the acidosis - for example, acetoacetic acid and beta-hydroxybutyric acid in diabetic ketoacidosis. The AG helps to determine the likely cause of the acidosis as outlined below.  
• The cause of a normal AG metabolic acidosis can be narrowed by checking the urinary AG: AG = [Na+] + [K+] − [Cl−]. If negative then the likely cause arises from the gastrointestinal tract; if not then consider renal causes.  
• AG correlates closely with albumin levels and must be adjusted in hypoalbuminaemia.

Causes of raised, normal and low AG

• Raised AG - can be due to low levels of unmeasured cations - eg, hypomagnesaemia, hypocalcaemia. For further causes, see table below.  
• Normal AG - for causes, see table below.  
• Low AG - can be the result of raised unmeasured cations such as in hypercalcaemia, hypermagnesaemia, and lithium toxicity. Hyperproteininaemia, hyperlipidaemia and hyperglycaemia can affect AG by falsely depressing measured sodium level. Bromide poisoning may cause Br ions to be mistaken for Cl ions by the autoanalyser, causing inappropriate depression of the AG.

<table>
<thead>
<tr>
<th>Correlation between anion gap and causes of metabolic acidosis</th>
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<tbody>
<tr>
<td><strong>Elevated AG metabolic acidoses</strong></td>
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<tr>
<td>Lactic acidosis caused by L-lactate, due to state of hypoperfusion, carbon monoxide/cyanide poisoning, biguanide toxicity, D-lactaemia in short bowel syndrome</td>
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<tr>
<td>Diabetic or alcoholic ketoacidosis caused by acetoacetate/beta-hydroxybutyrate</td>
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<tr>
<td>Renal failure caused by urate, hippurate, sulphate and phosphate</td>
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<tr>
<td>Saliolate poisoning</td>
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<tr>
<td>Methanol or formaldehyde poisoning caused by formate</td>
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<td>Ethylene glycol poisoning caused by glycolate and oxalate</td>
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<td>Paraldehyde poisoning caused by a variety of organic acids</td>
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<td>Sulfur poisoning caused by sulphate</td>
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<tr>
<td>Pyroglutamic acidaemia caused by 5-oxoprolate</td>
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<tr>
<td>Rhabdomyolysis is caused by direct proton release from lysed muscle cells</td>
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<table>
<thead>
<tr>
<th>Normal AG metabolic acidoses (hyperchloraemic acidosis)</th>
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<tbody>
<tr>
<td>Gastrointestinal bicarbonate loss - eg, diarrhoea, pancreatic or intestinal fistulae</td>
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<tr>
<td>Renal bicarbonate loss - eg, type 2 RTA</td>
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<tr>
<td>Some causes of renal failure/impairment</td>
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<tr>
<td>Hypoaldosteronism in type 4 RTA</td>
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<tr>
<td>Hyperventilation</td>
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<tr>
<td>Ingestion of ammonium chloride</td>
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<tr>
<td>Use of carbonic anhydrase inhibitors</td>
</tr>
<tr>
<td>Parenteral or hyperalimentation feeding</td>
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<tr>
<td>Partially treated diabetic ketoacidosis</td>
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Further general investigations

• Elevation of urea and creatinine will indicate that renal failure is the likely cause.  
• Hyperkalaemia often accompanies a normal AG acidosis, and some cases of acute renal failure.  
• Potassium may also be elevated in diabetic ketoacidosis but usually minimally so for the degree of acidosis.  
• Plasma and urinary glucose and ketones need to be checked to look for evidence of diabetic ketoacidosis.  
• Alcoholic ketoacidosis will show evidence of ketone formation without grossly elevating plasma glucose in most cases. A random alcohol level or expired breath alcometer reading may help to make the diagnosis, along with details from the history.  
• FBC should be checked but is usually nonspecific and unhelpful, except in the case of severe anaemia, where it is likely that lactic acidosis is the cause, or grossly elevated WCC indicating sepsis or haematological neoplasm.  
• LFTs should be checked to look for evidence of chronic liver disease, indicating alcohol abuse as a likely aetiology.  
• Send any appropriate samples for culture, particularly blood and urine if sepsis leading to lactic acidosis is possible.  
• ECG helps to detect arrhythmias.  
• Consider CXR to look for evidence of infection/cardiac failure or ingested iron/other radio-opaque toxins.

Investigations for specific causes

• Osmotic or osmolar gap. This is the difference between the laboratory-measured osmolality and the calculated osmolality. Calculated osmolarity can be worked out using one of the formulae below:

\[
\text{Calculated osmolarity} = 2[Na \text{ mmol/L}] + [\text{urea mmol/L}] + [\text{glucose mmol/L}] \\
\text{OR} \\
\text{Calculated osmolarity} = 2[Na \text{ mmol/L}] + [K \text{ mmol/L}] + [\text{urea mmol/L}] + [\text{glucose mmol/L}] 
\]

Where the osmotic gap is elevated, it indicates a disparity between the actual osmolality (measured by the laboratory) and the calculated osmolality. This indicates the presence of other osmotically active solutes which are not taken into account in the calculated osmolality. It is normally less than 10-15 mOsmol/kg (see local laboratory for range and bear in mind the different calculations). It is elevated by methanol or ethylene glycol ingestion.
• Plasma lactate, where lactic acidosis is a potential cause. Values >2 mmol/L indicate hyperlactataemia and >5 mmol/L indicate definite lactic acidosis.
• Plasma salicylate levels. Levels >350 mg/L (2.5 mmol/L) indicate salicylate toxicity. Levels >700 mg/L (5.1 mmol/L) indicate severe toxicity.
• Iron levels if there is a suspicion of deliberate or accidental overdose. Levels >300 mg/dL are considered toxic. An abdominal X-ray may be of use if there is suspected ingestion of iron tablets.
• Urine microscopy may show the presence of needle-shaped oxalate crystals which is indicative of ethylene glycol toxicity. Usually urine pH will be <5.0-5.5. Alkaline urine in the face of acidosis is usually caused by type 1 RTA or salicylate poisoning.
Management

Patients with metabolic acidosis are often very ill and prone to rapid deterioration. Make your assessment of their condition and its likely cause as quickly and calmly as possible. Arrange any investigations, as above, that will help to reveal its aetiology. Ask for advice from senior colleagues/other appropriate specialties early in the course of the presentation.

General measures

- Put the patient in the resuscitation area, or transfer to a high-dependency area as soon as feasible.
- Put the patient on an ECG monitor, SaO$_2$ monitor and BP/HR monitor.
- In patients who are clinically unwell and have deteriorating SaO$_2$ levels or conscious levels, consider intubation and assisted ventilation, after taking senior A&E/medical/anaesthetic advice.
- Intubation and ventilation can lead to decompensation and caution is advised. Patients with a metabolic acidosis are relying on their hyperventilation; induction agents and setting the ventilator to a normal respiratory rate may lead to further decompensation.
- Get large-bore IV access (a central venous line may be needed) and rehydrate aggressively.
- Consider catheterisation to monitor urine output and obtain urine for analysis.
- If there is any possibility of drug or toxin ingestion, give initial therapies such as activated charcoal/chelating agents/emetics, dependent on the specific compound ingested and latest local guidelines for poisoning.
- Liaise with local or national toxicology/poisoning services if there has been ingestion of a potentially dangerous substance.
- Obtain specialist input (usually the on-call general medical team initially) as soon as possible.

Correction of acidosis

Treatment of the underlying cause is the aim. Use of bicarbonate infusions is not recommended, as it can lead to a fatal outcome. It should be used only where advised in cases of poisoning.

Specific therapy for the underlying cause

This is the most important and efficient way to correct the acidosis and improve the patient's outlook. Toxicological/general medicine/renal medicine expertise should be engaged to offer specific therapy for the identified underlying problem.

Complications

The major problem is suppression of myocardial contractility and unresponsiveness to catecholamines caused by the acidæmic state. This may lead to a vicious cycle of hypoperfusion, worsening lactic acidosis and further cardiac suppression, causing multi-organ failure. If pH is <7.1-7.2 then cardiac arrhythmias are likely.

Prognosis

This is largely dependent upon the underlying cause and severity of the illness in a given patient. There is no doubt that metabolic acidosis can be life-threatening and carries significant mortality and morbidity. Appropriate initial management and ongoing expert input will improve the outlook for individual patients.

Further reading & references


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