Metabolic Alkalosis

2 factors are responsible for generation and maintenance of metabolic alkalosis – this includes a process that raises serum bicarbonate and a process that prevents excretion of the excess bicarbonate in urine.

Processes that raise serum bicarbonate include:

- loss of H⁺ ions through - the urine (primary mineralocorticoid excess, Chronic respiratory acidosis, Bartter, Gitelman syndrome, hypercalcaemia etc)
  - the GI tract (vomiting, diarrhoea, NG tube)

- movement of H⁺ ion into cells (seen mostly in Hypokalaemia)

- volume contraction around a constant amount of bicarbonate ( for example with use of a loop diuretic or thiazide diuretic )

Common causes for impaired excess bicarbonate excretion in patients with metabolic alkalosis are:

- Reduced effective circulatory volume
- Hypokalaemia
- Hypochloraemia
- Acute or chronic kidney disease

Assessment should include thorough history including drug history (to establish possible aetiology ), assessment of fluid status, urinary chloride and serum potassium.

Treatment:-Try to establish cause of metabolic alkalosis and treat this. Correct hypovolaemia, hypochloraemia and hypokalaemia.

Use potassium sparing diuretics or acetazolamide in conditions like heart failure, cirrhosis or post hypercapnic metabolic alkalosis. Post Hypercapnic metabolic alkalosis is seen when chronic hypercapnic patients, have their carbon dioxide levels corrected rapidly, for example by ventilation. This can cause seizures.

Metabolic alkalosis that is resistant to treatment can be considered for dialysis in the context of advanced acute or chronic kidney disease.

Rarely, patients with bicarbonate >50 or pH>7.55 can be given IV hydrochloride or ammonium chloride. These patients shouldn’t be dialysed.

Metabolic Acidosis

This is the process that increases the concentration of H⁺ ions in the body and reduces the bicarbonate concentration in the body. Acidemia is the condition when the pH is <7.35.

Metabolic acidosis is diagnosed when there is a low pH and bicarbonate is < 22.
There are numerous causes for metabolic acidosis: Diabetic ketoacidosis, renal tubular acidosis, lactic acidosis (secondary to seizures, sepsis, heart failure, liver failure, shock, medications such as salicylates) and drug overdoses (aspirin, ethylene glycol etc).

Detailed history, physical examination, electrolytes and calculating the anion gap are often sufficient to establish the aetiology of metabolic acidosis.

Treatment of metabolic acidosis centres around treatment of the underlying cause. After addressing this, the approach to treatment depends on whether the metabolic acidosis is acute or chronic.

In acute settings: Bicarbonate can be considered when bicarbonate is very low and pH is less than 7.1.

Tromethamine (THAM/TRIS) is an alternative to sodium bicarbonate with the advantage that it does not increase the sodium load. Again this is used in severe acidaemia caused by processes such as sepsis, permissive hypercapnia, DKA, RTA, gastroenteritis etc. Its use in lactic acidosis has not been evaluated.

In chronic settings: eg, diarrhoea, CKD etc – consider sodium or potassium bicarbonate depending on sodium and potassium levels.

**Hyponatraemia**

This is very common in daily clinical practice.

The key to understanding hyponatraemia is understanding the role of ADH, serum osmolality and fluid status in maintaining serum sodium.

So a good approach to identifying the cause of hyponatraemia is a thorough history, clinical examination especially assessment of fluid status and investigations such as paired urine and serum osmolalities, urinary sodium and potassium.

Making sense of osmolalities:

\[
\text{Serum osmolality} = (2 \times \text{serum} \left[\text{Na}\right]) + \left[\text{glucose}\right] + \left[\text{urea}\right]
\]

Normal range is 275-295.

In hyponatraemia, there is usually a low serum osmolality i.e. less than 275. (From the above equation, it can be seen that sodium is an important determinant of osmolality; so when the sodium is low, you would expect a low serum osmolality).

A serum osmolality of less than 275, can be seen in 2 settings; one in the setting of appropriate or expected suppressed ADH and the other in the setting of elevated ADH.

To differentiate if the ADH is appropriately suppressed or not, it’s good to check the urine osmolality (see below).

Causes of hyponatraemia with low serum osmolality and appropriately suppressed ADH include Beer Potomania (a specific hypo-osmolality syndrome related to massive consumption of beer), advanced renal failure and primary polydipsia.
Causes of hyponatraemia with low serum osmolality and elevated ADH are SIADH, true effective circulating volume depletion (true volume depletion, heart failure, cirrhosis, thiazide diuretics), adrenal insufficiency, hypothyroidism and pregnancy.

If the osmolality is normal or high, it implies there is some other molecule that is pushing the osmolality up despite a low sodium.

Hyponatraemia with normal osmolality – consider pseudo hyponatraemia eg cholestatic jaundice, multiple myeloma, high triglycerides, mannitol, sorbitol etc.

Hyponatraemia with high osmolality – consider hyperglycaemia, alcohol intoxication, renal failure, mannitol etc.

Urine osmolality: A urine osmolality of less than 100 implies appropriately suppressed ADH. It means the urine is maximally dilute.

A urine osmolality >100 implies an inability to normally excrete free water due to persistent ADH secretion.

Urinary sodium:
Less than 20 implies hypovolaemia unless there is use of diuretics.
Greater than 40 often seen in SIADH.
If urinary sodium is between 20-40, serial monitoring of serum sodium in response to isotonic saline can be performed.

Treatment should be aimed at the underlying aetiology. Treatment options include hypertonic saline, fluid restriction, drugs such as Tolvaptan in SIADH, steroids in adrenal insufficiency etc. When correcting sodium, aim to increase sodium by less than 9 meq/L over any 24 hour period.

Hypernatraemia

Occurs because of retention of salts like sodium and potassium without water or when water is lost without loss of salts or a combination of the two.

The commonest cause of hypernatraemia is dehydration. Primary hypothalamic disease that impairs thirst and administration of hypertonic saline are other causes.

Treatment is administration of 5% dextrose or desmopressin in the case of diabetes insipidus. Remember to correct any concomitant hypokalaemia.

Aim to lower the sodium by less than 10 meq/L over 24 hours.

Hypokalaemia

Remember potassium is predominantly an intracellular ion.

Common causes of hypokalaemia include decreased intake, translocation into cells (eg. increased insulin activity, increased Beta adrenergic activity, elevated pH) and most often due to loss of
potassium from urine (diuretic, increased mineralocorticoid activity) or GI tract (vomiting and other losses of gastric secretions).

The underlying cause of the hypokalemia should be identified, particularly the presence of hypomagnesemia or redistributive hypokalemia. Patients with hypomagnesemia can be refractory to potassium replacement alone, and potassium replacement can result in rebound hyperkalemia in patients with redistributive hypokalemia. Among patients with redistributive hypokalemia due to increased sympathetic tone (as in hypokalemic thyrotoxic periodic paralysis), the administration of a nonselective beta blocker, such as propranolol, can rapidly reverse the hypokalemia and associated symptoms.

**Treatment:**

Mild to moderate (3 – 3.4): Consider oral potassium salts (up to 80 meq/L over 24 hrs).

If potassium is not improving consider possible renal wasting of potassium (eg diuretic use, primary aldosteronism, Barter / Gitelman syndrome) – in these cases consider using spironolactone /eplerenone or amiloride.

Severe (<2.5 -3): Consider IV replacement, oral replacement or combination of both.

Clinical manifestations of hypokalaemia include arrhythmia, marked muscle weakness and rhabdomyolysis.

**Hyperkalaemia**

Hyperkalemia is most often due to impaired urinary potassium excretion due to acute or chronic kidney disease and/or disorders or drugs that inhibit the renin-angiotensin-aldosterone axis. Less commonly, redistributive hyperkalemia results from the movement of potassium out of the cells, even though the total body potassium may be reduced eg uncontrolled hyperglycemia.

The urgency of treatment of hyperkalemia varies with the cause and the presence or absence of the symptoms and signs associated with hyperkalemia. Marked tissue breakdown can be associated with rapid and substantial elevations in serum potassium.

Start calcium infusion in addition to other therapies in patients who have severe manifestations of hyperkalemia such as widening of the QRS complex or loss of P waves, in whom it would be potentially dangerous to wait the 30 to 60 minutes for insulin and glucose to act.

Administer insulin + glucose (10 units of actrapid in 50 mls of 50 % dextrose/500 mls of 10% dextrose)
- in patients with a serum potassium concentration greater than 6.5 to 7 meq/L
- less severe hyperkalaemia but associated with electrocardiographic changes
- a serum potassium that is rapidly increasing.
Glucose is usually given with insulin to prevent the development of hypoglycemia. However, insulin should be given alone if the serum glucose is ≥ 13.9 mmol/L.

Salbutamol can be considered as transient therapy in patients who have symptoms or serious ECG manifestations of hyperkalemia despite therapy with calcium and insulin with glucose.
Sodium bicarbonate is **not** indicated as a single agent for the acute management of hyperkalemia, but may be given for the treatment of significant metabolic acidosis.

Remember to treat any reversible causes.

Loop or thiazide diuretics can be considered for patients with moderate hyperkalemia whose renal function is not severely impaired.

Dialysis is indicated if the potassium remains significantly raised despite the measures listed above or if the potassium is expected to increase rapidly as could occur with marked tissue breakdown such as muscle injury. Haemodialysis is preferred since the rate of potassium removal is much faster than with peritoneal dialysis.

---

**Calcium and phosphate management in chronic kidney disease patients**

Reduced excretion of phosphate tends to develop early in renal disease. High phosphate levels are associated with increased mortality.

Secondary hyperparathyroidism encompasses most of the biochemical abnormalities that characterize CKD-MBD (mineral and bone disorders). Causes of secondary hyperparathyroidism include phosphate retention; decreased free calcium concentration; decreased 1,25-dihydroxyvitamin D (calcitriol) concentration; and the reduced expression of vitamin D receptors (VDRs), calcium-sensing receptors (CaSR), fibroblast growth factor receptors (FGFRs), and klotho in the parathyroid glands.

In CKD patients, aim to keep phosphate in normal range (up to 1.3 mmol/L) with appropriate diet restriction. If not controlled with diet alone, then consider starting phosphate binders.

In dialysis patients, aim to keep phosphate between 1.13 – 1.78.

If persistently high despite diet and binders, then options would be to consider either nocturnal/daily dialysis or to consider a calcimimetic (a drug that mimics the action of calcium on tissues) or a parathyroidectomy.

Phosphate binders can be calcium containing (eg calcium carbonate, calcium acetate) or non calcium containing (eg sevelamer, lanthanum). Calcium containing binders are better options for hypocalcaemic patients. Non calcium containing binders are used in normo or hypercalcaemic patients or in patients with adynamic bone disease or evidence of calcification on imaging.

Aluminium hydroxide should not be used for long term, chronic management of hyperphosphataemia because of risk for aluminium toxicity.

---

*The Resource used for preparation of these teaching notes was UpToDate*
Dr Legate Philip, CT 2
Q.A Hospital, Portsmouth