SydPath
ST VINCENT'S PATHOLOGY

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CHLORIDE AND THE ANION GAP INFORMATION SHEET

CHLORIDE

Chloride is the major intra- and extra-cellular anion found in the body. Its concentration in plasma appears to be regulated by the requirement to maintain electrical neutrality although other theories exist. It is commonly measured in serum as part of the electrolyte profile but its utility in this fluid is restricted to calculation of the anion gap. Chloride in CSF is about 20 mmol/L higher than in serum but there is no utility in measuring chloride in this fluid. For assessing a fluid as a possible CSF leak, detection of Beta-2-transferrin is the recommended investigation. Measurement of chloride in urine is occasionally useful to assist in determining the cause of a metabolic alkalosis. A low urine chloride (< 20 mmol/L) is consistent with metabolic alkalosis caused by vomiting, gastric suction or chloride diarrhoea.

ANION GAP

The plasma anion gap is the difference between the major measured cations (sodium and potassium) and the major measured anions (chloride and bicarbonate). The formula for the anion gap is as follows: AG = Na + K - (Cl + HCO3) (all values in mmol/L). The reference interval at SydPath is 10 - 18 mmol/L. Due to the requirement of electrical neutrality the anion gap also corresponds to the difference between the cations not included in the equation (eg magnesium, calcium, immunoglobulins) and anions not included in the equation (eg sulphate, phosphate, albumin, lactate, ketone bodies).
The common causes of a raised anion gap are as follows:

- Elevated serum lactate (L- or D-lactate)
- Ketoacidosis (raised beta-hydroxybutyrate and acetoacetate)
- Renal failure (raised phosphate and sulphate)
- Toxins (ethanol, methanol, ethylene glycol, salicylates)

The anion gap should be calculated whenever there is a metabolic acidosis (low serum bicarbonate) of unknown cause. If the anion gap is elevated the above causes should be considered, otherwise other causes are more likely.
Note also that a raise anion gap may be the only serum marker of a combined metabolic acidosis and metabolic alkalosis (eg lactic acidosis together with vomiting) as the bicarbonate may be normal in these cases. A low anion gap may be caused by low serum albumin (low unmeasured anion) or a high level of paraprotein (high unmeasured cation).
Note that the anion gap calculation is made up of four measurements, each of which has a measurement uncertainty. Because of this the result for the anion gap can only be considered accurate within about +/- 5 mmol/L. Thus the anion gap can only be considered a rough guide to the cause of a metabolic acidosis.
Please refer to the Anion Gap Calculator here