

Anion Gap

Serum normally has no net charge and is a balance of anions and cations.

The predominant cation is Na⁺ which is measured (but also K⁺, Mg⁺⁺, Ca⁺⁺-unmeasured)

This must be balanced out by anions, the main ones being HCO₃⁻ and Cl⁻ (measured). There are also more unmeasured anions (serum proteins, phosphate, sulfate, lactate, ketoacids)

Thus Anion Gap AG= [Na⁺+K⁺]-([HCO₃⁻]+[Cl⁻])

Normally 12 +/- 4 mEq/L

Usually raised in conjunction with a metabolic acidosis;

Diagnostic Category	Species	Origin	Diagnostic adjuncts
Renal failure (uraemia)	PO ₄ , SO ₄	Protein metabolism	Urea/Creatinine
Ketoacidosis Diabetic (DKA) Alcoholic (SKA) Starvation (SKA)	Ketoacids β-hydroxybutyrate Acetoacetate	Fatty acid metabolism	Serum/urine ketones
Lactic Acidosis	Lactate	Metabolism	Lactate level
Exogenous poisoning methanol ethylene glycol salicylate	formate oxylate & organic anions salicylate	methanol metabolism EG metabolism also results in high lactate salicylate, lactate, ketoacids	osmolal gap osmolal gap oxylate crystals resp alkalosis and metabolic acidosis

A paper from 2004, showed a high anion gap to be the most predictive of mortality following major vascular trauma (area under ROC curve of 0.991 [95% CI 0.972-0.998]) in a series of 64 non-survivors and 218 survivors of major vascular trauma³.

Osmolality

Number of osmoles/kg solvent (1 osmole equals the molecular weight of the substance in grams divided by the number of freely moving particles each molecule liberates in solution). Osmolal concentration of a substance in a fluid is measured by the degree to which it depresses the freezing point.

Can be measured or calculated by:

$2(\text{Na}^+ + \text{K}^+) + \text{Glu} + \text{Urea}$ (all in mmol/L)

The calculated vs measured (ie Osmolar gap) should be within 15-20mmol/kg H₂O

This is due to:

- Lab error
- Spuriously lowered (reduced serum water) , such as in hyperlipidaemia, or hyperproteinaemia
- Increased osmolytes such as radioactive contrast, mannitol, isopropyl alcohol, ethylene glycol, ethyl ether, ethanol, methanol, acetone, paraldehyde, lactate

Though there have been 2 case reports of ethylene glycol poisoning without an elevated serum osmolal gap⁴.

Interestingly osmolality increases 22mg/dl for every 100mg/dl of ethanol and so can be used to estimate blood alcohol level. The relationship between ethanol and the osmolar gap was found to be linear with a Pearson coefficient of correlation of 0.99. This was validated and also tested in vitro. A formula was derived using linear regression;

osmolal gap (mOsm/kg)=1.25 (Ethanol [mmol/l])-0.35.⁵

References:

1. Tintinalli JE. et al 'Emergency Medicine: A Comprehensive Study Guide' McGraw-Hill 2000
2. Kasper DL et al (ed) 'Harrison's Principles of Internal Medicine' 16th Ed, McGraw-Hill 2005
3. Kaplan LJ, Lewis J, Kellum JA, John A 'Initial pH, base deficit, lactate, anion gap, strong ion difference, and strong ion gap predict outcome from major vascular injury' Critical Care Medicine 32(5):1120-4. 2004 May
4. Darchy B, Abruzzese L, Pitiot O, Figuerdo B, Domart Y 'Delayed admission for ethylene glycol poisoning: lack of elevated serum osmol gap' Intensive Care Medicine 25(8):859-61, 1999 Aug
5. Pursell RA, Pudeck M, Brubacher J, Abu-Laban RB 'Derivation and validation of a formula to calculate the contribution of ethanol to the osmolal gap.' Annals of Emergency Medicine 38(6):653-9 2001 Dec