2019 ACMT Annual Scientific Meeting
Open Mic Competition

Title: From Electrode to Bedside: Spanning the Anion Gap

Presenter: Josh J. Wang, MD, First Year Fellow, New York University

Abstract: The anion gap (AG) is a historically important tool for evaluating acid-base disorders when assays for specific anions were rare. While still frequently used, the AG is laden with statistical noise and biases which make it unreliable.

At the level of the patient, electrolyte analyzers quantify sodium and chloride via ion-selective electrodes (ISE) (1.5% coefficient of variation) and bicarbonate via an enzymatic process (5% coefficient of variation). Propagating the measurement error from these analyzers generates a 95% confidence interval of ± 4 mmol/L on most calculated AG's.

Institutions may use direct or indirect ISE's. In one hospital, changing from direct to the indirect method decreased the AG's upper 97.5th percentile from 17 mmol/L to 12 mmol/L. Further, the FDA only requires that manufacturers provide reference ranges for directly measured analytes, not calculated values. The responsibility for setting the AG's reference range therefore falls on the clinical chemist of each institution, who must choose between various flawed methods of doing so.

Finally, clinicians interpreting the AG may use their own reference range with little consideration to these issues above. Medical toxicologists consulting across multiple institutions face even greater complexity. I conclude that a "low" AG is almost always statistical noise, a "normal" AG is often elevated, and an "elevated" AG is sometimes normal. Given the ease and low-cost of measuring most clinically relevant anions, medical toxicologists should have a low threshold for doing so if their clinical suspicion is strong, regardless of the AG.

Objectives:

1. Explain how statistical noise makes the anion gap a low-precision instrument
2. Illustrate sources of bias when measuring the anion gap
3. Demonstrate how to rationally use the anion gap in clinical practice