

## Clinical impact of glycolysis inhibition on plasma glucose results requires caution

Clinical laboratories should strive to produce accurate results as much as possible. In the case of plasma glucose (PG) measurement, sources of preanalytical bias have been identified.<sup>1</sup> In their recent letter, Carta et al.<sup>2</sup> compared the performance of several specimen tubes that use blood acidification. Except for Venosafe tubes (Terumo Europe N.V., Leuven, Belgium), alternatives using citrate gave results that were significantly biased when compared to the reference. (The Venosafe tubes have been withdrawn from the market.) The reported results corroborate our previous data.<sup>3</sup> We concluded that caution needs to be exercised in applying recommendations regarding the use of citrate in the light of the available experimental evidence on the performance of different tubes.

We wish to highlight another point regarding the potential impact of the use of citrate on patient classification. In our experience, the percentage of outpatients with fasting PG  $\geq 5.6$  mmol/L increased from approximately 25 to 45%, when Venosafe tubes replaced classical fluoride/oxalate tubes.<sup>4</sup> Although expert groups recommended as urgent the introduction of citrate tubes,<sup>5</sup> we still await the official position of professional groups representing clinical diabetes specialists regarding the decision limits that should be applied to fasting PG – should these be redefined when tubes are used that promptly inhibit *in vitro* glycolysis – or should they be maintained, so that more subjects at increased risk for diabetes will be identified earlier?

This is not the only example where adoption of a novel approach to specimen collection in laboratory medicine has affected the results obtained, raising issues for decision limits.<sup>6</sup> The effect of analytical and preanalytical changes on patient results requires that decision limits be reviewed, if patient expectations and even outcomes are not to be adversely affected. Current fasting PG cut-off points are derived from studies using sodium fluoride tubes.<sup>7</sup> Thus, the decision limits used by physicians are based on data that were generated with approaches in collecting blood that were negatively biased. This applies to other clinical settings

as well as diabetes diagnosis and management. For example, paediatricians measure PG during insulin tolerance test in children with suspected growth hormone deficiency. Decision limits for hypoglycaemia are likewise based on studies using sodium fluoride tubes. Revised blood collection procedures involving the use of citrate challenge these clinical criteria, putting into the normoglycaemic range subjects previously categorized as hypoglycaemic. Thus, it is essential that the clinical decision limits should be adjusted to ensure that patient care remains consistent despite the changes. Alternatively, clinicians must advise patients on the clinical improvement deriving from the change.

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MP.

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