OBSERVATIONS

It's Time for a Better Blood Collection Tube to Improve the Reliability of Glucose Results

Glucose is unstable in whole blood (1). Fluoride-containing tubes are used to reduce glycolysis, especially when very accurate glucose results are required. Complete inhibition of glycolysis by fluoride can take as long as 4 h, during which time glucose can fall as much as 10 mg/dL (0.6 mmol/L) at room temperature (1), even in samples with normal blood cell counts. This is because fluoride inhibits the enzyme enolase, which acts late in the Embden-Meyerhof pathway, thus allowing the "breakdown" of glucose to intermediate molecules earlier in the glycolytic cycle (2). Is there a better fluoride formulation available that can prevent this problem?

Inclusion of citrate buffer and EDTA in a fluoride tube produces immediate inhibition of glycolysis, with no loss of glucose prior to centrifugation for at least 8 h at 77°F (25°C) (3). Even after 24 h, the loss of glucose is only 1.3 mg/dL (0.07 mmol/L). Hexokinase, which converts glucose to glucose-6-phosphate in the initial step of the glycolytic pathway, is ineffective below pH 5.9, a pH that is achieved by the addition of citrate buffer to the modified fluoride tube. Although the advantage of this tube has been clearly confirmed in the U.S. (4), it remains unavailable for routine use in America.

Some laboratories try to prevent significant glycolysis by separating plasma from cells in the shortest possible timeframe. The World Health Organization suggests this must be done within 30 min, with samples collected in an ice slurry (1). We believe that this is impractical, and there is an urgent need for a better glucose blood tube for obtaining accurate glucose results (5). This is important when the goal is as follows:

- To diagnose diabetes (although decision points that were derived using suboptimal samples may need fine-tuning)
- To prevent incorrect classification of individual patients
- To obtain reliable estimates of the prevalence of diabetes in epidemiological studies
- To ensure that biological variation is not overestimated (and inconsistent) because of poor preanalytical procedures
- To ensure that glucose reference intervals are not falsely wide because of preanalytical variation
- To prevent pseudohypoglycemia, particularly in neonates (for whom the in vitro glycolysis rate is faster than in adults)
- To ensure that laboratory results used to assess glucose meters and other point-of-care devices are themselves reliable
- To determine, when preanalytical variation is minimized, if the oral glucose tolerance test is more reproducible than is suggested by currently available data

Introduction of citrate-acidified fluoride tubes can solve these problems, thus preventing falsely low laboratory glucose results that may lead to misclassification and mismanagement of patients. Their use for obtaining more reliable laboratory glucose results is overdue.

MICHAEL J. PEAKE, MSC[1]
DAVID E. BRUNS, MD[2]
DAVID B. SACKS, MB, CHB[3]
ANDREA R. HORVATH, MD, PHD[4]

From the [1]Biochemistry Department, Flinders Medical Centre, Bedford Park, South Australia, Australia; the [2]Department of Pathology, University of Virginia Medical School, Charlottesville, Virginia; the [3]Department of Laboratory Medicine, National Institutes of Health, Bethesda, Maryland; and the [4]Screening and Test Evaluation Program, School of Public Health, University of Sydney, School of Medical Sciences, University of New South Wales and SEALS Department of Clinical Chemistry, Prince of Wales Hospital, Sydney, Australia.

Corresponding author: Andrea R. Horvath, rita.horvath@sesiahs.health.nsw.gov.au.

DOI: 10.2337/dc12-1312

Acknowledgments—No potential conflicts of interest relevant to this article were reported.

References

1. Sacks DB, Arnold M, Bakris GL, et al.; National Academy of Clinical Biochemistry; Evidence-Based Laboratory Medicine Committee of the American Association for Clinical Chemistry. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. Diabetes Care 2011;34:e61–e99
2. Mikesh LM, Bruns DE. Stabilization of glucose in blood specimens: mechanism of delay in fluoride inhibition of glycolysis. Clin Chem 2008;54:930–932
3. Uchida K, Matuse R, Toyoda E, Okuda S, Tomita S. A new method of inhibiting glycolysis in blood samples. Clin Chim Acta 1988;172:101–108
4. Gambino R, Piscitelli J, Ackattupathil TA, et al. Acidification of blood is superior to sodium fluoride alone as an inhibitor of glycolysis. Clin Chem 2009;55:1019–1021
5. Bruns DE, Knowler WC. Stabilization of glucose in blood samples: why it matters. Clin Chem 2009;55:850–852