Q&A column

Editor: Frederick L. Kiechle, MD, PhD

Submit your pathology-related question for reply by appropriate medical consultants. CAP TODAY will make every effort to answer all relevant questions. However, those questions that are not of general interest may not receive a reply. For your question to be considered, you must include your name and address; this information will be omitted if your question is published in CAP TODAY.

Q. When a patient has a hematocrit level of ≥55 percent and a normal PT and APTT, do you still correct sodium citrate and ask for a redraw? Is it crucial to ask for a redraw when the emergency department orders a stat PT and APTT?

A.July 2022—CLSI document H21-A5 addresses the need to adjust citrate concentration for patients with high hematocrits since hematocrits above 55 percent lead to a relative excess of citrate in blue top tubes that may cause prolonged clotting times. I am not aware of guidance that addresses the need to redraw a sample for which citrate has been adjusted if the prothrombin time (PT) and activated partial thromboplastin time (APTT) are normal, which means laboratory directors can use their discretion in managing such situations.

Our laboratory would allow the normal results to be reported since the high hematocrit may lead to erroneous prolonged clotting times but would not be expected to cause erroneous normal clotting times.

The decision whether to redraw should take into consideration which tests are ordered since expected effects and potential clinical significance may be different for different assays. Therefore, the laboratory's written procedure outlining the handling of polycythemic specimens should address the potential for erroneous results for calcium-dependent clotting tests, including routine (e.g. PT, PTT) and specialized (e.g. clottable protein C, protein S) coagulation testing.

Clinical and Laboratory Standards Institute. H21-A5: Collection, Transport, and Processing of Blood Specimens for Testing Plasma-Based Coagulation Assays and Molecular Hemostasis Assays; Approved Guideline, 5th ed.; 2008.

College of American Pathologists. HEM.36900 Elevated hematocrits—coagulation. In: Hematology and coagulation checklist. Sept. 22, 2021.

Marlar RA, Potts RM, Marlar AA. Effect on routine and special coagulation testing values of citrate anticoagulant adjustment in patients with high hematocrit values. *Am J Clin Pathol*. 2006;126(3):400–405.

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Q. Obtaining an accurate blood glucose level is hindered by continued glycolysis in the evacuated tube post collection, even if a gray top tube is used. This leads to falsely low blood glucose levels.

What can laboratories do to limit ex vivo glycolysis?

A.The reader has identified an important practical problem. Loss of glucose from a blood sample via glycolysis, predominantly in red and white blood cells, contributes substantially to preanalytical error when measuring glucose. Glucose decreases in whole blood at room temperature ex vivo at five to seven percent per hour. To put this in context, the reduction in glucose at one hour exceeds the desirable limit of total analytical error for glucose based on biological variation.

Some clinicians erroneously believe that a gray top tube, which contains sodium fluoride, completely prevents glycolysis. However, this is true only for long-term glycolysis, as sodium fluoride, which inhibits the glycolytic enzyme enolase, does not stop glycolysis until two to four hours after sample collection. The rate at which glucose is lost during the first 60 to 90 minutes is the same with or without sodium fluoride. After four hours, the glucose concentration is stable in whole blood for 72 hours at room temperature in the presence of sodium fluoride.

An American Association for Clinical Chemistry and American Diabetes Association guideline addresses the practice of measuring plasma glucose to diagnose diabetes. The guideline recommends removing plasma from whole blood samples immediately after blood collection or immediately immersing the blood collection tube in an ice-water slurry and removing the plasma within 30 minutes of collection. However, these methods are rarely feasible in routine patient care.

A proposed alternative is to use blood tubes containing citrate, which immediately blocks the activity of glycolytic enzymes by acidifying the blood (pH, 5.3–5.9), thereby preventing glycolysis. Several studies that validate this concept have been published over the past few years. Tubes containing granulated citrate buffer with sodium citrate and sodium EDTA are used clinically, predominantly in Europe, but are not yet available in the United States. I strongly encourage manufacturers to make these blood collection tubes available worldwide.

Sacks DB, Arnold M, Bakris GL, et al. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. *Clin Chem*. 2011;57(6):e1–e47. *Diabetes Care*. 2011;34(6):e61–e99.

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