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. What is the best method to quantify ketones in serum? Can urine strips be used to detect ketones in serum?

A.March 2023—The body's primary source of energy is carbohydrates. When this pool is depleted, the body begins to use fat to meet its energy needs. The citric acid cycle is the primary process for breaking down fats into energy. When the capacity of the citric acid cycle is exceeded, ketone bodies are formed. The human body goes into a state of ketosis when the concentration of ketone bodies is higher than normal. The three ketone bodies that compose ketosis are beta-hydroxybutyrate (BHB, 78 percent), acetoacetate (20 percent), and acetone (two percent). BHB not only increases during periods of starvation but also during hypoglycemic episodes. Acetoacetate is present in significantly lower concentrations than BHB and is unstable. It spontaneously converts to carbon dioxide and acetone.

BHB is not only the predominant ketone but also the most sensitive and specific marker for assessing ketosis in diabetic ketoacidosis. Under normal circumstances, the ratio of BHB to acetoacetate is 1:1, but the ratio can be 10:1 or higher in ketoacidosis. BHB increases more rapidly in blood during ketogenesis than either acetoacetate or acetone and thus is a better marker for ketosis.

For the aforementioned reasons, the best ketone to quantify is BHB. The enzymatic method is most commonly used for this purpose. It is the best method because of its specificity. However, continuous ketone monitoring devices that measure BHB using enzyme electrochemistry are being evaluated.[1] Urine test strips for measuring ketones use a nitroprusside reagent that reacts well with acetoacetate but not BHB. Therefore, they are not as helpful as the enzymatic BHB method.[2,3] Furthermore, urine test strips may need to be validated if serum is used for measurement, as this is an off-label use. Review the manufacturer's package insert to determine if validation is needed.

1. Zhang JY, Shang T, Koliwad SK, Klonoff DC. Continuous ketone monitoring: a new paradigm for physiologic monitoring. *J Diabetes Sci Technol*. 2021;15(4):775–780.
2. Vanelli M, Chiari G, Capuano C, Iovane B, Bernardini A, Giacalone T. The direct measurement of 3-beta-hydroxy butyrate enhances the management of diabetic ketoacidosis in children and reduces time and costs of treatment. *Diabetes Nutr Metab*. 2003;16(5–6):312–316.
3. Laffel LMB, Wentzell K, Loughlin C, Tovar A, Moltz K, Brink S. Sick day management using blood 3-hydroxybutyrate (3-OHB) compared with urine ketone monitoring reduces

hospital visits in young people with T1DM: a randomized clinical trial. *Diabet Med*. 2006;23(3):278–284.

Stanley F. Lo, PhD, DABCC
Associate Director, Clinical Laboratory
Technical Director, Clinical Chemistry andPoint-of-Care Testing
Children's Wisconsin
Milwaukee, Wis.
Member, CAP Clinical Chemistry Committee

Q. Is it acceptable to run hemolyzed specimens for coagulation testing? We have a Stago analyzer for coagulation testing and some of my co-workers run hemolyzed specimens on it.

A.It is common for hyperbilirubinemia, hyperlipidemia, and hemolysis to adversely affect laboratory analyses. Their impact is variable and sometimes unpredictable, and it most frequently results from interference with optical detection methods.

Test manufacturers sometimes address the effects of interfering substances on their tests. However, it is ultimately the laboratory's responsibility to be aware of the effects and impact of these substances.

The consequences of hemolysis on hemostasis testing depend on the test or analyzer used and the degree of hemolysis in the specimen. Coagulation analyzers employ optical or mechanical detection methods. Hemolyzed specimens may interfere with optical-based tests if the detection wavelength overlaps the absorbance spectrum of free hemoglobin. Mechanical-based tests are generally less susceptible to interference by hemolysis, but studies have shown that high concentrations of dissolved hemoglobin falsely prolong clotting times when using mechanical methods.[1,2] One must remember that hemolysis will spill not only free hemoglobin but also phospholipids.

It is important to consider the type of test and whether the manufacturer or others have performed interference studies on the analyzer. For example, hemolysis does not appear to significantly affect prothrombin time and fibrinogen on the Stago STA Compact Max analyzer, but it shortens activated partial thromboplastin time.[3]

The soundest approach is for the laboratory to validate the effects of hemolysis by performing interference studies with the tests and analyzers in question. Without such data, the safest practice is to reject coagulation samples with more than trace hemolysis, unless the patient is experiencing in vivo hemolysis. Patients with in vivo hemolysis, such as those who have hemolytic anemia or are on ECMO circuits, may require coagulation testing, and their samples will be hemolyzed regardless of the phlebotomy technique and sample transport method used. Those samples should be analyzed and resulted in consultation with the clinical service. All specimens determined to have hemolysis merit a comment or disclaimer regarding the presence of hemolysis, particularly if the result is beyond the reference interval.

1. Moreira PL, Lansden CC, Clark TL, Gawryl MS. Effect of Hemopure on prothrombin time and activated partial thromboplastin time on seven coagulation analyzers. *Clin Chem*. 1997;43(9):1792.
2. Nougier C, Jousselme E, Sobas F, Pousseur V, Négrier C. Effects of hemolysis, bilirubin, and lipemia interference on coagulation tests detected by two analytical systems. *Int J Lab Hematol*. 2020;42(1):88–94.
3. Woolley A, Golmard JL, Kitchen S. Effects of haemolysis, icterus

and lipaemia on coagulation tests as performed on Stago STA-Compact-Max analyser. *Int J Lab Hematol*. 2016;38(4):375–388.

Clarence Chan, MD, PhD
Fellow, Clinical Chemistry
Department of Pathology
University of Chicago
Chicago, Ill.
Junior Member, CAP Hemostasis and Thrombosis Committee

Jacob Ritter, MD
Post-graduate Year-four Pathology Resident
Department of Pathology and Laboratory Medicine
UT Health San Antonio
Long School of Medicine
San Antonio, Tex.
Junior Member, CAP Hemostasis and Thrombosis Committee

Q. I am a medical laboratory scientist who would like to move into a laboratory information technology/information systems career to support the growing need of professionals in that aspect of health care. What education is advised and what licensing is required, and do you have any suggestions on how to make such a move?

A.In my organization, the majority of our laboratory informatics team members come to us with prior bench experience as clinical laboratory scientists (CLS). Their ability to understand local testing workflows and the data generated from testing is often key to guiding and supporting each of our testing departments with their laboratory information system and EHR requests.

A good way to get involved is to become the point person from your testing department who works with your local IT teams on any LIS-related changes, such as adding new test orders, interfacing new instruments, modifying test orders or results, and reviewing security needs for patient-protected health information. Learning to translate your testing department's needs to the LIS/EHR and IT requirements should give you real-world experience that will help you determine whether this might be a good career move. Beyond that, I don't think there are necessarily any required special certifications, but different job postings may have different needs, which should be spelled out in the job requirements or by inquiry to the recruiter.

Ji Yeon Kim, MD, MPH
Physician Director, Laboratory Informatics
Kaiser Permanente Southern California
Los Angeles, Calif.
President, Association for Pathology Informatics

Submit your pathology-related question

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.

Submit a Question