Answering your questions

Benzoylcegonine without cocaine?

Q Is there any other way for benzoylcegonine to be in your body other than the use of cocaine?

A Benzoylcegonine is one of several metabolic products of cocaine. It is formed from the hydrolysis of cocaine and is a very specific marker for the presence of that drug. If, however, benzoylcegonine is found in the urine, it is not evidence of illicit cocaine use.

There are at least two other ways that cocaine can get into a person’s system. One way is from medical administration. Cocaine is a component of a topical anesthetic used by ear, nose, and throat specialists. These physicians should always tell their patients that they have used a cocaine-containing anesthetic and warn them that they could have a positive drug test for up to 48 hours after the use of the anesthetic.

If, however, benzoylcegonine is found in the urine, it is not evidence of illicit cocaine use.

Another, less obvious route of ingestion is drinking mate de coca, a coca leaf tea, which is also sold in health food stores as Health Inca tea. We reported a case in which a person drank some of the tea as part of a meal in a Bolivian restaurant in the United States. The next day he had a positive drug screen. Although the imported tea is supposed to be de-cocainized, some may still contain cocaine in small amounts.

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Usefulness of reporting RBC morphology

Q Can you comment on the usefulness of reporting red-blood-cell (RBC) morphology on specimens submitted for a complete blood count (CBC), as opposed to a CBC with differential? We are currently scanning a slide for any specimen with RBC distribution width (RDW) <11.0 or >17.0 or “other abnormal indices,” or unusual RBC/hemoglobin (HGB) ratio. Are these guidelines clinically useful? Also, I am wondering about the correlation between indices and morphology. Is it usual to see hypochromia with a normal mean cell hemoglobin concentration (MCHC) or microcytosis with a normal mean cell volume (MCV)?

A There are certainly instances where a morphologic assessment of the red cells is useful, even if a differential is not ordered. Notably, the presence of spherocytes (hemolysis), teardrop cells (myelofibrosis, bone marrow metastases), or sickle cells (sickle-cell anemia), as examples, give information beyond that of the standard indices. Abnormal indices can give a clue to these morphologic abnormalities, so having some parameters in place is useful. An unusual RBC/HGB ratio may highlight patients with both anemia and an elevated RBC count, such as those with a hemoglobin disorder, including thalassemia. In general, a smear review for an increased RDW (such as >17.0) could be very useful, as it may show dimorphic populations and other abnormal red-cell morphology, which provide important clinical information. A low RDW (<11.0), which would indicate a more uniformly sized RBC population, however, is not clinically significant.

There is a correlation between indices and morphology. The instrument is very accurate, especially for size (MCV) and variation in size (RDW), since it looks at many more red cells than a morphologic assessment alone and evaluates them in their three-dimensional configuration. But that does not mean the instrument is perfect. The instrument would not detect any red-cell inclusions, such as Howell-Jolly bodies, basophilic stippling, and Pappenheimer bodies. It may also have trouble detecting a minor abnormal population. The MCV may be normal in these situations, but a subpopulation of microcytic cells may be present. Correlating the MCV with the other RBC indices is extremely helpful in these situations, such as increased RDW, reflecting the increased spectrum of cell size. Finally, the usefulness of morphology in these cases depends on your patient population. If you have a diverse population that includes patients of many different ethnic backgrounds, there may be more usefulness to these analyses.

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Minimal monoclonal gammopathy

Q How large should a monoclonal gammopathy be when doing serum protein electrophoresis before it is considered to be clinically significant?

A Monoclonal gammopathy of undetermined significance (MGUS) is the term used to denote the presence of a monoclonal protein (M-protein, myeloma protein, or paraprotein) in persons without evidence of plasma-cell myeloma,
Waldenstrom macroglobulinemia, primary amyloidosis, or related disorders. The incidence of MGUS is 3% in persons older than age 70 and 1% in those over 50 years of age. Approximately 75% of these cases are represented by monoclonal IgG, with IgM in 15% and IgA in 10%. IgD and IgE represent less than 1% of cases. Patients with MGUS are, by definition, asymptomatic and have low levels of plasma cells (less than 10% in bone marrow), but a proportion of these patients will evolve over time. Several large studies have shown that with more than 20 years of follow-up, approximately 25% of MGUS patients developed plasma-cell myeloma, macroglobulinemia, amyloidosis, or a related lymphoplasmaemic disorder.1 The risk of progression to multiple myeloma was about 1% per year and is unrelated to the type of M-protein.

There is no lower limit for the concentration of serum M-protein to be designated MGUS. A recent series of 1,384 MGUS patients, however, showed an increased risk of progression with increasing M-protein concentration.6 Those with M-protein values of 1.5 g/dL were nearly twice as likely to progress to multiple myeloma as those with values of 0.5 g/dL; the risk of progression with values of 2.5 g/dL was 4.6 times the risk in those with values of 0.5 g/dL. An IgA or IgM M-protein is associated with a slightly increased risk of progression than IgG. M-proteins greater than 3.0g/dL very often indicate the presence of underlying plasma-cell myeloma. The World Health Organization uses the values of serum IgG over 3.5 g/dL and IgA greater than 2.0 g/dL as major criteria for diagnosis of plasma cell myeloma.3 Thus, any value below this is consistent with MGUS in the absence of other clinical findings. Due to the risk of developing disease that requires treatment, patients with MGUS should be periodically monitored indefinitely for evidence of progression.

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Urine micro volume

Is there any standard as to the volume of urine to be spun down for a urine microscopic? If so, if less urine is submitted, would the results of the microscopic need to adjusted for volume of sample submitted? We use the BD urinalysis tube (8 mL) and some labs require 10 mL to be spun down, if less if submitted, a comment was reported with the results.

The standard volume for urine to be spun down for a microscopic varies per institution (10 mL, 12 mL, or 15 mL).1,2 Manufacturers of commercial systems have varying sediment concentrations (30:1, 15:1, and 12:1).3 I recommend that the standard volume for urine to be spun down for a microscopic is a 10:1 concentration of urine.4 This can be achieved one of two ways when you only have 8 mL of urine:

1. Centrifuge 5 mL and remove 4 mL and multiply times two; or
2. Centrifuge 8 mL. Reduce the final volume to 0.8 mL to maintain the 10:1 concentration.

—G. Berry Schumann, MD
Medical Director
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Seymour, CT

Tests for DIC

In my laboratory, we are suddenly getting quite a few requests for disseminated intravascular coagulation (DIC) related testing. We currently do prothrombin time (PT), partial thromboplastin time (PTT), fibrinogen (FIB), D-dimer, and CBC. Based on my experience in a coag lab a few years ago, I am suggesting fibrin monomer as additional testing. Would this be helpful, or is our current testing adequate?

The Scientific Subcommittee (SSC) on Disseminated Intravascular Coagulation of the International Society on Thrombosis and Haemostasis (ISTH) published a definition of DIC as well as clinical and laboratory criteria for diagnosis in the December 2001 issue of Thrombosis and Haemostasis. In this publication, the Subcommittee distinguished overt DIC from non-overt DIC. The Subcommittee defined overt DIC as that which occurs in a decompen-sated hemostatic system and non-overt as a compensated phase in which there is subtle hemostatic dysfunction.

In an effort to standardize diagnosis and determination of the severity of DIC, the ISTH Subcommittee on DIC has developed a five-step diagnostic algorithm that can be used to calculate a DIC score. A five-year overview of this scoring system was published on behalf of the SSC on DIC of the ISTH in the March 2007 issue of Thrombosis and Haemostasis and concluded that a score of five or greater can identify overt DIC. The diagnostic algorithm for the diagnosis of overt DIC is provided in Table 1.

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In this report, it was stressed that assays used in the diagnosis of overt DIC should be readily available laboratory tests. According to the ISTH Subcommittee on DIC, major laboratory criteria for the diagnosis of overt DIC include platelet count, prothrombin time, fibrinogen level, and a marker of the presence of fibrin, which can be ascertained by one of the following assays: soluble fibrin monomer, fibrin degradation products, and/or D-dimer. In the

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References
Dilution terminology

Q In the hospital where I work, we are having a “dilution debate,” because while documenting a sample before it is verified, most of us enter it as a x2 or x10 dilution — though some people prefer the 1:2 or 1:10 format. Confusion occurs when someone uses “1:1” as a dilution because if 1:10 means one part diluted with nine parts, making a total of 10 parts, then what does 1:1 mean? One part out of a total of one part, meaning “neat,” or, as some people loudly state, “one part plus one part,” meaning a x2 dilution? What proper terminology should we be using?

A Sharon Miller, a member of the MLO editorial advisory board, assisted me in answering this question. Clinical laboratory sciences students at Northern Illinois University receive the following information as part of their initial lab guidelines:

Terminology of dilutions is very important. Unfortunately, there is inconsistency in how dilutions are described. When water is added to relatively concentrated solutions or mixtures, they are being diluted. We say, for example, that we make a “1 in 10” dilution. This means that one volume of concentrate is mixed with nine volumes of water. A “1 in 100” dilution is one volume of concentrate in 99 volumes of water.

Avoid the expression “one-to-one dilution” or “one-to-two dilution.” Those expressions are actually proportions, not dilutions. We can express dilutions as follows: a “1 in 10” dilution = 1:10; and “1 in 100” dilution = 1:100. A 1:2 or “1 in 2” dilution is prepared by taking 200 mL of dilute and adding 200 mL of water to create 400 mL of solution.

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There is probably no single physiologic explanation for why capillary whole blood measurements are affected by poor peripheral perfusion, edema, or hypotension.

systematically underestimated venous glucose in this patient population. In contrast, another study performed on 75 patients with systemic hypoperfusion (defined as systolic blood pressure less than 90 mm Hg or requirement for vasoactive agents) found relatively good agreement between capillary whole blood and arterial whole blood glucose, with 95% limits of agreement of approximately ± 30 mg/dL.

Finally, a recent study comparing capillary whole blood to venous plasma glucose in patients with poor peripheral perfusion related to vasopressor use or peripheral edema found that in both categories of patients (poor perfusion and peripheral edema), capillary whole blood glucose systematically overestimated venous plasma glucose. Even in this study, however, almost all results agreed within approximately 2 mmol/L (36 mg/dL) glucose.

Because studies in these various patient populations have reached different conclusions, there is probably no single physiologic explanation for why capillary whole blood measurements are affected by poor peripheral perfusion, edema, or hypotension. Variables most likely include patient population under consideration (edema, hypotension, or poor perfusion); meter device characteristics and measurement technology (in particular extent of hematocrit effect but also any effect of oxygen content or pH); sample volume requirements for the measuring device; and range of glucose values encountered

Tips from the clinical experts

2003 meeting of the SCC on DIC, D-dimer was proposed as the ideal fibrin marker.

Therefore, the following battery of assays, PT/FIB/D-dimer/CBC, should be adequate in the evaluation of overt DIC, without the inclusion of a fibrin monomer assay. This is advantageous, as there is currently no manufactured kit available in the United States for the quantitation of soluble fibrin monomer. Diagnostica Stago offers a rapid qualitative slide test for soluble fibrin monomer complexes in plasma by the hemagglutination technique (F.S. Test). This assay, however, is not as sensitive to the presence of fibrin monomers in plasma as a quantitative immunologic-based soluble fibrin monomer assay.

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References

POCT glucose and patients with poor circulation

Q Lately, we have had several instances of getting 450+ glucose readings on patients who have an underlying circulatory issue that probably should not be having capillary glucose testing. When a specimen is sent to the lab to confirm, of course the glucose drops at least to one-half of what it was at bedside. What causes such a wide swing in values? Does glucose tend to “sit” in the extremities when circulation is poor? I am having a hard time explaining this to nurses when they call to say the glucose meter is broken ... and after asking a few questions, find out the patient has circulatory issues.

A A number of different studies have examined the accuracy of bedside glucose meters in various patient populations with either hypotension, poor peripheral perfusion, or edema. Two studies done on patients in the emergency department and ICU with hypotension (systolic blood pressure less than 80 mm Hg) both found that capillary glucose measurement...
To read HR 3453 and S 2099, please visit http://thomas.loc.gov/. Search using HR 3453 or S 2099 respectively.

The combined lobbying and grassroots efforts of the laboratory community are having an impact. In addition to Rep. Velazquez, HR 3453 now has 14 co-sponsors. In addition to Sen. Salazar, S 2099 has three co-sponsors.

The House Small Business Committee hearing definitely raised the profile of competitive bidding on Capitol Hill. On Aug. 7, 2007, House Energy and Commerce Chair John Dingell (D-MI) sent a letter to Department of Health and Human Services Secretary Michael Leavitt asking CMS to respond to a list of questions before the agency proceeds with the demonstration. On Aug. 14, 2007, Reps. Jim Matheson (D-UT) and Anna Eshoo (D-CA), both members of the Subcommittee on Health, requested an Energy and Commerce hearing on the demonstration.

References
4. Kanji S, et al. Reliability of point-of-care testing for capillary whole blood glucose results relative to a laboratory plasma measurement. I would start by looking at collection technique and meter dosing or as you mentioned a process for avoiding capillary sampling on these patients.

—Bradley S. Karon MD, PhD, Director Hospital Clinical Laboratories and POCT Mayo Clinic, Rochester, MN

Editor’s note: Dr. Baer also alerted us that in the September issue, on page 42 — the first page of the Tips in the third column — CBG is not “cell biology and genetics” but, rather, “capillary blood glucose.” We apologize for this egregious error. ☐

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Call to action
CMS is mandated by Congress to implement a competitive-bidding-demonstration project for clinical-laboratory services. Now that the first site has been announced, the only way to stop competitive bidding is to lobby Congress to enact legislation to repeal the demonstration project. Laboratory professionals must ask Congress to repeal the demonstration project now!
Please contact your Members of Congress and ask them to support HR 3453 and S 2099, either through your professional organization or by visiting www.senate.gov and www.house.gov.

Katharine I. Ayres is currently the director of Legislative and Regulatory Affairs for the Clinical Laboratory Management Association (CLMA), where she serves as staff liaison to CLMA’s Health Care Policy Committee, Medicare Billing Issues Committee, and PAC Board of Directors. She also interacts with government agencies such as CMS, FDA, and CDC on behalf of CLMA. She authors CLMA’s Regulatory Email Alerts and PAC Email Updates.