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. Is it necessary to perform a manual cell count for body fluids, including CSF, using a hemocytometer? Can clinical decisions be made based on low cell counts in body fluid reported by automated cell counters since these instruments have decreased precision and accuracy with low counts?

A.April 2022—In some cases, clinical decisions can be made from body fluids that have low cell counts. Although automated cell counters are a valuable tool for evaluating body fluid specimens, they have limitations, particularly with body fluids that have low cell counts. Therefore, automated cell counters should not be relied on below a certain threshold.

CAP hematology and coagulation checklist item HEM.35452 states, "The laboratory defines the upper and lower limits for counting body fluid cells (erythrocytes, nucleated cells) outside of which the use of automated or semi-automated cell counters is not reliable."[1] In addition, HEM.35528 indicates that the methods for evaluating body fluids should be appropriate for the intended clinical use.[1] Therefore, although a manual cell count and differential may not be required for all body fluid specimens with low cell counts, they may impact clinical care in some instances, so the appropriate testing should be performed.

For example, a cytocentrifuged cerebrospinal fluid sample should be obtained from patients who have acute lymphoblastic leukemia and are receiving intrathecal therapy. It should be manually reviewed to ensure an accurate cell count and differential, including enumeration of blasts, despite a low nucleated cell count.[2-5] Manually examining synovial fluid, despite a low total nucleated cell count, may also be beneficial to identify the presence or absence of neutrophils, microorganisms, or crystals, which in turn may aid in determining the etiology of these effusions.

In other clinical scenarios, it may not be necessary to perform a manual count for body fluids, including CSF, using a hemocytometer. For example, when evaluating for subarachnoid hemorrhage, it is reasonable to report the presence of a small number of erythrocytes without giving a precise count (i.e. less than 500 RBC/µL), as studies have shown that values below 2,000 RBCs/µL are not correlated with acute subarachnoid hemorrhage.[6]

As technology for automated cell counters continues to improve, the need for manual slide review may decrease. However, at present, manual review is still essential in certain clinical scenarios for identifying malignant cells, microorganisms, crystals, and other pathologic findings, regardless of the nucleated cell count.

1. College of American Pathologists. HEM.35452 Acceptable limits; HEM.35528 Quantitative differentials. In: Hematology and coagulation checklist. Sept. 22, 2021.
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acute lymphoblastic leukemia. *Cancer*. 1990;66(8):1748–1754.
3. Bürger B, Zimmermann M, Mann G, et al. Diagnostic cerebrospinal fluid examination in children with acute lymphoblastic leukemia: significance of low leukocyte counts with blasts or traumatic lumbar puncture. *J Clin Oncol*. 2003;21(2):184–188.
4. Pui CH, Howard SC. Current management and challenges of malignant disease in the CNS in paediatric leukaemia. *Lancet Oncol*. 2008;9(3):257–268.
5. Arber DA, Borowitz MJ, Cessna M, et al. Initial diagnostic workup of acute leukemia: guideline from the College of American Pathologists and the American Society of Hematology. *Arch Pathol Lab Med*. 2017;141(10):1342–1393.
6. Perry JJ, Alyahya B, Sivilotti ML, et al. Differentiation between traumatic tap and aneurysmal subarachnoid hemorrhage: prospective cohort study. *BMJ*. 2015;350:h568.

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Q. Is there a time limit for a critical value—for example, when a specimen is drawn at 8 AM, the lab receives it at 5 PM (due to courier issues) and has a result at 10 PM, and the value falls in the critical range? Since it is now 14 hours after the draw, the lab value may no longer be actionable. No clinician would act on a critical value that is a week old, so at what point is the lab value no longer considered critical?

Our hospital administration maintains that if a value is critical, the lab must contact the physician immediately or contact the patient, if the physician can't be reached, regardless of the time from draw to result.

A.George Lundberg, MD, is widely credited with developing the critical value system based on a foundational definition: A critical, or panic, laboratory value represents a pathophysiological state at such variance with normal as to be life-threatening unless something is done promptly and for which some corrective action could be taken.[1]

The clinical laboratory's responsibility to rapidly communicate critical values was incorporated into CLIA regulations. It states that the laboratory must "immediately alert the individual or entity requesting the test and, if applicable, the individual responsible for using the test results when any test result indicates an imminently life-threatening condition, or panic or alert values." The CAP all common checklist COM.30000 note defines requirements for critical value notification[2]:

> Alert or critical results are those results that may require prompt clinical attention to avert significant patient morbidity or mortality. The laboratory director, in consultation with the clinicians served, must define the critical values and critical results that pertain to its patient population. The laboratory may establish different critical results for specific patient subpopulations (for example, dialysis clinic patients).
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> An appropriate notification includes a direct dialog with the responsible individual or an electronic

> communication (eg, secure email or fax) with confirmation of receipt by the responsible individual . . . . Allowing clinicians to "opt out" of receiving critical results is strongly discouraged.

Determining which tests and exceeded result limits qualify as critical values is a frequent topic of discussion among laboratory professionals. Several Q-Probes studies provide guidance.[3-5]

Clinical laboratories are obligated to follow their own policies and procedures for critical value results and notify the patient's health care provider as soon as testing is completed. The requirement still applies when there are delays between sample collection and result.

During a delay in obtaining critical value results, the patient's pathophysiologic condition that was detected by the test may change, requiring repeat testing to guide management. Nevertheless, the delayed critical value notification can initiate investigations that might mitigate a patient's risk of harm. For example, an asymptomatic patient on warfarin anticoagulation whose critical international normalized ratio result of 6.5 is delayed for 24 hours beyond the expected collection-to-result turnaround time of four hours would continue to be at risk for bleeding complications until the laboratory informs the ordering physician and he or she takes action. Such steps as instructing the patient to hold subsequent warfarin doses, arranging for repeat INR monitoring, and advising the patient to seek immediate medical attention for signs and symptoms of bleeding would be triggered by the delayed critical value notification.

Some critical values are delayed due to analytical turnaround time. For example, blood and cerebrospinal fluid cultures can take several days to turn positive. Delays in collecting, transporting, and analyzing patient samples to obtain electrolyte and blood gas critical results may diminish the utility of the information. However, the physician who receives the critical result, and not the laboratory, should make that assessment.

1. Lundberg GD. It is time to extend the laboratory critical (panic) value system to include vital values. *MedGenMed*. 2007;9(1):20.
2. College of American Pathologists. COM.30000 Critical result notification. In: All common checklist. Sept. 22, 2021.
3. Valenstein PN, Wagar EA, Stankovic AK, Walsh MK, Schneider F. Notification of critical results: a College of American Pathologists Q-Probes study of 121 institutions. *Arch Pathol Lab Med*. 2008;132(12):1862–1867.
4. Howanitz PJ, Steindel SJ, Heard NV. Laboratory critical values policies and procedures: a College of American Pathologists Q-Probes study in 623 institutions. *Arch Pathol Lab Med*. 2002;126(6):663–669.
5. Wagar EA, Friedberg RC, Souers R, Stankovic AK. Critical values comparison: a College of American Pathologists Q-Probes survey of 163 clinical laboratories. *Arch Pathol Lab Med*. 2007;131(12):1769–1775.

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Q. Given that blood specimen collection tubes are in short supply, many laboratories may need to switch to an alternative collection tube manufacturer. What validation studies are necessary before an alternative collection tube can be implemented?

A.The CAP has an accreditation program checklist requirement for the change of specimen containers, and in the long list of references that follow it is one for a Clinical and Laboratory Standards Institute guideline on the validation and verification of tubes for specimen collection, which is also cited in the note accompanying the requirement.

The CAP's requirement, GEN.40942 Specimen Container Analytic Interference (phase two), says the laboratory director or designee must evaluate significant changes to specimen containers to ensure they do not contribute to analytic interference in the assays to be performed and approve them for use. The note reads as follows:

> Significant changes include new container types, a different container type (eg, a plain container to one with an additive), and when changing to a different vendor. To ensure that the specimen containers do not contribute to analytic interference, the laboratory director or designee must review clinical literature, as available, and evaluate information from specimen collection container and instrument/method manufacturers. Based on the information reviewed and the test systems that will be impacted, the laboratory director or designee determines whether verification by the laboratory is indicated.
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> Manufacturers of collection containers must perform studies to demonstrate safety and efficacy of the product prior to marketing their products. However, it is not feasible for manufacturers to evaluate all assays on all instruments and methods. The CLSI Guideline GP34-A, Validation and Verification of Tubes for Venous and Capillary Blood Specimen Collection, recommends performing a comparative tube evaluation when changing to a different type of tube (eg, gel, additive, different vendor). A sample protocol for end user evaluation is provided in the CLSI guideline.
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> For some analytes it may be necessary to evaluate the effectiveness of the specimen collection containers to accurately maintain analyte stability over time.

The requirement says the evidence of compliance are records of specimen container evaluation for analytic interference with approval for use.

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