Q & A Column, 9/14

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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

Effect of diurnal variation, postural changes on CBC

Using “transference” to standardize reference intervals throughout a regional health system

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Q. Occasionally on certain patients, when we draw for a CBC in the early morning, we get a low Hgb of 6 or 7 g/dL. We draw the same patient for a CBC in the afternoon and we get a higher Hgb by at least 1–1.5 g/dL. Can you explain the reason for this difference?

A. The CBC, and specifically hemoglobin, is affected by a number of different parameters. These include diurnal variation and posture-related changes, for example. Diurnal variation has been reported with many of the measurements of the complete blood count, including hemoglobin, from as early as 1947.[1] Specifically, the RBC count, hemoglobin, and hematocrit show diurnal variation with gradually falling mean levels throughout the day, with the nadir at midnight. In contrast, the WBC count and individual leukocyte counts (neutrophil, eosinophil, monocyte, lymphocyte) gradually increase mean levels throughout the day, peaking at midnight. In one study[2] hemoglobin and leukocytes showed the highest amount of variation when measured in healthy young men. In another study of athletes, hemoglobin decreased over the day by approximately 0.55 g/dL.[3]

In contrast, postural changes (supine to standing) increase hydrostatic pressure in dependent regions, resulting in a loss of plasma volume and subsequent hemoconcentration. In one study of hematocrit, a relative increase of 11 percent ± 3.6 percent was seen in individuals within 30 minutes of standing.[4] Given the situation described in the question, one can wonder if the individual who has a higher hemoglobin later in the day has had some loss of plasma volume and subsequent hemoconcentration (e.g. postural, diuresis).

1. Renbourn ET. Variation, diurnal and over longer periods of time, in blood haemoglobin, haematocrit, plasma protein, erythrocyte sedimentation rate, and blood chloride. *J Hyg* (Lond). 1947;45(4):455–467.
2. Sennels HP, Jørgensen HL, Hansen AS, et al. Diurnal variation of hematology parameters in healthy young males: the Bispebjerg study of diurnal variations. *Scand J Clin Lab Invest.* 2011;71:532–541.
3. Schumacher YO, Wenning M, Robinson N, et al. Diurnal and exercise-related variability of haemoglobin and reticulocytes in athletes. *Int J Sports Med.* 2010;31(4):225–230.
4. Jacob G, Raj SR, Ketch T, et al. Postural pseudoanemia: posture-dependent change in hematocrit. *Mayo Clin Proc.* 2005;80(5):611–614.

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Q. We would like to standardize reference ranges throughout our system of regional facilities, using our main laboratory to establish the ranges. How does the CAP view using the transference process as described in CLSI document C28-A3C, Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline? Is this an approved method for establishing reference ranges? Is it an acceptable process once the laboratory director approves it?

A. CAP Laboratory Accreditation Program checklist requirement COM.50000, Reference Intervals Established/Verified, says "The laboratory establishes or verifies its reference intervals (normal values)." The CAP does not give preference for one method over another but would fully support the practice of transference, as we will describe here.

The goal of having standard reference intervals throughout a regional health care system is laudable. To achieve this goal, there are two critical prerequisites: The facilities must have comparable patient populations, and the assays they use must generate comparable values.

In the situation described, the plan is to establish reference intervals at the main laboratory and then have the other facilities adopt those intervals as their own. According to CLSI EP28-A3C (formerly C28-A3C), this is exactly the situation in which one would use "transference." Each facility would compare its method to the main laboratory's method by performing correlation studies using fresh patient samples. Of note, the samples used in these studies can come from any patients; they do not need to come from reference individuals. If the values between the two methods match, the regional facility can adopt the main laboratory's proposed reference intervals. If the values do not match, then the regional facility, before adopting the proposed reference intervals, would have to incorporate slope and intercept changes in its method to make the values match. (This entire exercise, of course, is straightforward if the regional facilities are all using the same method as the main laboratory; one would fully expect the correlation studies to yield matching results.)

As noted in EP28-A3C, it is always a good idea, as a final step, to verify the proposed new reference intervals by collecting samples from 20 reference individuals at each facility and ensuring that no more than two of those values, for each analyte, are outside the proposed limits. If your institution is able to confirm the reference interval arrived at by transference in this fashion, it would represent exemplary performance.

1. College of American Pathologists Laboratory Accreditation Program All Common Checklist, April 21, 2014.
2. EP28-A3C—Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline—Third Edition. Wayne, Pa.: Clinical and Laboratory Standards Institute; 2010.

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