LifeLabs® Medical Laboratory Services

Inside Diagnostics

CAUSES OF DISCREPANT HEMOGLOBIN RESULTS

At LifeLabs, we occasionally receive calls regarding discrepant hemoglobin results. The motivation for the call is often that our reported hemoglobin value is lower than that of another laboratory. Frequently the patient is transferred to a hospital setting for a red cell transfusion that is later cancelled because of a higher repeat hemoglobin result. This is understandably frustrating and inconvenient for the patient, their family, and medical staff.

We value this feedback and investigate these inquiries thoroughly. Often, after careful review of our laboratory performance, we are unable to find a root cause. While this could mean the other laboratory hemoglobin value is inaccurate, it is more likely that both laboratories are analytically correct and that the discordant values are the work of unavoidable factors causing variation in results.

Regarding laboratory values, a certain amount of variation is allowable and expected. Specifically with regard to hemoglobin values, there are several sources of variability that can account for discordant results:

Pre-analytical

Careful handling of blood specimens, including collection, transportation, and storage, is very important. If any of these aspects of specimen handling are not optimized it can lead to compromise of the sample and discrepant values.

Physiological

Physiological causes of variation include diurnal variation (hemoglobin values are highest in the morning and drop mildly throughout the day), postural variation (standing or even sitting causes hemoconcentration therefore from upright to recumbent position the hemoglobin value will drop), and also hydration status of the patient. The expected sample to sample variation from physiological causes for hemoglobin measurement is 2.8%.

NOTE: Variation from physiological causes is not accounted for in the analytical variation.

Analytical

A certain amount of analytical imprecision and inaccuracy is allowed for each CBC parameter measured. The total allowable error (including inaccuracy and imprecision) for measurement of hemoglobin is 4.1%.

Therefore, analytical, preanalytical, and physiological factors are all contributing factors leading to inconsistency of hemoglobin results. Keep in mind that the analytical variation refers to a single laboratory analyzing a single specimen. There will be a greater amount of variation when hemoglobin results are compared to that of another laboratory, especially if they use different equipment and different reagents. This type of variation is unavoidable and very difficult to measure. In fact, due to this unpredictable variation, our provincial laboratory External Quality Assessment provider (QMPLS) compares proficiency testing results only to other laboratories that use the same hematology equipment and reagents.

Therefore, with reference to hemoglobin, there are many reasons for variant results. One should be cautious when deciding to transfer a patient with a hemoglobin result very close to the transfusion threshold as this value may not be sufficient to warrant a transfusion. The decision to transfuse should be based on laboratory values in addition to clinical signs and symptoms. If the laboratory value is unexpected or not consistent with the clinical picture, a repeat value should be obtained.

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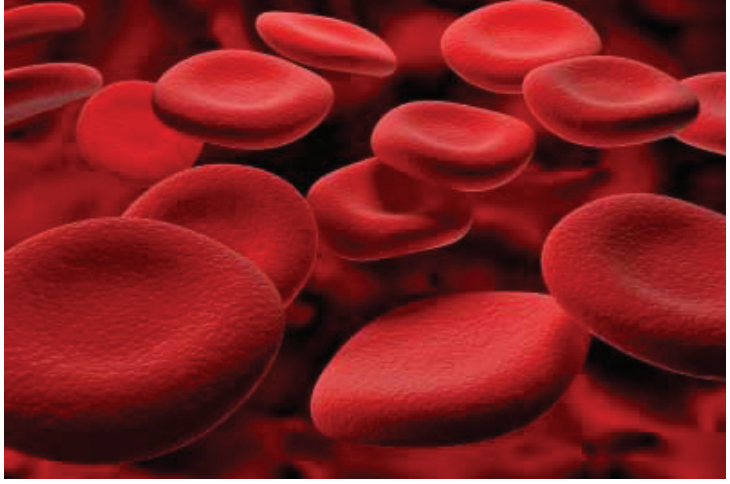

Discrepancies in hemoglobin results is not an infrequent occurrence as the nature of laboratory hematology testing is complex and variable. To guarantee quality results, the commitment required by each laboratory is to strictly follow the standards specified by the Ontario Laboratory Association (OLA) and demonstrate performance within the fixed limits of proficiency testing, a responsibility that LifeLabs strongly upholds.

References

1. "Desirable Specifications for Total Error, Imprecision, and Bias derived from intra- and inter-individual biologic variation". Westgard QC. http://www.westgard.com/biodatabase1.htm (9 May 2011).
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3. Pocock S, Shby D, Shaper A, Walker M, Broughton P. Diurnal variations in serum biochemical and haematological measurements. J Clin Pathol. 1989;42:172-179.

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DRUGS OF ABUSE URINE TESTING: *How long after use will a urine sample test positive for a drug?*

This is a commonly asked question and one that is difficult to answer as there are many physiological and analytical factors that determine the presence of a drug in urine.

Physiological factors include the amount and frequency of use, metabolic rate, body mass, as well as urine pH.

Metabolic Rate: Individuals with slower body metabolism are prone to longer periods of urine drug detection. In general, human metabolism slows with age or during periods of deteriorating health, resulting in longer drug detection periods. When tolerance to a drug is established, a shorter detection period is expected due to faster metabolism of the drug.

Body Mass: In general, human metabolism slows with increased body mass, resulting in longer period of drug detection. In addition, chronic users, physically inactive users, and individuals with a high percentage of body fat in relation to total body mass are prone to prolonged detection for drugs known to accumulate in fatty lipid tissue, such as Cannabinoids and Phenycyclidine.

Urine pH: Urine pH can impact drug detection periods. Typically, acidic urine results in shorter drug detection periods.

Pre-analytical issues such as addition of specimen adulterants will affect detection of the urine drug. Dilution of the urine with water or common household products such as dish-soap, may result in a false negative test even when the drug is present at concentrations above the analytical cut-off value. LifeLabs assesses the integrity of the urine specimen using semi-quantitative analysis of the urine pH, specific gravity and creatinine. Samples exceeding normal expected values are rejected with a note to explain the reason.

Analytical considerations include the cut off value used to assess a detected or non-detected response, as well as the analytical sensitivity and specificity of the method used for analysis. LifeLabs performs urine drug screening using class specific immunoassays designed to detect compounds of similar chemical structure. Drugs are typically excreted in the urine as a free drug, metabolite or as a conjugate with glucuronic acid. Therefore, the length of time for detection of the drug in the urine may vary depending on whether the method in use detects all excreted forms of the drug in question. On the other hand, the same analyte assessed by a different immunoassay, may generate a negative result due to differences in method antibody specificity.

Urine drug screen from LifeLabs are reported as "detected" when the drug level is above the cutoff point defined by the Substance Abuse and Mental Health Services (SAMSHA). These results must be considered "presumptive positive" unless confirmed by an alternate technology, such as gas chromatography with mass spectrometry (GC/MS). To request confirmation testing on a urine specimen, please call LifeLabs at 1-877-849-3637 or 416-675-3637.

The following table is a summary of approximate time since last use, that a urine specimen will test positive for a selection of more common drugs of abuse. These values should be used as a general guideline only.

Approximate Period of Drug Detection in Urine

Drug	Days Since Last Use Detection	SAMSHA Cutoff Value for Drug (ug/L)
Amphetamines or Methamphetamines	1-4	1000
Barbiturates	2-30	200
Benzodiazepines	1-42	200
Cannabinoids	1-35	50
Cocaine or Cocaine Metabolites	1-4	300
Methadone	1-7	300
Opiates	1-3	300
Phencyclidine	2-30	25

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RENIN ANALYSIS: LIFELABS CHANGES TO METHOD AND REPORTING

Plasma renin has an important role in the clinical assessment of hypertensive patients and is measured as plasma renin activity assay or as direct renin antigen.

Plasma Renin Activity (PRA)

Measurement of PRA in plasma involves quantitation of Angiotensin I by ***renin enzymatic activity*** acting on endogenous or exogenous plasma angiotensinogen. The concentration of Angiotensin I produced is proportional to the amount of active renin in the plasma. Currently, Lifelabs uses the Diasorin PRA radioimmunoassay and reports renin activity in ng/L/s.
Note: the "ng" refers to the amount of Angiotensin I produced.

Direct Renin

Direct renin immunoassays measure the concentration of renin protein in the plasma. These methods are calibrated to the International Reference Preparation of human renin (68/356).

Direct sandwich immunoassays for renin protein offer improved precision and lower limits of detection, compared to PRA methods. These characteristics are particularly important as they provide a more accurate calculation of the Aldosterone/Renin Ratio at a low renin concentration, which is commonly seen in patients with primary aldosteronism.

In June 2011, LifeLabs will implement a direct renin chemiluminescent immunoassay (Diasorin Liaison) and, at that time, will begin to report renin in units of ng/L.
Note: In this case, the "ng" refers to the amount of renin protein.

A patient correlation between the Diasorin PRA RIA method and the Diasorin Liaison direct renin method was conducted. Although a positive overall correlation was demonstrated between the two methods, many samples, particularly those with low results, deviated from the line of best fit. It is important to remember that the two types of assays are measuring very different properties of renin. For these reasons, a universal factor for "converting" results from one method to the other is not available.

Aldosterone/Renin Ratio (ARR)

One of the primary clinical indications for renin measurement is the evaluation of patients with suspected primary aldosteronism (PA). The Endocrine Society, cosponsored by the European and International Societies of Endocrinology and Hypertension, recently published guidelines for diagnosis and management of patients with PA.[2] The guideline indicates that the ARR is the most reliable available means for screening for PA and is superior to measurement of potassium or aldosterone or of renin in isolation.
The guideline reports that the ARR is most sensitive when used in patients who have had unrestricted dietary salt intake before testing. It is recommended that samples be collected in the morning, after patients have been ***upright,*** (i.e. sitting, standing, or walking), for at least 2 hours.
Note: No interpretative guidelines are provided for samples collected from patients in a supine position.

While beyond the scope of this article, the reader may refer to the published guideline for a comprehensive list of factors, including medications, to be considered when preparing the patient and in interpretation of renin results.[2]
With the introduction of the new direct renin method, LifeLabs will also include calculation and report of the ARR for samples collected from patients in the upright position. ARR results will be calculated using Aldosterone measurements in units of "pmol/L" and Renin in units of "ng/L". On the lab report, ARR results will be reported as "pmol/ng".

Using these units and the methods specifically used by LifeLabs, the following guidelines have been developed to aid in the interpretation:

ARR (pmol/ng)	Interpretation
<40	Aldosteronism is unlikely when the Aldosterone/Renin Ratio (ARR) is less than 40.
40-65	Aldosteronism is possible when the Aldosterone/Renin Ratio (ARR) is between 40 and 65.
>65	An Aldosterone/Renin Ratio (ARR) greater than 65 is significant evidence of aldosteronism.

References
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2. Funder JW, Carey RM, Fardella C, Gomez-Sanchez CE, Mantero F, Stowasser M, Young WF Jr., and Montori VM. Case Detection, Diagnosis, and Treatment of Patients with Primary Aldosteronism: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab* (2008) 93(9): 3266 – 3281.

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LIPOPROTEIN ELECTROPHORESIS TESTING NO LONGER AVAILABLE

The referral laboratory which has been performing Lipoprotein Electrophoresis for LifeLabs has informed us that they will be discontinuing this testing as of June 01, 2011.

Historically, lipoprotein electrophoresis was a tool used for the classification of hyperlipidemias and dyslipidemias. This test is now considered obsolete and is not offered by any lab in Canada.

The Canadian Cardiovascular Society released "Guidelines for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease in the adult" in 2009. In this guideline, they indicate that assessment of dyslipidemia should include the following tests: total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), triglycerides, low-density lipoprotein cholesterol (LDL-C), and a TC/HDL-C ratio.

Other tests which may be valuable for assessment of cardiovascular disease risk include apolipoprotein B (Apo B), apolipoprotein A1 (Apo A1), Apo B/Apo A1, and high-sensitive CRP (hs-CRP).

For more information regarding these tests, please see the Ontario Association of Medical Laboratories "Guideline for lipid testing in adults".

References

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DISCONTINUATION OF CK-MB TESTING AT LIFELABS

Early diagnosis of acute myocardial infarction (AMI), within 3-6 hours after chest pain, is required to properly manage patients with suspected AMI and minimize the amount of myocardial necrosis.

Current laboratory biomarkers used in the diagnosis of acute myocardial infarction may include creatine kinase – MB (CK-MB or CK-2). Measurement of this analyte is most useful when available to the physician with a turnaround time of <1 hour from the time of collection. In a community environment, testing of cardiac biomarkers cannot be accomplished within the timeframe required to be clinically useful. For this reason, LifeLabs will discontinue offering CK-MB testing, effective July 4th, 2011.

Patients suspected of having an AMI should be immediately referred to the closest emergency department for appropriate clinical management.

Note: CK fractionation will continue to be offered for follow-up assessment of patients with elevated total CK in suspected cases of muscle disease, or for patients on statins. The test is performed only once per week.

References

1. National Academy of Clinical Biochemistry and IFCC Committee for Standardization of Markers of Cardiac Damage Laboratory Medicine Practice Guidelines. Analytical Issues for Biochemical Markers of Acute Coronary Syndromes. Clin Chem (2007) 53: 547-551.
2. Wu A. Use of Cardiac Markers as Assessed by Outcome Analysis. Clin Biochem (1997) 30: 339-350.

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MEDSCI LIFELABS CLIENT SURVEY

We are interested in your feedback!

LifeLabs will be conducting a client survey beginning in June 2011 related to the quality of our Medical-Scientific services. You can access the survey online by visiting www.lifelabs.com.

The survey should take less five minutes of your time and is completely confidential. The results will help us understand how we are doing today and where we need to make improvements.

Thank you in advance for participating in the survey. We look forward to receiving your feedback.

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