LabWire
Laboratory News and Analysis for Clinicians October 2020

Retesting Recovered COVID-19 Patients

Dr. Richard Van Enk, Director of Infection Prevention

Our region is seven months into the COVID-19 pandemic and Bronson has provided diagnosis and care to well over 2000 patients with confirmed COVID-19 infection. Many of those patients will return to us for care, and it is important to understand the difference in management between recovered COVID-19 patients and others. A variety of protocols include COVID-19 testing of patients prior to procedures as a way to reduce risk and improve care during those encounters. Recovered COVID-19 patients are different because they should not be retested for COVID-19, and if they return with a new infectious disease presentation, we should look for causes other than COVID-19.

Patients with COVID-19 respiratory infection normally show positive PCR tests of nasopharyngeal specimens beginning about 2 days prior to symptoms and remain positive for several days after symptoms. The PCR test, however, does not detect intact, infectious virus; it detects segments of viral nucleic acid. Viral culture studies show that immunologically competent COVID-19 patients stop producing infectious virus by approximately day 8, and subsequent positive PCR tests are detecting remnants of old virus, not replicating, intact virus. Studies on the half-life of PCR-detectable viral remnants show that it takes at least 20 days for half of recovered patients to be PCR negative and nearly 50 days for 95% of patients to be negative. Also, recovered patients can produce intermittent positive PCR tests separated by negative tests post-recover for up to 3 months. Based on the biology of the virus and the nature of PCR testing, recovered COVID-19 patients should not be retested for at least several months, and the PCR test is not a test of cure.

A currently open question is whether people can get COVID-19 infection more than once, and if so, when immunity wanes enough to allow another infection. There are a few case reports of people getting what could be a second COVID-19 infection, but these are unconfirmed and it is unclear if the second presentation is a COVID-19 infection. The CDC currently says that there are no confirmed reinfections with COVID-19 at least seven months into the pandemic. For now, it is safe to assume that if a recovered COVID-19 patient presents with a subsequent respiratory infection, it is not COVID-19, and other causes should be sought. It can also probably be assumed that if a recovered patient has anti-COVID-19 antibody, they have protective immunity against reinfection, so the COVID-19 serology test may be helpful in resolving questions about a new presentation.

- Patients are considered recovered from acute COVID-19 infection when they are afebrile and their pulmonary symptoms are improving
- Functional recovery from COVID-19 infection can take a long time and there appear to be several significant sequellae resulting from infection, but they do not represent continued infection
- Recovered COVID-19 patients can give positive PCR tests for months
- Do not retest recovered COVID-19 patients
- If recovered COVID-19 patients are retested and the test is positive, it does not mean that they are still infected or that they are reinfected
- The presentation of COVID-19, influenza and other viral respiratory infections significantly overlap, so look for typical causes of respiratory infection in recovered COVID-19 patients

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CASE STUDY: Pseudohyperkalemia – Falsely Elevated Potassium Test Results

Paul Guthrie, Lab Technical Clinical Consultant

The causes of pseudohyperkalemia (PHK) include: Leaving tourniquet on for more than 1 minute, excessive fist clenching, arm in upward position, carryover of potassium containing anticoagulants when tubes are not filled in the correct order of draw, drawing above an IV site, difficult/traumatic draw, use of small gauge needles, syringe/catheter draws, forced transfer of blood from syringe into evacuated tubes, unpadded transport of samples in pneumatic tube systems, vigorous mixing of tubes, delays in processing sample beyond 2 hours, chilling of whole blood beyond 2 hours before centrifugation and certain patient conditions. [1]

Many of the aforementioned causes introduce hemolysis, the rupture of red blood cells. At Bronson's laboratories, all serum and plasma samples tested for potassium have a direct measurement of the level of hemolysis. That "serum index" allows for reporting the potassium (K^+) result with a comment indicating how the results are affected for mild or moderate hemolysis. Samples with severe hemolysis are rejected and redrawn.

Some of the causes for PHK do not cause hemolysis. These are more difficult to detect. False increases in K^+ can occur even when all collection, processing and testing steps are performed correctly. The following case illustrates a patient condition causing PHK.

The laboratory was presented with this Patient Safety Report:

Situation: The patient received unnecessary treatment due to falsely increased potassium results.
Background: The patient was admitted and had three critically high potassium draws in a row. The patient was treated to lower the potassium. A repeat lab we drew came back normal. The patient may not have needed to be treated.
Assessment: The patient continued to have very high potassium labs drawn by phlebotomy that were incorrect. We continued to assess the patient who was placed on telemetry as a result of the incorrect labs.
Recommendation: Check with the phlebotomists to see if there was a technique issue causing the samples to hemolyze. Check the lab equipment to see if there was an issue with the results it produced.

It should be noted that a false increase in potassium will not always result in a critically high potassium as in this example. It is even possible for a critically low potassium to be "masked" by the false increase. In this case, the laboratory investigation ruled out phlebotomy technique and laboratory equipment issues as the cause of PHK. Rather, the problem was the patient's white blood cells. An elevated WBC (typically over 50 x 10^9/L) can falsely raise the serum or plasma potassium, particularly in conditions such as chronic lymphocytic leukemia (CLL). Studies have shown the false increase from CLL averages 1 mmol/L K^+ per 100 x 10^9/L WBC count. [2] In CLL, the WBCs are fragile, and easily lysed to release their intracellular contents, which contain K^+. Unlike the lysis of red blood cells, this increase in potassium cannot be measured by a serum index, or grossly observed. Under the microscope however, these cells may be seen as broken "smudge" cells as shown below.

Continued on next page

LabWire
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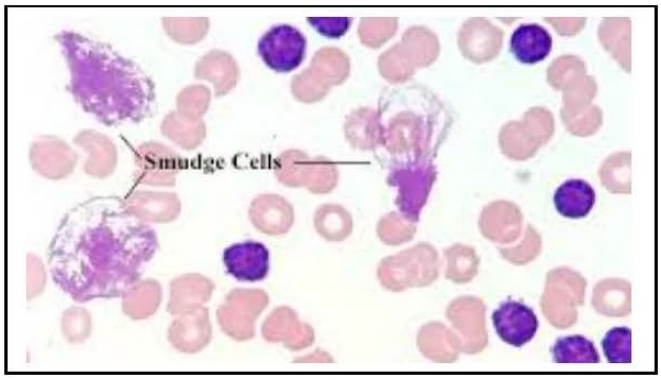
Continued from previous page



The routine testing process for K^+ includes several steps which can lyse the abnormally fragile WBCs. These include: transfer of the blood into a vacuum tube, potential rough handling during transport in an unpadded pneumatic tube system, and centrifugation to separate the cells from the plasma or serum required for testing by most chemistry analyzers. However, if one knows that the WBC count is significantly elevated with a condition like CLL, there is a way to obtain a more accurate K^+ value for these patients. If the sample is collected directly into a blood gas syringe, carefully transported it to the laboratory, and tested on a whole blood analyzer (typically a blood gas machine), the results will be much less affected. In this case study, the patient had plasma potassium values as high as 9.9 mmol/L. When the sample was tested as whole blood, the value was 3.2 mmol/L.

A similar cause for PHK is thrombocytosis. When a sample clots, the platelets (PLT) release potassium. In cases where the PLT is >500 x 10^9/L this may lead to an increase in potassium. The increase is approximately 0.1 mmol/L K^+ per each 200 x 10 10^9/L platelet count. [2] The collection of a sample in heparin will reduce this impact, as the clotting process is inhibited.

In retrospect, we were able to identify the reason for this patient's falsely elevated potassium values that led to unnecessary treatment. However, our challenge is to detect future instances of PHK and inform clinicians at the time of testing. To those ends, the following changes are being made effective November 21, 2020:

- The potassium analyzer interface has been programmed to search for the WBC count. If the WBC is >50 x 10^9/L the following comment will be attached. *"Potassium value in serum or plasma may be falsely elevated due to high WBC count. Suggest ordering whole blood potassium (LAB4502) and submitting sample in blood gas syringe."*
- The potassium analyzer interface has been programmed to search for the Platelet count. If that is >750 x10^9/L, the laboratory technologist will be alerted to see if sample is serum or plasma. If plasma, the K^+ will be reported. If serum, the following comment will be attached. "*Potassium value in serum may be falsely elevated due to high platelet count. Suggest ordering whole blood potassium and submitting sample in blood gas syringe."*
- A new test code (LAB4502) is available in Epic that allows whole blood potassium to be ordered by clinicians if they suspect pseudohyperkalemia due to elevated WBC or PLT.

Please bring any question to Paul Guthrie at guthriep@bronsonhg.org

References:

1. BD Vacutainer Systems, LabNotes, Volume 13, No 3. Summer 2003.
2. Establishing evidence-based thresholds and laboratory practices to reduce inappropriate treatment of pseudohyperkalemia, Clin Biochem, 2017 Aug; 50(12):663-669, Ranjitkar , et. al.

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LabWire
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Order Options for Serum Immuno-Fixation Electrophoresis (IFE)

Effective 11/24/20, Bronson Laboratory will be adopting the practice of national and other regional laboratories for the ordering of serum Immuno-Fixation Electrophoresis (IFE). Electronically, the IFE test will only orderable as part of a profile or algorithm as noted below. If a paper order for IFE alone is received, it will be converted to the Serum Protein Electrophoresis with Serum Immunofixation (SPIFE). These changes are being made to ensure an optimal diagnostic approach along with the most efficient test utilization.

IFE is available as follows:

- **Serum Protein Electrophoresis (SPEP) with reflex to IFE,** Epic: LAB119 - If indicated by interpretation of the electrophoretic pattern and the patient history, the clinical pathologist will order an IFE. Note: If a monoclonal peak is present in the SPEP will be quantified.
- **Monoclonal Protein Electrophoresis (MPE),** Epic: LAB2226 **-** This algorithm beings with a serum protein electrophoresis and serum free light chains. If indicated by interpretation of the electrophoretic pattern and the patient history, the clinical pathologist will order an IFE.
- **Serum Protein Electrophoresis with Serum Immunofixation (SPIFE),** Epic: LAB4715 **-** Both tests will be performed and accompanied by a pathologist interpretation.