Handling Hemolytic Blood Samples from High-Risk Clinical Areas: A Call to Action

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Alan H B Wu, Jerrold H Levy, W Franklin Peacock, Ramzy Rimawi, Manuel Sanchez Luna, Christopher Farnsworth, Hugo Stiegler, Robert H Christenson.
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Guest: Dr. Alan Wu from the University of California, San Francisco and Zuckerberg San Francisco General Hospital.

Randye Kaye: Hello and welcome to this edition of *JALM* Talk from *The Journal of Applied Laboratory Medicine*, a publication of the Association for Diagnostics & Laboratory Medicine. I'm your host, Randye Kaye.

The pre-analytical phase of clinical laboratory testing is the stage that includes specimen collection and transport before analysis. This phase is known to be the most error-prone, with hemolysis, the rupture of red blood cells, being a leading cause of pre-analytical issues in blood testing.

Hemolyzed specimens can bias test results, particularly for intracellular analytes like potassium, potentially leading to misdiagnoses, delayed or inappropriate treatments, and longer hospital stays. While central laboratories often use spectrophotometric analyzers to detect hemolysis in serum or plasma samples, point-of-care devices that test whole blood usually lack this capability, increasing the risk of undetected interference.

Fortunately, recent advancements now make hemolysis detention in whole blood possible. The availability of this technology has prompted a renewed emphasis on standardized practices and clinical awareness of hemolysis to promote patient safety and optimal care.

The September 2025 issue of *JALM* features a special report authored by experts from clinical labs emergency departments and intensive care units. The report highlights current practices in the US and Europe and offers key recommendations to improve hemolysis management. Today, we are joined by the article's corresponding author, Dr. Alan Wu.

Dr. Wu is a Professor of Laboratory Medicine at the University of California, San Francisco, and Co-Core Laboratory Director at Zuckerberg San Francisco General Hospital. Welcome Dr. Wu.

Hemolysis can be a significant problem for clinical labs, but not all hemolysis is the same. What's the difference between in vivo and in vitro hemolysis?

Alan Wu: In vivo hemolysis is when red cells that are circulating in blood lyse and release their contents directly into the circulation. This is due to various medical conditions such as insect bites, like from spiders or snakes, or incompatible blood transfusions. In vitro hemolysis is when the red cells lyse during the process of collection, phlebotomy or finger stick, and after the blood is in the tubes, if it is handled incorrectly.

Randye Kaye: All right, thank you. So how and how often does in vitro hemolysis occur?

Alan Wu: Well, in vitro hemolysis is pretty common in certain areas of the hospital, notably, the emergency department and their critical care units. There is a procedure known as ECMO [extracorporeal membrane oxygenation] that can also facilitate hemolysis as the process of conducting ECMO, and the frequency can be anywhere from 5-25%. So it is a non-trivial problem.

Randye Kaye: Yeah, that's significant. So how does central hospital labs typically detect hemolysis in blood specimens?

Alan Wu: It's something called an HIL index. And so, when blood is sent to the lab for testing of electrolytes say, the samples are first centrifuged to separate the serum or plasma from the red cell layer. Then the sample is delivered to the chemistry analyzer, where a sample of the serum or plasma is inspected for color. Now, it's not done visually, although it can be because hemolysis is red. But in the HIL index of a chemistry analyzer, photometric checks are made at various wavelengths to detect the presence of hemolysis, which is why the H comes into play, for turbidity or lipemia, which is the L. And then the middle one is I, stands for icterus, which is caused by excess of bilirubin.

So it's not just hemolysis. It's these other two that we can routinely test all samples that are being subjected for analysis in our chemistry analyzer.

Randye Kaye: All right, thank you. So, if in vitro hemolysis is undetected, what are the medical consequences?

Alan Wu: Well, there can be severe, it's mostly a pre-analytic error. Anything that's found in the red cells at higher concentrations than what is found in the serum or plasma will falsely increase that constituent into serum or plasma. So, for example, lactate dehydrogenase is an enzyme that's produced in various tissues of our bodies.

When you have hemolysis, LDH is released into the sample to produce a high value. Now, LDH is not one of the uber critical

tasks where really life and death decisions are being made, really, it is potassium. Potassium has a very narrow reference range typically between 3.5 and 5 milli equivalents per liter. And if you have a hemolytic situation, your potassium concentrations can go from normal to abnormal.

A high potassium, if it's real, is a medical emergency and requires immediate therapy because it can cause a life-threatening arrhythmia. Now, if you have a normal potassium, but your hemolytic sample is producing a high value, you don't want these measures to lower the potassium to take place because it is an artifact and doing so from a normal potassium, might move the patient to a hypokalemia situation, which in itself, has medical consequences.

Now going the opposite direction, if you have a patient, who has hypokalemia, or low potassium and the patient's sample is hemolyzed, you can then move the result from low to normal and that's even worse to some extent because nobody would pay attention to a normal result. They would not suspect that in fact, the patient was low. So when it comes to medical consequences, the majority of them center around erroneous potassium results.

Randye Kaye: All right, thank you. Now hemolysis is, it's not a new issue. So why did your author group decide to publish this call to action at this time?

Alan Wu: Yes, we have known that hemolysis can produce falsely results and that we have these countermeasures that can be done in a central lab. There are numerous studies that have documented this, but up until now, there has never been a way to determine hemolysis when an electrolyte test is performed on whole blood.

Now, these are more recently developed technologies, we are not talking the last year or two. So, 20 years ago, we started testing whole blood for electrolytes and the problem is that if you do an HIL index on a whole blood sample, it doesn't work because you're looking for a red color and whole blood is red by definition. And so those measures don't work and up until now we did not have any methodologies to detect hemolysis in whole blood and therefore this call to action really was not needed.

But today we can test for whole blood hemolysis and we wanted to revisit this issue to talk about hemolysis as a pre-analytic error because it continues to occur at high rates and to point out that we have solutions for point-of-care testing. New equipment that allow us to detect hemolysis and really should begin to be used.

Randye Kaye: All right, thank you, final question. So, these are newly available technologies to detect hemolysis in whole blood. How do you think these technologies will influence laboratory practice?

Alan Wu: Well, it is my opinion that these new analyzers are the new gold standard for electrolyte testing at the point of care using whole blood. Unfortunately, there's only one vendor to date that is able to achieve this and so if you are a hospital lab that don't use this particular equipment, it's not available to you today.

But I suspect that in the ensuing years to come all blood gas electrolyte, whole blood analyzers will have some feature for detecting hemolysis and that this will be standard medical laboratory practice.

Randye Kaye: All right, thank you so much for joining us today Dr. Wu.

Alan Wu: Well thank you Randye.

Randye Kaye: That was Dr. Alan Wu from University of California, San Francisco, describing the *JALM* article "Handling Hemolytic Blood Samples from High-Risk Clinical Areas: A Call to Action."

Thanks for tuning into this episode of *JALM* talk. See you next time and don't forget to submit something for us to talk about.