Clinical pathology selected abstracts

Editor: Deborah Sesok-Pizzini, MD, MBA, chief medical officer, Labcorp Diagnostics, Burlington, NC, and adjunct professor, Department of Clinical Pathology and Laboratory Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia.

Awareness of donation-related iron depletion among high-risk blood donors

April 2022—Iron deficiency in repeat blood donors is a medical concern. Donors undergo standard hemoglobin testing as part of the donation process, but the testing is not sensitive enough to detect nonanemic iron deficiency. Therefore, some donors may be iron deficient and still meet the requirements for blood donation. Researchers are investigating the impact of iron loss on the health and well-being of routine blood donors. These donors would benefit by understanding the risks of low iron levels and strategies to mitigate these risks. Some studies have shown the benefits of providing iron supplementation to donors, but the practice of offering this without full knowledge of a patient's health history poses dilemmas. The authors conducted a study in which they undertook a more cautious approach to donor education and examined online messaging about iron supplementation sent to blood donors after they left the donation setting. The authors hypothesized that online messaging would raise awareness of the risk of iron depletion after blood donation and that adding action planning would lead to changes in behavior that support a healthy iron state. For the study, they randomly assigned frequent (n=904) and young (n=629) blood donors to a control (n=548) or intervention (n=985) group. The control group answered questions in an online baseline survey and a six-month follow-up online survey regarding their awareness of the risks of blood donation and iron depletion and whether they were taking action to mitigate the risk of iron deficiency. The intervention group completed the same online baseline survey and six-month follow-up online survey. However, after completing the baseline survey, the intervention group received a one-page educational message that was customized based on whether they were a frequent or young donor. The message included information about the relationship between blood donation and iron stores and actions to mitigate iron deficiency. It also encouraged donors to tell their doctors that they had donated blood as this information is helpful when interpreting iron-related laboratory results. Furthermore, the messages provided a reminder about the constant need for blood, advocated for donation, and contained directions on how to get more information about iron depletion. The intervention group was also asked if they wanted to develop an action plan to improve their health status. Those who responded affirmatively received information on using simple implementation intention and cueing techniques to translate intentions into actions. The study results showed significant improvement in awareness and intervention with regard to blood donation and iron depletion when action planning was paired with education. In comparison to the control group, the intervention group showed greater awareness of iron loss overall for the action-plan and nonaction-plan groups. This suggests that the interventions enhanced concern for blood donation iron depletion. However, the interventions did not impact donor retention. The authors noted that a strategy of education combined with encouragement is likely to have the most impact among donors who are already concerned about their risk for iron deficiency and motivated to mitigate that risk.

France JL, France CR, Rebosa M, et al. Promoting awareness of donation-related iron depletion among high risk blood donors. *Transfusion*. 2021;61:3353–3360.

Correspondence: Dr. Christopher R. France at france@ohio.edu

Performance of surrogate tests for detecting SARS-CoV-2–neutralizing antibodies

SARS-CoV-2 produces neutralizing and binding antibodies. In this infection, neutralizing antibodies are primarily directed against the receptor-binding domain (RBD), and approximately 10 percent of them are targeted against the N-terminal domain. In contrast, binding antibodies can bind to several SARS-CoV-2 regions and signal a current or past infection. Several licensed tests use binding antibodies to target the spike protein (S) or parts of it—for

example, the S1/S2 or RBD domain—or nucleocapsid antigens. Despite the ability to test for SARS-CoV-2 binding antibodies, gaps still exist in the correlation between serological SARS-CoV-2 antibody assays and neutralizing antibody titers in COVID-19 convalescent plasma donors. Furthermore, testing for neutralizing antibodies is very limited because it needs to be conducted in sophisticated laboratories using advanced methods that generally are not available. The authors conducted a study that involved building a validation panel based on neutralizing antibody titers to evaluate the surrogate role of some of the commercially available anti-SARS-CoV-2 antibody tests used in Brazil. They studied a panel of antibody tests consisting of 180 samples from convalescent plasma donors tested for neutralizing antibodies and 11 controls between March 2020 and January 2021. The neutralizing antibody titers ranged from negative to 10,240. The samples were coded for surrogate testing, which consisted of a surrogate virus-neutralization test based on a competitive anti-RBD inhibition test, two anti-spike tests, and four anti-nucleocapsid tests, either isolated or combined. All tests were performed blindly following manufacturer instructions or according to FDA authorization for COVID-19 convalescent plasma collection. High-titer neutralizing antibodies were defined as those with titers of 160 or more. The study found that, except for combined tests and anti-NP IgA/IgM tests, all isolated surrogate tests performed well for detecting neutralizing antibodies. The latter had a sensitivity of 98.3 to 100 percent, specificity of 85.7 to 100 percent, positive predictive value of 98.9 to 100 percent, negative predictive value of 81.3 to 100 percent, and area under the curve of 0.93 to 0.96 using receiver operating characteristic analysis. There was a variable decrease in sensitivity and typically lower specificity when simultaneously evaluating samples with high levels of neutralizing antibodies (160 or more) and following FDA authorization for surrogate tests. To address the issue of varying sensitivities across different commercial anti-SARS-CoV-2 antibody tests, the surrogate testing panel was derived from only SARS-CoV-2 convalescent individuals, usually 28 or more days after the onset of symptoms. The authors noted that if a surrogate test is used only for those who are vaccinated, it is likely to be positive, but this does not necessarily indicate the presence of neutralizing antibodies. This means that vaccinated adults should not be allowed to donate plasma unless a previous SARS-CoV-2 infection has been documented. Furthermore, COVID-19 convalescent plasma screening performed on normal blood donors who had a previous SARS-CoV-2 infection during a time of low prevalence of the virus in the community may result in a low positive predictive value. In this case, using two independent surrogate antibody tests may enhance the estimated positive predictive value. The authors stated that the newly released World Health Organization anti-SARS-CoV-2 standard likely will prompt manufacturers to review their tests with the aim of achieving better standardization for neutralizing antibodies and binding assay formats. They concluded that there was no benefit in using IgA or IgM antibodies for COVID-19 convalescent plasma screening. However, they showed that other surrogate tests exhibit good clinical performance for detecting neutralizing antibodies for clinical diagnosis on a qualitative basis. Yet those tests are not precisely correlated with the gold-standard method (20 or more neutralizing antibodies by the cytopathic effect virus neutralization test), particularly with high neutralizing antibody titers.

Wendel S, Fachini R, Fontao-Wendel RCL, et al. Surrogate test performance for SARS-CoV-2 neutralizing antibodies (nAbs) for convalescent plasma (CCP): How useful could they be? *Transfusion*. 2021;61:3455–3467.

Correspondence: Dr. Silvano Wendel at snwendel@terra.com.br