Don’t order a factor V Leiden (FVL) mutation assay as the initial test to identify a congenital cause for a thrombotic event. First, order a phenotypic activated protein C resistance (APCR) ratio assay.

There exist several acquired APCR conditions such as elevated factor VIII and antibody-mediated APCR that can lead to thrombotic events such as deep venous thrombosis or pulmonary embolism. Further, several factor V Leiden-independent mutations may be associated with thrombosis. Best practice guidelines recommend testing for APCR using one of several phenotypic clot-based APCR ratio assays as an initial assay and following up positive APCR ratio results with the molecular factor V Leiden assay. Most currently available phenotypic tests are economical, have a greater than 95% concordance with molecular testing and up to 99% clinical sensitivity. Based on Medicare reimbursement rates, switching to initial-phase phenotypic testing and relying on its negative predictive value with follow-up genotypic testing on APCR-positive samples could result in a 75% reduction in costs. Although the FVL mutation assay is often ordered to determine the cause of venous thromboembolic disease, the APCR ratio assay provides greater clinical sensitivity at a lower cost. In instances when clot-based thrombosis risk testing is indicated during acute thrombosis, line-associated thrombosis, or anticoagulant therapy, the APCR is compromised and the FVL mutation assay is used as a primary assay.

Do not use herpes simplex virus (HSV) polymerase chain reaction (PCR) testing for genital HSV infection screening in adults and adolescents. Real-time HSV PCR testing should only be used to confirm herpes diagnosis in patients with suspected herpes.

HSV shedding is intermittent. Therefore, testing swabs from asymptomatic patients is not recommended for routine diagnosis since it is unlikely to yield confirmation of carrier status. However, laboratory confirmation in all patients with suspected herpes is recommended. HSV DNA detection by real-time PCR is considered the gold standard for diagnosis. Swabs for testing are taken from the base of the lesion (vesicles should be unroofed with a needle or scalpel blade). HSV typing into HSV-1 and HSV-2 is recommended in all patients with first-episode genital herpes to guide counselling and management.

Do not transfuse red blood cells as the sole intervention for expansion of circulatory volume unless deemed necessary for patients experiencing severe hemorrhage.

The Canadian Transfusion Requirements in Critical Care (TRICC) trial was the first to investigate a liberal versus restrictive approach to red blood cell (RBC) transfusions. The trial included a total of 838 hemodynamically stable, critically ill patients who had a hemoglobin (Hgb) concentration less than 9 g/dL (adult transfusion trigger 7–8 g/dL). The trial defined two categories for the study, a “liberal” approach that required allogeneic RBC transfusions for patients with Hgb less than 10 g/dL and a “restrictive” approach for patients with a Hgb concentration less than 7 g/dL. Patients were randomly divided between both study groups and were evaluated at 30 days. There was no significant mortality difference. The trial also noted a significantly better survival rate among patients less than 55 years old within the restrictive group; including in particular less acutely ill patients. Subsequent studies have shown that clinically stable patients may benefit more from a restrictive approach by reducing the percentage of patients exposed to allogeneic RBCs. It is not recommended to transfuse RBCs as the sole intervention for volume expansion. The World Health Organization recommends volume-expanding solutions such as crystalloids or colloids to expand fluid volume. These promote blood circulation through vital organs and tissues. RBC transfusions should be used to treat conditions such as severe hemorrhage that otherwise lead to significant mortality. Recent evidence for blood transfusions suggests that a restrictive transfusion approach is safer and as effective as a liberal approach for post-operative stable patients, normovolemic critically ill-patients with a hemoglobin transfusion trigger of 7–8 g/dL and patients with clinical symptoms of anemia.

The exception to the restrictive approach is comprised of patients with clinically significant cardiovascular conditions. Blood products carry the risk of transmitted infectious diseases and adverse effects of blood transfusion (e.g. immunosuppressive complications).
Avoid using hemoglobin to evaluate patients for iron deficiency in susceptible populations. Instead use ferritin.

Iron depletion is a progressive process with anemia as the final phase. Thus, screening for iron deficiency using hemoglobin (Hgb) will only identify the most severe cases. Moreover, Hgb is not specific for iron deficiency or iron deficiency anemia. Iron deficiency is one of the most common nutritional deficiencies worldwide. Prevalence of iron deficiency in USA women ages 12–49 years rose from 11% in 2003 to 14.8% in 2010. Pregnant women and young children are also high-risk groups and must be evaluated. Iron deficiency in U.S. toddlers, without anemia, is estimated at 6.6%–15.2%.

Serum ferritin is a measure of iron stores and is the most sensitive biomarker to test for early stages of iron deficiency as well as iron deficiency anemia. Sensitivity of ferritin test is 89% for diagnosis of iron depletion compared to hemoglobin, which is only 26%. Moreover, a ferritin cut off of ≤30 ng/mL provides 92% sensitivity and 98% specificity for iron deficiency anemia and is the best screening test for this disorder.

Evaluating patients for iron deficiency with ferritin will identify early stage iron deficiency and will potentially result in iron therapy, preventing iron deficiency anemia. Iron deficiency anemia has been long associated with psychomotor and cognitive abnormalities but even iron deficiency without anemia has been related to negative neurodevelopmental outcomes in children.

Ferritin is an acute phase reactant, and occasionally in inflammatory conditions, ferritin levels may be normal or elevated even in the presence of iron deficiency. Additional laboratory tests such as reticulocyte hemoglobin content (CHR or Ret-He), mean corpuscular volume (MCV), red cell distribution width (RDW), and additional iron studies such as percent transferrin saturation and total iron binding capacity, accompanying clinical correlation are also helpful to determine iron deficiency.

Do not order a comprehensive stool ova and parasite (O&P) microscopic exam on patients presenting with diarrhea less than seven days’ duration who have no immunodeficiency or no history of living in or traveling to endemic areas where gastrointestinal parasitic infections are prevalent. If symptoms of infectious diarrhea persist for seven days or longer, start with molecular or antigen testing and next consider a full O&P microscopic exam if other testing is negative.

The comprehensive O&P microscopic exam often requires submission of multiple stool samples, it is labor intensive, requires significant expertise to perform, and typically has lower sensitivity when compared to many other tests now available. Instead, consider ordering antigen detection tests (i.e. direct fluorescent antibody, enzyme immunoassay, indirect immunofluorescence assay, rapid immunochromatographic tests), modified acid-fast stain, or molecular tests that detect specific gastrointestinal parasites most commonly acquired in the U.S. When investigating cases of gastrointestinal disease, it is important to take a comprehensive clinical history that considers the patient’s exposure risk, mechanism(s) of transmission, and immune status. Patients lacking international travel history or residence in areas where parasites are endemic are most likely to be exposed to intestinal parasites associated with outbreaks from exposure to contaminated food or water. In the U.S. these pathogens include *Giardia duodenalis* (*G. lamblia, G. intestinalis*), *Entamoeba histolytica*, *Cryptosporidium*, and *Cyclospora*. For most individuals with healthy immune systems, symptoms self-resolve without treatment. In individuals with prolonged symptoms, risk for development of severe infection, or when pathogen identification is necessary for public health reasons, testing is recommended. Numerous antigen detection assays and molecular tests, including multiplex panels, have been developed for targeted detection of the most common gastrointestinal parasites acquired in the U.S.
The committee collaborated with respective ASCLS Scientific Assemblies in developing and reviewing recommendations, which the Board of Directors reviewed and accepted for publication. The recommendations were subsequently reviewed in collaboration with the ASCP Test Utilization Steering Committee prior to submission.
The American Society for Clinical Laboratory Science (ASCLS) and its 9,000 clinical laboratory professional, student, and educator members in more than 50 state and regional constituent societies work to advance the expertise of clinical laboratory professionals who, as integral members of interprofessional healthcare teams, deliver quality, consumer-focused, outcomes-oriented clinical laboratory services through all phases of the testing process to prevent, diagnose, monitor and treat disease. The Society promotes high standards of practice by holding the profession accountable to a Code of Ethics, through dissemination of knowledge at educational programs and through publications; maintains a supportive community to advocate on behalf of current and future laboratory professionals; and provides laboratory professionals a voice to legislators and regulators through collective, grassroots efforts.

About the ABIM Foundation

The mission of the ABIM Foundation is to advance medical professionalism to improve the health care system. We achieve this by collaborating with physicians and physician leaders, medical trainees, health care delivery systems, payers, policymakers, consumer organizations and patients to foster a shared understanding of professionalism and how they can adopt the tenets of professionalism in practice.

To learn more about the ABIM Foundation, visit www.abimfoundation.org.

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For more information or to see other lists of Five Things Physicians and Patients Should Question, visit www.choosingwisely.org.