Coagulation Dos and Don'ts

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The quality of a coagulation result is crucial, and there are many variables with which to contend—reagents, instruments, different test kits and lack of standardization for calibration curves. Pre-analytical variables, in fact, account for 64 percent of all errors in testing.[1] Following are some dos and don'ts to help your coagulation laboratory deliver quality results.

DO be ruthless about your specimen. Make sure that you adhere to the 1:9 ratio. Keep the NCCLS guideline of a +/- 10 percent fill rate. **DON'T** think that you are helping give a result out by ignoring that guideline; you may be doing more harm than good. If the tube is under-drawn, there will be excess anticoagulant and an otherwise normal result can become prolonged.
DO remember that APTTs have a four-hour window of time to be performed, while PTs have 24-hour stability. **DON'T** add an APTT to a PT that has exceeded the four-hour window. You may be tempted to report out the result if it is normal; however, when plasma remains in contact with platelets, there may be a release of PF4 that neutralizes the presence of heparin. If the patient is on a low dose of heparin, the result may falsely appear in the normal range.
DO confirm any PTs and APTTs that result in no clot by an alternative method or by checking the cuvette for an unclotted specimen. **DON'T** assume that they are just prolonged. They may have clotted prior to the instrument reading. This can occur in specimens with small clots or specimens from patients receiving recombinant VIIa.
DO find out if patients are on heparin, coumadin or direct thrombin inhibitors. **DON'T** think that just unfractionated heparin or coumadin can prolong results. Depending on the molecular weight, several low molecular heparins may be capable of prolonging your APTTs. In addition, direct thrombin inhibitors (Hirudin, Refludan and Argatroban) will prolong screening tests as well as any clot-based test.
DO make sure that your normal range reflects your patient population, using a minimum of 20, with equal numbers of males and females. **DON'T** use ER or Pre-OP patients. They may have "acute phase reactants." These are elevated during times of stress and inflammation. Two common ones are fibrinogen and factor VIII. If these are elevated it can shorten your normal range.
DO realize the importance of your normal range. It is used in calculating the INR, determines what is normal versus abnormal, and is used in looking at the therapeutic range for heparin (1.5-2.5 times the mean of the normal range). **DON'T** prepare your range all in one day. Rather, run it over a period of time to introduce inter-day variation.
DO know your reagents; they can be your worst nightmare. **DON'T** assume that a normal PT and APTT reflects a normal patient, unless you know your reagents.
DO know how sensitive your reagents are for factors, even if you only do PTs and APTTs. **DON'T** run a lot of reagents unless you know how many seconds the PT or APTT will be that will reflect a factor deficiency. For example, if the upper limit of your APTTs is 37 seconds but reflects only a 19 percent factor IX, that patient may bleed in surgery.

DO know the actual therapeutic range for unfractionated heparin.
DON'T think that using 1.5-2.5 times the mean of the APTT normal range will be good enough.

DO perform a heparin therapeutic range by collecting 50 specimens of patients on all doses of heparin. They must have a normal PT. Run an APTT on each specimen with the lot of reagents as well as a heparin level. Plot a graph of the APTT versus the heparin level. Read off the graph the seconds that correspond with 0.3-0.7U/ml; this represents your actual therapeutic range.
DON'T just spike normal plasma with known concentrations of heparin and run an APTT. This method eliminates the biological variations seen with patients on heparin.

DO make sure that you are working with platelet poor plasma (PPP), plasma with a platelet count of less than 10,000.
DON'T assume that centrifuging specimens make them platelet poor. Check your centrifuges. Be careful with the Stat-spin. Specimens spin fast, but if they are allowed to stand, platelets diffuse back to the plasma.

DO remember that platelets are phospholipids, and so are coagulation reagents.
DON'T forget that the presence of platelets will shorten clotting times.

DO be careful when you are separating and freezing specimens.
DON'T think that getting more plasma is better. If you pick up platelets from the buffy coat you will shorten clotting times. If you freeze and thaw specimens, the platelets will burst and interfere with the phospholipid in the reagent, shortening clotting times.

DO use a PT reagent with an international sensitivity index (ISI) <1.5.
DON'T use insensitive reagents with high ISIs. Remember: In the formula for the international normalized ratio (INR), the ISI is exponential, so the higher the ISI, the greater the error in calculating the INR.

DO understand that the INR is only valid on patients who are on a stabilized dose of coumadin. It takes two weeks for a patient to become stable.
DON'T use the INR for diagnosing other possible coagulopathies.

DO report out INRs up to 6.0.
DON'T report out higher INRs. If you run your PTs only up to 50 seconds, that is where the instrument is linear. A PT above that is not accurate and will not reflect an accurate INR.

DO understand when you switch from plastic to glass tubes you must perform new normal ranges.
DON'T think it has to be done only when you change a lot of reagents. According to NCCLS guidelines, it must be done when you change instruments, lots, collection systems or annually.

DO use only 3.2 percent sodium citrate for testing. The specimens are more stable, your results are more accurate and this anticoagulant has a closer osmolality to plasma.
DON'T use 3.8 percent sodium citrate. Your testing will contain more variability and 3.2 percent is an important factor in standardizing methods.

DO avoid traumatic venipunctures; it can release tissue factor and initiate coagulation.
DON'T assume that a bad draw with normal results is OK; times may be artificially shortened.

DO understand that a hematocrit >55 percent will cause a prolonged coagulation result.
DON'T forget that a hematocrit of <20 percent may not contain a sufficient amount of anticoagulant and cause a clotted specimen.

DO remember that every accession number and medical record number is attached to a patient.
DON'T think that just giving a number for a result is enough. Understand the importance of giving quality results and the role it plays in patient care.

Donna D. Castellone is technical specialist, Department of Coagulation, New York (NY) Presbyterian Hospital, and an ADVANCE *editorial advisory board member.*
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Reference: Becan-McBride K. Avoiding specimen transport error. *MLO* 2002:38.