To address current variation in aPTT comments, mixing study variability, communication of results with ordering clinicians, and interpretation timing across BC, as a guide, the Special Coagulation specialists' team from St. Paul Hospital have come up with a summary of Acquired Hemophilia A testing recommendations and an interpretative comment for isolated prolonged aPTT.

Acquired Hemophilia A (AHA): Summary of Testing Recommendations

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1. AHA should be suspected in patients with recent onset of abnormal bleeding and an isolated prolonged activated partial thromboplastin time (aPTT) (normal PT/INR), especially the elderly, peripartum and postpartum women. [1]

   An example of an interpretive comment for isolated prolonged PTT:
   - **Isolated prolonged PTT**: The differential diagnosis includes deficiency/deficiencies of intrinsic coagulation pathway factor/factors versus inhibitor. Possible inhibitors include anticoagulant therapy, lupus anticoagulant and specific inhibitors (e.g., acquired FVIII inhibitor). Correlation with medication history and the clinical picture is required. **If there are new bruising or bleeding symptoms raising clinical concern of an acquired FVIII inhibitor, emergency hematology or bleeding disorder clinic consultation is recommended to guide additional investigations**.

2. AHA should be suspected in a non-bleeding patient not on anticoagulation with an isolated prolonged aPTT, an aPTT mixing study consistent with an inhibitor (see point 5 and 6), and negative lupus anticoagulant (LA) testing. [1]

3. An isolated prolonged aPTT (cutoff to be determined by the local laboratory) should always be investigated. The effects of anticoagulants (heparin, direct oral anticoagulants (DOACS), etc.) should be appropriately ruled out.

4. An appropriate comment for an isolated prolonged aPTT should be added in a timely manner (preferably < 24 hours). This comment preferably should be added by a pathologist and if not possible at smaller sites, automated comments (LIS, middleware, etc.) should be considered.

5. An aPTT mixing study (1:1 ratio) including incubation step (see point 6, below) is recommended in the investigation of an isolated prolonged aPTT. If the aPTT of the "mix" fails to show correction or any partial correction, this is suggestive of an inhibitor. Correction of the immediate mix is usually suggestive of factor deficiency. However, since factor VIII inhibitors display time dependency, correction of the immediate mix does not rule out the presence of an inhibitor; therefore, an incubation step is recommended. [2]

6. The mix, patient plasma and normal pooled plasma (NPP) should be incubated for 1 to 2 hours (preferably 2 hours) at 37˚C. If the inhibitor demonstrates delayed acting properties, AHA should be suspected. Prolongation of aPTT after incubation can be less than 10 seconds. [2]

7. Variable definitions of mixing correction exist. Correction may be expressed relative to the normal aPTT reference range (i.e., within 2 or 3 standard deviations), the NPP (mix ≤ NPP results plus five seconds), as a ratio or absolute difference (subtraction method), as a percentage correction, or using the Rosner index. [2]

8. If there is a suspicion for AHA and Factor VIII assay is available, FVIII may be measured first based on the site preference.

9. A FVIII inhibitor should be confirmed and quantified by the Bethesda Assay (BA) or Nijmegen Bethesda Assay (NBA). [1]

10. If AHA is confirmed, verbal notification of result should be given to the ordering clinician (or designated coverage physician) urgently. Additionally, recommendation for the ordering provider to contact a hematologist on call at Vancouver General Hospital, St. Paul's Hospital or Royal Jubilee Hospital.

Based on lab's availability for additional testing (i.e., mixing studies, etc.), individual site should develop its own interpretive comment(s) or consult SPH for sample comments.

References:

1. Kruse-Jarres et al. Am J Hematology. 2017; 92:695 – 705
2. Clinical and Laboratory standards institute guidelines: H47-Ed3 One-stage PT and aPTT Test. March 2023