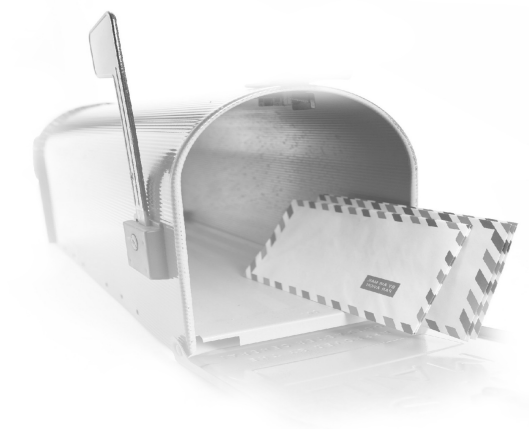

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Letter to the Editor

"Indeterminate lupus anticoagulant" as the third category

TO THE EDITOR: Laboratory testing for the detection of lupus anticoagulant (LAC) is important for the diagnosis of antiphospholipid syndromes and hypercoagulable states. LACs are heterogeneous circulating autoantibodies directed against epitopes found on negatively charged phospholipids and proteins associated with the cell membrane and inhibit phospholipid-dependent coagulation tests *in vitro*. However, LAC is actually prothrombotic agents and cause thrombosis *in vivo*; therefore, accurate diagnosis is critical for risk assessment and long-term patient management with anticoagulants.

To improve the diagnostic sensitivity of LAC testing, the International Society of Thrombosis and Haemostasis (ISTH) published testing guidelines in 1995 [1], and in 2009, it updated guidelines for LAC detection, patient selection, choice of tests, calculation of cut-off value, and interpretation of results [2]. Although mixing studies are simple in principle, interpretation of their results poses a considerable challenge. The 2009 ISTH guidelines recommended using the 99th percentile of the normal values as a cut-off for determining clotting time correction. When the concentrations of LAC are low, the clotting time after mixing can erroneously return to the normal range, and the results may be interpreted as negative. This shows that low concentrations of LAC cannot be detected when the 99th percentile of the normal values is used as a cut-off.

Therefore, it is necessary to adopt a more stratified diagnostic strategy for LAC, especially for the clotting- time based test, to reduce the possibility of a false-negative result when the concentration of LAC is low. In this context, separate, third strategy should be introduced for individuals with "indeterminate LAC". The results can be classified as "indeterminate LAC" when the outcomes of both LAC screening and the confirmatory test are positive but that of the mixing test is weakly positive. By introducing "indeterminate LAC" as a separate category, we can focus on patients who are thought to have a low concentration of LAC.

Alkayed and Kottke-Marchant reported that indeterminate LAC results were common, and that the clinical characteristics of these individuals differed from those with negative results [3]. In our laboratory, we classify LAC test results into 3 different categories: positive, negative, and indeterminate. Our data also show that patients with "indeterminate LAC" have heterogeneous clinical characteristics, from absence of clinical symptoms to evident deep-vein thrombosis, pulmonary thromboembolism, or recurrent fetal loss. If indeterminate LAC results are ignored, these thrombotic diseases may remain undiagnosed.

We think that adding this third category will prove to be a good strategy both practically and clinically. We completely agree with the opinion of Alkayed and Kottke-Marchant.

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