



## COMPARATIVE CLINICAL PERFORMANCE OF READS® ANTIPHOSPHOLIPID ANTIBODY TESTS: AN INTERPRETIVE TOOL

In the last issue of *THE READER* (April 1999), the interpretive ranges for the current READS antiphospholipid antibody assays (aCL, aPS and anti-B2GPI) were reviewed and updated to assist the clinical laboratory with more accurate interpretation of their results. This review process involved testing a large population of healthy and diseased serum samples (including infectious and autoimmune diseases). In addition to interpretive ranges, clinical laboratories and physicians should be familiar with the performance characteristics of each assay with various patients populations, as well as the advantages (and disadvantages) of each antiphospholipid assay. The results from the interpretive range study were further analyzed to compare the performance of each assay with the various patient populations.

The IgG antibody isotype was used in this analysis, as it is most commonly tested and generally regarded as the most clinically significant isotype. Results from a total of 290 serum samples included in the study are summarized in the table below. (Refer to technical updates distributed with the previous 2 issues of *THE READER* for more details on the study).

In this study, 2-3% of the healthy individuals were positive for aCL and aPS antibodies; none were positive for aB2GPI. Based on these results, healthy

individuals seem less likely to demonstrate elevated levels of aB2GPI antibodies compared to aCL and aPS, whereas the prevalence rate reported in the literature for aCL antibodies in healthy populations is up to 7%.

About half of the syphilis patients were positive for aCL and aPS; only 1 of 41 (2%) was borderline for aB2GPI. Published studies show that a majority of syphilis patients may react to CL. Thus aB2GPI may help to distinguish "infectious" from "autoimmune" antiphospholipid antibodies, as previously suggested by various research groups. Only "autoimmune" (rather than "infectious") antiphospholipid antibodies are associated with thrombosis.

More patients in the autoimmune disease groups (PSS, RA and SLE) were reactive for aCL or aPS antibodies compared to the normal population, which resulted in slightly higher mean levels for these populations. However, only the SLE group showed a higher incidence of aB2GPI antibodies (with an elevated mean level), most likely attributable to "autoimmune" antiphospholipid antibodies. These findings are similar to the results of other prevalence studies reported in the literature.

As expected, primary and secondary antiphospholipid syndrome (APS) groups showed a greater number (cont. on pg. 2)

Sample Population	IgG aCL		IgG aPS		IgG aB2GPI	
	Mean GPL	% positive	Mean GPS	% positive	Mean G units	% positive
Healthy (controls)	11	3	9	2	2	0
Syphilis	28	48	18	48	3	2
PSS	14	2	12	20	2	2
RA	18	29	16	37	2	0
SLE	18	23	20	53	24	23
Primary APS	43	64	45	84	111	89
Secondary APS	34	59	42	75	69	58

Healthy = blood bank donors; PSS = progressive systemic sclerosis; RA = rheumatoid arthritis; SLE = systemic lupus erythematosus; APS = primary and secondary (to SLE) antiphospholipid syndrome.

## THE READER RESPONSE

**Q.** A young male was recently admitted to our hospital with recurrent deep vein thrombosis. His clinical picture was consistent with a diagnosis of antiphospholipid syndrome, however, his serum tested negative for anticardiolipin (aCL) antibodies (IgG, IgM, and IgA). In our laboratory, the aCL assay is used to screen for antiphospholipid syndrome (APS); further antiphospholipid testing (aB2GPI) is performed only on aCL positive samples. At the physician's request, the patient was tested for B2GPI antibodies and was shown to have elevated levels of IgG aB2GPI. What changes can we make in our testing protocol to avoid missing clinically relevant phospholipid antibodies?

**A.** This case illustrates the need for effective communication between the laboratory and referring physicians. As with all laboratory procedures, aCL results need to be interpreted in context with the patient's history and other clinical findings. A patient may develop anti-phosphatidylserine (aPS) and/or aB2GPI antibodies in the absence of aCL, which could be related to the stage of the disease process. For these reasons, an algorithm was proposed by Dr. Jeffrey S. Dlott and Dr. Douglas A. Triplett, in *CAP Today* (March 1999, pp. 84-88), which recommends testing all clinically suspicious aCL negative patients for antibodies to phosphatidylserine and B2GPI. Patients with low titers of IgG aCL antibodies, or who present with only IgM and/or IgA aCL antibodies should also be tested for aB2GPI. Repeat testing in 8-10 weeks is also recommended to demonstrate antibody persistence, and to detect the emergence of additional antiphospholipid antibodies. The most conclusive serological evaluation of patients with clinical manifestations of APS would be provided by a panel that includes all three assays (aCL, aPS, and aB2GPI). In addition, offering all three assays as individual tests would allow physicians the option to test for aPS and aB2GPI on clinically suspicious, aCL negative patients.

**Corgenix** was recently awarded **ISO 9001 certification**, after demonstrating our continuing commitment to quality during the extensive review and audit process.

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## FEATURE ARTICLE (cont. from p.1)

of positives with higher population mean levels in all three assays. These results suggest:

- IgG aB2GPI antibodies are more relevant for APS, whereas other phospholipid assays (aCL and aPS) may give false positive results. The phospholipid antibodies in patients who test positive for only aCL or aPS are likely to be of an "infectious" rather than "autoimmune" nature. Neither APS group showed a 100% positive rate for any of the three assays, suggesting that any single test may miss some APS patients. This supports the use of more than 1 assay to increase the detection rate for APS.
- aCL and/or preferably aPS (with a higher prevalence in autoimmune disease groups) may be used to screen for antiphospholipid antibodies. Follow-up testing of positive samples for aB2GPI would then add valuable, more specific information to the serologic evaluation of APS.
- The exact clinical significance of high levels of aCL or aPS antibodies in the absence of aB2GPI in autoimmune diseases remains unclear and should be investigated.

This information should help clinical laboratories and physicians interpret the significance of individual or a combination of antiphospholipid assay results in the serologic evaluation of APS.

## READER ANNOUNCEMENTS

**AACC's 51st Annual Meeting** will be held in New Orleans on July 25-29, 1999. Corgenix invites you to stop by our booth (#3102) during the **Clin Lab Expo** from Tuesday, July 27 - Thursday, July 29, at the Ernest N. Morial Convention Center to learn about our latest products or discuss your testing needs. The following abstracts will be presented during the poster sessions and published in *Clinical Chemistry*:

**Detection of antiphospholipid antibodies: efficient evaluation of hypercoagulable states.** Dier K, Whittier A, Fink CA, Lopez LR. Abstract # 265.

**Quantitation of antibodies to Beta 2 Glycoprotein I in human serum by ELISA.** Dier K, Whittier A, Fink CA, Lopez LR. Abstract # 558.

**Direct Quantitation of Free Protein S in human plasma by a monoclonal-based ELISA.** Whittier AM, Taylor DO, Fink CA, Lopez LR. Abstract # 212.

An article was recently published in *American Clinical Laboratory* (1999) 18;2, 24-25, entitled, "**The measurement of Free Protein S by a monoclonal ELISA**," by Whittier A, Taylor DT, Fink CA, Lopez LR.