



A DECADE OF ANTIPHOSPHOLIPID ANTIBODY TESTING: UPDATE ON THE CLINICAL PERFORMANCE AND INTERPRETIVE RANGES

The 10th anniversary of the introduction of the REAADS ELISA test kit for anti-cardiolipin (aCL) antibodies is fast approaching. During this time, Corgenix has witnessed several remarkable discoveries in this constantly evolving field of antiphospholipid antibody testing. At present, the clinical importance of measuring serum levels of these antibodies for the assessment of thrombotic risk and the diagnosis of the antiphospholipid syndrome is widely accepted. Furthermore, the current understanding of the mechanism(s) by which antiphospholipid antibodies play a role in the production of blood clots has resulted in more effective preventive measures and treatment schedules.

The introduction of the ELISA technology for aCL antibodies in the mid 1980's opened new possibilities for better and more specific clinical studies of antiphospholipid antibodies. However, in spite of several standardization efforts, significant variability in the results between laboratories and procedures is frequently seen. The reasons for this variability are now better understood, as the antiphospholipid antibodies represent a heterogeneous group of autoantibodies. The role of protein cofactors such as Beta-2 Glycoprotein I (B2GPI) allowed the differentiation of antiphospholipid antibodies associated with thrombosis, and suggested that other antibodies may be more specific markers for the antiphospholipid syndrome and thrombotic risk. As a result, ELISA tests for anti-phosphatidylserine (aPS) and anti-B2GPI antibodies have been developed and recently introduced to the clinical laboratory. Other related ELISA assays may soon follow, i.e. anti-prothrombin, and, as you may very well have concluded, healthcare providers will be faced with interpreting results from different tests with different performance characteristics and clinical significance.

With 10 years of experience in this field, Corgenix has reviewed the performance of the commercially available REAADS ELISA tests for antiphospholipid

antibodies (aCL, aPS and anti-B2GPI), with additional and more clinically relevant patient populations. This data has been incorporated into our analysis to propose the following updated interpretive ranges for these assays. Our data for the new REAADS anti-B2GPI tests including their respective interpretive ranges was published as a technical update and distributed with the previous issue of *THE READER*. The revised REAADS aCL, aPS and anti-B2GPI interpretive ranges are shown below. The attached technical updates for aCL and aPS show the test results for these patient populations and support the proposed interpretive ranges. This information is made available to laboratory personnel and healthcare providers to facilitate a more accurate clinical interpretation of the results obtained with the REAADS test kits for antiphospholipid antibodies.

Summary of updated interpretive ranges:

REAADS Anti-Cardiolipin ELISA Ranges			
	IgG	IgM	IgA
Normal	< 23 GPL	< 11 MPL	< 22 APL
Low Positive	23 - 35	11 - 20 MPL	22 - 35 APL
Moderate Positive	36 - 50	21 - 30 MPL	36 - 45 APL
High Positive	> 50 GPL	> 30 MPL	> 45 APL

REAADS Anti-Phosphatidylserine ELISA Ranges		
	IgG	IgM
Normal	< 16 GPS	< 22 MPS
Low Positive	16 - 30 GPS	22 - 35 MPS
Moderate Positive	31 - 50 GPS	36 - 50 MPS
High Positive	> 50 GPS	> 50 MPS

REAADS Anti-B2GPI ELISA Ranges	
	IgG, IgM, IgA
Normal	< 20 units
Low Positive	21 - 50 units
Moderate Positive	51 - 100 units
High Positive	> 100 units

The READER RESPONSE

Q. Our laboratory recently added REAADS anti-Beta-2 Glycoprotein I assay to our antiphospholipid testing panel, and have noticed some samples that test positive for anti-cardiolipin antibodies are negative for anti-B2GPI. What is the clinical significance of these results? Are these patients at risk for thrombosis? What additional diagnostic information does the anti-B2GPI test provide?

A. The aCL assay can detect antibodies of differing specificities, including antibodies specific for the cardiolipin (CL) molecule itself, and antibodies that are directed against either a cofactor molecule such as B2GPI or a special binding site created by the interaction of a cofactor with CL (cofactor dependent antibodies). Antibodies directed against CL may be associated with infectious disease, or may be specific for a different cofactor, such as prothrombin. The clinical significance of these antibodies must be assessed in conjunction with the patient's symptoms, clinical history, and other laboratory findings. Follow-up testing of these patients is recommended in 3-6 months to confirm reactivity. Only B2GPI cofactor dependent antibodies react in the anti-B2GPI assay; these antibodies show a higher correlation with thrombosis and are more specific for the antiphospholipid syndrome.

READER ANNOUNCEMENTS

The following papers were submitted by Corgenix and published in *American Clinical Laboratory*:

Dier K, Fink C, and Lopez LR, Antiphospholipid syndrome: Determination of antibodies to Beta 2 Glycoprotein I (anti-B2GPI) by ELISA. *Amer Clin Lab* (1998) 17;8, 20-21.

Taylor D, Buckner TR, Ridgway HJ, and Lopez LR, The determination of von Willebrand Factor (vWF) by ELISA. *Amer Clin Lab* (1998) 17;8, 26-27.

InterMed '99, North America's International Exhibition for Medical, Healthcare, Surgical & Pharmaceutical, Equipment, Supplies & Services, will be held at the National Trade Centre, in Toronto, Ontario, Canada June 21-23, 1999. In addition to the exhibits, International Conference / Seminar programs on more than 20 different subjects are scheduled during the show. Dr. Luis R. Lopez, CEO of **Corgenix, Inc.**, will discuss the immunology and laboratory determination of antiphospholipid antibodies (anti-cardiolipin, anti-phosphatidylserine, and anti-beta 2 glycoprotein I), at the seminar on the Laboratory Evaluation of Hypercoagulable Diseases, along with other world renowned experts in the field. Corgenix

(cont. in next column)

READER PRODUCT FEATURE

REAADS Anti-Phosphatidylserine IgG/IgM Semi-Quantitative Test Kit

For *In Vitro* Diagnostic Use

Assay format -	96-well microtiter plate (8 x 12 strips) with breakaway wells
Antigen substrate -	Phosphatidylserine
Conjugate -	Horseradish peroxidase (HRP) / goat anti-human IgG/IgM
Chromogenic substrate -	TMB (single component)
Stopping solution -	0.36 N Sulfuric acid
Sample dilution -	1:50, human serum
Incubations	
Sample -	15 min @ room temperature
Conjugate -	15 min @ room temperature
Substrate -	10 min @ room temperature
Wavelength -	450 nm
Clinical specificity -	IgG 98%; IgM 98%
Clinical sensitivity -	SLE with thrombosis: IgG 75%, IgM 16%; Primary APS: IgG 84%, IgM 60%
Product number -	030-001 aPS IgG/IgM

ANNOUNCEMENTS (cont.)

representatives will be available at Booth #951 during the Exhibition to answer your questions or discuss your testing needs. For more information on InterMed '99 visit their Web-site: <http://www.mpe.ca/intermed>, or call +1 (514) 731-1015 in Montreal, Quebec.

The First Annual Symposium on Hemostasis and Thrombosis, will be presented by University Coagulation Consultants (UCC) at the Omni Severin Hotel in Indianapolis, Indiana on May 20-21, 1999. The Symposium will focus on arterial and venous thrombosis, providing a comprehensive review of pathophysiology, laboratory testing, genetics, and treatment modalities for physicians and health care workers whose practices deal with the evaluation and management of patients with thrombotic events. A wet workshop is scheduled on May 20, to allow hands on experience with several coagulation instruments. Contact Ball Memorial Hospital, Medical Education Department by phone (765) 747-3366, or fax (765) 747-0137 to register before May 7, 1999.

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