

THE 8TH INTERNATIONAL SYMPOSIUM ON ANTIPHOSPHOLIPID ANTIBODIES

The 8th International Symposium on Antiphospholipid Antibodies was held in Sapporo, Japan on October 6 - 9, 1998. Professor T. Koike from Hokkaido University School of Medicine, Sapporo, Japan organized a comprehensive antiphospholipid scientific program with cultural events that attracted researchers from various parts of the world. The traditional Japanese hospitality during the symposium which made this event even more memorable. A brief summary of the most relevant topics discussed which represent new trends and developments in the field of antiphospholipid antibody testing is presented below. The state of the art lectures and scientific abstracts have been published in *Lupus*, 1998: 7(2) for further reading by those interested in expanding their knowledge of antiphospholipid antibodies.

As seen in the previous symposiums, the role of B2GPI in antiphospholipid testing continued to be a dominant topic of scientific research and clinical studies. It is becoming clear that B2GPI is the most common and best characterized "cofactor" for antiphospholipid antibodies. For example, genetic studies have confirmed that mutations of the fifth domain of the B2GPI molecule can interfere with the interaction between B2GPI and anionic phospholipids which may also affect their binding with antiphospholipid antibodies. There is growing evidence that lupus anticoagulants (LA) are more strongly associated with thrombosis than classic aCL antibodies, and that B2GPI-dependent LA may be more relevant than prothrombin-dependent LA. Results from these studies lead to the proposal that anti-B2GPI antibodies bind with low affinity to B2GPI in circulation. These complexes (anti-B2GPI-B2GPI) may now have high affinity for phospholipids present on procoagulant surfaces. These complexes may compete with coagulation factors for phospholipids *in vitro* or may promote clotting reactions *in vivo*. Studies

on the possible role of anti-prothrombin antibodies in thrombosis yielded mixed results, and it appears that the clinical relevance of these antibodies has not yet been fully established. These studies emphasized the importance of B2GPI in antiphospholipid testing and thrombosis, and lead to the recommendation that anti-B2GPI antibody testing should be included in the evaluation panel for thrombosis (antiphospholipid syndrome).

Antiphospholipid antibodies have been described in patients with infectious diseases including those with viral infections. "Autoimmune" antiphospholipid antibodies that caused fetal death and spinal cord infarction were induced in mice by immunization with foreign B2GPI. It is thought that *in vivo* binding of B2GPI to phospholipids created immunogenic complexes which led to the production of antiphospholipid antibodies in these mice. Small peptides from the phospholipid binding region of the B2GPI molecule also induced antiphospholipid antibodies in this animal model. Furthermore, viral peptides with homology sequence to the phospholipid binding region of B2GPI also produce high levels of antiphospholipid antibodies (including anti-B2GPI antibodies) in experimental mice. These results suggest that viral products may be the initial stimuli for antiphospholipid antibody production in patients with the antiphospholipid syndrome.

Several scientific abstracts from independent groups showed increased levels and high prevalence of IgA antiphospholipid antibodies (including anti-B2GPI) in various patient populations. Patients with IgA antiphospholipid antibody as the only isotype present were also reported. The significance of IgA antiphospholipid antibodies was the subject of a plenary lecture in which previously published papers were reviewed. A study by L.R.Lopez *et al* on the

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Q. Our normal control is consistently recovering at the upper end of the assayed range with REAADS Protein S Antigen assay. We are using the same controls with the REAADS Protein S ELISA that we routinely use for all of our other coagulation testing. Should we be concerned about this trend?

A. Your routine coagulation controls can be used with REAADS Protein S, monoclonal Free Protein S, Protein C, and von Willebrand Factor Antigen ELISAs, however, it is important to understand which technology was used by the manufacturer to establish control ranges. As with most laboratory tests, control ranges can be influenced by differences in technology, equipment, and manufacturers' products, among other things. Protein S control ranges that were assigned using Laurell Rocket immunoelectrophoresis may not be identical with ranges assigned by ELISA. It may be necessary to establish your own control ranges in your laboratory, especially if the manufacturer's ranges were not assigned by ELISA. For your convenience, Corgenix offers two levels of Coagulation Controls with assayed ranges for REAADS ELISAs. For more information, please contact our Customer Service Department at (800) 729-5661 or (303) 457-4345.

READER ANNOUNCEMENTS

- **Corgenix** will be operating on a limited schedule during the holidays, beginning at 12:00 noon on Thursday, December 24 until Monday, January 4, when regular operations will resume. All standing orders due by the end of the month will be shipped the week of December 21, to arrive before Christmas. Please check your inventory and plan ahead to assure an adequate supply of product during the holidays. For technical assistance or an emergency delivery, please call and leave a message at (800) 729-5661 or (303) 457-4345, and a Customer Service Representative will return your call.
- **Corgenix** announces that REAADS IgA Anti-Cardiolipin Test Kit is now available in a convenient three (3) plate format. The new kit (catalog number 026-006) includes proportionally larger serum and wash buffer volumes to facilitate automated testing.
- The following **Corgenix** abstract was published in *BLOOD*, 1998: 92, No. 10, Suppl 1: 102b, #3423:

Evaluation of a Monoclonal Antibody based ELISA for the Detection of Free Protein S in Human Plasma. A.M. Whittier, D.O. Taylor, C.A. Fink, L.R. Lopez.

REAADS Monoclonal Free Protein S Test Kit

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Assay format -	96-well microtiter plate (8 x 12 strips) with breakaway wells
Sample matrix -	citrated human plasma
Capture antibody -	Monoclonal antibody to Free Protein S
Detection antibody -	Horseradish peroxidase (HRP) conjugated polyclonal rabbit anti-human Protein S
Chromogenic substrate -	TMB (single component)
Stopping solution -	0.36 N Sulfuric acid
Sample dilution -	1:26
Incubations	
Sample -	40 min @ room temperature
Conjugate -	10 min @ room temperature
Substrate -	10 min @ room temperature
Wavelength -	450 nm
Assay calibration -	Six point curve prepared from reference plasma included in kit
Assay sensitivity -	≤ 6% of normal
	*FDA Clearance pending

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clinical significance of IgA aCL antibodies in SLE patients published in 1992 played a central role in these discussions. It was concluded that experimental evidence suggests that IgA antiphospholipid antibodies (including anti-B2GPI) are as prothrombotic as the IgG and IgM isotypes.

Other interesting associations, i.e. antiphospholipid antibodies with atherosclerosis and myocardial infarction were discussed by some groups. Although too early to establish firm conclusions, these associations are, to say the least, "very intriguing" at this point. Finally, in addition to updated clinical and therapeutic reviews, one plenary lecture addressed the need to revise the criteria for the diagnosis of the antiphospholipid syndrome. A panel of experts further discussed this issue in a post symposium seminar; the revised criteria with their new recommendations will be published soon.

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