

THE SIXTH INTERNATIONAL SYMPOSIUM ON ANTIPHOSPHOLIPID ANTIBODIES

The Sixth International Symposium on Antiphospholipid Antibodies was held in Leuven, Belgium on September 14 - 17, 1994. More than 300 scientists actively investigating antiphospholipid antibodies representing diverse disciplines such as immunology, hematology (hemostasis and thrombosis), rheumatology, neurology, obstetrics, biochemistry, etc., met and discussed their most recent results. Significant progress has been made towards elucidating the interaction between phospholipids and plasma proteins known as cofactors, which generates antigenic determinants responsible for binding with antiphospholipid antibodies. Other recent serologic and clinical studies on antiphospholipid antibodies were reviewed and hypothetical models presented to explain the pathogenic role of these antibodies in thrombosis. A brief summary of some of the most relevant topics is presented below. For further reading, the Symposium's state of the art lectures and abstracts have been published in the August 1994 issue (Volume 3, Number 4) of the international journal *Lupus*.

The plasma protein B₂ glycoprotein I (B₂GPI) with anticoagulant properties *in vitro* has been identified as a cofactor for the binding of antiphospholipid antibodies in solid phase assays. The most likely site of the interaction between B₂GPI and the negatively-charged phospholipid molecule has been localized and characterized as an amino acid sequence in the B₂GPI molecule with a highly positive charge. The new antigenic determinant exposed when B₂GPI binds the phospholipid is also found in this region of the molecule. Unlike those associated with infectious diseases, autoimmune antiphospholipid antibodies appear to be more dependent on B₂GPI for optimal immunological binding. Due to B₂GPI's anticoagulant properties, their participation in the binding of autoimmune antiphospholipid antibodies provides an explanation to a possible mechanism(s) of thrombosis in patients with the antiphospholipid syndrome.

The heterogeneity of the antiphospholipid antibodies has been well documented but its nature has been difficult to ascertain. Variations at any of the following levels may

account for the differences observed in the antiphospholipid antibodies: avidity of the antiphospholipid antibodies, cross reactivity (cardiolipin, phosphatidylserine), dependency for B₂GPI-phospholipid complexes, other cofactor molecules, phospholipid conformation, antibody isotypes, etc. Although better recognized at this time, these differences need to be further clarified to understand and address important practical problems encountered in routine serologic determination, standardization efforts, and in the interpretation of antiphospholipid antibody levels. In the coming years, these aspects as well as the role of other plasma proteins acting as cofactors may further elucidate the clinical significance of antiphospholipid antibodies.

Laboratories are continually challenged with the problem of determining the presence of antiphospholipid antibodies in patient samples. It has been recommended that laboratories develop a well-planned strategy to identify these antibodies. Both coagulation assays and ELISAs should be performed. ELISAs for antiphospholipid antibodies should provide information such as the antibody isotype and concentration to improve the clinical interpretation of the results. The use of phosphatidylserine as the antigen (in the presence of B₂GPI) should also be included in the serologic evaluation of antiphospholipid antibodies as it may provide a better and perhaps a more physiologic antigenic site for the interaction with antiphospholipid antibodies. The determination of both anticardiolipin and antiphosphatidylserine antibodies has been shown to enhance the correlation with clinical manifestations of the antiphospholipid syndrome.

New developments in antiphospholipid antibody research including their role in thrombosis will be discussed again in 1996 at the Seventh International Symposium on Antiphospholipid Antibodies to be held in the U.S. (New Orleans). It can be anticipated that the progress in this field will continue to improve the diagnosis, treatment and prevention of diseases where thrombosis is an important factor for morbidity and mortality.

THE READER RESPONSE



Q. What is the clinical significance of IgM anticardiolipin antibodies? We have a patient who tests positive for IgM aCL, but negative for IgG and IgA aCL antibodies.

A. The detection of IgM aCL antibodies in a patient testing negative for IgG and IgA aCL antibodies is reported to have a poor clinical correlation with thrombosis. Although some patients produce IgM aCL antibodies of undetermined clinical significance, patients with high levels of IgM antibodies should be monitored over time to see if they represent an early manifestation of the antiphospholipid syndrome (APS). Low antibody levels may represent a non-specific serological reaction, and have been described to occur secondary to drug-induced and infectious disorders. These antibodies are usually transient, and should disappear with time. As with all laboratory tests, the clinical symptoms and history of the patient need to be considered in the interpretation of aCL test results.

Q. How do you interpret aCL test results in a patient with syphilis?

A. Patients with syphilis may produce antibodies which react with cardiolipin. In fact, cardiolipin is one of the active antigenic components in the VDRL test for syphilis. Historically, some individuals were found to test positive by VDRL with no clinical or epidemiological evidence of syphilis. A high incidence of autoimmune disease, particularly SLE was found to occur in these individuals. More recently, the clinical utility of quantitatively measuring anti-cardiolipin (aCL) antibodies by ELISA was recognized with the observation that many of these individuals with high levels of aCL antibodies experienced recurrent thrombosis, fetal abortions and/or thrombocytopenia (antiphospholipid syndrome, APS).

Patients confirmed to have syphilis may test positive for aCL antibodies, however this finding cannot be considered diagnostic for APS. Recent evidence has suggested that autoimmune aCL antibodies can be distinguished from those elaborated in syphilis by their dependence on a cofactor, such as B₂GPI. Syphilis antibodies are not associated with thrombosis and react independent of a cofactor. Most ELISAs contain B₂GPI as a cofactor and favor the detection of autoimmune associated aCL antibodies.

READS Medical Products, Inc. would like to wish all of our customers and their families a very Merry Christmas and a happy and safe holiday season. We appreciate your continued support in the coming new year.



READER ANNOUNCEMENTS

- READS will be closed during the holidays from 12:00pm MST on December 23 to 8:00am January 2, 1995 in order for our employees to celebrate the holidays with their families. Please check your inventory and place your orders early to assure timely delivery in December. If you need technical service or an emergency delivery during this period, leave your phone number and message at (800) 729-5661, and one of our Customer Service representatives will return your call.
- READS is currently completing clinical studies with our new ELISA anti-phosphatidylserine (aPS) assay for submission to the FDA. We will begin marketing the kit as soon as we secure FDA clearance.
- READS is also considering expanding our autoimmune product line to provide our customers with a complete range of autoantibody assays in the ELISA format. More information will appear in upcoming editions of **THE READER**.

Additional questions or requests for references regarding the information or opinions presented in this newsletter, current applications and clinical significance of anticardiolipin antibodies or autoantibodies detected by ELISA may be directed to our customer service / technical support staff at READS Medical Products, Inc.

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