EDITORIAL

This supplement contains review articles addressing several important concepts regarding the antiphospholipid antibodies (aPL) and the antiphospholipid syndrome (APS). Since its recognition as a separate entity in the early 1980s, the APS has increasingly gained the interest of haematologists, obstetricians and rheumatologists. It is an autoimmune disorder in continuous evolution and our knowledge has greatly improved in the last years. Nevertheless it is also a clinical area with several open questions. Some of them are discussed in this series of reviews.

The last International consensus document that updated the classification criteria for APS was published at the beginning of 2006. However, there are several authors suggesting that only patients with thrombosis and/or pregnancy morbidity with triple aPL positivity must be considered as definite APS. This implies that lupus anticoagulant (LA), anticardiolipin (aCL) and anti-$\beta_2$glycoprotein I (anti-β_2GPI) antibodies should be simultaneously positive. Different laboratory criteria for thrombosis- and pregnancy morbidity-related APS are now recommended.

The most relevant antigenic targets involved in APS are β_2GPI and prothrombin. But, a rising number of other phospholipid-binding proteins with central functions in the regulation of blood coagulation and fibrinolysis are also targeted by APS-related autoantibodies. New studies show convincing evidence that anti-β_2GPI from the majority of patients with APS preferentially bind the domain I of β_2GPI. The detection of specific β_2GPI antibodies targeting domain I could perhaps help in the best characterization of pathogenic autantibodies.

The updated version of the recommendations for LA detection and diagnosis was recently published. It is important to strictly follow the guidelines and the recommendations in order to minimize the source of variability and to increase reliability of the tests. The future of laboratory diagnosis of APS seems to be promising and further improvement could be achieved through multicenter collaborative prospective studies.

The clinical utility of aPL assays to phospholipids other than cardiolipin and to phospholipid-binding proteins other than β_2GPI remains unclear. Their application should be restricted only to research rather than to routine diagnostic use.

Both aPL and APS are more commonly associated to systemic lupus erythematosus (SLE). However, APS is also associated to a very large and yet not well defined group of other autoimmune diseases. A series of clinical cases is presented in one the articles in order to illustrate the wide spectrum of clinical manifestations of APS.

Our knowledge on the thrombogenic mechanisms in APS has greatly improved in the last years. The strongest evidence that aPL are pathogenic *in vivo* come from studies utilizing animal models of thrombosis and pregnancy loss. Pathogenic mechanisms include effects on the coagulation cascade, cellular activation and complement activation. Recently much has been advanced in the knowledge of cellular receptors that participate in signaling transduction. Understanding intracellular events in aPL-mediated cellular activation may help in designing new targeted therapies for thrombosis in APS.

The mainstay of the clinical management of thrombosis in APS is anticoagulation but there is some debate on the optimal duration. Considering the thrombosis risk seems to be particular according to the different aPL profile (multiple or single positivity), it is vital to carry out large scale randomized clinical trials to identify the most appropriate management for primary or secondary prevention of thrombosis. Well designed clinical trials are essential in order to evaluate the potential effectiveness of new therapeutic agents. Questions such as whether the newer agents could be used in addition to current treatment in preventing recurrence thrombosis despite oral anticoagulation probably should be answered in the future.

This series of reviews address some aspects of this intriguing disease in order to contribute to a best understanding of the APS.

Ricardo R. Forastiero

Department of Physiology/Favaloro University
Thrombosis and Haemostasis/University
Hospital/Favaloro Foundation
Buenos Aires
Argentina
Tel: +54 11 4378 1145
Fax: +54 11 4378 1311
E-mail: rforastiero@favaloro.edu.ar