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# Introduction

As part of the XIII International Congress on Thrombosis in Bilbao, Spain (June 6–10, 1994), a special symposium was held to address a number of recent advances in the field of antiphospholipid antibodies (APA).

APA are a family of related antibodies which have arbitrarily been defined by in vitro laboratory test systems. This family of antibodies includes reagin, lupus anticoagulants (LA) and anticardiolipin antibodies (ACA). Initially, LA and ACA were thought to be the same antibody; however, recent studies have clearly identified differences in antigenic specificity and cofactor requirements. Furthermore, various in vitro schemes of purification have been able to separate the two antibodies. Patients with APA have a spectrum of clinical findings including recurrent arterial and venous thromboembolic events, spontaneous abortions, thrombocytopenia, and a variety of neurologic disorders. A wide variety of medical specialists are interested in the field of APA. As a result, requests to the laboratory for analysis of patient plasmas for these antibodies have increased dramatically.

A comprehensive review of laboratory diagnostic strategies was presented. A number of new test systems have been identified for use in the diagnosis of LA. These include integrated screening and confirmatory tests: dilute Russell Viper Venom Time (dRVVT) based and Activated Partial Thromboplastin Time (APTT) based. These integrated approaches employ a sensitive screening procedure, incorporation of a mixing step, and confirmation by the presence of either an excess of phospholipids (or platelets) or, alternatively, specifically configured phospholipids (hexagonal phase II). A new snake venom assay based on a component of Pseudonaja textilis venom (Textarin) was also discussed. This venom can also be used in a comprehensive assay integrated system. Advan-ces in the field of ACA include the use of gamma irradiated polystyrene pla-tes which provide greater sensitivity to the presence of ACA.

A prospective epidemiologic study on LA and ACA was presented. Increasingly, both animal models as well as prospective clinical trials suggest APA are causative rather than a coincidence or consequence when identified in the context of clinical complications.

The term APA is a misnomer. Initially, these antibodies were thought to be specific for anionic phospholipids. However, recent studies would suggest the antibodies recognize a variety of proteins when complexed with anionic phospholipids or other negatively charged surfaces. Beta2 Glycoprotein I was first described as a cofactor necessary for the ACA assay. Recent studies suggests the epitope for ACA is exposed when Beta2 Glycoprotein I undergoes a configurational change following interaction with a negatively charged surface (either anionic phospholipids or negatively charged microtiter plates without phospholipid). Lupus anticoagulant activity may be Beta2 Glycoprotein I dependent or, alternatively, may require the presence of human prothrombin. The species specificity of LA has been appreciated for some time. Bevers and colleagues were the first to clearly demonstrate the requirement of human prothrombin for a subset of LA. Other plasma proteins which may represent putative targets for APA include protein C, protein S, factor X, and factor XI.

The standardization of solid phase immunoassays for APA/ACA has been the focus of studies for a number of years. Several international workshops have attempted to bring clarity to this field. Unfortunately, there remains a lack of interlaboratory consistency for ACA testing. The availability of reference sera for IgG, IgM, and IgA ACA isotypes has proved helpful in the semiquantitation of the antibodies. Controversy remains regarding the optimal lipid to be used in solid phase assays. Physiologically, phosphatidylserine would seem to be a better antigen than cardiolipin. However, there are limited data available from studies analyzing antibodies to phosphatidylserine.

Antiphospholipid antibodies represent a model of autoimmune-induced thrombosis. As such, they potentially could provide a paradigm for other antibody-induced thrombotic conditions. There are pathologic as well as clinical similarities between patients with heparin-induced thrombocytopenia, thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, and the antiphospholipid antibody syndrome. The laboratory's challenge remains one of identifying the presence of these antibodies and hopefully being able to elucidate characteristics of given antibodies which identify them as being pathogenic and persistent in contrast to the antibodies which are innocent and transient.