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Review

14th International Congress on Antiphospholipid Antibodies Task Force. Report on antiphospholipid syndrome laboratory diagnostics and trends

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ABSTRACT

Current classification criteria for definite Antiphospholipid Syndrome (APS) require the use of three laboratory assays to detect antiphospholipid antibodies (aCL, anti-β2GPI and LA) in the presence of at least one of the two major clinical manifestations (i.e. thrombosis or pregnancy morbidity) of the syndrome. However, several other autoantibodies shown to be directed to other proteins or their complex with phospholipids have been proposed to be relevant to APS but their clinical utility and their diagnostic value remains elusive.
This report summarizes the findings, conclusions and recommendations of the "APS Task Force 3—Laboratory Diagnostics and Trends" meeting that took place during the 14th International Congress on Antiphospholipid Antibodies (APLA 2013, September 18–21, Rio de Janeiro, RJ, Brazil).

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1. Introduction

Current classification criteria for definite Antiphospholipid Syndrome (APS) require the use of three laboratory assays to detect antiphospholipid antibodies (aPL) in the presence of at least one of the two major clinical manifestations (i.e. thrombosis or pregnancy morbidity) of the syndrome [1]. Anticardiolipin antibodies (aCL), anti-β2 glycoprotein I (anti-β2GPI) antibodies and the lupus anticoagulant (LA) are the laboratory tests included in the revised criteria for the classification of the APS.

However, several other autoantibodies shown to be directed to other proteins of the coagulation cascade (i.e. prothrombin and/or phosphatidylserine–prothrombin complexes) or their complex with phospholipids other than cardiolipin, or to some domains of β2GPI, have been proposed to be relevant to APS [2] but their clinical utility and their diagnostic value remain elusive. The clinical relevance of IgA aPL and whether these isotype tests should be part of the routine diagnostic algorithm is also being a subject of hot debate.

A task force of worldwide scientists in the field firstly met, discussed and analysed critical questions related to "criteria" and "non-criteria" aPL tests in an evidence-based manner during the 13th International Congress on Antiphospholipid Antibodies (APLA 2010, April 13–16, Galveston, TX, USA) [3,4]. Members of these task forces continued to work and reunited to evaluate the utility of various laboratory assays.

This report summarizes the findings, conclusions and recommendations of the "APS Task Force 3—Laboratory Diagnostics and Trends" meeting that took place during the 14th International Congress on Antiphospholipid Antibodies (APLA 2013, September 18–21, Rio de Janeiro, RJ, Brazil). This task force comprised a group of clinical laboratory scientists, researchers and clinicians, involved within 7 subgroups (Table 1) according to their expertise. All available data was assigned a level of evidence according to the design of the study [5] (Table 2) and the grading system was applied to evaluate the quality of that available evidence (Table 3) [6,7].

Last but not least, this manuscript is dedicated to the memory of Prof. Silvia Pierangeli (1955–2013), an exceptional friend, a remarkable colleague and one of the main contributors to the study of APS, including the standardization of aPL tests. Prof. Pierangeli embarked on a tireless effort to promote standard test performance through multiple publications and workshops, and by providing proficient advice worldwide. Her efforts culminated in the assembly of experts for this task force to which she devotedly dedicated during the last months of her life.

1.1. Subgroup I—harmonization of aCL and anti-β2GPI

This session was dedicated to the memory of Drs. John A McIntyre and Doug A Triplett.

Table 1
Task force 3—laboratory diagnostics and trends.

Subgroup	
I	Harmonization of aCL and anti-β2GPI
II	Lupus anticoagulant
III	IgA aPL tests
IV	Tests for antibodies to negatively charged phospholipids and antibodies to phosphatidylethanolamine (aPE)
V	Tests for antibodies to prothrombin (aPT) and phosphatidylserine/prothrombin (aPS/PT)
VI	Tests to antibodies to domain I
VII	aPL as risk factors

2. Standardization of antiphospholipid immunoassays

A report from the 'criteria' aPL task force formed at the 13th International Congress on Antiphospholipid Antibodies outlined critical issues relating to the performance of antiphospholipid (aPL) immunoassays and made several recommendations to improve their standardization [3]. Among these recommendations were the need for an international consensus protocol for anticardiolipin (aCL) and anti-□eta2 glycoprotein I (anti-β2GPI) tests (which have subsequently been published) as well as the establishment of international units (IUs) of measurement for anti-β2GPI assays and the development of internationally recognized polyclonal and monoclonal standards for this assay [8,9]. Members of subgroup I were charged with continuing the development of international units and reference materials for anti-β2GPI testing and more broadly with critical examination and discussion of proficiency testing programs, cut-off establishment and the significance of low-positive titers for aPL immunoassays.

3. Development of polyclonal and monoclonal reference material and international units for anti-β2GPI measurement

According to an approved protocol prepared by Drs Silvia Pierangeli, Pier Luigi Meroni and Gabriella Lakos, IgG and IgM polyclonal reference sera (IgG and IgM reference material) were each prepared by pooling serum from well-characterized APS patients with very high anti-β2GPI levels of the desired isotype. Once prepared, IgG and IgM anti-β2GPI fractions were purified from their respective reference material utilizing combinations of affinity and ion-exchange chromatography; then were subsequently pooled, concentrated, sterile filtered and their binding

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