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Review of International Consensus Statement On An Update of the Classification Criteria for Definite Antiphospholipid Syndrome

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Introduction:

The international consensus statement update of the classification criteria for definite antiphospholipid syndrome (APS) was published in 2006 in the *J Thromb Haemost*¹. These criteria were revised as a large body of work on the laboratory and clinical manifestations of APS have appeared since the original Sapporo criteria published in 1999². Both the lupus anticoagulant criteria and the anticardiolipin (aCL) IgG and IgM isotypes have been maintained.

The present criteria differ in the following aspects:

a) The original criteria required persistent positivity for at least 6 weeks and this interval has been increased to 12 weeks, b) beta-2-GPI IgG and IgM antibodies have been included as criterion antibodies, c) a subclassification based upon aPL positivity has been proposed and d) an improved definition of clinical criteria has been included. The clinical criteria require only one event for arterial/venous thrombosis or fetal complications >10 and < 34 weeks of gestation, and have added three or more fetal losses < 10 weeks (see below).

Revised classification criteria for the antiphospholipid syndrome¹:

Antiphospholipid syndrome (APS) is present if at least one of the clinical criteria and one of the laboratory criteria that follow are met:

Clinical Criteria:

1. Vascular thrombosis: One or more clinical episodes of arterial, venous or small vessel thrombosis in any tissue or organ. This does not include superficial venous thrombosis.

a. Thrombosis must be confirmed by objective, validated criteria – i.e. unequivocal findings of appropriate imaging or Histopathologic confirmation – thrombosis should be present without significant inflammation in the vessel wall.

2. Pregnancy mortality:

a. One or more unexplained deaths of a morphologically normal fetus at or beyond the 10th week of gestation, with normal fetal morphology documented by ultrasound or direct examination of the fetus,

or

b. One or more premature births of a morphologically normal neonate before the 34th week of gestation because of: (i) eclampsia or severe preeclampsia defined according to standard definitions³, or (ii) recognized features of placental insufficiency,

or

c. Three or more unexplained consecutive spontaneous abortions before the 10th week of gestation, with maternal anatomic or hormonal abnormalities and paternal/maternal chromosomal causes excluded.

Testing:

Revised classification criteria for the antiphospholipid syndrome¹:

Antiphospholipid syndrome (APS) is present if at least one of the clinical criteria and one of the laboratory criteria that follow are met:

Laboratory Criteria:

1. Lupus anticoagulant (LA) present in plasma, on two or more occasions at least 12 weeks apart and not greater than 5 years after the clinical event. These should be detected according to the guidelines of the International Society on Thrombosis and Haemostasis (Scientific Subcommittee on LA's/ phospholipid-dependent antibodies) ⁴

2. Anticardiolipin (aCL) antibody of IgG and/or IgM isotype in serum or plasma (in titer > 40 GPL or MPL, or > the 99th percentile, on two or more occasions, at least 12 weeks apart and not greater than 5 years after the event, measured by standard ELISA assays. ^{5,6,7}

3. Anti-beta-2-GPI IgG and/or IgM isotypes in serum or plasma (in titer > the 99th percentile, present on two or more occasions, at least 12 weeks apart, and not greater than 5 years after the clinical event, by a standard ELISA assay⁹.

Proposed classification for investigators based upon antiphospholipid antibody results¹:

Investigators are strongly advised to classify APS patients in studies into one of the following categories based on laboratory results: I. More than one laboratory criteria present (any combination); IIa. (LA present alone), IIb. (aCL antibody present alone) and IIc. anti-beta-2-GPI antibody alone.

Features associated with APS, but not included in the revised criteria:

It should be noted, although not reviewed here due to space limitations, that these investigators also listed criteria for some of the clinical and laboratory features which are not included in the revised classification. These include: (i) heart valve disease, (ii) livedo reticularis, (iii) thrombocytopenia, (iv) nephropathy, (v) neurologic manifestations, (vi) IgA aCL, (vii) IgA anti-beta-2-GPI antibodies, (viii) antiphosphatidylserine antibodies, (ix) antiphosphatidylethanolamine antibodies, (x) antibodies against prothrombin alone, and (xi) antibodies to the phosphatidylserine-prothrombin complex. Their association has been well recognized, but the adoption of these criteria may decrease diagnostic specificity. Nevertheless this is very useful information for physicians who care for patients with APS.

Summary:

The updated revised clinical and laboratory classification of the antiphospholipid syndrome has changed. Physicians evaluating patients for this disorder should now order the standard lupus anticoagulant panels plus anti-beta-2-GPI IgG and IgM testing. The criteria for length of time of positivity has been increased from 6-12 weeks. In addition, only one clinical event for arterial, venous thrombosis or a pregnancy mishap after 10 weeks gestation is now required. In addition, three successive fetal losses < 10 weeks is a new criterion.

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