

21. Antiphospholipid antibodies

Last Updated: 2/13/2005

Q1: "My hemo just ran five new tests on me, looking for another cause of clotting. It looks as if the beta-2-glycoprotein test is an indicator of APS (= antiphospholipid antibody syndrome). My IgG and IgA are both normal, but my IgM is 34 (should be <15 U/ml). There's another test; I am not sure how to read most of it, but the bottom says "Phoslip IgM INT = weakly positive. I also flunked lipoprotein(a) (I am 121 mg/dL, should be < 30), but don't think that's involved in APS. Would someone be willing to fill me in a bit?"

A1: Presence of β 2-glycoprotein-I antibodies is an indicator of the antiphospholipid antibody syndrome. "Phoslip IgM INT" may stand for "antiphosphatidyl-inositol IgM antibody", which is one of the many different types of antiphospholipid antibodies. The significance of anti-phosphatidylinositol antibodies is not known. A weakly positive level is of questionable significance. Lipoprotein(a) is not associated with the antiphospholipid antibody syndrome. Elevated levels are, however, a risk factor for arteriosclerosis, arterial thrombosis, and possibly venous thrombosis.

Q2: "Do I have a lupus anticoagulant? On my lab report under "Coagulation - Miscellaneous" is "Lupus Anticoagulant". APTT is 44.9 sec (range 23.0 - 33.0) and DRVVT test is 90 (range 40.0 - 54.4). I'm on coumadin® and don't know if that makes a difference on any of this."

A2: The aPTT is typically not prolonged in patients on coumadin, but the DRVVT is. Many reasons can cause the aPTT to be prolonged; lupus anticoagulant is just one of them. The lab needs to do a so-called "confirmatory test" (adding extra phospholipids to the sample) on both the aPTT and the DRVVT, before a lupus anticoagulant can be diagnosed. With the data presented by the patient one can not conclude that she has a definite lupus anticoagulant.

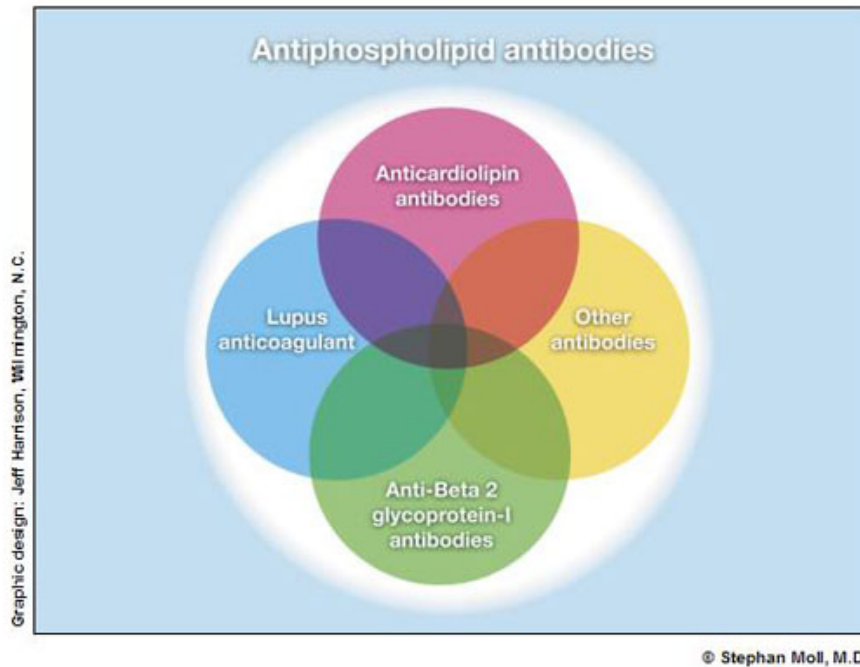
Q3: "Lupus anticoagulant testing should not be done during anticoagulation."

A3: This is not correct. A lupus anticoagulant test can be done and is often reliable while the patient is taking coumadin if the "confirmatory test" (addition of extra phospholipids to the sample) is done. For correct interpretation of the test the physician needs to know what kind of lupus anticoagulant test kit the lab is using.

The term "antiphospholipid antibodies" (= APLA) is the general term for a variety of different antibodies (see figure 1) which, in some people, are associated with venous clots (deep vein thrombosis or pulmonary embolism. etc.), arterial clots (heart attack, stroke, leg artery clots, etc.), or pregnancy loss. These antibodies are directed against several types of phospholipids (or phospholipid binding proteins). Thus, one could theoretically run multiple tests for antiphospholipid antibodies:

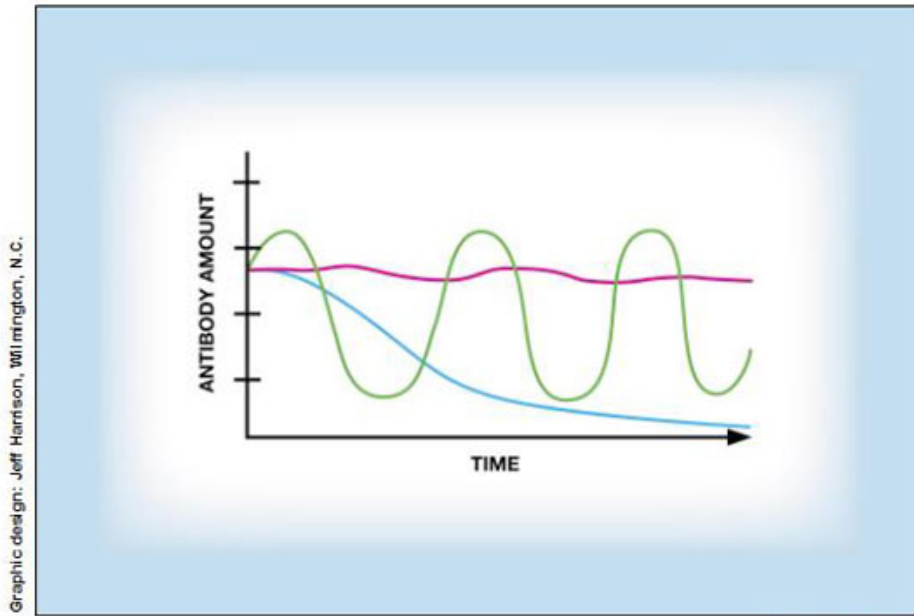
1. anticardiolipin antibodies
2. lupus anticoagulant
3. anti- β 2-glycoprotein-I antibodies
4. anti-phosphatidylserine antibodies
5. anti-phosphatidylinositol antibodies
6. anti-phosphatidylethanolamine antibodies
7. anti-prothrombin antibodies

Only anticardiolipin antibodies and lupus anticoagulant have been studied well enough, to be used routinely in clinical practice. Research data also indicate that the anti- β 2-glycoprotein-I antibodies are a clear risk factor for blood clots. One can therefore make some arguments to also test for anti- β 2-glycoprotein-I antibodies (along with anticardiolipin antibodies and lupus anticoagulant) when working up a patient with a blood clot. However, test kits for these antibodies are very poorly standardized and testing for anti- β 2-glycoprotein-I antibodies has therefore not made its way into routine clinical practice. Results of clinical studies on all the other antibodies have not been convincing enough yet, that these tests would be useful for routine clinical purposes. However, some physicians already test for all these different antibodies; however, it is unclear how to interpret the results and what clinical consequences they have.

Figure 1

Antiphospholipid antibodies are often positive at the time of an acute clot, but turn negative a few weeks later. They can also fluctuate over time or be persistently positive at a steady level (figure 2). Positive tests should therefore be repeated 6 or more weeks after a positive test has been obtained, to make sure that they are persistently positive. Only if they have been persistently positive (and the patient has had venous or arterial clot or recurrent 1st trimester pregnancy loss or one or more pregnancy losses after week 10) does one say that the patient has the antiphospholipid antibody syndrome.

Figure 2



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