Antiphospholipid Syndrome

Antiphospholipid antibody syndrome (antiphospholipid syndrome, APS) is a recently identified autoimmune disease present in mostly a young female population. For these individuals, proteins called anti-phospholipid autoantibodies in the blood can cause blood to flow improperly, leading to dangerous clotting in arteries and veins, and/or pregnancy miscarriage and fetal complications. These antibodies develop, for unknown reasons, against the person's own tissues. People with this disorder may otherwise be healthy, or may also suffer from an underlying disease, most frequently systemic lupus erythematosus (SLE).

Fast facts
- Anti-phospholipid antibodies account for 15-20% of all episodes of deep vein thrombosis (clotting) and one-third of new strokes occurring in patients under the age of 50.
- Anti-phospholipid antibodies are accepted as the major cause for recurrent miscarriages and pregnancy complications in the absence of other known causes.
- Once the disease is diagnosed, adequate therapy can prevent the recurrence of the symptoms in most cases.

What is APS?
Antiphospholipid syndrome (APS) is an autoimmune disease associated with frequent clotting in arteries and veins and/or miscarriages. The clotting results from the presence of proteins in the blood called anti-phospholipid autoantibodies (aPL) formed against the person’s own tissues. In circulation, these autoantibodies are able to interfere with some mechanisms of coagulation leading to clot formation or thrombosis (stopping blood flow due to clot).

The damage caused by this clotting can vary depending on the site of the formation. For instance, repeated small thrombotic events may cause heart problems (cardiac valve thickening or damage), with the risk of releasing clots into blood (arterial embolism). There is recent evidence that aPL also may be associated with myocardial infarction in young people without any known risk factor (heart attack). A reduction or even a stoppage of blood flow in these arteries is actually the cause of damage to the heart.
(myocardial infarction). Thrombosis in the arterial circulation can occur anywhere in the body, but usually occurs in the brain circulation, causing strokes. Patients with arterial clots can experience problems in movement or vision, and repeated clots can lead to cognitive impairment.

Clots forming in the veins most frequently affect the lower legs. This can be complicated by the possibility of pulmonary embolism, a released clot that can reach the pulmonary (lung) vessels where it stops blood flow so that part of the lung dies (pulmonary infarction).

In a few cases, repeated thrombotic events may take place in a short time, leading to the progressive damage of several organs. This is an acute and life-threatening condition (also called catastrophic APS).

Patients with APS also may have a reduced number of platelets, and may have skin involvement in the form of mottled purplish discoloration (livedo reticularis), or of skin ulcerations.

For pregnant women, aPL can lead to early and late miscarriage, and pre-eclampsia (high blood pressure and presence of protein in the urine during pregnancy). Originally it was suggested that aPL were responsible for clots in the placenta’s blood vessels. As a consequence, it was thought that the blood exchange between mother and fetus was impaired, causing fetal growth retardation (resulting in a small baby) or death. We now know that the autoantibodies also may directly attack the placental tissues blocking their maturation and development. So, miscarriages associated with aPL may be caused by a defective placentation (i.e. placental development) without necessarily involving thrombosis (clotting in the placental vessels).

**What causes APS?**
Why patients develop these autoantibodies is not yet completely understood. Some evidence points to environmental factors, such as infections in the presence of a genetic-predisposing background, as playing a role in triggering the production of these autoantibodies.

aPL can be present in the circulation for a long time, but thrombotic events result only occasionally. In fact, aPL may be necessary but not sufficient to induce clotting alone (in other words, aPL are strong risk factors for thrombosis). Instead, thrombotic events frequently take place when other conditions that favor clotting are present, such as prolonged immobilization (e.g., being restricted to bed), surgery, or pregnancy. Also, additional risk factors for thrombosis are hypertension, obesity, smoking, atherosclerosis (hardening of the arteries), use of estrogens, as well as some congenital defects or alterations in some blood proteins.

**Who gets APS?**
APS usually affects women five times more commonly than men. It is typically diagnosed between the ages of 30 and
40. While up to 40% of patients with SLE will test positive for the anti-phospholipid autoantibodies, only half will develop thrombosis and/or experience miscarriages.

Like most autoimmune disorders, APS has a genetic component, although there is not a direct transmission from parent to offspring.

**How is APS diagnosed?**

The diagnosis of APS is made through blood testing for aPL in patients with thrombosis and/or recurrent miscarriages. Screening is done using two kinds of assays, called a clotting functional assay (the Lupus Anticoagulant test) and solid-phase assays (the anti-cardiolipin and the anti- b 2 glycoprotein I antibody test).

Tests vary because of the differences in the aPL population. Each single test cannot detect all of the possible autoantibodies, so their combined use is strongly advised. At least one of these tests must prove positive, and be confirmed on two occasions no less than three months apart to rule out transient positivity.

**How is APS treated?**

Most often, aPL is detected after a thrombotic event or recurrent miscarriages. Therefore, the main target is prevention of recurrences, given that the persistent presence of the antibodies puts the patient at strong risk for future episodes.

**Vascular events.** All acute thrombotic events (both arterial and venous) are treated the same, whether aPL is present or not. Typically, the blood is anticoagulated (“thinned”) using heparin infusion into the veins, followed by oral anticoagulant drugs (e.g., coumadin). Some patients also are given compounds that dissolve clots.

For venous events, oral anticoagulation is required to avoid recurrences, possibly over a period of years. For arterial events, recurrences also are prevented with drugs that inhibit platelet function.

**Obstetrical manifestations.** Subcutaneous injections of heparin and low-dose aspirin are the standard therapy for preventing new miscarriages. The therapy is started at the beginning of the pregnancy and prolonged in the period immediately after the delivery. This therapeutic approach has been shown to be effective in the majority of the cases, with delivery of healthy babies. In non-responsive cases, alternative therapies such as intravenous immunoglobulin infusions may help.

The same combination of heparin and low-dose aspirin—but with higher doses of heparin—is used in pregnant women who
had previous thrombotic events [to prevent new thrombotic events favored by the pregnancy itself].

The therapy with heparin and aspirin has been shown to be safe for both the mother and the baby in the majority of the cases.

When antibodies are detected in patients with no prior thrombotic events or pregnancies, the need of preventive therapy must be evaluated case by case. However, it is generally accepted that treatment is not necessary if no additional risk factors for clotting are present.

**Broader health impacts**
Thrombosis per se is a devastating consequence in APS patients and may affect any organ in the body. The recurrence of thrombosis and miscarriages in patients with aPL is high and, combined with high morbidity (chance of disease), calls for an adequate treatment. In addition, the disease can have significant socio-economical impact as it involves long-term disability and costly treatments.

**Living with APS**
The need for a long-term oral anticoagulant therapy significantly affects the lifestyle of the patients, creating the need for regular controls for the anticoagulation (blood-thinning) effect and special attention paid to the diet and to situations with a bleeding risk (e.g., falls). Correction of conventional risk factors for thrombosis (diabetes, hypertension or high blood pressure, hypercholesterolemia or high cholesterol, obesity, smoking and estrogen therapy for menopause or contraception) is mandatory in APS patients and significantly impacts lifestyle.

Present treatment for the prevention of the obstetrical manifestations is quite effective. The majority of the women can have healthy babies eventually.

**Points to remember**
- The presence of aPL represents an important risk factor for recurrent thrombosis and miscarriages.
- The mainstay of the therapeutic intervention is the prevention of clinical manifestations through oral anticoagulation or anti-platelet drugs.
- However, other risk factors for thrombosis such as diabetes, hypertension or high blood pressure, hypercholesterolemia or high cholesterol, obesity, smoking and estrogen therapy for menopause or contraception also must be corrected.

**To find a rheumatologist**
For a listing of rheumatologists in your area, click here.

Learn more about rheumatologists and rheumatology health professionals.

**For more information**
If you want more information on this or any other form of arthritis, contact the Arthritis Foundation at (800)283-7800 or visit the Arthritis Foundation Web site at www.arthritis.org.
Updated August 2009
Written by Pier Luigi Meroni, MD and reviewed by the American College of Rheumatology Patient Education Task Force.

This patient fact sheet is provided for general education only. Individuals should consult a qualified health care provider for professional medical advice, diagnoses and treatment of a medical or health condition.

© 2010 American College of Rheumatology