

# **Hughes Syndrome: Antiphospholipid Antibody Syndrome**

The antiphospholipid antibody syndrome, also known as Hughes Syndrome, is a disorder characterized by multiple different antibodies that are associated with both arterial and venous thrombosis (clots). There are three primary classes of antibodies associated with the antiphospholipid antibody syndrome: 1) anticardiolipin antibodies, 2) the lupus anticoagulant and 3) antibodies directed against specific molecules including a molecule known as beta-2-glycoprotein 1.

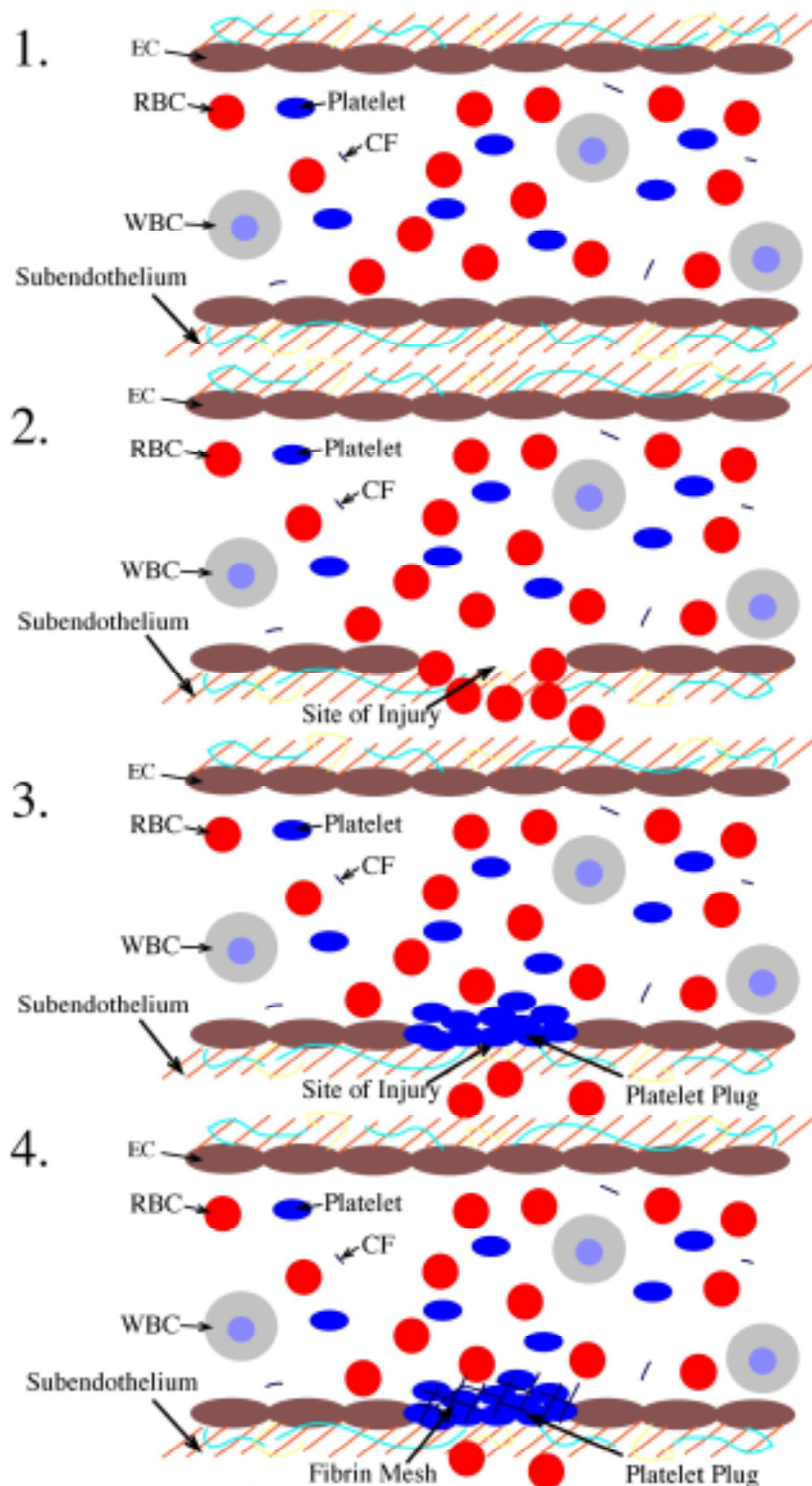
Historically, antiphospholipid antibodies were first noted in patients who had positive tests for syphilis without signs of infection. Subsequently, a clotting disorder was associated with two patients with systemic lupus erythematosus in 1952. In 1957 a link between recurrent pregnancy loss and what is now called the lupus anticoagulant was established. Ultimately, the lupus anticoagulant was further described in 1963 and in 1972 the term lupus anticoagulant was given. In 1983, Dr. Graham Hughes described the association between antiphospholipid antibodies and arterial as well as venous thrombosis.

There are two main classifications of the antiphospholipid antibody syndrome. If the patient has an underlying autoimmune disorder, such as systemic lupus erythematosus, the patient is said to have secondary antiphospholipid antibody syndrome. If the patient has no known underlying autoimmune disorder, it is termed primary antiphospholipid antibody syndrome.

## **Mechanism of the Antiphospholipid Antibody Syndrome:**

The antiphospholipid antibody syndrome is an autoimmune phenomenon. The immune system's function is to watch for and defend against foreign substances in the human body (for instance, bacteria or viruses). One component of this defence system is the antibody. An antibody is a protein that can recognize and bind to a foreign substance. Once it has bound to this substance, it can attract other molecules and cells to destroy the offending molecule.

In some disease states, the immune system is not able to differentiate between foreign invading substances and normal components of the body; this is referred to as autoimmunity. There are a number of well known autoimmune disorders, including systemic lupus erythematosus, and studies on other diseases have suggested autoimmune components in a number of other illnesses.



The Formation of a Clot. Panel 1 depicts a normal artery or vein in the body composed of an endothelial cell (EC) wall with a subendothelial layer of collagen and other substances. Some of the normal components of the blood are depicted including red blood cells (RBC), white blood cells (WBC), platelets and clotting factors (CF). Panel 2 shows a break in the EC wall, resulting in bleeding from the site. Panel 3 shows platelets coming together (aggregation) to form a platelet plug. Panel 4 shows the final step, where the coagulation cascade forms a fibrin network to secure the clot in place.



In general, anticardiolipin antibodies are more common than the lupus anticoagulant; anticardiolipin antibodies occur approximately 5 times more often than the lupus anticoagulant in patients with the antiphospholipid antibody syndrome.

In patients with an initial presentation of primary antiphospholipid antibody syndrome, around 10% will eventually go on to be diagnosed with an autoimmune disorder such as systemic lupus erythematosus or a mixed connective tissue disorder.

### **Risks of the Antiphospholipid Antibody Syndrome:**

The role of the antiphospholipid antibody syndrome in both arterial and venous thrombotic disorders is an active area of clinical research. To date, studies examining the role of the antiphospholipid antibody syndrome in thrombosis are numerous. Clearly, the antiphospholipid antibody syndrome is associated with both arterial and venous thrombosis. However, a review of the literature clearly demonstrates continued controversy regarding the degree of risk these antibodies confer. Studies have not shown any clear differences between patients with the primary antiphospholipid antibody syndrome versus the secondary antiphospholipid antibody syndrome.

A risk of recurrent thrombi, both arterial and venous, is associated with the antiphospholipid antibody syndrome as well. Most studies suggest that patients who have a recurrent episode will have it in a similar blood vessel type. In other words, patients who have a stroke initially will most often have a stroke if they have a recurrence. None-the-less, patients are reported that have multiple different types of thrombotic events.

The antiphospholipid antibody syndrome is also associated with miscarriages as well as other complications of pregnancy including preterm labor and preeclampsia. An association with thrombocytopenia (low platelets) has also been established. This occurs in 20-40% of patients with the antiphospholipid antibody syndrome.

### **Treatment of the Antiphospholipid Antibody Syndrome:**

Studies of the optimal treatment for the antiphospholipid antibody syndrome are currently under way. Treatment of the initial thrombosis in patients with the antiphospholipid antibody syndrome does not generally differ from treatment of patients with the same disorder who do not have the antiphospholipid antibody syndrome. Anticoagulation with heparin and then subsequently with oral anticoagulation is initiated. The duration of anticoagulation in patients without the antiphospholipid antibody syndrome is generally 3-6 months. In patients with the antiphospholipid antibody syndrome, the risk of recurrence is relatively high for both arterial and venous thrombotic events. As a result, patients are generally started on long-term (in some cases life-long) oral anticoagulation.

The treatment of women who are pregnant and have the antiphospholipid antibody syndrome can result in a much higher success rate for the pregnancy. Several regimens have been studied including heparin.

The role of medications generally used in autoimmune disorders to try and control the immune system is extremely limited. The primary role of these medications is in patients who have secondary antiphospholipid antibody syndrome, and they generally have no effect on the antiphospholipid antibody syndrome, but can help control the systemic lupus erythematosus, for example. Anti-platelet drugs, such as aspirin, are also used. At this time, a large study looking at the use of aspirin versus oral anticoagulation is underway in patients with the antiphospholipid antibody syndrome and stroke. Use of low-molecular-weight heparins instead of warfarin or in combination with other medications is also sometimes used.

In the case of patients who are discovered to have the antiphospholipid antibodies without any known thrombotic problems, the question of preventative (prophylactic) treatment is unresolved. Currently, aspirin is the general recommendation.

The use of long-term anticoagulation has risks associated with it (approximately a 3% chance per year of having a major hemorrhage, of which approximately 1/5 are fatal). Beginning long-term anticoagulation is influenced by the patient's overall risk of recurrent thrombosis balanced against the risks associated with long-term anticoagulation on an individual basis.

#### **Pregnancy and the Antiphospholipid Antibody Syndrome:**

As mentioned above, the antiphospholipid antibody syndrome is associated with complications in pregnancy. These complications can include miscarriages, preterm labor, low birth-weight and preeclampsia. For women with known antiphospholipid antibody syndrome, it is recommended that pre-pregnancy counseling is obtained. This allows the patient to be monitored closely from the beginning of the pregnancy.

Treatments during pregnancy are a subject of active investigation at this time. Currently, several studies have examined the use of heparin along with low-dose aspirin (doses are generally that of a baby aspirin) throughout the pregnancy and have demonstrated improved fetal outcomes. Other regimens that have been examined the use of aspirin and prednisone. Further studies of aspirin and prednisone combinations suggested that complications associated with prednisone use, in most cases, outweigh the benefits and thus prednisone is not a commonly used agent in addition to aspirin.

In patients for whom the above treatments are not successful, use of intravenous immune globulin (IVIG) has been used. At this time, the studies suggest this may be helpful in refractory cases, but is not recommended for use on a routine basis.

#### **Further Information:**

For further information, please visit the University of Illinois – Urbana/Champaign and Carle Cancer Center webpages on coagulation disorders at:  
[www-admin.med.uiuc.edu/hematology](http://www-admin.med.uiuc.edu/hematology).

This information is provided as a resource to patients and health care providers. The information contained above represents common diagnostic and treatment modalities, but

individual circumstances may require additional or different tests or medications. All medical decisions should be made with the advice and consultation of a physician or other health care provider.