

Antiphospholipid syndrome (APS)

This booklet provides information
and answers to your questions
about this condition.



Arthritis Research UK produce
and print our booklets entirely
from charitable donations.

What is antiphospholipid syndrome (APS)?



Antiphospholipid syndrome (APS) is a condition that causes blood clotting and is also a major cause of recurrent miscarriage. In this booklet we'll explain the main facts about APS, including the main symptoms and what causes it. We'll also look at what treatments are available and where to get more information.

At the back of this booklet you'll find a brief glossary of medical words – we've underlined these when they're first used.

What's inside?

- 2 Antiphospholipid syndrome (APS) at a glance**
- 4 What is antiphospholipid syndrome (APS)?**
- 4 What are the symptoms of APS?**
- 5 Who gets APS?**
- 5 What causes APS?**
- 6 What is the outlook?**
- 8 How is APS diagnosed?**
 - What tests are there?
- 9 What treatments are there for APS?**
 - Drugs
- 12 Self-help and daily living**
 - Exercise
 - Diet and nutrition
 - Reducing your own risk of getting clots
 - Helping yourself with APS
- 13 Research and new developments**
- 14 Glossary**
- 15 Where can I find out more?**
- 15 Further reading**
- 16 We're here to help**



At a glance

Antiphospholipid syndrome (APS)

What is antiphospholipid syndrome?

Antiphospholipid syndrome (APS), also known as sticky blood syndrome, is a condition that causes blood clotting in the arteries or veins and is also a major cause of recurrent miscarriage. It can occur on its own or alongside a condition called lupus.

What are the symptoms?

The two main symptoms are **blood clotting** and **pregnancy problems**. Blood clotting can occur:

- in the veins
- in the arteries
- in the brain.

In pregnancy, APS can cause recurrent miscarriage. APS can also cause other pregnancy problems such as high blood pressure (pre-eclampsia), small babies and early deliveries.

What causes it?

APS is an autoimmune disease, which means that it's caused by your immune system attacking particular parts of the body and producing symptoms.

APS usually affects people between the ages of 20 and 50.

In people with APS, the immune system produces harmful antibodies called antiphospholipid antibodies (aPL). These aPL affect cells in the blood and in the walls of blood vessels in such a way that the blood becomes 'sticky' and more likely to clot inside the vessels. Clotting inside vessels is called thrombosis. In a pregnant woman aPL can also affect the womb and the placenta in a way that can make the baby grow more slowly and increase the risk of miscarriage.

There are a number of other factors that make it more likely for you to develop blood clots, including:

- smoking
- immobility (related, for instance, to the thrombosis seen after long-haul flights)
- the contraceptive pill
- genetic factors.

How is it diagnosed?

Diagnosis is made from the clinical history of blood clots and/or pregnancy loss, confirmed with one or more of three particular blood tests:

- the anticardiolipin test
- the lupus anticoagulant test
- the anti-beta-2-glycoprotein I test.

Although these tests measure broadly the same thing, around 20% of people with APS will have a negative test result in one or the other, so one test alone could miss the diagnosis. The diagnosis is made if there has been a blood clot or miscarriage **and** positive blood test on two occasions at least 12 weeks apart.

What treatments are there?

APS can be treated and its effects controlled, often with drugs that thin the blood:

- If you carry the antiphospholipid antibodies but have no history of clotting, you'll probably be given low-dose aspirin.

- If you have APS and a history of clotting, you'll probably be given warfarin (a blood-thinning drug) to prevent further clots.
- If you've had a number of miscarriages but no history of clotting, you'll probably be given low-dose aspirin during pregnancy to prevent another miscarriage. You may be given injections of heparin as well. After giving birth you may be advised to continue low-dose aspirin to prevent clotting.
- If you've suffered both miscarriages and clotting you'll probably be given warfarin when you're not pregnant, but this will be changed to heparin when you're pregnant and aspirin will be added.



What is antiphospholipid syndrome (APS)?

Antiphospholipid syndrome, often referred to as APS, is sometimes known as sticky blood syndrome or Hughes Syndrome after a doctor who researched and published widely on the condition in the early 1980s. APS can cause blood clotting in the arteries or veins and is also a major cause of recurrent miscarriage. It's also one of the most common causes of strokes in young people. It's estimated that 1 in 5 people who've had a stroke before the age of 40 may have APS.

APS affects all age groups but is most common between the ages of 20 and 50. It was first diagnosed in people who had lupus (systemic lupus erythematosus) but it was later discovered that APS can exist in people who don't have lupus or any other disease. APS that exists on its own is called primary APS.

i See Arthritis Research UK booklet
Lupus (SLE).

What are the symptoms of APS?

The two main problems caused by APS are blood clotting and pregnancy problems, particularly recurrent miscarriage.

Blood clotting can occur:

- in the veins, causing pain and swelling, typically in the calf (deep vein thrombosis or DVT) – this

can sometimes lead to pulmonary embolism if a piece of the clot breaks away and travels to the lung

- in the arteries, causing high blood-pressure or strokes
- in the brain, which can cause memory loss, migraines, forgetfulness, slurred speech, fits or sight problems.

In pregnancy, APS can cause repeated miscarriage. This can happen at any time during the pregnancy but is most common between 3 and 6 months. APS can also cause other pregnancy complications, such as high blood pressure (pre-eclampsia), small babies and early deliveries. APS is now recognised as one of the most important causes of treatable recurrent miscarriages. Other problems sometimes associated with APS include:

- **heart problems:** the heart valves may thicken and fail to work, or the arteries may narrow because their walls get thicker, leading to angina
- **kidney problems:** APS can cause narrowing of the blood vessels, including those serving the kidneys, resulting in high blood pressure
- **infertility:** testing for antiphospholipid antibodies is becoming routine in infertility clinics
- **skin problems:** some people develop a blotchy rash, often seen on the knees or arms and wrists, with a lacy pattern (known as livedo reticularis)

- **low platelet count:** platelets are small cells in the blood which are involved in the control of bleeding. Some people with APS have very low platelet levels – often there are no symptoms, although people with very low counts may bruise easily or experience strange or excessive bleeding.

Very rarely, APS can cause clots to develop in small blood vessels in several parts of the body at once, causing damage to several organs at the same time and making you seriously ill. This is called catastrophic APS and is **very rare**. It's thought to be triggered by things like infection, trauma, medication or surgery. You should have quick and easy access to your rheumatology or haematology team in these circumstances.

Who gets APS?

All age groups can be affected, from infants to the elderly, but most people with APS are aged between 20 and 50 years. It seems to affect the health of women more than men because of its effect in pregnancy.

What causes APS?

APS is an autoimmune disease, which means that it's caused by your immune system attacking parts of the body and producing symptoms.



With the right treatments, the outlook is usually good.

If you have APS, your immune system produces harmful antibodies called antiphospholipid antibodies (aPL). These aPL attack proteins linked to fats in your body. The most important of these proteins is called beta-2-glycoprotein I. When aPL stick to this protein they can interfere with blood cells. The cells change in such a way that the blood becomes 'sticky' and more likely to clot inside the vessels. In a pregnant woman aPL can also affect the cells of the womb and the placenta, which can make the baby grow more slowly and increase the risk of miscarriage.

Although people with APS have a higher risk of thrombosis than other people, this doesn't mean that they suffer clots all the time. In fact, they may go for many years without suffering clots. The risk can be reduced by certain drugs and by reducing or monitoring other factors that can cause clots, including:

- smoking
- keeping still for long periods (linked, for example, to the thrombosis seen after long-haul flights)

- the contraceptive pill
- genetic factors – there may be a family history of clots, miscarriages, other autoimmune diseases such as lupus, or thyroid problems.

Occasionally, the thrombosis occurs during an infection such as a sore throat; however, in the vast majority of people the thrombosis comes 'out of the blue'.

What is the outlook?

Many people with APS feel very well and have no symptoms. The aim of treatment is usually to prevent thrombosis or miscarriage. This is achieved by an early diagnosis and the right combination of drugs. Other people with APS have symptoms like rash, joint pain, migraine and tiredness even when they don't suffer thrombosis and are not pregnant. This is especially true in people who have lupus as well as APS.

Because these drugs are being used to prevent symptoms rather than to treat them after they happen, it means that you may be taking drugs for many years without having symptoms. These drugs can have side-effects so it's critical to balance the risk of suffering APS symptoms against the risk of side-effects.

In summary, the outlook for most patients with APS is good but it's important to use the right drugs and to be aware of the side-effects.



How is APS diagnosed?

APS can only be diagnosed if you have a positive blood test (see below) **and** you've have suffered either thrombosis or a miscarriage. More and more people who have thrombosis or a miscarriage are routinely tested for APS. If you've had either of these problems, especially if they've happened more than once, you should discuss with your doctor whether you need these blood tests. Depending on the results, your doctor may want to refer you to a specialist (either a rheumatologist or a haematologist).

What tests are there?

There are three main blood tests used to diagnose APS. These are:

- the anticardiolipin test
- the lupus anticoagulant test
- the anti-beta-2-glycoprotein I test.

All three tests detect whether aPL are present in the blood. The result of the lupus anticoagulant test is either positive or negative, and the results of the other two tests are given as numbers. The higher this number is, the more aPL a person has in their blood. Although these tests all measure aPL, they do so in different ways so that around 20% of people with APS will have a negative result in one test or the other. One test alone could miss the diagnosis.

The tests are usually repeated after 12 weeks as levels of aPL vary and can sometimes go up when you have an infection. If you only have one positive test and it quickly becomes negative again then you probably don't have APS.

Higher levels of antibodies (i.e. higher numbers in the anticardiolipin or anti-beta-2-glycoprotein I tests) suggest you may be at greater risk of blood clots and other symptoms. Being positive in more than one of the three tests also suggests a higher risk.

I repeatedly test positive for aPL. Does this mean I'll definitely get APS?

No, this doesn't mean that you'll definitely get APS. In fact, many people who have lupus are tested for these antibodies as part of their routine lupus blood tests and about 20–30% will be positive for aPL. People who carry the antibodies but who've never had either clots or miscarriages are not said to have APS. They are aPL-positive people without symptoms, and doctors have to decide whether they're at high or low risk of getting APS in the future. There's no foolproof way of deciding, but factors that may help include:

- how high the aPL level is
- how many of the three tests are positive
- whether there are other risk factors for thrombosis
- whether you have other typical symptoms of APS (such as migraine).

Am I being tested for lupus?

No, this confusion often arises because one of the blood tests for APS is called the 'lupus anticoagulant' test. This is because it was first invented by doctors who were studying patients with lupus. In fact it is a test for APS, NOT a test for lupus. There are other, better blood tests for lupus itself and many people who are positive in the lupus anticoagulant test do not have lupus.

What treatments are there for APS?

Drugs

At present APS can't be cured, but the effects can be controlled. For example, treatment with anticoagulant (blood-thinning) drugs can help prevent both blood clots and miscarriages. The most commonly used drugs are aspirin, warfarin and heparin.

If you have aPL but no history of clotting, your doctor will probably recommend daily low-dose aspirin (75–100 mg).



This isn't guaranteed to prevent blood clots but is known to make the blood less 'sticky'. If you have other factors which increase your risk, for example a family history of clots, or if you suffer from typical APS symptoms such as migraine or livedo reticularis, your specialist may advise you to take warfarin instead of aspirin. It's very important to do whatever you can to reduce your own risk of clots (see section Self-help and daily living).

If you have APS and a history of clotting, you're likely to be given warfarin to prevent further blood clots. Warfarin is taken by mouth. You'll have regular blood tests (this is called an INR) to check what effect the drug is having, and if necessary your dose will be adjusted. The INR blood tests can be just a finger-prick test or a more formal assessment by a laboratory. The most serious side-effect of warfarin during treatment is bleeding. This means that your dosage will be closely monitored.

Warfarin can interact with a number of drugs and foods (for example grapefruit juice), and so it's important that you're aware of this and take steps to ensure your other medications or diet won't affect the results of the blood tests.



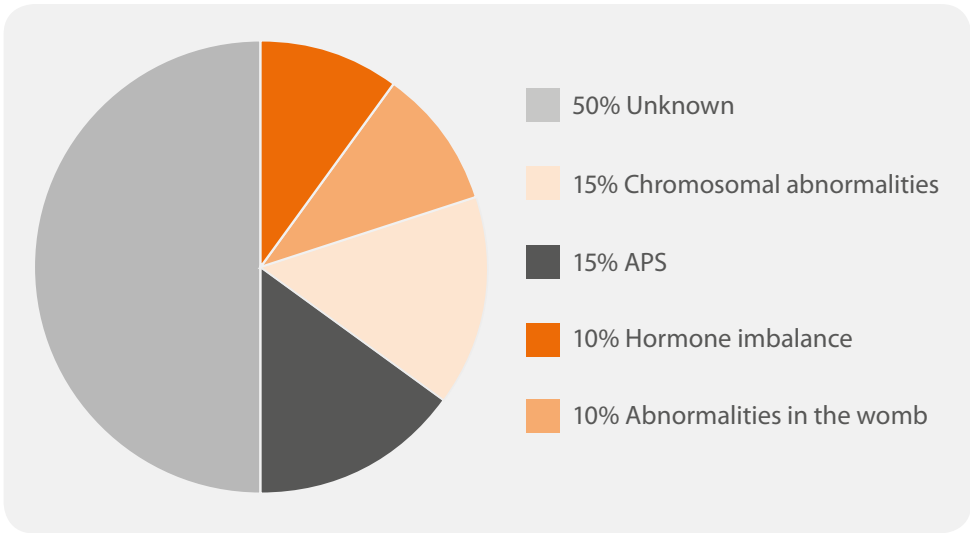
If you've had a number of miscarriages but no history of clotting, there are two considerations – treatment during pregnancy to prevent another miscarriage and treatment outside pregnancy to prevent clots. During pregnancy the usual treatment is low-dose aspirin; however, it's common for pregnant women with APS to be given daily injections of heparin as well as aspirin, especially if the previous miscarriages happened in mid- to late pregnancy or if there have been other pregnancy complications such as pre-eclampsia. It's a good idea to be seen in a special pregnancy clinic where the doctors have experience of APS, as well as by your normal obstetrician. Most APS specialists have access to these clinics and you should ask about this if you're planning to get pregnant.

If you've suffered miscarriages and have APS you may have an increased risk of clots as well, even when you're not pregnant, so you may be advised to take low-dose aspirin even after your baby is born.

If you're on warfarin and you become pregnant you'll probably be changed over to heparin. This is because warfarin is potentially harmful to the baby.

Even with treatment, complications can sometimes occur towards the end of pregnancy. However, advances in the understanding and treatment of APS have resulted in many more successful pregnancies in women with the condition. With close monitoring of the pregnancy, there's now a very good chance that your baby will do very well with no long-term problems.

Figure 1 Causes of recurring miscarriages



Self-help and daily living

Exercise

Although there aren't any specific exercises that can help with the condition, taking regular exercise will help keep you fit and keep your heart healthy.

Diet and nutrition

It's been suggested that increasing the amount of essential fatty acids in your diet, particularly omega-3 fatty acids found in oily fish, could help reduce the risk of thrombosis. However, there are no clinical trials to support this idea.

As well as this, fish oils contain large amounts of vitamin A which can be harmful in pregnancy, so we wouldn't recommend this if you're thinking of having a baby.

Eating a healthy, balanced diet is important for your general health and may help prevent you from developing blood clots. You should also keep to a healthy weight and stop smoking.

At present, no complementary medicine has been shown to help with APS.

Reducing your own risk of getting clots

There are several things that you can do to help reduce the risk of getting clots:

- Don't smoke – smoking will increase your risk of clots.
- Don't drink excessive amounts of alcohol.



- Think very carefully about what sort of contraception to use and discuss it with your doctor, as some types of contraceptive pill increase the risk of clotting.
- If you're thinking about hormone replacement therapy after the menopause, this may also increase your risk of clots so you should discuss it with your doctor.
- Think ahead if you know you'll soon have to keep still in one place for a long time (for example on a long-haul flight). It may be possible to get your travel agent to book you a seat with room to stretch your legs, and some people like to wear elasticated stockings during the flight to reduce the risk of clots building up in the lower legs. Ask your specialist whether this would be good for you.
- If you have another condition that can increase your risk of blood clots (e.g. diabetes, high blood pressure or high cholesterol) you should make sure you have regular checks to keep these factors under control.

Helping yourself with APS

It's always important that you understand the features of APS and therefore when to ask for help. You should have access to your local specialist team, which may include a specialist nurse who you can call for advice.

If you're taking drugs such as warfarin you should be careful about accidents, as bruising can be worse. If you're pregnant it's important that you attend your clinic appointments and keep in touch with your specialist obstetric consultant, whose aim is always to keep you and your baby healthy.

Research and new developments

There are many groups around the world carrying out research into APS. The following questions are being researched:

- Can we develop better blood tests to predict whether people with aPL in their blood are likely to get clots or have miscarriages? This will help us decide who needs treatment with warfarin and for how long.
- Can we develop new drugs to block the effects of aPL on cells? The idea is that these will be as effective as warfarin and heparin but with fewer side-effects.
- Can we find out more about exactly what aPL do to cells to cause clots and miscarriages? This will also help us to develop new treatments.

Arthritis Research UK is funding a programme of research into all these areas in the UK.

Glossary

Angina – severe chest pain characterised by a choking or crushing sensation below the breastbone. It occurs when the heart muscle isn't receiving enough oxygen.

Anti-beta-2-glycoprotein I test – A blood test used to diagnose APS. This test measures the amount of anti-beta-2-glycoprotein I antibodies in the blood.

Antibody – A naturally occurring molecule produced by the body to combat infections.

Anticardiolipin test – A blood test used to diagnose APS. This test measures the amount of antiphospholipid antibodies in the blood.

Antiphospholipid antibody (aPL) – An antibody which attacks proteins in the phospholipids (see below). Because the antibody attacks the body's own cells, rather than bacteria, it's called an auto-antibody.

Autoimmune disease – A disorder of the body's defence mechanism (immune system), in which antibodies and other components of the immune system attack the body's own tissue – these are called auto-antibodies.

Beta-2-glycoprotein I – A protein in the blood, which attaches itself to phospholipids in the walls of blood cells. When aPL and beta-2-glycoprotein I joined together attach to phospholipids it causes changes in the cells, which leads to clotting.

Deep vein thrombosis – a blood clot that forms in the deep-lying veins (usually in the leg or pelvis).

Haematologist – A hospital specialist who has an interest in disease of the blood.

Heparin – a daily injection to slow blood clotting.

Immune system – the tissues that enable the body to resist infection. They include the thymus (a gland that lies behind the breastbone), the bone marrow and the lymph nodes.

Livedo reticularis – A rash which occurs in APS. It looks blotchy and is seen most often on the knees and wrists. It gets its name because of its lacy pattern on the skin.

Lupus – A short name for systemic lupus erythematosus, a condition often linked to APS.

Lupus anticoagulant test – A blood test used to diagnose APS. This test measures the effect of the anti-phospholipid antibodies on the blood clotting time. It's not a test for diagnosing lupus.

Obstetric consultant – a doctor who specialises in helping women who have medical problems during pregnancy.

Phospholipids – A type of fat found throughout the body, particularly in the outer coating of cells or cell membrane.

Placenta – an organ within the womb that provides nourishment to the developing baby. The placenta is discharged after the baby is born and is sometimes known as the afterbirth.

Arthritis Research UK

Antiphospholipid syndrome (APS)

Pre-eclampsia – A common condition in the second half of pregnancy in which three things occur: high blood pressure, protein in the urine and fluid retention. Pre-eclampsia occurs more commonly in first pregnancies as well as APS.

Pulmonary embolism – the blockage of the pulmonary artery or one of its branches in the lungs, usually caused by detached fragments from a blood clot in a leg or pelvic vein.

Rheumatologist – A hospital specialist with an interest in diseases of joints, bones and muscles. As lupus is one of the conditions treated by rheumatologists, they often have an interest in APS.

Thrombosis – A blood clot which may occur in an artery or a vein.

Warfarin – a drug used to prevent blood clots from forming or growing larger. It works by thinning the blood, making it less 'sticky' and reducing the blood's ability to clot.

Where can I find out more?

Arthritis Research UK

Copeman House
St Mary's Court
St Mary's Gate
Chesterfield
Derbyshire S41 7TD
Phone: 0300 790 0400
www.arthritisresearchuk.org

Related organisations

The following organisations may be able to provide additional advice and information:

Hughes Syndrome Foundation

Conybeare House
Guy's Hospital
London SE1 9RT
Phone: 0207 188 8217
www.hughes-syndrome.org

Arthritis Care

Floor 4, Linen Court
10 East Road
London N1 6AD
Phone: 020 7380 6500
Helpline: 0808 800 4050
Email: info@arthritiscare.org.uk
www.arthritiscare.org.uk

Further reading

Available from the Hughes Syndrome Foundation and major bookshops:

Hughes Syndrome: A Patient's Guide, by Dr Graham Hughes, Springer-Verlag London 2001, ISBN 9781852334574

Hughes Syndrome: Antiphospholipid Syndrome (textbook), by Dr Munther A. Khamashta (Editor), Springer-Verlag London 2000, ISBN 9781852332327



We're here to help

Arthritis Research UK is the charity leading the fight against arthritis.

We're the UK's fourth largest medical research charity and fund scientific and medical research into all types of arthritis and musculoskeletal conditions.

We're working to take the pain away for sufferers with all forms of arthritis and helping people to remain active. We'll do this by funding high-quality research, providing information and campaigning.

Everything we do is underpinned by research.

We publish over 60 information booklets which help people affected by arthritis to understand more about the condition, its treatment, therapies and how to help themselves.

We also produce a range of separate leaflets on many of the drugs used for arthritis and related conditions. We recommend that you read the relevant leaflet for more detailed information about your medication.

Please also let us know if you'd like to receive our quarterly magazine, *Arthritis Today*, which keeps you up to

date with current research and education news, highlighting key projects that we're funding and giving insight into the latest treatment and self-help available.

We often feature case studies and have regular columns for questions and answers, as well as readers' hints and tips for managing arthritis.

Tell us what you think

Please send your views to:

feedback@arthritisresearchuk.org

or write to us at:

Arthritis Research UK, Copeman House, St Mary's Court, St Mary's Gate, Chesterfield, Derbyshire S41 7TD

A team of people contributed to this booklet. The original text was written by Dr Munther Khamashta, who has expertise in the subject. It was assessed at draft stage by specialist nurses Sue Brown and Gail Melling. An **Arthritis Research UK** editor revised the text to make it easy to read and a non-medical panel, including interested societies, checked it for understanding. An **Arthritis Research UK** medical advisor, Prof. Anisur Rahman, is responsible for the content overall.

Get involved

**You can help to take the pain away
from millions of people in the UK by:**

- volunteering
- supporting our campaigns
- taking part in a fundraising event
- making a donation
- asking your company to support us
- buying products from our online and high-street shops.

To get more **actively involved**, please
call us on **0300 790 0400**, email us at
enquiries@arthritisresearchuk.org
or go to
www.arthritisresearchuk.org



Arthritis Research UK

Copeman House
St Mary's Court
St Mary's Gate, Chesterfield
Derbyshire S41 7TD

Tel 0300 790 0400

calls charged at standard rate

www.arthritisresearchuk.org

Registered Charity England and Wales No. 207711, Scotland No. SC041156
© Arthritis Research UK 2011
Published April 2014 2059/APS/14-1

