



Alpha-1-antitrypsin deficiency

This information is for people in the UK who have been diagnosed with alpha-1-antitrypsin deficiency, their families, friends and carers. It explains what alpha-1-antitrypsin deficiency is, what causes it, what the symptoms are, how it's diagnosed and options for treatment.

Alpha-1-antitrypsin deficiency is also known as AATD or A1AD.

What is alpha-1-antitrypsin deficiency?

Alpha-1-antitrypsin deficiency (AATD) is a rare, inherited condition, which can cause lung and liver problems. It's thought that about 12,000 people in the UK have the ZZ genetic type of the condition, and up to 73,000 have the SZ genetic type. In both groups most people remain healthy, so few have been diagnosed. Proportionally more people who have the SZ type remain well, compared to ZZ.

People with AATD lack a protective chemical in the body called alpha-1-antitrypsin. This makes them much more vulnerable to the effects of inhaling smoke or other toxic materials like dust, fumes or chemicals.

Having these low levels of alpha-1-antitrypsin increases the risk of lung disease. If you have AATD, you're more likely to develop chronic obstructive pulmonary disease (COPD). You may also develop COPD at a younger age than usual, and it may progress more rapidly than normal COPD, especially if you smoke.

It can also sometimes cause liver problems, skin rashes and immune problems.

What is alpha-1-antitrypsin?

Alpha-1-antitrypsin (AAT) is an enzyme inhibitor. This means it controls enzymes in your body.

What are enzymes?

Enzymes are proteins that make chemical processes happen in your body. They do lots of different jobs. For example, some are involved in building up and breaking down parts of the body. Some help digestion. Others help you move by using energy to make your muscles contract. When enzymes are not properly controlled they can cause damage to your body tissue.

AAT is mainly produced by your liver. It's released into your blood and works in all parts of your body. It especially works in the lungs to control the enzymes that can cause lung damage.

What does alpha-1-antitrypsin do in my lungs?

When you have an infection, white blood cells in your body work to fight off the infection. As part of their defence, they produce enzymes that allow them to move into the lung and break down the bacteria causing the infection. They also do this as part of your body's response to breathing in cigarette smoke. But as well as breaking down proteins in the bacteria, these enzymes can also damage the proteins which your lungs are made of. To stop this, alpha-1-antitrypsin (AAT) damps down the effect of the enzymes, reducing the damage to the surrounding lung.

If you have a low level of AAT, the surrounding lung isn't protected as well as it should be. So when you breathe in smoke or have a lung infection, the enzymes will cause much more damage to the surrounding healthy lung. This can lead to the development of chronic obstructive pulmonary disease (COPD). It's especially damaging to the small air spaces (alveoli) where oxygen and carbon dioxide are exchanged – these become bigger leaving holes referred to as emphysema.

What is the cause of alpha-1-antitrypsin deficiency?

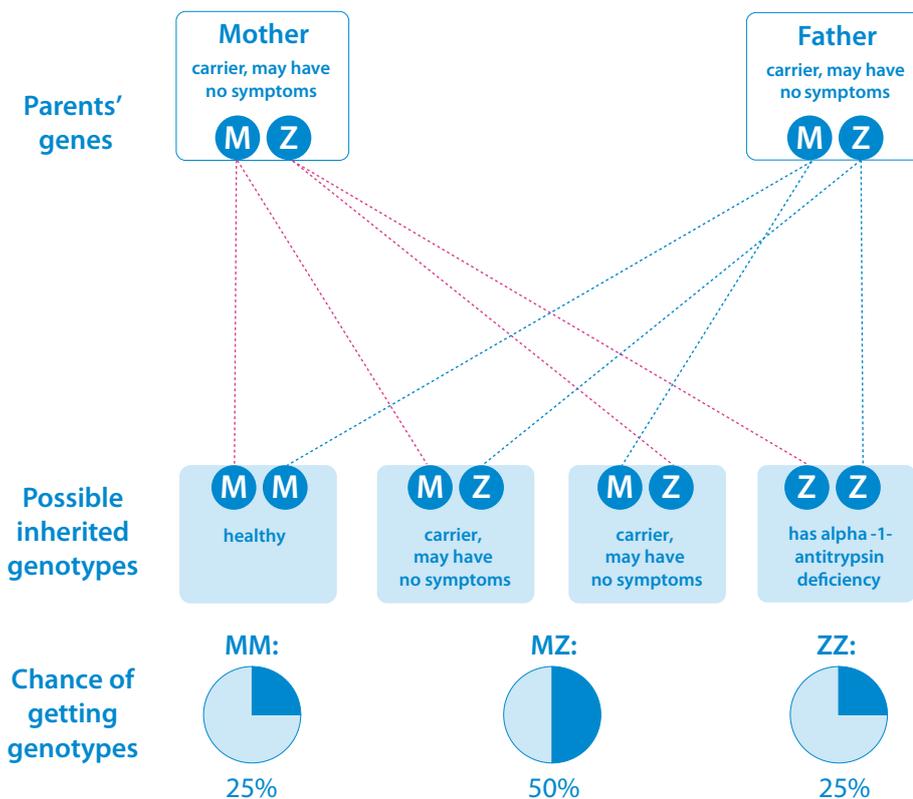
Everyone has 2 genes that make alpha-1-antitrypsin (AAT). You inherit 1 from your mother and 1 from your father. If you have children, you pass on 1 of your 2 genes to them. Which one you pass on to each child is random, like tossing a coin.

The gene which produces AAT in the normal way is called **M**. The main gene which causes AAT deficiency is called **Z**. Because everyone inherits 2 genes, there are 3 possible combinations of these genes: **MM**, **MZ** or **ZZ**. These combinations are called genotypes. There is another gene which causes a milder AAT deficiency, called S. In general, the S gene only causes a low AAT level when combined with the Z gene (**SZ** genotype)

- **MM**: If you have two M genes, you'll have a normal level of AAT in your blood. It's estimated that 90-95% of the population have the MM genotype.
- **MZ**: If you have one M gene and one Z gene, you'll have a lower than normal level of AAT in your blood. Usually the level isn't low enough to cause major problems – you'll probably have enough AAT to protect against damage. You may be more susceptible to lung disease, but if you don't smoke, this is rarely a problem. If you have the MZ genotype, you are a carrier – this means you can pass the Z gene on to your children.
- **ZZ**: If you inherit 2 Z genes, you'll have a very low level of AAT in your blood – only 10%-20% of what it should be. You're at high risk of getting lung disease especially if you smoke.
- **SZ**: If you inherit a S gene and a Z gene you have a milder form of AAT deficiency. There is a lower risk of lung disease compared to ZZ patients, and smoking is the major risk factor for getting lung problems.

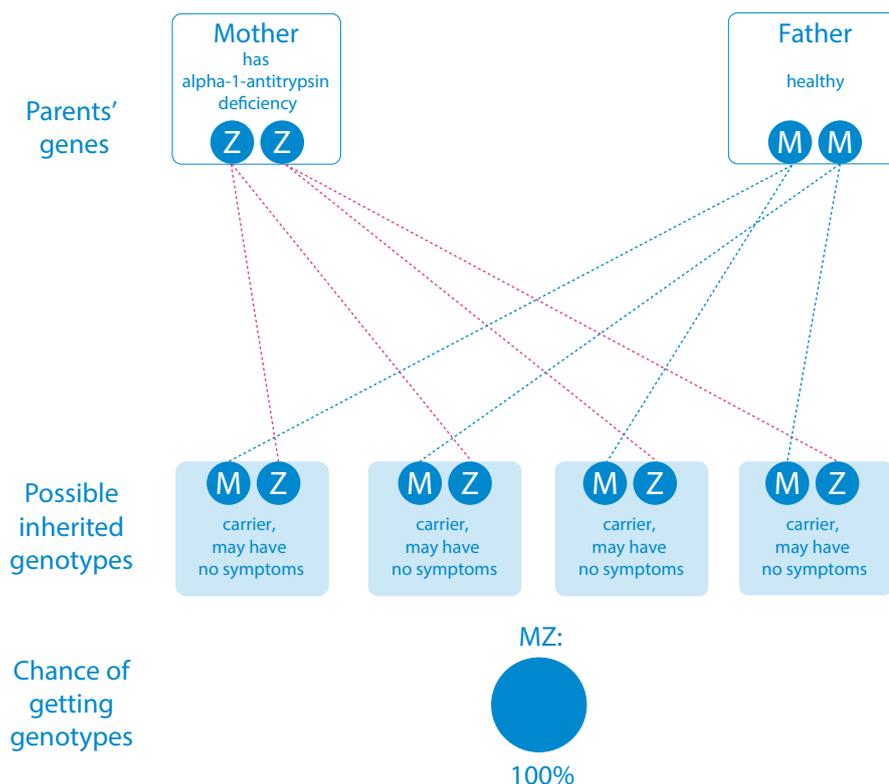
Risk of AATD if both parents are carriers

The diagram below shows how 2 parents who are carriers (MZ) can pass on different genotypes to their children. The parents may be entirely healthy but notice that they could have a child with the ZZ genotype.



Risk of AATD if one parent has AATD, and the other doesn't

This diagram is an example of what happens if one parent has alpha-1-antitrypsin deficiency (ZZ) and the other doesn't (MM). All of their children will inherit one Z gene, so they'll all be carriers. But they'll also all inherit one M gene so they're unlikely to be affected by AATD.



There are also some other possible genotypes linked to AATD. In some people the AAT gene is missing or does not work properly. These are referred to as Null genes. They are very rare, so it is hard to be very clear about their effects and how they are inherited. But M Null and Z Null combinations generally have the same effect on health as MZ and ZZ.

It's important to remember that there are other things that influence how much you'll be affected by smoking. Two people with AATD may have very different lung conditions. This may vary in families too.

What health problems can alpha-1-antitrypsin deficiency cause?

Lung conditions that can be caused by AATD

The main lung problem caused by AATD is chronic obstructive pulmonary disease (COPD). COPD is caused by lung damage as a result of breathing in smoke and other toxic materials.

The symptoms include:

- breathlessness during exercise or physical activity
- a cough that lasts a long time
- production of phlegm
- wheezing
- repeated chest infections

COPD describes a group of lung conditions, including emphysema and bronchitis. If you have AATD, the COPD you're more likely to have will be emphysema. This is because emphysema is when the small air sacs in your lungs are damaged. There may also be damage and widening of the airways, called bronchiectasis.

If you have AATD, your lungs are much more likely to be damaged from breathing in smoke. So, it's common for smokers with AATD to get COPD at a much younger age than other people with COPD.

Not everyone with AATD will get COPD. Only people with the lowest levels of alpha-1-antitrypsin in their blood are likely to develop the condition.

Liver disease caused by AATD

Children who have AATD may have problems with their liver in early life. This is usually temporary and most have normal liver function by late adolescence. Serious problems are rare. Of infants who have AATD, it's estimated that between 4-10% could have problems with their liver. In new-born babies, AATD can be associated with a yellowing of the skin and eyes, called **jaundice**. This is usually managed safely without long-term consequences.

In some people with AATD, abnormal alpha-1-antitrypsin proteins collect in the liver. This can lead to liver disease in older people, usually those who are over the age of 50, and may lead to liver failure and the need for transplantation. However, this is rare.

The Children's Liver Disease Foundation has more information on liver disease caused by alpha-1-antitrypsin deficiency (childliverdisease.org/liver-information/childhood-liver-conditions/alpha-1-antitrypsin-deficiency).

Rarer problems that can be caused by AATD

AATD can occasionally cause other problems. It can lead to a skin condition in the form of painful red lumps which sometimes become ulcers. This condition is called **panniculitis**.

In rare cases, people can get inflammation in their blood vessels affecting their kidneys, called **vasculitis**.

How is alpha-1-antitrypsin deficiency diagnosed?

Alpha-1-antitrypsin deficiency (AATD) is diagnosed by a blood test. This measures the level of AAT in the blood. In this section we cover why your doctor might test you for AATD, and what you should do if a family member is diagnosed.

If the level is lower than it should be, some more tests will be done on the blood sample to see what the type is – for example, MZ or ZZ. You should only need this test once.

There are a few reasons why your doctor might decide to test for AATD:

- They might suspect that you have AATD – for example if you've developed emphysema or another lung condition at a young age.
- Sometimes they do it as a routine test if you've been diagnosed with COPD.
- They might do the test as part of family screening, looking at relatives of people who have diagnosed AATD.
- They might do the test as part of the investigation of liver disease, particularly in children born with jaundice.

If you're diagnosed with COPD and especially if you are under the age of 45, you should ask your doctor to consider testing you for AATD. You should also be tested if you're diagnosed with COPD but have never been a smoker or have only smoked for a few years.

Testing is important to make sure that you're receiving the correct treatment. AATD causes COPD at an earlier age than usual, so it may be misdiagnosed as asthma. A test will ensure that you're not being treated for something that you don't have.

Should I be tested if a family member is diagnosed?

Because AATD is an inherited condition, you're more likely to have it if a family member has it. If a family member has been diagnosed with AATD, particularly a brother or sister, you should consider being tested yourself. Being aware of your risk helps you take steps to minimise the impact of AATD, for example quitting or never smoking.

How is alpha-1-antitrypsin deficiency treated?

At the moment, NICE does not recommend any specific treatment in the UK for alpha-1-antitrypsin deficiency (AATD). If you have a condition caused by AATD, such as COPD or liver disease, the focus is on usual treatment for those conditions.

If you're a smoker and you have AATD, the most important thing you can do to avoid damage to your lungs is stop smoking.

Treatment for COPD

Your treatment might include **inhalers** (blf.org.uk/support-for-you/copd/treatment/medications), **pulmonary rehabilitation** (blf.org.uk/support-for-you/keep-active/pulmonary-rehabilitation), or **oxygen therapy** (blf.org.uk/oxygen). There's also some evidence that people with AATD can benefit from **lung volume reduction procedures** (blf.org.uk/support-for-you/copd/treatment#surgery), though the benefits for people with AATD may be less than for people with usual COPD. You should also have your regular flu vaccination.

It's also very important to recognise and **treat chest infections as quickly as possible** (blf.org.uk/support-for-you/copd/flare-ups) to minimise damage to your lungs. Make sure you have an action plan that you've agreed with your health care professional so you know what to do if you have a flare-up of your symptoms. Take a look at **our checklist** (blf.org.uk/support-for-you/copd/flare-ups#checklist).

Lung transplant

For the small number of people with AATD whose lungs become severely damaged, a **lung transplant** (blf.org.uk/support-for-you/copd/treatment#surgery) might be an option which may significantly improve your quality of life.

Because people with AATD often develop COPD at a younger age than other people with COPD, they may be more suitable for a lung transplant. This is because they are often fitter with fewer other health conditions compared to older people so they cope better with the surgery and treatment. Though there's no absolute cut-off age for a lung transplant, it's unusual for people to have this much over the age of 65.

You'll only be considered for a lung transplant after very careful assessment and advice. Potential candidates need:

- a healthy body mass index (BMI) (www.nhs.uk/live-well/healthy-weight)
- no other significant medical conditions or infections
- an emotional and physical support network

To be considered suitable you'll first have lots of tests to make sure your other major organs – such as the heart, kidneys and liver – will work well after the transplant. You'll be assessed by a regional transplant centre. If you're accepted, your name will be placed on a lung transplant waiting list for a suitable organ to become available.

Unfortunately, there aren't enough organs available for transplant to meet the current demand in the UK. Not all people who are suitable will get one in time. In March 2019, 331 people were waiting for lung transplants. In 2018-19, 158 people had lung transplants (www.odt.nhs.uk/statistics-and-reports/organ-specific-reports).

Treatment for liver disease

The Children's Liver Disease Foundation has more information on treating liver disease caused by AATD (childliverdisease.org/liver-information/childhood-liver-conditions/alpha-1-antitrypsin-deficiency).

Possible future treatments

AAT augmentation therapy is a treatment where alpha-1-antitrypsin (AAT) is given into your veins to increase the levels in your body. The idea is to try to slow down the progression of COPD caused by AATD. It's available in some other countries, but not currently approved in the UK.

Trials so far show that augmentation therapy can have a measurable effect on the appearance of emphysema on patients' CT scans. It's not clear how this finding translates into a meaningful clinical benefit for people with AATD. One possibility is that augmentation therapy will become available in the future for some people – for example those whose symptoms and lung damage get worse very quickly, once they've stopped smoking and are receiving the best possible treatment. The decision will depend on a review by experts in AATD management considering all the evidence about risks and benefits.

Research is also looking at drugs that have the same function as AAT, ways to correct the gene that causes AATD, to stop AAT collecting in the liver and to promote the release of AAT into the blood.

How can I stay healthy with alpha-1-antitrypsin deficiency?

If you have alpha-1-antitrypsin deficiency, there are a number of things you can do to help keep yourself healthy.

If you're a smoker, stop smoking

This is essential to slow down the development of COPD and improve symptoms. Stopping smoking (blf.org.uk/smoking) is both prevention and treatment. You should be offered help to quit if needed. If not, ask for it.

Avoid being regularly exposed to irritants such as dust and gas

If you're exposed to irritants, for example at work, this might cause COPD to develop faster.

Avoid getting chest infections and colds

If you have AATD, chest infections can cause your lungs to become damaged more quickly. If you have a cough that produces mucus or phlegm you should see your doctor as you probably have an infection. You may need a course of steroids and, if your phlegm is a different colour (green or yellow) or a thicker consistency than usual, you may also be given a course of antibiotics. Stay away from friends or family when they have chest infections or colds.

Get vaccinated

Get a flu jab every year. This will help you avoid chest infections. Ask your doctor about having a one-off vaccination against pneumonia.

Lead a healthy lifestyle

This will help you manage your symptoms. Make sure you eat a balanced diet, manage your weight and get regular exercise.

Keep an eye on your alcohol intake

There's no need to avoid alcohol completely but it's wise to keep to the safe drinking guidance (www.nhs.uk/live-well/alcohol-support/calculating-alcohol-units) – less than 14 units spread throughout a week. You might have blood tests and scans to keep an eye on your liver.

We have more information on lung conditions caused by alpha-1-antitrypsin deficiency. Read about **COPD** (blf.org.uk/copd) and **bronchiectasis** (blf.org.uk/bronchiectasis) and find advice on **coping with breathlessness** (blf.org.uk/breathlessness).

Alpha-1 UK Support Groups

You can find support from these groups for people with alpha-1-antitrypsin deficiency, their families and carers:

www.alpha1.org.uk

Alpha-1 Awareness UK (geneticalliance.org.uk/member/alpha-1-awareness-uk)

University Hospitals Birmingham NHS Foundation Trust AATD service

www.uhb.nhs.uk/alpha-1-antitrypsin-deficiency-aatd-clinic.htm

Tel: **0121 371 3885**

Email: **ADAPT@uhb.nhs.uk**

Get in touch with us to find support near you.

Helpline: 03000 030 555

Monday to Friday, 9am-5pm

Ringing our helpline will cost the same as a local call.

helpline@blf.org.uk

blf.org.uk

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blf.org.uk/aatd

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We value feedback on our information. To let us know your views, and for the most up to date version of this information and references, call the helpline or visit **blf.org.uk**