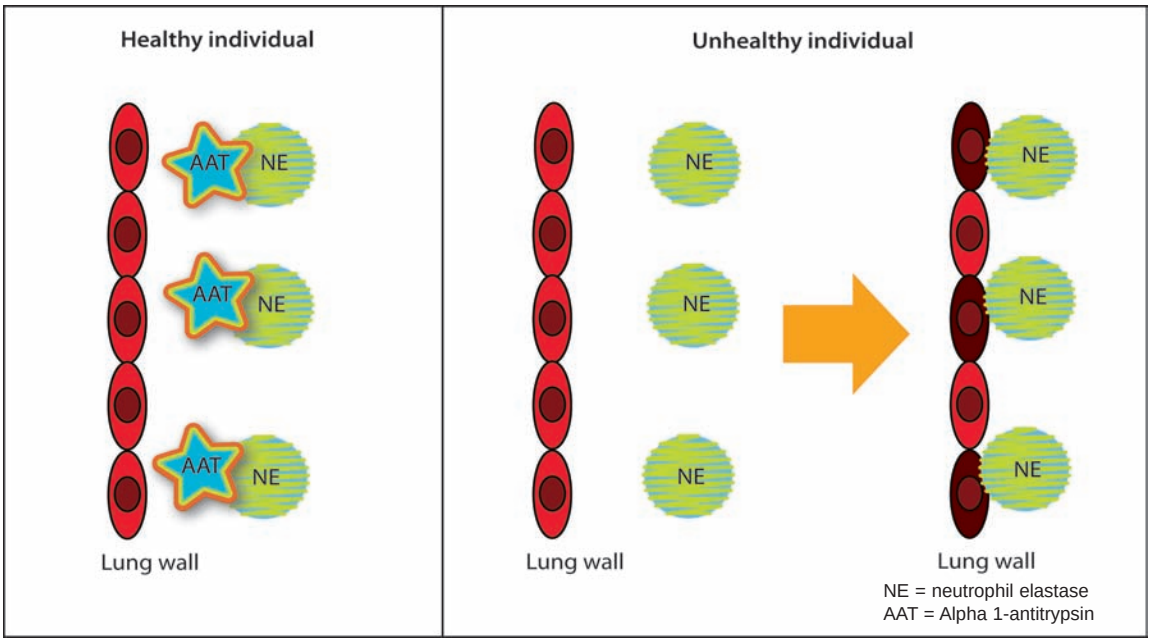
Alpha 1-antitrypsin deficiency

Alpha 1-antitrypsin (AAT) deficiency is a genetic disease. People with AAT deficiency have low levels of AAT protein in their blood and are more likely to get lung disease earlier in their life than someone with higher levels of AAT. The most common lung disease that people with AAT deficiency are likely to get is chronic obstructive pulmonary disease (often called COPD). It is thought that only about 5% of people with AAT deficiency have been diagnosed. This means that most people with the disease are unaware that they could benefit from changes to their lifestyle which could reduce their chances of getting lung disease, or from medical help.

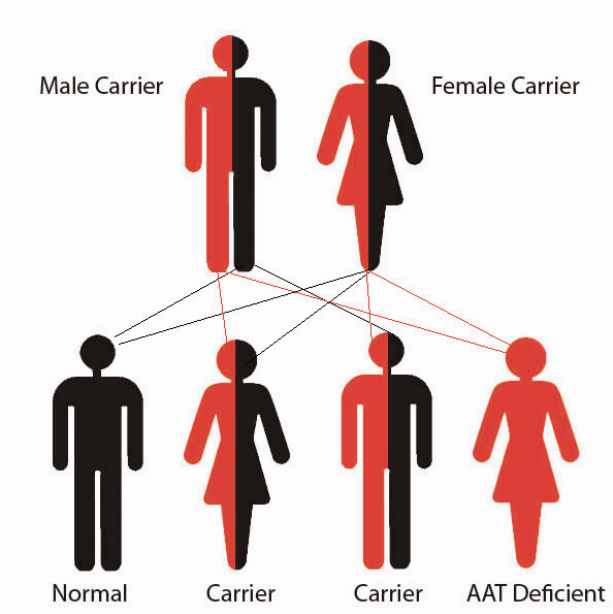
How does a lack of AAT cause lung disease?

AAT protein is made in the liver and released into the blood. It enters the lungs from the blood and its job is to protect the lung tissue from being damaged, especially by another protein called neutrophil elastase, which is made by white blood cells. The job of neutrophil elastase is to destroy damaged cells and bacteria. AAT stops it from attacking healthy lung cells.



How can genes cause AAT deficiency?

DNA carries the information to create all of the components of our body. We have two copies of almost all our DNA, one from each of our parents. AAT deficiency is caused by an abnormality in one of the genes of our DNA, called SERPINA1. AAT deficiency is called a 'recessive' disease, because two abnormal copies of the gene are needed to cause the disease. People who have one abnormal and one normal SERPINA1 gene are called carriers as they can pass their one abnormal gene to their children, but they do not have the disease themselves. Their AAT levels are usually lower than normal, but not low enough to cause a serious risk of health problems.



The children of two carriers can inherit two normal genes, one normal and one abnormal gene and become carriers themselves, or two abnormal genes and have AAT deficiency. This is shown in the diagram above. If a person with two abnormal genes has children, the children will either have the disease or be a carrier, depending on the SERPINA1 genes of the other parent.

Several different abnormalities in the SERPINA1 gene have been found that result in different amounts of AAT protein being made. This means the disease can be more severe in some people than others.

How common is AAT deficiency?

In Europe, between 1 in 1,600 and 1 in 2,000 people are thought to have AAT deficiency, totalling about 125,000 people.

Although AAT deficiency is thought of as a rare disease, it is actually one of the most common inherited diseases in some parts of the world, such as Europe. The reason that people think it is rare is because it is often not recognised or diagnosed. There is often a long delay before people are diagnosed with the disease even after visiting a doctor with symptoms. One scientific study found that a diagnosis of AAT deficiency was made on average 7 years after the first symptoms appeared.

The reasons that most people with AAT deficiency are either not properly diagnosed or are never diagnosed include:

- symptoms can be very different in different people;
- COPD, or asthma symptoms, can have many other causes;
- some people have no symptoms at all.

What are the symptoms of AAT deficiency?

AAT deficiency can cause similar lung symptoms to those seen in COPD or asthma. Early symptoms include:

- cough;
- excess sputum;
- wheezing.

Symptoms may not appear all the time at first, which means that some patients who just have wheezing may be diagnosed with asthma by mistake.

Many people with the disease have no symptoms, which makes a diagnosis very difficult. Therefore, if COPD is seen in people who do not smoke or if COPD is seen in young smokers (less than 40 years old), then a doctor may suspect AAT deficiency.

There may also be symptoms such as jaundice, caused by the disease's effect on the liver, or panniculitis, an inflammation of the fatty layer under the skin.

How will a doctor know that you have AAT deficiency?

A doctor who thinks someone might have AAT deficiency will take blood samples and do some laboratory tests that measure the amount of AAT in the blood. Gene testing can also be carried out to look at the SERPINA1 gene.

Because AAT deficiency is genetic and inherited, relatives of people with the disease are also likely to be carriers or to have the disease. Therefore, family members should also be told and tested. It may also be a good idea for partners to be tested, to find out whether there is a chance that any children will have AAT deficiency.

What can you do to prevent lung disease if you have AAT deficiency?

There are many things that people with AAT deficiency can do to ensure that they have less chance of getting lung disease or to slow its progress. Most of these involve trying to avoid damaging the lungs as there will not be enough AAT to protect them.

- Not smoking. Smoking is even more harmful to people with AAT deficiency, as their lungs have less protection.
- Avoiding highly polluted areas, for example by staying away from busy roads at peak traffic times (for more information see the ELF factsheet 'Outdoor air pollution and the lungs').
- Preventing bacterial and viral infections by avoiding people who are unwell and by being careful about personal hygiene.
- Eating a balanced diet, rich in protein and vitamins (for more information see the ELF factsheet 'Diet and the lungs').
- Performing breathing exercises as recommended by your doctor.

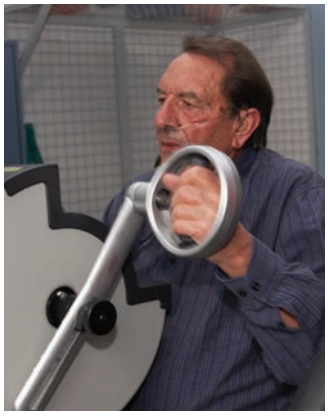
How can AAT deficiency be treated?

AAT deficiency can be controlled but not cured. However, early diagnosis is very important so that treatment can begin as soon as possible.

General treatments for lung damage

Treatments that might be prescribed for patients with other respiratory problems such as asthma or COPD include the following:

- Inhaled bronchodilators.
- Corticosteroids.
- Supplemental oxygen.
- **Pulmonary rehabilitation (below).**



Treatment to replace AAT

Augmentation (replacement) therapy is available in some European countries and it has been suggested that this could be a limited 'cure' for the disease. This involves a weekly dose of AAT that boosts the level of AAT in the blood and the lungs. Once the level is high enough, the AAT will start to protect the lungs. Patients must still stop smoking cigarettes and avoid environmental pollutants. Some studies have suggested that replacement therapy helps to slow the progression of emphysema, which is one of the components of COPD. There is not yet a clinical trial proving this, however.

Surgical treatment for damaged lungs

Lung transplantation is an option for people with AAT deficiency who have serious lung disease. One or both lungs can be transplanted, and sometimes patients also receive a heart transplant. The number of lung transplants has increased considerably over the past 15 years.

Another surgical procedure, lung volume reduction surgery, may help some AAT deficiency patients with lung disease. Although lung volume reduction surgery is not an alternative to lung transplantation, it can help patients to cope until a lung transplant is available, as it may reduce symptoms and improve exercise tolerance.

Useful websites

The Alpha One International Registry
The registry is an international research organisation covering 16 countries, mostly in Europe. Centres in the countries pool information about AAT deficiency in order to improve the progress of research.
www.aatregistry.org

ATS/ERS Statement: Standards for the diagnosis and management of individuals with AAT deficiency
This document spells out the way in which doctors should recognise and treat AAT deficiency.
www.thoracic.org/sections/publications/statements/pages/respiratory-disease-adults/alpha1.html

Patient support groups

Alfa Europe
Alfa Europe is an alliance of groups in 11 countries devoted to improving the lives of people with AAT deficiency.
www.alfaeurope.org

Alpha-1 Foundation
The foundation is a US organisation that provides resources for patients, doctors and scientists.
www.alphaone.org

This factsheet has been prepared with the assistance of M. Luisetti and B. Balbi. The factsheet was based on the following article by M. Luisetti: Diagnosis and management of α_1-antitrypsin deficiency. Breathe 2007; volume 4: pages 38–46.

This can be found online at www.ersnet.org/ers/lr/browse/viewPDF.aspx?id_attach=17735.