CONDITION

Homozygous alpha-1-antitrypsin deficiency

An inherited condition causing very low alpha-1 antitrypsin, which can damage the lungs and liver.

WHAT IT IS
Inherited low alpha-1 antitrypsin affecting lungs and liver

BODY SYSTEM
Lungs and liver

MAIN SYMPTOMS
Shortness of breath, cough, wheeze, jaundice

WHAT CAUSES IT
Two inherited matching SERPINA1 gene variants

HOW IT IS DIAGNOSED
Blood AAT level plus phenotype or genetic testing

MAIN TREATMENT
Lung care, liver monitoring, selected augmentation therapy

CAN IT BE CURED?
Sometimes - liver transplant restores normal AAT production

IS IT AN EMERGENCY?
Sometimes - severe breathing trouble, coughing blood, or confusion

LONG-TERM OUTLOOK
Often good with protection, monitoring, and timely treatment

Overview

Alpha-1 antitrypsin, often shortened to AAT, is a protein made mainly in the liver. It travels through the blood and protects lung tissue from enzymes released during inflammation.

Homozygous alpha-1-antitrypsin deficiency means you inherited two matching altered copies of the SERPINA1 gene, one from each parent. The most common severe form is called * Pi ZZ**, or simply ZZ. Other homozygous forms exist and may have different effects.

In severe deficiency, too little working AAT reaches the lungs. This makes lung tissue more vulnerable to damage, especially from cigarette smoke, dust, fumes, and repeated inflammation. The altered protein may also collect inside liver cells and cause liver injury.

Some people develop emphysema, a condition in which the lung's small air sacs are damaged.

Others develop liver problems. Some develop both, while many remain well for years. Knowing about the condition matters because avoiding smoke, monitoring the lungs and liver, and treating problems early may reduce further harm.

Symptoms

Many people have no symptoms when the condition is first found. Symptoms may begin in childhood, adulthood, or not at all.

Lung symptoms can include:

Emphysema related to AAT deficiency often appears at a younger age than smoking-related emphysema, particularly in people who smoke. However, age alone cannot identify the cause.

Liver problems can occur in babies, children, or adults. Possible signs include yellow skin or eyes, called jaundice; dark urine; pale stools; itching; abdominal swelling; or swelling in the legs. Liver injury can also be present without noticeable symptoms and may first appear on blood tests.

A rare complication called panniculitis causes painful, inflamed lumps beneath the skin. These may break down and leak an oily fluid.

- Shortness of breath during activity
- A long-lasting cough or wheeze
- Reduced exercise tolerance
- Frequent chest infections

Causes and risk factors

This condition is inherited. The SERPINA1 gene gives the liver instructions for making AAT. In the common ZZ form, the altered protein folds incorrectly. Much of it remains trapped in liver cells instead of entering the bloodstream.

The low blood level leaves the lungs less protected. The trapped protein can injure the liver, although not everyone with the same gene pattern develops liver problems.

Inheritance is autosomal codominant . This means each parent passes on one copy of the gene, and both copies influence the amount and type of AAT produced. Parents and siblings may be carriers or may also have deficiency.

Genes cause the condition, but other exposures affect whether organ damage develops and

how quickly it progresses. Important factors include:

These factors do not explain every case. A person who has never smoked can still develop lung or liver problems.

- Smoking or breathing second-hand smoke
- Workplace exposure to dust, smoke, vapours, or fumes
- Repeated lung infections
- Heavy alcohol use or other causes of liver injury
- Excess body weight, which may contribute to fatty liver disease

Diagnosis

Diagnosis begins with a blood test measuring the AAT level. A low level suggests deficiency but does not identify the exact inherited form.

Confirmation usually requires one or both of the following:

AAT levels may rise during infection, inflammation, pregnancy, or some other health conditions. For that reason, a level that appears normal does not always exclude an inherited variant. Results need to be interpreted together.

Tests used to assess the effects of the condition may include breathing tests, also called pulmonary function tests. Spirometry measures how much air you can breathe out and how quickly. A chest CT scan can show emphysema, but it is not required in every person.

Liver assessment may include blood tests, ultrasound, or tests that estimate liver stiffness and scarring. The choice depends on your age, symptoms, examination, and earlier results.

Because the condition runs in families, biological parents, siblings, and children may be offered testing. Genetic counselling can help family members understand what results may mean for them and their children.

- Phenotyping , which identifies the type of AAT protein in the blood
- Genetic testing , which looks for changes in the SERPINA1 gene

Treatment and management

Treatment aims to protect the lungs and liver, manage symptoms, and slow further organ damage. The inherited gene pattern itself cannot be changed with current routine treatment.

Avoiding tobacco smoke is one of the most important steps. If you smoke, stopping can substantially reduce ongoing lung injury. It is also helpful to limit exposure to workplace dust and fumes. Suitable protective equipment or changes in duties may be needed.

Treatment for lung symptoms is similar to care for other forms of emphysema or chronic obstructive pulmonary disease, known as COPD. Depending on the problem, this may include inhaled medicines that open the airways, pulmonary rehabilitation, oxygen for confirmed low blood oxygen, and treatment of respiratory infections. Recommended vaccinations may help lower the risk of serious respiratory illness.

AAT augmentation therapy is an intravenous treatment made from purified human AAT. It may be considered for selected adults who have severe deficiency and established emphysema. Evidence suggests that it can slow the loss of lung tissue in appropriate patients, but it cannot rebuild damaged lungs or reliably remove existing symptoms. It is not used to treat liver injury because adding AAT to the blood does not remove the abnormal protein trapped in liver cells.

Liver management depends on the degree and cause of injury. It may involve avoiding substances that can harm the liver, addressing fatty liver risk, treating other liver conditions, and monitoring for scarring. People with cirrhosis may need regular checks for complications, including liver cancer.

Lung transplantation may be considered for advanced respiratory failure. Liver transplantation may be considered for severe liver failure or certain liver cancers. A transplanted liver produces the donor's normal AAT protein, although transplantation is major treatment with lifelong follow-up.

Complications

Possible lung complications include emphysema, COPD, respiratory failure, and a collapsed lung caused by air leaking around it. Lung damage that has already occurred is generally permanent.

Liver complications include persistent inflammation, fibrosis or scarring, cirrhosis, liver failure, and liver cancer. Liver problems can develop even when breathing remains normal.

Panniculitis is uncommon but can cause painful skin wounds and infection. The condition has also been associated with a rare inflammation of blood vessels called granulomatosis with polyangiitis, though most people with AAT deficiency do not develop it.

Prevention

Homozygous AAT deficiency cannot be prevented because it is inherited before birth. Having the gene pattern does not mean that organ damage is certain.

You can reduce avoidable risks by not smoking, avoiding second-hand smoke, and limiting exposure to dust and fumes. Keeping vaccinations current and seeking timely care for significant chest infections may help protect lung health.

Protecting the liver includes avoiding heavy alcohol use and addressing other causes of liver injury, such as viral hepatitis or fatty liver disease. The safest approach to alcohol depends on whether liver damage is present.

Genetic counselling cannot prevent the condition, but it can explain inheritance and reproductive testing options.

Living with it and what to expect

The course differs widely. Some people remain active and symptom-free for decades. Others develop progressive lung or liver problems. Smoking history, workplace exposures, the exact gene variant, and existing organ damage all influence the outlook.

Lung tissue lost through emphysema does not grow back. However, avoiding smoke and using appropriate treatment may slow further decline. Breathing tests over time are more useful than a single result for showing whether lung function is changing.

Liver test results may stay stable, improve, or worsen. Normal blood tests do not always rule out scarring, so follow-up may include imaging or other assessments.

Routine follow-up commonly focuses on symptoms, breathing function, liver health, smoking status, and exposure risks. The timing is based on your results and whether organ damage is present.

Most daily activities, work, exercise, travel, and family life remain possible. Pulmonary rehabilitation, adjusted exercise, workplace protection, and practical planning can help if breathlessness develops.

When to get medical help

Arrange routine medical review if you develop a lasting cough, wheeze, reduced exercise tolerance, unexplained abnormal liver tests, or yellowing of the skin or eyes. Review is also appropriate if symptoms are gradually changing or if a close relative has been diagnosed.

Seek prompt medical advice for a sudden worsening of breathlessness, fever with worsening

respiratory symptoms, new jaundice, a rapidly swelling abdomen, leg swelling, or painful skin lumps that break down.

Call emergency services for:

These symptoms can have several causes. They require urgent assessment rather than waiting for a routine appointment.

- Severe difficulty breathing or blue-grey lips
- New confusion, extreme drowsiness, or collapse
- Coughing or vomiting blood
- Black, tar-like stools
- Sudden chest pain with marked breathlessness

Common questions

Is alpha-1-antitrypsin deficiency the same as COPD?

No. AAT deficiency is an inherited condition that can cause emphysema and COPD. COPD also has many other causes. A person can have AAT deficiency without COPD, especially before lung damage develops.

Can I have homozygous AAT deficiency without symptoms?

Yes. Some people are diagnosed through family testing or unrelated blood tests before symptoms appear. A lack of symptoms does not show whether early lung or liver changes are present, so an initial assessment and planned follow-up are useful.

Will my children inherit it?

Every biological child inherits one SERPINA1 gene copy from you. If you have two matching deficiency variants, each child will inherit one of those variants. Whether the child has severe deficiency also depends on the gene copy inherited from the other biological parent.

Does augmentation therapy treat the liver as well as the lungs?

No. Intravenous augmentation raises AAT in the blood and may protect lung tissue in selected adults. It does not clear the abnormal AAT trapped inside liver cells and is not a treatment for AAT-related liver injury.

Can I drink alcohol?

Alcohol does not cause the inherited condition, but it can add to liver injury. If you have abnormal liver tests, fibrosis, or cirrhosis, you may be advised to avoid it. Your liver results are important when deciding what is safest.

Does this condition shorten life expectancy?

It can, particularly when severe emphysema, cirrhosis, or liver cancer develops. Many people, especially those who never smoke and have limited organ damage, do well for many years. An individual outlook is better judged from lung function, liver assessment, exposures, and changes over time.

Sources

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