CONDITION

Alpha-1 antitrypsin deficiency

Learn how alpha-1 antitrypsin deficiency can affect the lungs and liver, how it is diagnosed, and which treatments and follow-up may help.

WHAT IT IS
Inherited condition affecting the lungs and liver

BODY SYSTEM
Lungs and liver

MAIN SYMPTOMS
Shortness of breath, wheezing, long-lasting cough, jaundice

WHAT CAUSES IT
Inherited SERPINA1 gene variants

HOW IT IS DIAGNOSED
Blood protein level with genotyping or protein phenotyping

MAIN TREATMENT
Exposure avoidance and organ-specific disease management

CAN IT BE CURED?
No, inherited gene variants cannot change

IS IT AN EMERGENCY?
Sometimes, with severe trouble breathing

LONG-TERM OUTLOOK
Variable, from no symptoms to severe lung or liver disease

Overview

Alpha-1 antitrypsin deficiency, often shortened to A1AT deficiency or AAT deficiency, is an inherited condition that can affect the lungs, liver, and, less often, the skin. It is caused by changes in the `SERPINA1` gene.

Alpha-1 antitrypsin is a protein made mainly in the liver. It travels through the bloodstream and protects lung tissue from neutrophil elastase, an enzyme released by certain white blood cells during inflammation. Without enough working alpha-1 antitrypsin, this enzyme can gradually damage the small air sacs in the lungs.

Some gene changes also cause abnormal alpha-1 antitrypsin to become trapped inside liver cells. This can injure the liver even though the protein level in the blood is low.

The condition affects people differently. Some never develop symptoms. Others develop emphysema, chronic obstructive pulmonary disease (COPD), liver disease, or both. Smoking and repeated exposure to lung irritants greatly increase the chance and severity of lung damage.

Identifying A1AT deficiency matters because avoiding tobacco smoke, managing lung or liver disease, testing close relatives, and considering condition-specific treatment may reduce risks or detect complications earlier.

Symptoms

Symptoms depend on which organs are affected and how much damage has developed. They may begin in infancy, adulthood, or later life. A person can have liver disease without lung symptoms, or lung disease without known liver problems.

Lung symptoms may include:

Emphysema means that the walls of the lung's tiny air sacs have been damaged. This reduces the surface available for oxygen exchange. In A1AT deficiency, emphysema often affects the lower parts of the lungs, although the pattern varies.

Infants with liver involvement may develop jaundice, which causes yellowing of the skin or eyes, or cholestasis, meaning bile does not flow normally from the liver. Most children with jaundice do not have A1AT deficiency, but persistent or unexplained liver problems may lead to testing.

Possible liver symptoms in children or adults include:

A rare skin complication called panniculitis causes painful, inflamed lumps under the skin. These areas may break open and release an oily fluid. A1AT deficiency has also been associated with granulomatosis with polyangiitis, an uncommon disease involving inflammation of blood vessels.

- Shortness of breath, especially during physical activity
- Wheezing or a whistling sound when breathing
- A long-lasting cough, with or without mucus
- Reduced exercise ability
- Frequent chest infections
- Symptoms of emphysema or COPD at a younger age than expected
- Bronchiectasis, in which damaged airways become widened and collect mucus

- Yellow skin or eyes
- Dark urine or unusually pale stool
- Itching related to poor bile flow
- Swelling of the abdomen or legs
- Easy bruising or bleeding
- Fatigue or reduced appetite
- Pain or discomfort in the upper right abdomen

Causes and risk factors

A1AT deficiency results from inherited variants in the `SERPINA1` gene. Everyone usually receives one copy of this gene from each biological parent. The combination of the two copies helps determine the amount and function of alpha-1 antitrypsin.

Gene variants are often described with letters. The M variant generally produces normal protein. The Z variant is the most common cause of severe deficiency, while the S variant usually has a milder effect. A person with two Z variants, sometimes written as Pi*ZZ, has a high risk of low blood levels and abnormal protein buildup in the liver. Other combinations and rare variants can also cause clinically important deficiency.

Having a gene variant does not predict exactly what will happen. Even people with the same genetic combination can have very different health outcomes.

Factors that can increase lung risk include:

Smoking is the most important avoidable risk factor. It increases inflammation and can weaken the protective activity of the alpha-1 antitrypsin that is present.

Liver disease is linked mainly to abnormal protein collecting inside liver cells. Alcohol, viral hepatitis, excess body weight, metabolic liver disease, and medicines or supplements that injure the liver may add to liver stress.

Because the condition is inherited, biological siblings, children, and parents of an affected person may carry a related gene variant. Their actual risk depends on which variants are present in the family.

- Cigarette smoking or regular exposure to secondhand smoke
- Vaping or inhaling other substances that irritate the lungs
- Workplace exposure to dust, fumes, smoke, or chemicals

- Repeated respiratory infections
- Asthma or another condition that adds airway inflammation
- Increasing age

Diagnosis

A1AT deficiency cannot be diagnosed from symptoms alone. Testing usually starts with a blood test that measures the alpha-1 antitrypsin level.

The protein level needs careful interpretation. Alpha-1 antitrypsin rises during infection, inflammation, pregnancy, and some other conditions. A result taken during an illness can therefore appear higher than a person's usual level. Liver disease can also affect the result.

Additional testing may include:

Spirometry measures how much air a person can breathe out and how quickly. It helps identify airflow obstruction, a feature of COPD, but normal spirometry does not rule out early lung disease.

Clinicians may consider A1AT testing in people with COPD, emphysema, otherwise unexplained bronchiectasis, unexplained chronic liver disease, necrotizing panniculitis, or a close relative with the condition. Some professional guidance recommends testing all adults diagnosed with COPD, regardless of age or smoking history.

Family testing should involve clear explanations about inheritance and the possible effects of genetic information. Genetic counseling can help people understand results, testing choices, and implications for relatives.

- Genotyping to look for common `SERPINA1` variants, especially S and Z
- Protein phenotyping to examine the type of alpha-1 antitrypsin in the blood
- Expanded genetic testing when initial results do not explain a low level or strong clinical suspicion
- Lung function tests, including spirometry and measurements of gas transfer
- Chest imaging when needed to evaluate emphysema or bronchiectasis
- Liver blood tests and, when appropriate, liver imaging or assessment of liver stiffness

Treatment and management

Treatment depends on whether the lungs, liver, or other organs are affected. It also depends

on symptoms, test results, genetic findings, and overall health. Treatment cannot change the inherited gene variants, but it can reduce avoidable injury and manage related disease.

Avoiding tobacco smoke is central to lung protection. People who smoke can ask about counseling, medicines, and structured quit programs. Avoiding secondhand smoke, occupational dust, and irritating fumes is also important. Workplace ventilation or protective equipment may reduce exposure in some settings.

People with lung disease may receive the same symptom-based treatments used for COPD or bronchiectasis. These can include inhaled bronchodilators, which relax the muscles around the airways, and other inhaled medicines when appropriate. Pulmonary rehabilitation combines supervised exercise, breathing education, and support for managing daily activities. Supplemental oxygen may be used when testing shows that blood oxygen remains too low.

Routine respiratory vaccinations can reduce the chance of infections that may worsen lung disease. A clinician may also discuss hepatitis A and hepatitis B vaccination when liver protection is relevant and immunity is absent.

Intravenous augmentation therapy is a condition-specific option for selected adults with severe A1AT deficiency and emphysema. It supplies purified human alpha-1 antitrypsin through a vein. It is intended to raise protective protein levels in the blood and lungs.

Augmentation therapy does not repair existing lung damage, treat liver disease, or correct the gene change. It is not appropriate for every genotype or every person with a low level. Decisions consider confirmed severe deficiency, evidence of emphysema, lung function, smoking status, expected benefit, treatment burden, and access. Infusions are ongoing and can cause reactions, so the risks and practical demands should be reviewed with a specialist.

Liver management focuses on reducing additional injury and monitoring for complications. This may include limiting or avoiding alcohol, maintaining a weight that supports liver health, treating viral or metabolic liver disease, and reviewing medicines and supplements. No supplement has been proven to remove the abnormal protein from liver cells. People should discuss herbal products with a clinician because some can damage the liver.

Severe lung or liver disease may lead to evaluation for organ transplantation. A lung transplant replaces damaged lung tissue but does not change production of abnormal protein by the liver. A liver transplant replaces the main source of abnormal alpha-1 antitrypsin and can restore the recipient's circulating protein pattern.

Complications

Long-term lung injury can lead to emphysema and COPD. These conditions may cause

progressive shortness of breath, reduced physical ability, low blood oxygen, and respiratory failure. Bronchiectasis can lead to repeated infections, mucus buildup, and coughing up blood.

Liver complications may include fibrosis, meaning scar tissue; cirrhosis, meaning advanced scarring that changes liver structure; and portal hypertension, which is increased pressure in veins that carry blood through the liver. Advanced disease can cause fluid buildup in the abdomen, swollen veins in the digestive tract, confusion from toxin buildup, or impaired blood clotting.

A1AT-related liver disease also increases the risk of hepatocellular carcinoma, the most common form of primary liver cancer. People with cirrhosis may need regular liver cancer surveillance based on established liver-disease guidance.

Not everyone with A1AT deficiency develops these complications. Individual risk is influenced by the gene variants, environmental exposure, other health conditions, and changes seen during follow-up.

Follow up

Follow-up should be tailored to the organs affected and the person's risk factors. A primary care clinician may coordinate care with a pulmonologist, hepatologist, gastroenterologist, genetic counselor, or other specialist.

Monitoring may include a review of breathing symptoms, smoking or workplace exposure, spirometry, oxygen levels, liver blood tests, platelet counts, physical examination, and liver imaging. The timing depends on previous results and whether disease is present. A person with stable test results may need routine visits, while new or worsening findings may require earlier review.

Contact a clinician promptly for a clear increase in breathlessness, a new persistent cough, repeated chest infections, worsening wheezing, jaundice, abdominal swelling, unusual bruising, or new painful skin lumps. These symptoms need assessment but are not always emergencies.

Seek urgent or emergency care for:

Relatives who are considering testing can ask whether genetic counseling is available. Test results should be interpreted with the measured protein level, medical history, and family findings rather than viewed in isolation.

- Severe trouble breathing, blue or gray lips, confusion, or fainting
- Chest pain, especially with shortness of breath or sweating
- Coughing up more than a small streak of blood

- Vomiting blood or passing black, tar-like stool
- Sudden confusion, extreme sleepiness, or rapidly increasing abdominal swelling
- Signs of a severe infusion reaction, such as throat swelling or difficulty breathing

Sources

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