

# Alpha-1 Antitrypsin Deficiency

## Overview

- What is Alpha-1 Antitrypsin deficiency? (<http://patients.gi.org/topics/acid-reflux/>)

Alpha-1 antitrypsin deficiency is an inherited disease that causes low blood levels of alpha-1 antitrypsin (AAT), a liver protein that blocks certain enzymes from destroying organs and tissues. The condition may lead to lung and liver disease, and in rare cases, skin disease.

## Causes

- What causes Alpha-1 Antitrypsin deficiency? (<http://patients.gi.org/topics/alpha-1-antitrypsin-deficiency/>)

Alpha-1 antitrypsin (AAT) is a protein that is produced mostly in the liver. Its main purpose is to destroy an enzyme called neutrophil elastase in the lungs. Neutrophil elastase is an enzyme that normally performs an important function in the lungs -it digests damaged or old cells and bacteria to promote healing. However, if left unchecked, it will also attack healthy lung tissue. AAT, in sufficient amounts, will trap and destroy neutrophil elastase before it has a chance to begin damaging delicate lung tissue. Consequently, if a patient doesn't have enough AAT, the enzyme goes unchecked and attacks the lungs.

AAT deficiency is an inherited defect due to a mutation in the proteinase inhibitor (Pi) gene on chromosome 14, which alters the structure of the AAT molecule and prevents its release from liver cells. As a result, serum levels of AAT are decreased. The amount of AAT in the lung consequently is low which results in unchecked activity of neutrophil elastase and damage to lung tissue. This can lead to lung disease. The resultant accumulation of excess AAT in liver cells leads to injury to the liver, which can progress to cirrhosis (excess scar tissue).

Cigarette smoke is especially harmful to patients with AAT deficiency. In addition to increasing the inflammatory reaction in the airways, cigarette smoke directly inactivates alpha 1-antitrypsin resulting in more severe lung damage.

## Risk Factors

- Who gets Alpha-1 Antitrypsin deficiency? (<http://patients.gi.org/topics/alpha-1-antitrypsin-deficiency/>)

Everyone receives one copy of the alpha-1 antitrypsin gene (Pi gene) from each parent. The most common type of Pi gene is called the M gene, which is the non-disease causing (normal) variant. Most people have two normal copies of the Pi gene and they are said to have type PiMM. These people have normal levels of AAT in the blood. People with AAT deficiency may have one normal copy and one damaged copy, or two damaged copies of the Pi gene. There are more than 70 different types of defective alpha-1 antitrypsin genes. The most common genotype leading to liver disease is PiZZ. Routine testing for AAT should include measuring levels of AAT and the genotype of an individual's AAT.

AAT deficiency has been identified in all populations, but it is most common in patients of Northern European and Iberian descent. AAT deficiency is 1 of the 3 most common lethal genetic diseases among adult white persons. In Scandinavia this disorder affects 1 in 1,500 to 3,000 individuals, but it is less common in Asian and black populations. In North America, AAT deficiency affects 1 in 5,000 to 7,000 people.

Current evidence suggests that there are about 100,000 people with clinically significant AAT deficiency in the United States.

## Symptoms

- What are the symptoms of AAT deficiency? (<http://patients.gi.org/topics/alpha-1-antitrypsin-deficiency/>)

This deficiency may predispose patients to several illnesses. It most commonly manifests as lung disease or emphysema, less commonly as liver disease, or more rarely, as a skin condition called panniculitis. Panniculitis is characterized by hardened skin with painful lumps or patches and is due to an inflammation in the fatty tissue under the skin. It can occur in both children and adults.

Lung disease is the most frequent cause of disability and early death among adults affected by the disease.

The first signs and symptoms of lung disease caused by alpha-1 antitrypsin deficiency usually manifest between ages 20 and 50. The earliest symptoms are shortness of breath following mild activity, reduced ability to exercise, and wheezing. Other signs and symptoms can include: unintentional weight loss, recurring respiratory infections, fatigue and vision abnormalities.

Advanced lung disease leads to emphysema or chronic obstructive lung disease (COPD), in which small air sacs in the lung are damaged. Characteristic features of emphysema include difficulty breathing, and a barrel-shaped chest.

Smoking or exposure to tobacco smoke accelerates the appearance of symptoms and damage to the lungs. AAT deficiency is also a major reason that patients undergo lung transplants.

Liver disease can affect both children and adults. About 10 percent of infants and 15 percent of adults with AAT deficiency develop scarring or cirrhosis of the liver because of progressive liver damage. In newborns, the typical symptoms of AAT deficiency are jaundice, swelling of the abdomen, and poor feeding. Symptoms of AAT deficiency may also appear in late childhood or adulthood and include fatigue, poor appetite, swelling of the abdomen and legs or abnormal liver tests and jaundice. It can cause progressive scarring or cirrhosis of the liver and is the leading genetic cause of liver transplantation in children. Cirrhosis can manifest as easy bruising, fluid retention and vomiting of blood or passage of black stool because of bleeding in the gut. It can also lead to confusion, which can progress to coma.

## Screening/Diagnosis

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- How is AAT deficiency diagnosed? (<http://patients.gi.org/topics/alpha-1-antitrypsin-deficiency/>)

The diagnosis of AAT deficiency is made by blood tests showing the low levels of alpha-1 antitrypsin. If they are abnormally low, the next step is to identify the exact alpha-1-antitrypsin protein variants the person carries. Abnormal types of the alpha-1-antitrypsin protein can be detected using dried blood as a sample for gel electrophoresis – this is known as phenotyping. Whenever genetic testing is done, genetic counseling must be available, and informed consent should be obtained. Other tests to confirm the severity of the disease include lung function tests, chest X-rays and chest CT scans and liver function tests.

A liver biopsy may be performed to check for evidence of damage to the liver.

## Treatment

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- What is the treatment for AAT deficiency? (<http://patients.gi.org/topics/alpha-1-antitrypsin-deficiency/>)

The most important factor in preventing disease or slowing disease progression in individuals with AAT deficiency is avoidance of risk factors. The biggest risk factor for lung disease is cigarette smoking. In addition to smoking cessation, it is important to avoid second-hand smoke, avoid infection, and avoid occupational inhaled irritant exposures. Similarly patients should be counseled regarding possible sources of liver injury such as alcohol abuse.

The lung-affected patients may receive intravenous infusions of alpha-1 antitrypsin, derived from donated human plasma. This augmentation therapy is thought to arrest the course of the disease and halt any further damage to the lungs. Long-term studies of the effectiveness of A1AT replacement therapy are not available. It is currently recommended that patients begin augmentation therapy only after the onset of emphysema symptoms.

Augmentation therapy is not appropriate for liver-affected patients; treatment of A1AD-related liver damage focuses on alleviating the symptoms of the disease. In advanced and decompensated liver disease, the only available approach is liver transplantation.

## Authors

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## Patient Links

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- American Liver Foundation (<http://www.liverfoundation.org/>)
- American Association for the Study of Liver Disease (<http://www.aasld.org/>)