



Research for a Cure

The mission of the **Alpha-1 Foundation** is to provide the leadership and resources that will result in increased research, improved health, worldwide detection, and a cure for Alpha-1 Antitrypsin Deficiency. The Foundation has invested nearly \$39 million to support Alpha-1 Antitrypsin Deficiency research in more than 70 insitutions in North America, Europe and Australia. For more information, visit: www.alpha-1foundation.org.



Support, Education and Advocacy

The **Alpha-1 Association** is the leading national patient membership organization serving the Alpha-1 community since 1991. Its mission is to identify those affected by Alpha-1 Antitrypsin Deficiency and to improve the quality of their lives through support, education, advocacy and to encourage participation in research. Its programs include a national Support Network of more than 70 Support Groups, Patient Hotline, national and regional educational programs, Genetic Counseling Service, and grassroots advocacy program. For more information visit: www.alpha1.org.

www.alpha-1foundation.org
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The Liver and Alpha-1 Antitrypsin Deficiency (Alpha-1)



What Is Alpha-1 Antitrypsin Deficiency?

Alpha-1 is a condition that may result in serious lung disease in adults and/or liver disease in infants, children, or adults. This condition is passed on from parents to their children through genes.

For the most part, for each trait a person has there are two genes. One gene is from each parent. People with Alpha-1 have received two defective alpha-1 genes. One defective gene came from their mother and one from their father. There are many types of defective alpha-1 genes. The most common of these genes is called S or Z. Normal genes are called M. A person who does not have Alpha-1 will have two M genes (MM). People with Alpha-1 most commonly have two Z genes (ZZ) or an S and a Z gene (SZ). The health risks to people with SZ Alpha-1 tend to be less than for people with the ZZ form of the deficiency.

The result of having two defective genes for Alpha-1 is a very low or even absent level of a protein called alpha-1 antitrypsin (AAT) in the blood. People with Alpha-1 (ZZ or SZ) will pass on one of their defective genes (S or Z) to each of their children.

An Alpha-1 Carrier is a person who has one normal AAT gene (M) and one defective AAT gene (usually S or Z). Being a carrier is very common. It is believed that over 20 million people in the U.S are carriers. Carriers (MZ or MS) may pass their defective AAT gene (S or Z) to their children. Carriers have lower blood levels of AAT protein, but their levels are rarely as low as people with Alpha-1.

What Are Some Important Facts About Alpha-1?

- It is an abnormality of the genes that leads to low or absent levels of AAT
- It may cause lung disease in adults
- It may cause liver damage that gets worse over time in adults, children and infants
- It can be treated, but cannot be cured
- It is easy to diagnose through a blood or mouth swab test

What Is Liver Disease?

The liver is one of the largest organs in your body. It is very important to your health because it cleans your blood and helps fight infections. The liver makes important proteins that travel throughout the body. It also stores vitamins, sugars, fats and other nutrients from the food that you eat. The liver breaks down alcohol, drugs and other toxic substances that may harm your body. "Liver disease" may refer to any number of diseases or disorders that stop the liver from working as well as it should.



What Causes Liver Disease In Alpha-1?

Liver disease is the second most frequent health problem that may result from Alpha-1. However, the exact cause of the liver disease is not known. The most widely accepted explanation is that it is caused by the build-up of abnormal AAT in the liver. The abnormal AAT protein is made in the liver of people with ZZ genes and 80-90% of this protein is kept (or gets stuck) in the liver. If the liver is not able to break down this abnormal protein, the build-up of the abnormal protein over time leads to liver damage.

How Common Is Liver Disease In People With Alpha-1 And In Alpha-1 Carriers?

Of newborns and children who have two defective AAT genes, such as ZZ, about 1 in 20 will, in their first year, develop liver disease that may be serious. Other children may have abnormal liver blood tests and few symptoms of liver disease. In most cases, the liver abnormalities resolve by the time the child reaches their teens and many ZZ children remain completely healthy. Adults with Alpha-1 can also develop liver disease, which often becomes more severe in middle age and beyond.

Cirrhosis, or scarring of the liver, is the most common liver disease in adults related to Alpha-1. The risk of chronic disease in MZ carriers is much less than that of people with Alpha-1. Research suggests that chronic liver disease might appear in MZ carriers only when the liver has been damaged first by something else. Things that could harm the liver are a virus, such as hepatitis B or C, or a chemical such as alcohol. There is no scientific evidence that carriers with the MS genes are at increased risk for liver disease.

What Are Some Symptoms Of Alpha-1 Liver Disease?

- Eyes and skin turning yellow (called “jaundice”)
- Swelling of the abdomen (called “ascites”) and/or legs
- Vomiting blood or passing blood in the stool
- Widespread itching (called “pruritis”)

How Is Alpha-1 Liver Disease Found?

Liver disease that is related to Alpha-1 can be found during routine exams and by lab tests. These may involve measuring the blood’s AAT level, blood tests of liver function and ultra-sound exams of the liver. A liver biopsy is rarely needed to make the diagnosis of liver disease due to AAT deficiency, although it may be helpful to find out how severe the liver disease is and to eliminate other causes for the liver disease.

Who Should Be Tested For Alpha-1?

- Newborns, children, and adults with unexplained liver disease
- People with a family history of liver disease
- Relatives of a person diagnosed with Alpha-1
- Everyone with emphysema, bronchiectasis, chronic obstructive pulmonary disease (COPD), chronic bronchitis, or asthma that is incompletely reversible after aggressive treatment

Informed Consent

Informed consent is the process through which a person receives appropriate information, understands that information, and agrees to testing. It originates from the legal and ethical right of the patient to direct what happens to their body and from the ethical duty of the physician to involve the patient in their

healthcare. You should discuss the decision to get tested for Alpha-1 with your doctor and make sure all of your questions are answered. (For more information on informed consent, please go to www.alpha-1foundation.org.)

How is Alpha-1 Liver Disease Treated?

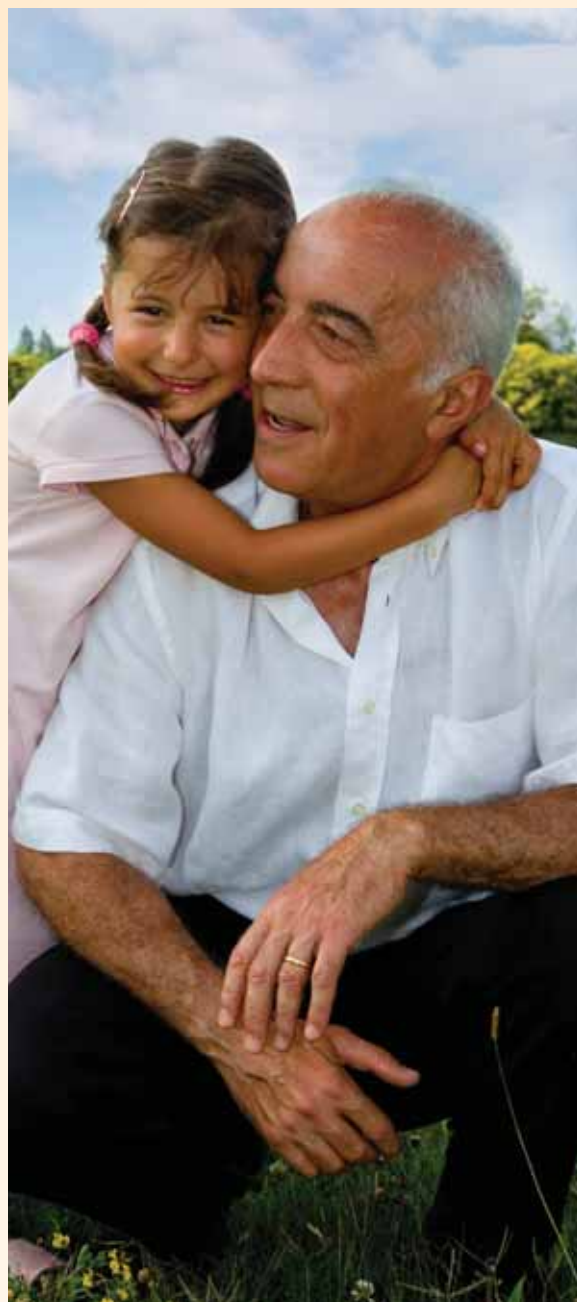
At this time, there are no specific treatments for Alpha-1 liver disease. In its most severe form, the only treatment is liver transplantation. Also, there is no treatment to prevent the onset of the liver disease. The focus of care is on managing health problems as they come up and keeping patients as healthy as possible. All patients with Alpha-1 should be immunized against hepatitis A and B. They should also have regular physical exams, liver function tests and abdominal ultrasound exams. People 50 and older who have decompensated (worsening) cirrhosis due to Alpha-1 are at increased risk for hepatoma (“liver cell cancer”). As a result, they should get periodic CT imaging of the liver. Staying away from tobacco smoke and alcohol while eating a nutritious, well-balanced diet is also important.

Unlike lung disease caused by Alpha-1, there is no role for “augmentation therapy” — periodic injections or doses of the missing or deficient AAT protein. This therapy does NOT help the liver.

Liver transplantation is surgery to remove a sick liver and replace it with a healthy one. A transplant is needed when a patient’s diseased liver gets worse over time until it is working so poorly that the patient may die. Most often, more than one doctor will decide if a person needs a liver transplant and if it is safe for them to have one. It can take a long time to get a healthy liver. The liver usually comes from someone who has just died. However, sometimes part of the liver from a living person is used. Due to the lack of donated organs, there is no guarantee that a donated liver will be available. For this reason, the decision to put someone on a transplant waiting list may be made long before a person truly needs one.

How Can I Learn More About Liver Disease In People With Alpha-1?

- Ask your healthcare provider
- Use the “Resources” listed in this brochure to access information



Alpha-1 Association

Toll Free: (800) 521-3025
 Patient Information Hotline:
 877-346-3212
 Genetic Counseling Program:
 800-785-3177
www.alpha1.org

The Association is a member-based nonprofit organization that provides programs and services to Alpha patients and their families including a free confidential Genetic Counseling Program, physician referral and an Alpha-1 Families Virtual Support Group that meets by telecall by-monthly.

Alpha-1 Foundation

Toll Free: (877) 228-7321
www.alpha-1foundation.org

The not-for-profit Foundation provides resources, educational brochures and information on testing and diagnosis for physicians and patients. It funds cutting-edge research to find treatments and a cure and supports worldwide detection of Alpha-1.

AlphaNet

Toll Free: (800) 577-2638
www.alphanet.org

AlphaNet assists patients and families with support, education and strategies to manage their health. It also sponsors clinical trials for Alpha-1 therapies and produces The Big Fat Reference Guide to Alpha-1, a complete guide to understanding, managing and living with Alpha-1, and includes key terms, testing, genetics and treatment options. It is available through the website or number listed above.



The Alpha-1 Research Registry

Toll Free: (877) 886-2383
www.alphaoneregistry.org

The Research Registry is a confidential database of Alphas and carriers. The Registry gives patients the opportunity to provide information to help advance research on the disorder through questionnaires and clinical trials. It also provides access to experts on Alpha-1 care. Individuals enrolled in the Registry have the ongoing opportunity to participate directly in clinical trials of new therapeutic approaches, in addition to other research opportunities.

Alpha-1 Kids

1 (877) 346-3212
www.alpha1kids.org

Alpha-1 Kids provides support and information for parents and children with Alpha-1.

The American Association for The Study of Liver Disease

(703) 299-9766

www.aasld.org

This is the leading organization of scientists and healthcare professionals committed to preventing and curing liver disease.

American Liver Foundation

Toll Free: (800) 465-4837

www.liverfoundation.org

The Foundation provides information on prevention, treatment and potential cures for liver diseases.

Children's Liver Association for Support Services

Toll Free: (877) 679-8256

www.classkids.org

This group serves the emotional, educational and financial needs of families and children with liver disease.

Cholestatic Liver Disease Consortium

(303) 837-2598

www.childrennetwork.org/families.html

The Consortium provides support and information for children and families with rare cholestatic liver diseases. For information on liver issues related to AAT, visit this website and click on the Alpha-1 link.

