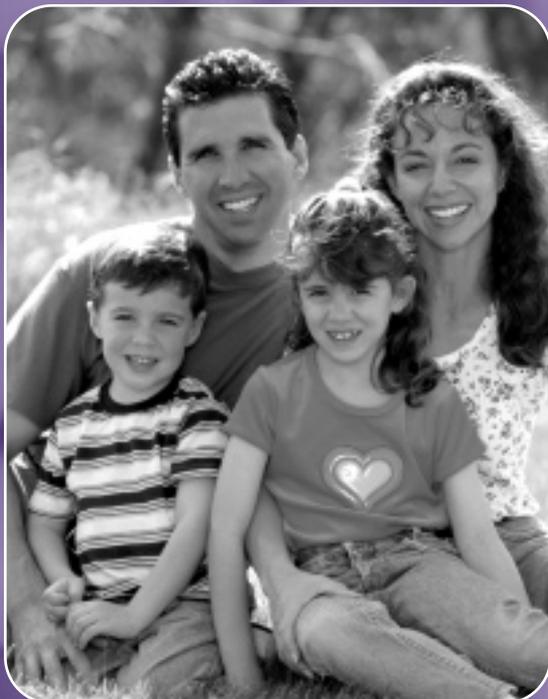


A Guide for the Recently Diagnosed Alpha-1 Carrier

Alpha-1 Antitrypsin Deficiency



A Guide for the Recently Diagnosed Alpha-1 Carrier

What Does it Mean to be a Carrier of Alpha-1 Antitrypsin Deficiency (Alpha-1)?

Finding out that you are an Alpha-1 Carrier can be a confusing and potentially upsetting experience. It is important to note that most people diagnosed as Alpha-1 Carriers live full and healthy lives. The information contained in this brochure is designed to help you and your family take charge of your health and slow disease progression by following preventive measures. Alpha-1 is an inherited disorder that can result in damage to the lungs or liver. Alpha-1 is one of the most common genetic disorders worldwide; over 100,000 people in the U.S. (and a similar number in Europe) are estimated to have the severe deficiency while between 16 and 21 million individuals in the U.S. are estimated to be Alpha-1 Carriers.



What are the most important facts I need to know about being an Alpha-1 Carrier?

- You have received an altered gene from one parent and a normal gene from the other.
- Many research studies suggest that some carriers are at risk for developing lung and/or liver disease; however, these risks are much less than those of individuals with severe Alpha-1 Deficiency. Carriers with an MS phenotype appear to have even less risk.
- The amount of AAT in a carrier's blood is sufficient to protect the tissues in most cases. You can modify your lifestyle to reduce the risks associated with Alpha-1.
- Carriers may be more susceptible to the damaging effects of cigarette smoke (including passive smoke), alcohol consumption, and other environmental risk factors than the general population. This appears to be especially true with regards to children.
- There are three test results that provide information about your carrier status, and if you may be at risk for developing any of the symptoms of AAT Deficiency:
 - The level of AAT in your blood
 - The type of AAT in your blood (phenotype)
 - Your specific AAT genetic makeup (genotype)
- You should discuss your test results in detail with your healthcare provider.
- More detailed information on being an Alpha-1 Carrier is outlined in this brochure.

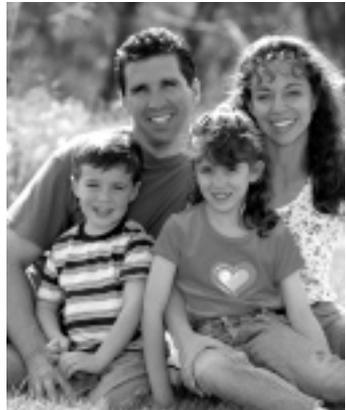
Why would I want to know if I'm an Alpha-1 Carrier?

Minimize your health risks through preventive measures; make informed decisions about family planning; evaluate the risks to other family members; be aware of the potential implications as it may relate to insurance and employment issues.

There is some evidence that Alpha-1 Carriers:

- Are found in higher than expected numbers among patients being treated for liver and lung disease.
- May be more susceptible to the damaging effects of cigarette smoke, alcohol consumption, and other environmental risk factors than the general population.

You may want to contact organizations that provide education and support resources for individuals affected by Alpha-1. You may also want to consider genetic counseling to better understand medical information about your diagnosis, help you consider all of the aspects of being diagnosed with a genetic disorder and provide emotional support if needed.



For a listing of resources please refer to the end of this booklet.

Understanding Test Results and Implications

Test Results

Testing for AAT Deficiency can include measuring the level of AAT in your blood, determining the type of AAT in your blood (phenotyping) and your specific genetic makeup (genotyping). The AAT phenotype and genotype of an Alpha-1 Carrier does not change throughout their life but the AAT level can vary.

In all normal individuals and almost all Alpha-1 Carriers, the level of AAT in the blood is higher than 11 micromolar (μM). Alpha-1 Carriers have, on the average, about half of the normal level of the AAT in their blood. In persons with severe Alpha-1, blood tests reveal a level of AAT less than 11 micromoles (μM). Most commercial labs measure AAT serum levels in milligrams/deciliter (mg/dl). To convert mg/dl to μM , divide the mg by 5. For example, an individual with a level of 50 mg/dl would have a level of 10 μM .

The most common Alpha-1 Carrier phenotype associated with increased risk for lung and liver disease is MZ. There are many other possible variants. You can discuss your phenotype in detail with your healthcare provider.

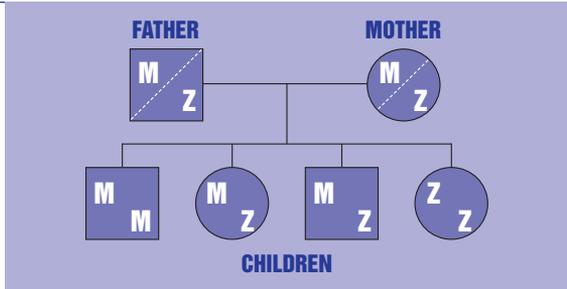
Risks to Alpha-1 Carriers

The risk of developing lung or liver disease caused by being a carrier of Alpha-1 compared to normal individuals appears small. At the present time, there are only known risks for those that are MZ. It is unclear at this time if there are any increased risks for MS carriers.

Genetic Transmission

One half of your genes are inherited from each parent. The figure below shows the possible outcomes for children if both parents are Alpha-1 Carriers (having one normal “M” and one “Z” gene).

Alpha-1 is a genetic disorder. Since one half of your genes are inherited from each parent, look at the figure to the right to see the possible outcomes for children if both parents are carriers of the AAT gene.



- Normal (MM)** Does not have the disorder and does not carry any altered AAT genes.
- Carrier (MZ)** Mild to moderate AAT Deficiency—may develop disease symptoms and does carry an altered AAT gene.
- Carrier (MS)** It is unclear whether there is a risk for developing disease symptoms but does carry an altered AAT gene (though most studies do not indicate an increased risk for disease).
- AAT Deficiency (ZZ) (SZ)** Moderate (SZ) to severe (ZZ) deficiency—could develop disease and does carry two altered AAT genes.
- AAT Deficiency (SS)** It is unclear whether there is a risk for developing disease symptoms but does carry two altered AAT genes (though most studies do not indicate an increased risk for disease).

Since You're an Alpha-1 Carrier

If your spouse has two normal AAT genes, each of your children will have a fifty-fifty chance of being an Alpha-1 Carrier. If both you and your spouse are carriers, each child has a 50% chance of being an Alpha-1 Carrier (i.e. MZ), a 25% chance of having a normal genotype (i.e. MM), and a 25% chance of inheriting severe Alpha-1 (i.e. ZZ). If you are an Alpha-1 Carrier and your spouse has Alpha-1 (i.e. ZZ) each child has a 50% chance of being an Alpha-1 Carrier (ie. MZ), and a 50% chance of inheriting severe Alpha-1 (i.e. ZZ).

What Symptoms can an Alpha-1 Carrier Develop?

It is recommended that Alpha-1 Carriers consult with their physician to ascertain if they have symptoms related to the lungs or liver that are associated with Alpha-1. Most Alpha-1 Carriers have no lung or liver symptoms related to their single altered AAT gene. The amount of AAT in an Alpha-1 Carrier's blood is sufficient to protect the tissues from injury in most carriers. You can modify your lifestyle to reduce your risks associated with Alpha-1.

If respiratory symptoms do occur, they may include:

- Shortness of breath at rest or with exercise
- Wheezing, persistent coughing
- Recurrent lung infections
- Persistent sputum (or phlegm) production
- History of suspected allergies and/or asthma
- Sinus infections

Alpha-1 Carriers with liver problems may notice:

- Increased liver enzymes
- Jaundice (yellowing of the eyes and skin)
- Enlarged liver and/or spleen
- Ascites or fluid collection in the abdomen
- Cirrhosis
- Coughing up or vomiting up blood
- Persistent itching
- Noticeable change in energy level or becoming easily fatigued
- Blackish, purplish or dark colored stools
- Poor appetite

Living as an Alpha-1 Carrier

There are some effects of being an Alpha-1 Carrier that are better understood and some that are still under study. Most Alpha-1 Carriers lead long and healthy lives and, in fact, will never know they are carriers. There are estimated to be over 16 million undiagnosed Alpha-1 Carriers in the U.S. and a similar number in Europe.

The vast majority of them are leading healthy lives. Scientific knowledge of the biochemistry and consequences of severe Alpha-1 and some evidence from studies involving Alpha-1 Carriers suggests that there are measures that will make it more likely that Alpha-1 Carriers will live full and healthy lives. Now that you know you are an Alpha-1 Carrier, you can begin to reduce your risk for developing health problems associated with Alpha-1. Just as you would modify your lifestyle if you found out that you had a high cholesterol level, you can also modify your lifestyle to reduce your risks associated with Alpha-1.

Some preventive measures you can take include:

- Stop smoking and avoiding second hand smoke
- Moderating or eliminating alcohol consumption
- Avoiding jobs that involve exposure to dust, fumes or smoke

Smoking Cessation:

Current smokers should stop smoking regardless of their AAT status. Alpha-1 Carriers who smoke are at increased risk for the development of more severe lung disease compared to smokers with normal AAT levels. If your child has been diagnosed as a heterozygote (an Alpha-1 Carrier), it is very important for YOU to stop smoking. Educate your child of the dangers of smoking, as well as secondhand smoke.

Avoid Pollutants & Infection:

Risk of infection is also important. Consideration should be given for immunizations against influenza (flu), streptococcus pneumonia (Pneumovax®), hepatitis A, and hepatitis B.

Medical Evaluation of Alpha-1 Carriers

If your healthcare provider does not know that you are an Alpha-1 Carrier, it may be advisable to inform him/her. This will allow him/her to monitor you and evaluate any possible medical conditions in light of your genetic condition. There are risks to providing this information that include potential genetic discrimination in employment or with life and/or health insurance, should your medical record become available to others. Although these risks are discussed further in this booklet it is recommended you seek genetic counseling in order to make informed decisions.

Basic tests of the lungs and liver should be considered and they may include: pulmonary function testing, lung x-rays, monitoring the level of oxygen in the blood and liver function testing. Any illness should be treated promptly and aggressively, especially if related to the lungs or liver.

Other Issues of Concern for Alpha-1 Patients

Here are some issues you may face after you have been diagnosed as an Alpha-1 Carrier. These are merely a starting point for discussion with your healthcare provider and genetic counselor and should be used as examples of various issues that may arise. Please use these for reference only. These issues may be easier to address with professional advice and family support.

Family Support

Q: What do I tell family members?

A: We recommend that you inform your spouse and blood relatives of the test result, because of the genetic nature of the disorder.

Q: Should I encourage family members to be tested?

A: Because of the genetic nature of Alpha-1, your blood relatives could be normal, be carriers, or have the severe disorder themselves. After consulting with your healthcare professional about Alpha-1, it may be appropriate to consider encouraging your blood relatives to seek testing.

Example:

If both parents are carriers, each child has a chance of inheriting severe Alpha-1, a chance of being an Alpha-1 Carrier, or a chance of having both normal genes. Since the genes for Alpha-1 had to be inherited from the grandparents, etc., more distant relatives are also at risk such as aunts, uncles, cousins, nephews, and nieces that are related by blood.

With the popularity of adoption, it is important to be sensitive regarding the approach to an adopted relative. In addition, an adopted child may be found to have an altered AAT gene, even if no others in the adopting family are affected.

Health Insurance

Q: Will being an Alpha-1 Carrier affect my health insurance?

A: It may. The answer to this question depends upon your current insurance coverage status.

If you are currently insured, it is important that you educate yourself about:

- Your specific insurance policy and benefits regarding coverage and reimbursement.
- Your lifetime maximum benefit, if any.
- The laws of your state regarding mandatory coverage.

If you are currently uninsured, having severe AAT Deficiency or being an Alpha-1 Carrier may be considered a pre-existing condition, and future insurance companies may not be obligated to cover costs for this specific condition for some period of time. You may wish to seek professional advice from your state insurance authority and familiarize yourself with your state's insurance regulations. Generally, you are obligated to inform an insurance company of any pre-existing condition when you apply for coverage. If you change jobs after diagnosis, the issue of disclosure of your carrier status may also affect the benefit status of future coverage.

Q: Who will have access to your medical records?

A: The results of your test should be included in your medical record. Although generally treated as confidential, insurance companies, healthcare facilities and other professionals may access this information.



Confidentiality

Q: To whom should (or must) I disclose my Alpha-1 diagnosis?

A: You should make your own decisions about discussing this information. It is highly recommended that you tell your spouse and blood relatives about the risk of Alpha-1 and urge them to be tested. You should also inform future healthcare providers. You may be required to inform insurance companies, if you change insurance policies.

Finding out that you are an Alpha-1 Carrier can be potentially upsetting. It may help to:

- Share this information with family.
- Learn as much as you can about the health implications and if your health is affected.
- Seek support groups and/or genetic counseling to answer questions you may have about having a genetic predisposition.

Where Can I Go for More Information and Support?

There are a number of organizations, which help and support people with Alpha-1.

Alpha-1 Foundation

Toll Free: 877-2-CURE-A1 (228-7321)

Web Site: www.alphaone.org

The Alpha-1 Foundation is a not-for-profit organization dedicated to providing the leadership and resources that will result in increased research, improved health, worldwide detection, and a cure for Alpha-1. The Foundation has realized continuous growth since its inception and has developed a solid infrastructure to promote research and the development of new therapies for improving the quality of life for those diagnosed with AAT Deficiency. It has fostered collaborations with investigators throughout the United States and in Europe, working closely with the National Institutes of Health (NIH), the U. S. Food and Drug Administration (FDA), individuals affected with AAT Deficiency, and the pharmaceutical industry to expedite the development of improved therapies for Alpha-1.

AlphaNet

Toll Free: 800-577-ANET (577-2638)

Web Site: www.alphanet.org

AlphaNet, a not-for-profit disease management company, currently employs more than 20 Alphas. AlphaNet provides a wide range of support services to patients, administers clinical trials involving Alpha-1 therapies, and has developed a comprehensive disease management program to enhance the quality of life for those affected by Alpha-1. Since its inception in 1995, AlphaNet has contributed over \$10 million to support Alpha-1 research and community programs.

Alpha-1 Association

Toll Free: 800-4ALPHA1 (425-7421)

Web Site: www.alpha1.org

The Alpha-1 Association is a not-for-profit, membership organization founded in 1991. The community of people who are affected by Alpha-1 governs this international organization. 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 research.” That mission is fulfilled through an international network of support groups; a Peer Guide program to help newly diagnosed individuals, and an array of educational materials. The Alpha-1 Association advocates for the community on a host of issues including genetic privacy and discrimination, insurance issues, and product safety and availability. The Association also encourages research and supports the programs of the Alpha-1 Foundation.

American Liver Foundation

Toll Free: 800-GO LIVER (465-4837)

Web Site: www.liverfoundation.org

The American Liver Foundation is a national, voluntary not-for-profit organization dedicated to the prevention, treatment, and cure of hepatitis and other liver diseases through research, education and advocacy.



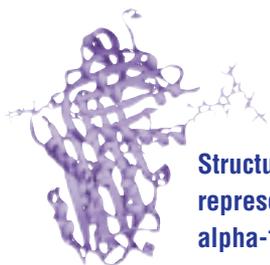
American Lung Association

Toll Free: 800-LUNG-USA (586-4872)

Web Site: www.lungusa.org

The American Lung Association (ALA) is a nationwide health organization. Since 1904, the American Lung Association has been fighting lung disease through education, community service, advocacy and research, seeking better treatments and cures. The ALA can also help you find information on smoking cessation programs that are available.

Glossary of Terms



**Structural
representation of
alpha-1 antitrypsin**

Alpha-1 Antitrypsin

alpha-1 antitrypsin (AAT) is a protein that is made in the liver and normally released into the bloodstream. AAT has many functions in the body, one of which

is to protect delicate tissue in the body from being destroyed by neutrophil elastase, a tissue-digesting enzyme.

Alpha-1 Antitrypsin Deficiency

Alpha-1 Antitrypsin Deficiency (Alpha-1) is a genetic condition. In individuals with Alpha-1, the AAT protein is not released from the liver into the blood stream. This creates a deficiency of AAT throughout the body. Some people with AAT Deficiency are not affected, while others develop liver or lung problems such as cirrhosis and emphysema.

Ascites

Fluid collection in the abdomen.

Asthma

A condition of the lungs characterized by widespread narrowing of the airways due to spasm of the smooth muscle, swelling of the mucous membrane lining the respiratory tract, and the presence of mucus in the inner spaces of the branches leading to the lungs.

Bilirubin

Bilirubin is a by-product of red blood cell breakdown that is normally formed in the liver. It creates the yellow tinge of normal serum, the yellow-green hue of bile, the brown color in stools, and



the yellow color of urine. In the presence of liver disease the bilirubin level can rise when the liver is not functioning normally. Increased bilirubin causes jaundice (yellowing of the eyes and skin).

Bronchiectasis

Chronic damage and dilation (widening) of the bronchial tubes within the lung is commonly associated with severe infections of the surrounding lung and bronchial tubes. Bronchiectasis is associated with the production of sputum.

Chronic Bronchitis

A lung disease characterized by the inability to move air in and out of the lungs combined with the production of sputum on most days of the year. This is one of the diseases caused by cigarette smoking.

Chronic Obstructive Pulmonary Disease (COPD)

COPD is a broad category of lung problems including emphysema, chronic bronchitis, bronchiectasis, and chronic asthma in adults. All these diseases cause the obstruction of inhalation and exhalation as a prominent component. COPD is responsible for more than 100,000 deaths each year and is the fourth leading cause of death in the United States.

Cirrhosis

Cirrhosis is characterized by extensive scarring and hardening of the liver. This condition is most often associated with advanced liver disease.

Emphysema

One of the conditions included in COPD, emphysema obstructs or blocks movement of air in and out of the lungs through destruction of the air sacks of the lung. It is thought that much of this destruction



is caused by the body's own defense mechanisms such as white blood cells and the digestive enzymes they contain.

Genotype

The human genome is a very long complex combination of gene sequences. The AAT gene sequence has many variations. The genotype is a description of the variation in the sequence of a particular gene. The specific change in an individual's AAT gene sequence (genotype) determines their phenotype.

Heterozygote/Homozygote

Every cell of the body has genes within it and every gene is comprised of a pair of alleles, one from the father and one from the mother. If a mother and father each give their child the same allele, this gene is called a homozygote. If a mother and father each give a child a different allele, this gene is called a heterozygote. When speaking of the AAT gene – a heterozygote would have two different alleles, often one normal allele (M) and one abnormal allele (Z, for example), referred to, in this example, as MZ. Individuals who are homozygote can have two normal AAT alleles (MM) or two abnormal alleles such as those with severe AAT Deficiency (ZZ). A very rare homozygote is the Null/Null individual in whom no AAT is made at all.

Influenza

Also known as the flu, influenza is a severe, contagious viral infection, commonly spread through populations. It is characterized by the swelling of the respiratory tract and by the sudden onset of fever, chills, muscular pain, headache, and severe fatigue.

Jaundice

A condition characterized by a yellowish tint of the skin, white portion of the eye, tissue lining of the mouth, and body fluids due to excess bilirubin in the blood.

Liver Enzymes

Proteins (specifically enzymes) found in high concentration in the liver and lower amounts in the blood and body tissue. These enzymes are released into the blood when liver cells are injured. Doctors can measure the amount of enzyme release from cells and estimate the extent of liver damage.

Micromolar

Abbreviated as μM , it is used to designate the amounts of alpha-1 antitrypsin in the blood when serum levels are tested. A person is considered alpha-1 antitrypsin deficient when their serum level is 11 μM or below.

Phenotype

The specific type of AAT protein circulating in your blood that is determined by the AAT genes passed on to you by your mother and father.

Phlegm

Thick, sticky, stringy mucus secreted by the mucous membrane of the respiratory tract, as during a cold or other respiratory infection.

Pneumonia

An acute or chronic disease marked by inflammation of the lungs and caused by viruses, bacteria, or other microorganisms and sometimes by physical and chemical irritants.

Sputum (also called phlegm)

This is the material in the airways that is brought up by coughing, such as mucus or pus, that is expectorated (ejected or spit out of the mouth) in diseases of the air passages.

Alpha-1 Carriers are encouraged to join the Alpha-1 Research Registry, a confidential registry of individuals diagnosed with Alpha-1 and carriers of the disorder. Your participation is important to advance research on Alpha-1.



The Alpha-1 Research Registry

Call Toll Free: 1-877-886-2383

Visit our Website at alphaoneregistry.org

Visit the Alpha-1 Foundation Website at: www.alphaone.org



The Alpha-1 Foundation

2937 SW 27th Avenue, Suite 302, Miami, FL 33133
Telephone: (877) 2-CURE-A1 (228-7321) • Fax: (305) 567-1317

Website: <http://www.alphaone.org>