

A Guide for the Recently Diagnosed Individual

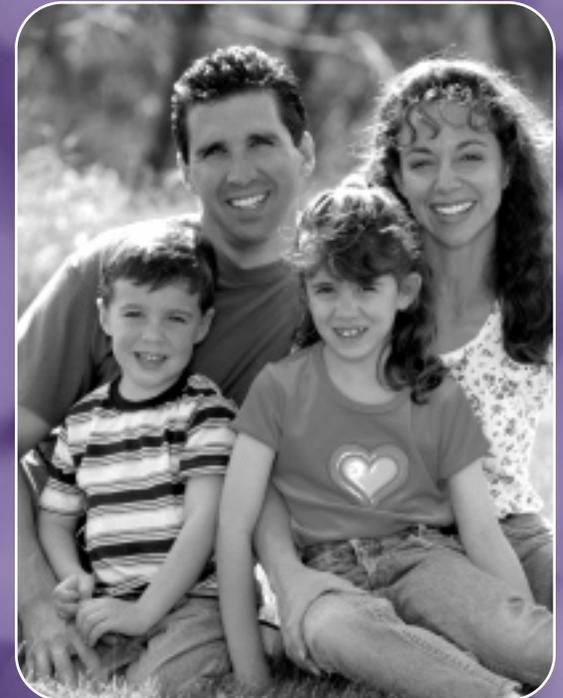
Alpha-1 Antitrypsin Deficiency



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>



A Guide for the Recently Diagnosed Individual

Finding Out About an Alpha-1 Diagnosis

Finding out about an Alpha-1 Antitrypsin Deficiency (also referred to as AAT Deficiency or Alpha-1) diagnosis can be an overwhelming and potentially upsetting experience. It is important to note that many Alphas, or individuals diagnosed with Alpha-1 Antitrypsin Deficiency, live full and productive lives. The following information is designed to help you and your family take the necessary preventive measures to keep you as healthy as possible. Listed here are four major medical and behavioral categories that can help:

- Behavioral and Lifestyle Modification
- Drug Therapy for Lung Problems
- Specialized Therapy for Alpha-1
- Surgical Options

Share this information with your family, and your healthcare professional. You may also want to seek professional genetic counseling if necessary, and contact organizations listed at the back of this brochure that provide resources for individuals diagnosed with Alpha-1 to obtain more information and support.

Understanding Alpha-1

Alpha-1 is an inherited disorder that may result in you developing a serious lung/ liver disease and passing the defective AAT gene onto your children. An estimated 100,000 people in the U.S. and a similar number in Europe are estimated to have the severe deficiency. In normal individuals large amounts of alpha-1 antitrypsin (AAT) is made in the liver and released into the blood. In AAT deficient individuals, the AAT made in the liver cannot be fully released into the blood.

Alpha-1 Is...

- A genetic disorder
- A reduced amount or lack of the protein called alpha-1 antitrypsin (AAT) in the blood
- Leading genetic cause of liver disease in infants and children
- One of the most common genetic disorders worldwide
- Often misdiagnosed

Alpha-1 Can Cause...

- Lung disease [i.e., asthma, chronic bronchitis, emphysema, chronic obstructive pulmonary disease (COPD), or bronchiectasis in adults].
- Liver disease (i.e., elevated liver enzymes, neonatal hepatitis, chronic liver disease, cirrhosis, and liver cancer)
- Skin disease known as Panniculitis

With Alpha-1...

- The lungs lack the enzyme inhibitor AAT, which protects the lungs from enzymes in white blood cells.
- Some newborns, toddlers, children, adolescents, and adults develop liver problems (i.e., chronic liver disease, cirrhosis, liver cancer) due to the inability of the misfolded AAT to exit the liver cells properly.

Test Results

A clinical diagnosis of Alpha-1 is determined by the level and a blood “phenotype” (Pi-type) of the protein alpha-1 antitrypsin (AAT) in the blood. Persons with severe Alpha-1 have blood levels of AAT less than 11 μ M (micromolar). Most commercial labs measure AAT serum levels in mg/dl. To convert mg/dl to μ M, divide the mg/dl by 5. For example, an individual with a level of 50 mg/dl would have a level of 10 μ M. In normal persons and most carriers (individuals with one normal gene and one deficient gene), the level of AAT in the blood is higher than 11 μ M.

The second test identifies the type(s) of AAT your body makes, and is called phenotyping or genotyping. Here are a few examples of possible results of this second blood test, showing possible phenotypes and their meaning as it relates to Alpha-1:

Phenotype	What it Means
Pi Z (ZZ)	You have Alpha-1 and will pass one of these genes on to your children
Pi MZ (Heterozygote)	You are a CARRIER of Alpha-1 and you can pass either one of these genes on to your children
Pi M (MM)	You do NOT have Alpha-1
Null Null (similar to PiZ)	You have Alpha-1 and will pass one of these genes on to your children

Note: *These are the most common variants of AAT. There are also many other possibilities. One of the other common forms of AAT that people can inherit is the S form; this is associated with milder reductions in AAT levels than the Z form. Combinations of these different forms of AAT are found in different people; for example, Pi SZ indicates that the person has both the S and the Z forms in their blood. You can discuss your phenotype in detail with your healthcare professional.*

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

Genetic Transmission

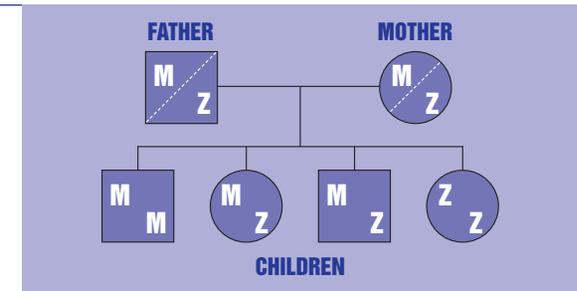
Because Alpha-1 is a genetic disorder, a person with the severe form of this disorder must have inherited two deficient genes (one from each parent). Depending on the phenotype of your parents, your brothers and sisters have a chance of either inheriting Alpha-1, being a carrier of the disorder (HETEROZYGOTE), or a chance of having a normal phenotype. Most carriers have, on average, 60% of the normal level of the protein and usually do not develop lung or liver disease.

Carriers are able to pass the gene to their offspring, and, if their spouses are also carriers, each child will have a chance of inheriting Alpha-1, a chance of being a carrier, or a chance of having a normal phenotype. While Alpha-1 Carriers are usually asymptomatic, there is some evidence that carriers may be at a slightly increased risk for injury to the lungs, especially if they smoke, and the liver.

Since half of your genes are inherited from each parent, the examples on the next page show four possible genetic combinations of children if both parents are Alpha-1 Carriers (having one normal “M” and one altered “Z” gene). Individuals with Alpha-1 could have parents who are both carriers, one parent who is a carrier and one who is severely deficient, or two parents who



are severely deficient. Please note that this figure represents the most common normal and deficient genes.



Risks Associated with Common Genetic Variants

- | | |
|-----------------------------|---|
| 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). |
| Alpha-1 (SZ) or (ZZ) | Moderate (SZ) to severe (ZZ) deficiency - could develop disease and does carry two altered AAT genes. |
| Alpha-1 (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). |

What Are the Symptoms?

If you do have respiratory symptoms, you may notice:

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

If you have liver symptoms, you or your physician may notice:

- Increased liver enzymes (a blood test performed by a physician)
- Jaundice (yellowing of the eyes and skin)
- Enlarged liver and/or spleen (may be noted by patient, parent of child, or physician)
- Ascites or fluid collection in the abdomen
- Cirrhosis (excessive accumulation of liver scar tissue noted by physician)
- Coughing up or vomiting up blood
- Persistent itching
- Noticeable change in energy level or becoming easily fatigued
- Blackish, purplish, dark or pale colored stools
- Poor appetite

You may not show signs of this disorder.

Even without symptoms, you should follow the recommendations in the next sections.

If you practice a healthy lifestyle and obtain appropriate medical care, you may remain healthy. However, this does not mean that you will not have symptoms in the future, so monitoring of your medical condition by a healthcare provider is suggested. If your healthcare provider is not knowledgeable on Alpha-1, you may request a copy of the Alpha-1 Foundation's Healthcare Provider's Guide for them. This Guide is also posted on the Alpha-1 Foundation's web site, at <http://www.alphaone.org>.

What Does Having Alpha-1 Mean to Me?

All of the following issues are potential major concerns of persons diagnosed with Alpha-1, who are also referred to as Alphas. The resources listed at the back of this brochure provide advice and support for newly diagnosed individuals in handling these issues. In addition, genetic counseling can provide the support and knowledge needed to make informed decisions for individuals diagnosed with a genetic condition.

Having Alpha-1 May Require:

Increased Doctor Visits:

People with Alpha-1 must seek expert medical treatment and may need to visit their healthcare provider more often.

Changes in Lifestyle:

If you or your child has Alpha-1, it may be necessary to make lifestyle changes to help the body stay healthy. This should include:

- Quitting smoking/keeping children away from second-hand smoke
- Avoiding exposure to dust and fumes
- Exercising regularly
- Eating well
- Drinking alcohol with caution, if at all
- Avoid exposure to chemicals that may be absorbed through the skin
- Read labels of over-the-counter medications/herbal supplements or vitamins carefully
- Advise your healthcare provider if you are taking vitamin supplements or herbal products

Various Treatments:

There are various treatment options for people diagnosed with Alpha-1. The most common types of treatments are:

- Behavioral and lifestyle modification
- Drug therapy for lung problems
- Specialized therapy for Alpha-1 lung disease
- Treatments for the complications of liver disease associated with AAT Deficiency are primarily supportive and focus on treating the specific liver dysfunction and attempting to alleviate and/or prevent complications.
- Surgical options

These treatments are discussed in greater detail in the following sections.

Environmental & Social Changes:

Environmental and social changes for people with Alpha-1 include avoiding pollutants that irritate the lungs and/or increase the risk of lung infection. Examples of such irritants are:

- Cigarette smoke, from personal smoking or second-hand tobacco smoke
- Industrial and occupational pollutants (i.e., dust, flower and tree pollen, ash, volatile compounds, fumes and other allergens)
- Air pollution
- Wood burning stoves
- Household cleaning fumes (i.e., bleach, ammonia)
- Paints and/or toxic agents
- Precautions should also be taken when handling chemicals and other materials that may be absorbed through the skin. The liver detoxifies poisonous chemicals that enter the body. If the liver is damaged, the detoxification process is altered.

- Alcoholic beverage consumption can cause damage to the liver in normal people. Many authorities recommend low, infrequent or no alcohol consumption for ZZ patients. Patients with any indication of Alpha-1 related liver damage should avoid alcohol completely.

What Do I Do Now?

As an individual with Alpha-1 you should NEVER smoke. Evidence shows that smoking tobacco products significantly increases the risk and severity of emphysema in individuals with Alpha-1 and may decrease their life span by as much as ten years or more. Exercise and nutritional programs also contribute to maintaining a healthier body. These issues are explored in sections that follow. You need to aim to achieve and maintain a healthy lifestyle. You can make a difference by following these recommendations:

Smoking Cessation:

If you smoke, it is extremely important that you quit smoking any form of tobacco. This is necessary because smoking destroys the small amount of AAT in the lungs of individuals with Alpha-1 and attracts white blood cells, with their damaging enzymes, to the lungs in large numbers, thus speeding the development of lung disease. With Alpha-1, your lungs do not have the normal defenses against white blood cells. If your child has been diagnosed with AAT Deficiency, it is so important for you to stop smoking to protect their lungs from second-hand smoke. Educate your children of the dangers of smoking as well as to avoid second-hand smoke.

Avoid Pollutants & Infection:

You should avoid occupational and environmental pollutants that can be inhaled (including pollen, dust, areas with high levels of pollutants or organic fumes, and second-hand tobacco smoke). These substances can cause irritation to your lungs, and cause or worsen lung problems.



Avoid air pollution and aerosolized sprays at all times. It is also important to realize that you may encounter pollutants and infections, both at home and at work.

In the Workplace

You should avoid exposure to inorganic or organic dust, (i.e., coal, hay, etc.) or irritating gases (i.e., chlorine, isocyanates, etc.). You should seek the healthiest possible work environment. Demand clean indoor air, with proper ventilation and filtration systems, and avoid second-hand tobacco smoke whenever possible. Wear protective clothing, i.e., rubber gloves, when coming in contact with chemicals or other agents that can be absorbed through the skin. Read labels closely.

In the Home

You should avoid:

- Household chemicals
- Respiratory irritants (i.e., second-hand smoke, wood burning stoves, dust and pollen)
- Chlorine and ammonia (found in common household cleaning products)
- Pesticides
- Pet dander

Since bacterial and viral infections are harmful to the lungs, you should try to avoid contact with sick or infectious people. Hand washing with soap is the single most effective way to avoid both contracting and spreading infectious diseases. Wear protective clothing, i.e., rubber gloves, when coming in contact with chemicals or other agents that can be absorbed through the skin. Read labels closely.



Develop an Exercise Program:

Routine exercise improves mental outlook, stamina and physical well-being. Exercise is essential to all Alphas. It is important to exercise muscles in the chest and upper body that are related to the functioning of your lungs.

Walking Programs

Walking programs (particularly in “climate controlled” local indoor shopping malls), strolling, swimming, and/or biking may improve your lung function and endurance.

A Pulmonary Rehabilitation Exercise Program

A Pulmonary Rehabilitation Exercise Program (PREP) is highly recommended for Alphas who have lung problems. A PREP that includes exercise, breathing retraining, education, smoking cessation, and nutrition counseling may help you achieve your fullest level of activity. As with all exercise programs, a PREP should be recommended by and discussed with your healthcare professional.

Personal Exercise Plan

You may want to have a personally tailored exercise program that is carefully monitored by your healthcare provider and/or exercise specialist. You should start exercising slowly and build the intensity of your program over time, as your tolerance for exercise increases.

Develop a Nutrition Program:

Proper eating habits may help to preserve lung and liver function. It is important to maintain an ideal body weight, whether you have lung/liver disease or not. Some scientific research indicates that people with lung disorders need to consume more calories than “lung-healthy” people, this affects the manner in which you should approach nutrition. You should establish or maintain good eating

Current Treatments for Alpha-1

habits. If you have lung and/or liver problems, it may help to work closely with a nutritionist or registered dietician who will be able to set up an appropriate individualized nutrition program.

Supportive nutritional needs in the patients exhibiting liver complications due to AAT Deficiency are highly individualized. While sodium and protein intake may become a consumption concern due to fluid retention, good nutrition is advised. Processed foods have high sodium content. Read labels carefully. Vegetable sources of protein are better than animal sources of protein. Vitamin A, B3 (Niacin), and iron supplements may stress an already compromised liver. In the Alpha-1 patient who exhibits signs of liver complications, fat absorption may be altered; therefore, your healthcare provider may recommend supplementing the diet with Vitamins A, D, E and K. In the infant that is experiencing feeding difficulties and shows poor growth and a failure to thrive, a special formula is often recommended. Sometimes, TPN (total parenteral nutrition) may be necessary to administer.

Reduce Stressors:

Persons with Alpha-1 report benefits with stress reduction techniques. There are many relaxation techniques that help in reducing stress. These relaxation techniques may also contribute to a positive outlook on life and may prevent depression. Here are a few:

- Breathing exercises
- Muscle relaxation
- Biofeedback
- Visualization
- Hypnotherapy
- Positive thinking
- Improving sleep patterns
- Yoga
- Meditation

What Are the Current Treatments for Alpha-1?

You may benefit from lifestyle modification. However, if you have lung and/or liver disease, you should seek expert medical care to treat your condition(s). There are specialized Clinical Resource Centers with healthcare professionals and staff that provide medical treatment and behavioral and lifestyle modification guidelines specifically for patients diagnosed with Alpha-1.

Drug Therapy for Lung or Liver Problems

These treatments require your healthcare provider's care. Discuss the plan you need to follow with your healthcare provider.

Vaccinations:

- It is important for you to have annual influenza (flu) shots. The use of these prophylactic (preventive) vaccinations is of the utmost importance
- The Pneumovax® vaccine may help prevent pneumonia. Repeating the pneumonia shot after six years should be considered
- Discuss hepatitis A vaccine with your healthcare provider
- Discuss hepatitis B vaccine with your healthcare provider

Aggressive treatment of lung infections:

It is important for you to notify your healthcare provider immediately when you suspect a lung infection. These are some symptoms to be aware of:

- Fever
- Increased shortness of breath
- Increased coughing
- Chills with fever
- Changes in color or thickness of sputum (phlegm)

Because the lungs contain more white blood cells when you have an infection, and hence, destructive enzymes, it is necessary to take antibiotics to fight the infection.

Additional Preventive Measures:

- Avoid direct contact with persons having respiratory illness
- Limit exposure to children less than five years of age (they are often infectious or exposed to infections)
- Wash your hands frequently with soap
- Limit exposure to liver toxins such as alcoholic beverages and organic solvents

Aggressive Treatment of Liver Complications

It is important for parents, caregivers, or significant others to be aware and advised of any indication of possible complications related to liver disease. Listed below is a list of common symptoms that they should be advised about:

- Increased abdominal swelling, chest or down into the lower groin area
- Coughing up or vomiting bright red blood
- Blood in toilet or diaper
- Blackish, purplish, dark, or pale colored stools
- Confusion, crankiness, unusual crying, disorientation, lethargy
- Little or no urine
- Dark urine
- Lack of energy, easily fatigued
- Fever
- Change in or the appearance of jaundice
- No appetite/refusal to eat or drink
- Enlarged abdomen
- Itching or increased itching
- Peripheral edema (swelling of hands and feet)

Liver Disease Associated With Alpha-1

A complete discussion of the diagnosis and treatment of severe liver disease is beyond the scope of this brochure. The treatment of liver disease is highly individualized and is treated symptomatically and preventatively. In older children and adults, liver damage can occur silently and with/without severe symptoms. Often, in infancy, a prolonged period of jaundice (neonatal hepatitis) is the first indicator that is indicative of liver disease. Other early warning signs may appear in the simple blood tests that measure liver function, as well as a low birth weight, poor growth and feeding difficulties and ascites. Even when there is severe liver damage present, most individuals with Alpha-1 can lead a relatively normal life with a low rate of progression of liver disease for extended periods of time. The majority of children with Alpha-1 lead normal lives.

Once liver injury is identified in an adult with Alpha-1, the first course of action is to evaluate your lifestyle for ingestion of potential liver toxins, such as alcohol, large doses of certain vitamins, and some medications. As with the pediatric population, careful follow-up of abnormal liver function by your healthcare provider is needed. Again, the liver disease is treated symptomatically and preventatively. In the adult population with Alpha-1 liver disease, symptoms may occur suddenly (i.e., after an esophageal varices hemorrhage) with no prior indication that liver disease exists.

Some medications (prescription or over the counter) and nutritional supplements (vitamins, herbs, protein drinks) may contain substances that are harmful to your liver. Making a list of any substances you use and reviewing it with your healthcare provider is suggested. Careful follow-up of abnormal liver function by your healthcare provider is needed and often the liver injury can prove to be mild and temporary.



In the most severe situations, the liver can be extensively damaged. Liver transplantation may be the only alternative to maintain life. Fortunately, in infants, toddlers, and children diagnosed with Alpha-1, this degree of injury is rare.

Common Therapies For Alpha-1 Lung Disease:

Antibiotics

Bacterial infections in the lung can lead to a dramatic influx of white blood cells into the lung tissue and airways. This may be one of the major causes of lung destruction in Alpha-1. To minimize this risk, many physicians advocate aggressive therapy with antibiotics at the first signs of a lung infection. While many so-called 'pulmonary exacerbations' may not be caused by infection or may be due to a viral infection (which would not be expected to benefit from antibiotics), the benefits of this approach to therapy may, in some patients, outweigh the risks of antibiotic use (which include selection of antibiotic resistant bacteria, overgrowth of yeast and other agents that can lead to disease, and allergic reactions).

Bronchodilators

Some of the symptoms of Alpha-1 are similar to common lung diseases, such as asthma and COPD. Medications called bronchodilators, which are usually administered by inhalers, may be useful in relieving lung symptoms of Alpha-1. There are a number of different types of bronchodilator medications and these may sometimes be combined to achieve maximal benefit.

Corticosteroids

Based on your healthcare provider's recommendation, the use of corticosteroids (or simply, steroids) can be an appropriate treatment for lung symptoms in some individuals. Steroids can be administered by inhalation, in pill form, or intravenously (into a vein). Steroids administered by mouth or vein are usually reserved to treat severe lung problems.

Supplemental Oxygen

Supplemental oxygen can be important and life saving therapy for individuals with low blood oxygen levels. Some people, however, need supplemental oxygen primarily during exercise or with sleep. For some, it is especially important when traveling by air or at high altitudes. Ask your healthcare provider about your need for this treatment.

Specialized Therapy for Alpha-1

Augmentation Therapy

Augmentation therapy is appropriate for many Alphas who have lung problems. As its name suggests, it increases, or augments, the AAT protein levels in your blood, and may help to slow the rate of lung function loss in Alphas. Augmentation therapy is not a cure; it will not reverse lung damage that has already occurred, nor treat or prevent Alpha-1-related liver problems. Augmentation therapy may help prevent lung problems from getting worse and thereby, help you live longer.

Augmentation therapy, a derivative of human plasma, is AAT that has been purified from the blood of normal donors. It is used to increase the concentration of AAT in your blood and lungs and is given intravenously once per week. Currently, augmentation therapy can only be prescribed for individuals with Alpha-1-related emphysema, under supervised professional health care. This is not a treatment option for Alpha-1-related liver disease.

Other Issues of Concern for Alpha Patients

Surgery Options for Alpha-1 Liver Disease:

There are several surgical options that may become necessary in end stage liver disease. They are: large volume paracentesis (LVP), sclerotherapy treatment to esophageal varices and portal vein decompression utilizing surgical shunts. Surgical treatment options are highly individualized to each patient, as is the decision as to the timing of liver transplantation. The option of living-related liver transplantation is available at some transplant facilities. If you decide to explore this option, check with the transplant center first to be certain that this choice is available to you.

Surgery Options for Alpha-1 Lung Disease:

Your healthcare provider determines rationale for the use of surgery. There are two types of surgery for those with Alpha-1: lung volume reduction and organ transplantation.

Lung Volume Reduction

This surgery may improve breathing by physically removing some of the most damaged lung tissue.

Organ Transplantation

Lung/Liver transplantation is an option for some individuals with severe lung and/or liver disease.

As with all surgery, outcomes depend on a number of issues specific to each person. There are no guarantees of the extent to which there will be an improvement of your medical condition. Please consult with your healthcare professional about these options.

Here are some issues you may face after you have been diagnosed with Alpha-1. These are merely a starting point for discussion and should be used as examples of the various issues that may arise. Please use these for reference only. These are issues, which may be better to face with professional advice from a physician or genetic counselor and familial support.

Psychosocial/Family Support

Q: What do I tell family members?

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

Q: Should I urge family members to be tested?

A: After consulting with your healthcare provider regarding the specific issues about Alpha-1, it is reasonable to encourage your blood relatives to seek testing. Because of the genetic nature of Alpha-1, your blood relatives could be carriers or have the disorder themselves. Issues related to genetic discrimination in employment and insurance need to be taken into account, however. It is possible to obtain confidential testing for Alpha-1 through the Alpha-1 Research Registry (contact information at the at the end of this brochure).

Example:

If both parents are carriers, each child has a chance of inheriting Alpha-1, a chance of being a carrier of Alpha-1, or a chance of having both normal genes.

Health Insurance

Q: Will the Alpha-1 diagnosis 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 benefit regarding coverage and reimbursement
- Your lifetime maximum benefit, if any
- The laws of your state regarding mandatory coverage

If you are currently uninsured

Alpha-1 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 and familiarize yourself with the insurance regulations in your state of residence. Generally, you are obligated to inform an insurance company of any pre-existing condition when you apply for coverage.

Employment

Q: Can I continue to work?

A: The answer to this question usually depends upon two conditions:

- The present state of your health
- The possibility of unwanted airborne exposures (i.e., dust & fumes) at work

It is good to work! If, after discussion with your healthcare professional, you are physically able and have no occupational exposure to dust and fumes, you should continue to work. Otherwise, your healthcare provider may suggest changing your job to reduce these exposures.

Please note that your eligibility to continue health insurance coverage may vary from state to state. If you change jobs after diagnosis, the issue of disclosure of your disorder may also affect the benefit status of future coverage.

Q: What role does disability insurance have?

A: If your physical condition does not allow you to work, it is important to discuss the availability of disability insurance payments with your healthcare provider and other professionals familiar with disability benefits.

Confidentiality

Q: Who will know that I have Alpha-1?

A: The results of your test will be included in your medical record. Although generally treated as confidential, insurance companies, healthcare facilities and other professionals may access this information. It is possible to obtain confidential Alpha-1 testing through the Alpha-1 Research Registry (contact information at the at the end of this brochure).

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

A: You must make your own decisions about discussing this information. However, it is highly recommended that you tell 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 about an Alpha-1 diagnosis can be an overwhelming and potentially upsetting experience. It is important to:

- Share this information with family
- Seek professional counseling, if necessary

Glossary of Terms

Actigall (Ursodiol)

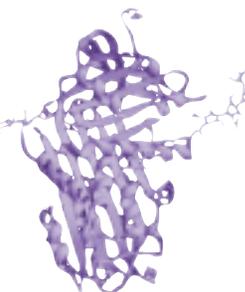
This is a medication commonly used by healthcare providers that will assist in the bile flow out of the liver and help to alleviate a build-up of bile acids in the liver, which may result in further damage to the liver.

Alpha-1 Antitrypsin

Alpha-1 antitrypsin (AAT) is a protein that is made in the liver. The liver normally releases this protein 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)

A genetic condition caused when the protein cannot pass out of the liver, as it should. This creates a deficiency of AAT throughout the body. Some people with Alpha-1 develop liver problems, some develop lung problems like emphysema, and some develop a skin disorder known as Panniculitis. Others are not affected at all.



Structural representation of alpha-1 antitrypsin

Ascites

Fluid collection in the abdomen.

Antibiotics

Antibiotics are drugs that can kill or stop the growth of bacteria. Sometimes the term is used to describe drugs that can treat any infections such as those caused by bacteria, fungus, tuberculosis, and even viruses.

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.

Augmentation Therapy

Intravenous administration of alpha-1 antitrypsin (AAT) purified from human plasma and given in sufficient amounts to protect the lungs from damage.

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).

Biopsy

A procedure to remove tissue from an organ or a piece of tissue to examine it under a microscope. There are basically three types of biopsies: a fine needle biopsy, a core needle biopsy, and a wedge biopsy.

Bronchiectasis

Chronic dilation (widening) of the bronchial tubes within the lung. This is often caused by inflammatory diseases or obstruction and leads to chronic lung infection.

Cholestasis

A backup of bile in the liver; may result in jaundice, dark urine, pale stools, and itching.

Chronic Bronchitis

A lung disease characterized by inability to move air in and out of the lung 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 have 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 extensive scarring and hardening of the liver. This condition is most often associated with advanced liver disease.

Corticosteroids (steroids, prednisone)

A class of drug modeled after hormones released by the body's adrenal glands. They are the most potent anti-inflammation drugs currently available and can be lifesaving to people with severe COPD and asthma but are also known for their serious side effects.

Emphysema

A lung disease which involves damage to the air sacs (alveoli) in the lungs. The damaged air sacs do not deflate normally so breathing is harder than normal. Lungs with emphysema may be slow to expel used-up air and unable to fill with enough fresh air to ensure an adequate oxygen supply to the body.

Esophageal Varices

Enlarged veins in the esophagus resulting from the increased pressure in the portal vein through which blood flows into the liver. This commonly occurs in cirrhosis.

Fibrosis

This is the presence of scar tissue made of collagen within the framework of the liver tissue. When the liver is badly scarred, the organ will not function properly.

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 of the sequence of a particular gene. The specific change in an individual's AAT gene sequence (genotype) determines their phenotype.

Hepatitis

Inflammation of the liver; can be caused by viruses, abnormalities of the immune system, and medications as well as AAT Deficiency.

Hepatomegaly

Enlargement of the liver so that the liver can be felt below the rib cage.

Hepatosplenomegaly

Enlargement of the liver and the spleen.

Heterozygote/Homozygote

Every cell of the body has genes within it and every gene is actually a pair of alleles, one from the father and one from the mother. If your mother and father each give you the same allele, this gene is called a homozygote. If your mother and father each give you a different allele, this gene is called a heterozygote. For Alpha-1 deficient

individuals – if you are a heterozygote most often you have one normal allele (M) and one abnormal allele (Z), for example. Thus you would be MZ. Full, deficient individuals have two abnormal genes, such as ZZ.

Icteric

Yellowing of whites of the eyes associated with jaundice.

Influenza

Commonly known as the flu, influenza is an acute, contagious viral infection, commonly occurring in epidemics. It is characterized by inflammation of the respiratory tract and by the sudden onset of fever, chills, muscular pain, headache and severe prostration.

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. The 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. These blood tests are specifically the AST (or SGOT), ALT (or SGPT), alkaline phosphatase, and GGT-P. There are other blood tests that are commonly performed as well to monitor liver function.

Micromolar

Abbreviated as μM , it is used to designate the amounts of alpha-1 antitrypsin protein when serum levels are tested. A person is considered alpha-1 antitrypsin deficient when their serum level is $11 \mu\text{M}$ or below.

Milk Thistle

This is an alternative medicine (an herb) that has been used in the European society for many years. The primary active ingredient of Milk Thistle is silymarin. It is thought to be helpful for individuals who have liver disease because of the cleansing and protective properties that silymarin appear to have related to the treatment of liver disease. It is extremely important that your healthcare provider be informed if you take, intend to take or intend to give this herb to your child. The National Advisory Council for Complementary and Alternative Medicine for the National Institutes of Health (NIH) are currently studying this herb extensively.

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.

Panniculitis

Panniculitis is an inflammation in the blood vessels beneath the skin, causing the skin to harden and form extremely painful lumps, patches, or lesions. It is likely that the damage is initiated by destructive action of unrestrained neutrophils. In some patients, damage from panniculitis may occur after an incident of trauma to

the affected area. It occurs in children as well as adults, and has been linked to the ZZ and MZ phenotypes and possibly other alleles as well.

Portal Hypertension

Blood flows from veins in the stomach, intestines, spleen, and pancreas and goes into the liver through the portal vein. When the liver is diseased, hardened and unable to function properly, the blood attempting to flow through the liver is impaired. Because of this impaired flow of blood, pressure builds up in the portal vein, and can cause a number of problems. This condition is known as portal hypertension.

Pruritus

Medical term for itching.

Sclerotherapy

A procedure that may be used in the treatment of bleeding from esophageal (in the esophagus) varices. Specific intravenous medication is injected directly into the enlarged veins to stop the bleeding.

Spleen

An organ that is a part of the lymphatic system in the human body. It functions as a body's defense mechanism, in the formation of certain blood cells, in the destruction of certain blood cells, and as a blood reservoir. Blood from the spleen goes into the liver.

Splenomegaly

Splenomegaly is an enlarged spleen. Splenomegaly occurs when the spleen has a disease or when portal hypertension develops due to liver disease.

Sputum

Matter coughed up and usually expelled from the mouth, especially mucus or pus that is expectorated (ejected or spit out of the mouth) in diseases of the air passages.

TPN

Total Parenteral Nutrition (TPN) is the administration of nutritionally adequate solution intravenously; may become necessary to provide nutrition to individuals with severe liver damage.

Vitamins A, D, E, K

These are fat-soluble vitamins that are necessary in the diet for proper nutrition. When liver disease is severe, these vitamins are not appropriately absorbed into the blood stream. Frequently, the healthcare provider will prescribe these vitamins as dietary supplements.



Where Can I Go for More Information and Support?

Listed below are a number of organizations, which help and support people with Alpha-1. Each of these organizations works with individuals with Alpha-1 in different ways.

Alpha-1 Foundation

Toll Free: 877-2-CURE-A1 (228-7321) or 305-567-9888

Web Site: <http://www.alphaone.org>

The Alpha-1 Foundation is a not-for-profit organization founded by individuals diagnosed with Alpha-1 Antitrypsin Deficiency. Its mission is to provide the leadership and resources that will result in increased research, improved health, worldwide detection, and a cure for Alpha-1. Through its expanding research network of experts in Alpha-1 related research, it fosters research collaborations with investigators throughout the United States and Europe. It also works closely with the National Institutes of Health (NIH), the Food and Drug Administration (FDA), individuals affected with AAT Deficiency, and the pharmaceutical industry and other organizations to expedite the development of improved therapies and to jointly resolve critical issues in the field of Alpha-1 research and treatment. Since its inception in 1995, the Foundation has funded more than \$10 million in research grants, awards and programs at 28 institutions in North America and Europe. To obtain additional educational materials on Alpha-1, or free test kits, please contact the Alpha-1 Foundation.

Alpha-1 Association

Toll Free: 800-521-3025 or 202-887-1900

Patient Services: 800-425-7421

Web Site: <http://www.alpha1.org>

The Alpha-1 Association is a nonprofit, membership organization founded in 1991. This grassroots social enterprise represents and is governed by the community of people who are affected by Alpha-1. Our 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.

Alpha-1 Research Registry

Toll Free: 1-877-886-2383 or 843-792-0260

Web Site: <http://www.alphaoneregistry.org>

The Alpha-1 Research Registry was created to provide a population base for the research studies necessary to develop improved treatments for individuals with Alpha-1. The Registry, established in accordance with the recommendations of the World Health Organization, is a confidential database of individuals diagnosed with Alpha-1 and is the only active national registry of its type in the United States. The Medical University of South Carolina operates the Registry Data Management Center. Individuals diagnosed with Alpha-1 should consider participating in the Alpha-1 Research Registry by completing a Registry enrollment Questionnaire.

AlphaNet

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

Web Site: <http://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.

American Liver Foundation

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

Web Site: <http://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: <http://www.lungusa.org>

The American Lung Association 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 American Lung Association can also help you find information on smoking cessation programs that are available.



Individuals diagnosed with Alpha-1 are encouraged to join the Alpha-1 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.



Alpha-1 Research Registry

Call Toll Free: 1-877-886-2383

Visit our Website at alphaoneregistry.org



Alpha-1 Foundation

2937 S.W. 27 Avenue, Suite 302

Miami, Florida 33133

Telephone: (877) 2-CURE-A1 (228-7321)

Fax (305) 567-1317

Web Site: <http://www.alphaone.org>