Alpha$_1$-Antitrypsin (AAT) Deficiency:

A guide to counseling patients from testing to treatment

Provided by Grifols

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ALPHA-1 ANTITRYPSIN DEFICIENCY: HEALTHCARE PROVIDER'S GUIDE

COUNSELING PATIENTS

As you begin to screen for Alpha$_1$-Antitrypsin (AAT) deficiency, it is important for you to be able to explain the disorder in a clear and concise manner and encourage testing of your patients at risk. Through a simple blood test, you can identify affected patients and receive results within two weeks.

Following are scenarios that were developed to assist you in encouraging screening, giving test results, and explaining the various aspects of an AAT deficiency diagnosis.

Promoting Screening

Setting: In-Office Visit

Objective: Request Blood Sample

"As one of my patients with the diagnoses of (emphysema, COPD, bronchiectasis, liver disease, etc.), I am advising you to consider being tested for the genetic disorder AAT deficiency.

"AAT deficiency is believed to affect as many as 100,000 people in the US alone, making it one of the most common genetic disorders in this country. Since AAT deficiency was only recently discovered, there is much to learn about its frequency, severity, treatment, and prevention. I am advising you to consider this test because this information will be important to help me take better care of you as a patient. By taking the test, you will learn whether or not you have the genetic disorder called AAT deficiency. Early detection of AAT deficiency is very important because there are medical interventions I can prescribe that are specifically indicated to treat severe AAT deficiency. I can discuss these interventions with you. You may also find that a genetic counseling service can be beneficial at this time.

"The only way to be tested for AAT deficiency is to have a blood test. This test will only take a few minutes and uses a finger stick. The results generally require a two-week period of time to receive. Once the test results are back, I will contact you by telephone to come in for a follow-up visit to discuss your results.

"There may be some mild physical discomfort and risk of an infection from obtaining the finger-stick blood sample for the blood test. You may experience slight discomfort at the needle site, and there is a risk of a bruise.

"Your life could be affected by learning information that may be discovered by genetic testing. There may be additional risks, including emotional distress, which I cannot predict at this time. All of these issues should be carefully considered prior to being tested.

"Your choice to be tested is totally voluntary. You are free to refuse to be tested at any time.

"Again, as your doctor, I would be happy to answer any questions concerning AAT deficiency and your possible risk."

At this point, provide the patient with the brochure, "What Is Alpha-1?" (access at www.alpha-1foundation.org). Additionally, you may direct your patients to these resources for more information on informed consent:

- National Genome Research Institute (access at www.genome.gov/10002332)
- E-Medicine Health (access at www.emedicinehealth.com/informed_consent/article_em.htm)

Giving Test Results

Scenario A

Setting: Office Visit

Objective: Explain a Negative Test Result (Pi M) for AAT deficiency

"After reviewing the results of the blood test we performed at your last visit to determine if you had the inherited genetic disorder AAT deficiency, I am pleased to inform you that they were negative. This means that you have enough AAT in your blood and indicates that you do not have the disorder."

Despite the negative result, you should still advise patients that it is important to avoid all tobacco smoke, whether

it is from directly smoking tobacco products or situations where it is inhaled secondhand.

Scenario B

Setting: Office Visit

Objective: Explain a Carrier Test Result (Pi MZ or Pi MS) for AAT deficiency

"After reviewing the results of the blood test we performed at your last visit to determine if you had the inherited genetic disorder AAT deficiency, I must inform you that they were positive for a special state of the disorder known as the carrier state.

"Heterozygotes (carriers) have one normal gene and one gene for the disorder. This combination of genes does NOT typically cause health problems.

"Currently, your risk for lung or liver problems appears to be low. There have been inconclusive published research findings that have indicated that there may be a higher risk for developing chronic liver disease in the adult Pi MZ population, either alone or in combination with other liver diseases.

"However, it is recommended that you should inform your blood relatives of the test result because of the genetic nature of the disorder. Since AAT deficiency is passed genetically from parents to child, it is possible that your blood relatives could be heterozygotes (carriers) such as yourself, or have AAT deficiency."

Example:

If both parents are carriers, each child has a chance of inheriting AAT deficiency, being a carrier of AAT deficiency, and having both normal genes. Most importantly, you should advise patients that it is important to avoid all tobacco smoke, whether it is from directly smoking tobacco products or situations where it is inhaled secondhand. At this point, you can provide the patient with the brochure "A Guide for the Recently Diagnosed Carrier" (access at www.alpha-1foundation.org) and the Alpha-1 Research Registry questionnaires for family members.

Scenario C

Setting: Office Visit

Objective: Explain a Positive Test Result (Pi Z) for AAT deficiency and Its Consequences Adult Patient — Pulmonary Disease

"After reviewing the results of the blood test we performed at your last visit to determine if you had the inherited genetic disorder AAT deficiency, I must inform you that the results were positive for the disorder. Because these results are so important, we recommend confirming the results of this test with a second blood test. The amount of AAT in your blood is low and slightly different from the normal type. This test result explains some of the health problems that you are experiencing (or have experienced), including [symptoms specific to this patient, eg, coughing, wheezing, shortness of breath].

"I know that this can be upsetting news due to the impact that having this disorder may have on your health. However, with behavioral and lifestyle modifications such as not smoking, exercise, nutrition, drug therapy, medical treatments, specialized therapy for AAT deficiency, and preventive measures, alpha patients can and do lead full lives.

"Before we go into the explanation of what this means and the questions you may have, let me review the information we have about alpha-1 at the present."

A. Explain:

- The course of AAT deficiency
- The progression of AAT deficiency
- Consequences, including the genetic risk to the patient's family

B. Review information in the manual, "A Guide for the Recently Diagnosed Patient" (access at www.alpha-1foundation.org)

C. Schedule the next patient visit

D. Complete the treatment checklist

E. Provide information and questionnaires for each family member from the Alpha-1 Research Registry

Scenario D

Setting: Office Visit

Objective: Explain a Positive Test Result
Pediatric Patient — Liver Disease

"After reviewing the results of the blood test we performed at your last visit to determine if your child had the inherited genetic disorder AAT deficiency, I must inform you that they were positive for the disorder. The amount of AAT in your child's blood is low and slightly different from the normal type. However, your child's liver disease is not due to this low level of AAT in the blood stream. Research studies indicate that these liver complications are the result of the misfolded protein not being secreted properly into the blood stream. This backup of AAT in the individual liver cells causes damage to the liver."

At this time, there is no specific treatment for liver disease associated with AAT deficiency. Clinical care is primarily supportive management for any liver dysfunction and prevention of complications. Each child is an individual and treatment is highly individualized. Liver transplantation may be required. It is difficult to say if your child will definitely need a liver transplant. The majority of these children diagnosed with AAT deficiency have a low rate of disease progression and lead a relatively normal life for extended periods of time.

A. Explain:

- The course of AAT deficiency
- The progression of AAT deficiency
- Consequences, including the genetic risk to the patient's family

B. Review information in the manual, "A Guide for the Recently Diagnosed Patient" (access at www.alpha-1foundation.org)

C. Schedule the next patient visit

D. Complete the treatment checklist

E. Provide information and questionnaires for each family member from the Alpha-1 Research Registry

Scenario E

Setting: Office Visit

Objective: Explain a Positive Test Result
Adult Patient — Liver Disease

"After reviewing the results of the blood test we performed at your last visit to determine if you had the inherited genetic disorder AAT deficiency, I must inform you that they were positive for the disorder. The amount of AAT in your blood is low and slightly different from the normal type. Liver disease is the second most frequent health problem that may result from AAT deficiency. Cirrhosis (scarring) of the liver is the most common liver disease related to AAT deficiency in adults. While the exact cause is not known, research studies indicate that these liver complications are the result of the misfolded protein not being secreted properly into the blood stream. This backup of AAT in the individual liver cells causes damage to the liver."

At this time, there is no specific treatment for liver disease associated with AAT deficiency. Clinical care is primarily supportive management for any liver dysfunction and prevention of complications. Each patient is an individual and treatment is highly individualized. Liver transplantation may be required. It is difficult to say if you will definitely need a liver transplant or if one will become available. Augmentation therapy to replace this missing or deficient AAT protein will not help the liver.

A. Explain:

- The course of AAT deficiency
- The progression of AAT deficiency
- Consequences, including the genetic risk to the patient's family

B. Review information in the manual, "A Guide for the Recently Diagnosed Patient" (access at www.alpha-1foundation.org)

C. Schedule the next patient visit

D. Complete the treatment checklist

E. Provide information and questionnaires for each family member from the Alpha-1 Research Registry

At this point, make sure that you note your counseling discussion in your patient's medical record.

TREATMENT CHECKLIST FOR AAT DEFICIENCY

Many patients will experience emotional upset and anxiety due to their diagnosis. It may be necessary to schedule an additional visit in order to complete the discussion about recommended medical treatment and behavioral changes.

Initial Visit(s)

- Discuss baseline testing (with subsequent follow-up)
- Discuss requirement for lung function tests (FEV_1, etc.)
- Discuss need for baseline liver evaluation or referral to a GI/liver specialist (pediatric or adult)
- Discuss need for baseline lung evaluation or referral to a pulmonologist (pediatric or adult)
- Discuss the use of drug therapy for lung problems:
  - Use of bronchodilators
  - Use of corticosteroids
  - Treatment of lung infections
- Discuss treatment of liver complication symptoms
- Discuss the need for vaccinations:
  - Influenza (annual)
  - Pneumovax® (Pneumococcal Vaccine Polyvalent) (every six years)
  - Hepatitis A
  - Hepatitis B
- Assess smoking status and give a strong message to quit if patients smoke any form of tobacco, including cigars and cigarettes
- Discuss risk of occupational and environmental exposures, including secondhand tobacco smoke and dust
- Avoid being around exposed individuals who are ill with the flu or a cold, etc.
- Discuss alcoholic beverage consumption
- Discuss developing an exercise program
- Discuss developing a nutrition program
- Discuss reducing stressors

- Discuss referring patient to a counselor (if necessary)
- Contact and refer patients to the resources listed at the end of this guide

Subsequent Visit(s)

- Discuss requirement of follow-up visits
- Discuss augmentation therapy (specialized therapy for AAT deficiency)
- Discuss use of supplemental oxygen (if necessary)
- Discuss surgery options (if appropriate)
- Discuss referring patient to a counselor (if necessary)

AAT Deficiency Physician Resources

The Alpha-1 Research Program at the University of Florida in Gainesville was established by the Alpha-1 Foundation and is devoted to the study of lung and liver disease associated with AAT deficiency (alpha-1). The resources and services offered by the program are an important access point for the national and international medical and scientific communities.

Resources:

The Alpha-1 Translational Research Laboratory is devoted to characterizing the molecular mechanisms responsible for the development of liver and lung disease in AAT deficiency and to the development of new treatments.

The Alpha-1 Gene Therapy Program is focused on the development of safer and more efficient vehicles for the delivery of therapeutic genes to the liver, lung, and other tissues.

The Alpha-1 DNA and Tissue Bank serves the international scientific community with the largest single-disease collection of DNA and tissue samples for research studies in the United States.

The Bronchoscopy Research Procedure Unit and the Lung Cell Biology Laboratory enable clinical studies on the fundamental process associated with lung injury in individuals with AAT deficiency and determine the efficacy of new therapies.

The Alpha-1 Genetics Laboratory is an international reference laboratory for AAT levels and phenotype and genotype analysis. Testing is provided free of charge to patients throughout the world and includes:

- AAT genotyping, phenotyping, and blood concentration
- Follow-up and/or referral for specialized care
- Genetic counseling referral
- Alpha-1–specific patient educational resources

The Alpha-1 Florida Detection Program is a state-sponsored, statewide, targeted population screening for AAT deficiency. The Alpha-1 Florida Detection Program targets Florida residents with chronic obstructive pulmonary disease (COPD) and liver disease. The program is dedicated to raising awareness among Florida medical professionals, the media, and the public about AAT deficiency. Through this program, diagnostic testing for AAT deficiency is offered free of charge and appropriate referrals for education and clinical care are made. To learn more about this program, visit www.alpha-1foundation.org and click on “Get Tested,” or call 877-2-CURE-A1 (877-228-7321).

University of Florida College of Medicine
Telephone: 866-284-2708
Email: alpha1lab@medicine.ufl.edu
Web site: www.alphaone.ufl.edu

Grifols supports the National Alpha-1 Detection Program that facilitates the nationwide, targeted detection and diagnosis of AAT deficiency. Test kits and laboratory processing are provided free of charge to pulmonary clinics for their at-risk patients. The test is administered through doctors’ offices using a finger-stick test available from Grifols. Your test results will be mailed back directly to the requesting physician to ensure accurate interpretation. For healthcare providers wishing to obtain a Grifols AlphaKit test kit, please call 800-562-7222.

COMMUNITY ORGANIZATIONS & RESOURCES

There are a number of organizations which help and support people with AAT deficiency. Each of these organizations works with the AAT-deficient individual in different ways.

Alpha-1 Foundation

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

Web site: www.alpha-1foundation.org

The Alpha-1 Foundation is a not-for-profit organization founded by individuals diagnosed with AAT 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. This mission is achieved through the following programs and activities:

The Alpha-1 Research Grants and Award Program has funded to date nearly $39 million in research and programs at more than 70 institutions in the United States, Europe, and Australia.

The Alpha-1 Research Registry is a confidential database of AAT-deficient individuals and alpha-1 carriers that provides the population base eligible for clinical trials and research studies. The registry is administered by the Medical University of South Carolina.

The Alpha-1 DNA and Tissue Bank serves the international scientific community with the largest single-disease collection of alpha-1 DNA and tissue samples for research studies. It is located at the University of Florida College of Medicine.

The Alpha-1 Research Network provides support for and consultation with an international network of scientists who volunteer their time and expertise through service boards, committees, and working groups. The network is also composed of over 75 clinical resource centers, including pulmonary and liver centers where AAT-deficient individuals are referred for expert care and have the opportunity to participate in clinical trials and research studies.

Scientific meetings, conferences, workshops, working groups, and symposia focus on specialized topics to advance knowledge of AAT deficiency and address critical issues in the areas of improved treatments, education, detection, and ethical issues.

An Alpha-1 Detection Program promotes worldwide awareness and the identification of AAT-deficient individuals in population groups at high risk for AAT deficiency, such as adults with chronic obstructive pulmonary disease (COPD), chronic asthma, and/or chronic liver disease.

Public policy and advocacy government relations activities in Washington, DC, respond to the challenge of increasing research funding, addressing product shortages, ensuring blood safety, developing new therapies, and advocating for access to care, which includes insurance reimbursement and genetic discrimination.

The University of Florida at Gainesville Alpha-1 Research Program was established by the foundation as a resource to the medical and scientific communities.

AlphaNet

Telephone: 800-577-2638

Web site: www.alphanet.org

AlphaNet, a not-for-profit disease management company, currently employs 33 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 $35 million to support alpha-1 research and community programs.

COMMUNITY ORGANIZATIONS & RESOURCES (continued)

American Lung Association
Telephone: 800-548-8252
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.

COPD Foundation
Telephone: 866-316-COPD (866-316-2673)
Web site: www.copdfoundation.org

The COPD Foundation is dedicated to developing and supporting programs which improve the quality of life through research, education, early diagnosis, and enhanced therapy for persons whose lives are impacted by chronic obstructive pulmonary disease (COPD). The COPD Foundation has several programs dedicated to informing, empowering, educating, and engaging individuals affected by COPD, including both diagnosed and undiagnosed individuals, their families and friends, and their medical professionals.

Alpha-1 Association
Telephone: 800-521-3025
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, and advocacy, and to encourage participation in 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, and product safety and availability. The Association also encourages research and supports the programs of the Alpha-1 Foundation.

American Liver Foundation
Telephone: 800-465-4837
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.