Letter from the Director

by Charlie Strange, M.D.
Professor of Pulmonary and Critical Care Medicine, Allergy and Clinical Immunology
Medical University of South Carolina

Dear Registry Members,

Welcome to the 2005 fall/winter edition of the Research Registry Update! Much has happened in the Alpha-1 Community over the past six months. This edition of the newsletter is dedicated to keeping the community informed and, as always, we welcome your comments and questions to all of us on the Registry staff.

Included with the newsletter, you will find a quick study questionnaire by physicians at Brigham and Women’s Hospital in Boston who have seen a case or two of kidney disease occurring in Alpha-1 patients and are curious if this is more generalized. As always, we would like to see responses from those of you without kidney disease as well. These normal responses serve as a control group to see what the risk factors for Alpha-1 kidney disease might be if there is such a thing.

Discussions are underway to change some procedures in the Alpha-1 Coded Testing (ACT) Study. We have found that some individuals who receive home testing and are found deficient do not seek the services of a physician to assist with their disease. Some individuals diagnosed with PiZZ severe deficiency remain smokers. A discussion with the Ethical, Legal, and Social Implications (ELSI) Working Group of the Alpha-1 Foundation was held in October to assist in determining whether continued home testing is the best thing to do. That discussion led to a reevaluation of the practice of de-linking contact information. De-linking involves the removal of a person’s identifying information from the database. Once contact information is de-linked from study results, we are unable to obtain the follow-up needed to assure that appropriate testing outcomes are being achieved.

Another change being discussed is an analysis of whether longer term outcomes need to be followed, particularly of children who are tested in the program. You may remember that the current protocol allows for five years of continuing follow-up. The suggestion was made by ELSI to continue follow-up without a time limit since it is impossible to predict the outcome of the political discussions concerning genetics and the insurance industry.

Lastly, the ACT study is changing its policies concerning rare allele testing. You may remember that the home finger stick test can look for the common deficient genes that cause Alpha-1 Deficiency. The S gene and the Z gene are the two most common deficiency genes; both of these are tested in every finger stick sample. However, when the Alpha-1 level is low but the S or Z gene is not present, then further testing is needed. These further tests are quite expensive for Dr. Mark Brantly’s Alpha-1 genetics lab in Gainesville, Florida. Sequencing of the Alpha-1 gene is often needed. Because these are anonymous samples to him from the ACT Study, some of these samples do not make it into the Alpha-1 Foundation’s DNA and Tissue Bank despite our best efforts to get these rare samples included. Therefore, the ACT study will inform participants when a rare gene is suspected. However, a blood tube sample will need to be submitted to the DNA and Tissue Bank in Florida for any further work up to continue. This program should bring enhanced collaboration between the ACT study and the DNA and Tissue Bank as core Foundation programs.

We remain happy to receive comments from the community about these proposed changes and will report any of your comments to the ELSI Working Group should you care to contact us.

There are two articles in this newsletter that report on the follow-up to the differences between Aralast and normal alpha-1 antitrypsin. We did circulate these articles to some Alphas in the community for a review before they were published in an attempt to be unbiased in the reporting of drug issues. The last thing we desire is to be alarmist. The important messages we will try to convey as facts. We realize that there is no good forum to keep the dialogue open other than the Registry newsletter and will commit to reporting on drug development issues of importance in this place.

Thank you for your continued interest in the publication. I thank Dr. Chris Cooper for his articles featuring UCLA in this edition of the Registry newsletter.

Sincerely,

Charlie Strange, M.D.
Walsh Receives Health Foundation Concern Award

Hometown Hero with Global Reach

John W. Walsh, president, CEO and co-founder of the Alpha-1 Foundation, was named one of two winners of the 2005 Concern Awards presented by the Health Foundation of South Florida. The award, which includes a $25,000 grant, recognizes South Floridians working to improve healthcare and health education in the community.

“It’s an honor to be recognized by the Health Foundation of South Florida for work to which I’ve dedicated my life,” said Walsh, who begins a term as chairman of the National Health Council in January. He was described as a hometown healthcare advocate with national and international scope. “This award is especially meaningful because, as a result of the Health Foundation’s early investment in our research infrastructure, we have been able to make a significant impact on Alpha-1 throughout the world.”

According to Health Foundation Board Member James Eckhart, a panel of community judges reviewed nominees submitted by community organizations and individuals. “They selected individuals whose invaluable contributions have enhanced the wellness and quality of life for people in Broward, Miami-Dade and Monroe Counties,” Eckhart said.

In 1989, Walsh was diagnosed with Alpha-1 Antitrypsin Deficiency, a condition that is passed on from parents to their children through genes and can cause serious lung and/or liver disease. There may be up to 100,000 people with Alpha-1 in the United States. An estimated 20 million people are “carriers,” who don’t have symptoms but may pass the defective gene on to their children.

Since its inception in 1995, the Alpha-1 Foundation has invested more than $23 million to support Alpha-1 research and research-related projects, which includes funding grant awards to more than 45 academic and research institutions in North America and Europe.

Walsh’s tireless dedication has put Alpha-1 in the national spotlight and increased international awareness of the disorder. Thanks to his efforts, advocates for rare genetic disorders have a voice.

The award was presented during a Dec. 2 luncheon at the J.W. Marriott Hotel in Miami.
Featured CRC

Alpha-1 program at UCLA COPD Center Provides Resources for West Coast
by Christopher B. Cooper, M.D.
Medical Director, UCLA COPD Center

With the increasing worldwide awareness of chronic obstructive pulmonary disease (COPD), it has become recognized that this group of diseases is treatable and in some cases preventable. Recent research has drawn attention to novel medical and surgical treatments for emphysema. We appreciate that emphysema is caused by a combination of genetic factors that place a person at greater risk for oxidant lung injury and harmful exposures such as tobacco smoking or environmental pollution. Alpha-1 Antitrypsin Deficiency is the best known genetic factor that predisposes individuals to the development of emphysema. While Alpha-1 only accounts for a small percentage of cases of emphysema, it is estimated that about 100,000 Americans have the disease. At the UCLA Medical Center, we are pleased to be part of the nationwide network of Clinical Resource Centers that provide services for patients with Alpha-1.

UCLA COPD Program

UCLA Medical Center is a large university teaching hospital that functions as a tertiary referral center for a substantial catchment area of patients in the southwestern United States. Over the past five years, in its evaluation of hospitals, US News and World Report magazine has consistently ranked UCLA Medical Center as the “Best in the West”. Within the medical center itself is the UCLA COPD Program. This program consists of a specialty outpatient clinic staffed by six attending pulmonologists with special interests in COPD. The clinic has three clinical research nurses and a database of several thousand COPD patients. The COPD program has featured prominently in COPD-related research and clinical advances in recent years. For example:

• The Lung Health Study: UCLA Medical Center was one of the principal centers in the nationwide Lung Health Study that evaluated the effects of smoking cessation, bronchodilator therapy and inhaled corticosteroids on the progression of COPD in about 6,000 patients.

• UCLA Pulmonary Fitness and Rehabilitation Program: Rehabilitation exercise in the form of a structured exercise program is vitally important for patients with all types of chronic lung disease. Established in its present format in 1994, the UCLA Pulmonary Fitness and Rehabilitation Program uses scientific principles of exercise assessment and prescription, both aerobic and resistance exercises, to recondition the patient and restore their optimal physical and social functioning.

• Transtracheal Oxygen Therapy: Some patients with advanced forms of lung disease cannot achieve adequate blood oxygen levels with conventional oxygen administration via nasal cannulae and facemasks are too intrusive. These are the type of patients who might benefit from transtracheal oxygen delivery via a thin catheter in the neck. UCLA remains active as a center providing transtracheal oxygen therapy for patients with refractory hypoxemia. The technique roughly halves the amount of oxygen needed as compared with nasal cannulae and thus allows patients greater mobility as well as an improved appearance.

• FORTE: Researchers at UCLA were the first to investigate the effects of drugs called retinoids that were thought to potentially help regeneration of the lungs in patients with emphysema. This research now continues in the form of a nationwide multi-center clinical trial in which UCLA is the lead center.

• Lung Volume Reduction Surgery: UCLA Medical Center participated in the National Emphysema Treatment Trial (NETT) and is one of the centers currently approved by the Center for Medicare and Medicaid Services (CMS) for the performance of these operations. Our physicians routinely evaluate patients for this type of treatment and recognize the importance of careful patient selection to optimize the benefits and minimize the risks.

• UCLA Lung Transplantation Program: The lung transplantation program at UCLA Medical Center has grown in recent years to be one of the leading centers in the nation in terms of its number of transplants per year and also the favorable survival statistics. Physicians from the Division of Pulmonary and Critical Care Medicine support the lung transplantation program and routinely evaluate our patients who have severe COPD, including emphysema.

• UCLA Liver Transplantation Program: The liver transplantation program at UCLA, established over 30 years ago, is foremost in the world and currently performs more than 300 transplants per year. End-stage liver disease is rare in Alpha-1, but liver function is an obvious concern. UCLA has considerable expertise in the management of cirrhosis and hepatologists associated with the UCLA Liver Transplantation Program are available to assess Alpha-1 patients.

Alpha-1 Involvement at UCLA

Here at the UCLA COPD Program, we are proud to be a part of the nationwide network of Clinical Resource Centers for patients with Alpha-1 Antitrypsin Deficiency. With this honor goes our commitment to make available all of the impressive resources of the UCLA COPD Program to patients with Alpha-1 disease. Our goal is to unite these patients in Southern California and to build a center that provides for their needs as well as for their interactions with each other and between their families. We currently provide Alpha-1 testing and replacement therapy as well as pulmonary rehabilitation and transplant evaluation. Over the past two years, we have partnered with the Alpha-1 Foundation to provide annual patient education days. They were held in March 2004 and 2005 and are now established as an annual event. The program typically consists of presentations by one or more nationally recognized speakers, patient advocates and local healthcare providers affiliated with the UCLA COPD Center. For example, last year we invited the Surgical Director of the UCLA Lung Transplantation Program and Dr. Alan Barker, from Oregon Health Sciences University, who is an expert on Alpha-1 and bronchiectasis. As we move ahead, we look forward to serving more Alpha-1 patients by offering the highest standard of up-to-date clinical care as well as the opportunity to participate in novel experimental treatments as they emerge for patients with Alpha-1 or emphysema in general.
**Trends in the Diagnosis of Symptomatic Patients With Alpha-1 Antitrypsin Deficiency Between 1968 and 2003**

by Michael Campos, M.D.

University of Miami Miller School of Medicine

Every few years, a new study is performed to highlight the Alpha-1 Community. The typical questions that are asked include ages, presentation, time until diagnosis and onset of symptoms. A recent study that many of you may have participated in was published in the journal “CHEST.”

Recently, a study of 1,020 members of AlphaNet was conducted. Questionnaires were given to each member of the study group. Since all participants reported symptomatic lung disease at the time of diagnosis, an initial baseline questionnaire contained questions devoted to the diagnosis of Alpha-1. The questions included: age at diagnosis, year of diagnosis, years with symptoms before diagnosis, the number of physicians seen before correct diagnosis, and general demographic, clinical, and epidemiological data.

The study observed that 15% of the subjects received a diagnosis after diagnosis was made in a relative. Three quarters had a physician diagnosis of chronic obstructive pulmonary disease (COPD) or emphysema, and nearly half reported a diagnosis of asthma with (39.1%) or without (41.1%) COPD.

The average age of the individuals responding was 54.2 years and the number of years since their diagnosis of Alpha-1 was 8.3 years. Most of the diagnoses were made in individuals between 40 and 49 years of age, but up to one fourth were diagnosed after age 50. Since the study encompassed diagnoses of Alpha-1 done during the past 50 years, it analyzed differences in the diagnostic experience of Alphas over time. One of the most important findings is that Alphas diagnosed in recent years are significantly older than before. This also correlated with the number of physicians seen and the amount of time an individual had symptoms until the correct diagnosis of Alpha-1 was made (both increasing over time). The average number of physicians seen by the study group was 2.7. One third reported a correct diagnosis by the first physician, and another third by the second physician, while one fifth had to see four or more physicians before being correctly diagnosed with Alpha-1.

This study shows that early detection has not improved over time, but the diagnosis has increased in older patients with advanced disease. A diagnostic delay is still present, and efforts to increase Alpha-1 awareness are needed to emphasize early diagnosis among healthcare providers and patients.

We hope that the article helps get the word to pulmonologists who read “CHEST.”


**AlphaNet Study Highlights:**

- 15% diagnosed after a relative received a diagnosis
- Three quarters diagnosed with COPD or emphysema
- Nearly half reported a diagnosis of asthma
- Average age of respondent: 54.2
- Average number of years since diagnosis of Alpha-1: 8.3
- Most were between 40 and 49 years old, but up to 25% were diagnosed after age 50
- Average number of physicians seen by the study group: 2.7
Alpha-1 After 60

by Laura Schwarz
Coordinator, Alpha-1 Research Registry

When Alpha-1 associated emphysema was first described, researchers discovered emphysema in young individuals and in individuals who did not smoke. Many physicians hear about this classic description of the disease while going through medical school and do not learn about the rest of the story: that Alpha-1 associated emphysema can present after the age of 60. Therefore, some physicians are not inclined to test patients over 60 years of age, even if they have advanced Chronic Obstructive Pulmonary Disease (COPD).

The other finding that has been discovered after studying large groups of Alphas is that there appear to be only small clinical differences in the lung disease of COPD that occurs from smoking and the COPD that occurs in Alpha-1 patients. Since augmentation therapy with Prolastin, Zemaira, or Aralast is the treatment most widely prescribed to Alphas, these patients being treated for emphysema would not have received the optimal treatment for their disease.

Our Alpha-1 Research Registry has 2,879 members as of Sept. 30, 2005. It allows us to look at the demographics of individuals diagnosed with Alpha-1 and individuals identified as Alpha-1 Carriers. For example, the total population of ZZ genotypes recorded in our registry is shown at right.

As you can see in the graph, a significant number of people age 60 and above have a severe deficiency of Alpha-1. The Registry is interested in clinically researching this age group to promote the relevance of Alpha-1 testing to physicians and the general population alike. In an initial evaluation of Registry participants over age 60, we find a heterogeneous group including some patients with lung disease, some with liver disease, and some that record no diseases.

The Alpha-1 Coded Testing (ACT) study doesn’t put an age limit on who can be tested. It is interesting that 559 individuals older than 60 years of age performed the test over the last 4 years. The percentage of those individuals who are diagnosed with a ZZ genotype (4.5%) actually may be higher than the percentage under age 60 diagnosed with a ZZ genotype (2.6%).

In summary, the Registry is beginning a series of studies to disprove the notion that age should be considered before testing an individual. Should one of our questionnaires arrive on your doorstep in the near future, please take the time to fill it out.

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Alpha-1 Foundation Research Registry PiZZ Population Compared to the General U.S. Population

![Graph showing percent of population by age group and ZZ genotype distribution between the general U.S. population and the current Registry ZZ population.](image-url)
Differences between Alpha-1 Products

by Charlie Strange, M.D.
Chairman, Medical and Scientific Advisory Committee,
Alpha-1 Foundation

When two independent laboratories found biochemical differences between the Alpha-1 augmentation product Aralast compared to normal circulating alpha-1 antitrypsin in the fall of 2004, the Alpha-1 Foundation felt a duty to inform the community. The letter generated and disseminated to the Alpha-1 Community promised that the differences would be explored and that further communication would be forthcoming. This article is an attempt to educate the Alpha-1 Community about the science that has evolved over the past six months and describe the continuing work that will follow.

On Sept. 27, 2005, partial results of the follow-up studies were presented to some members of the Medical And Scientific Advisory Committee (MASAC) to the Alpha-1 Foundation and representatives of the Food and Drug Administration (FDA) and the Center for Biologics Evaluation and Research (CBER) in Bethesda, Maryland. The science that was presented was performed in laboratories of Baxter Pharmaceuticals, the makers of Aralast, in Vienna, Austria. In addition, Baxter hired consultants in the United States and in Europe to perform specific tests on different parts of the drug.

Missing One of 394 Amino Acids

The data presented showed that the difference originally noted between Aralast and naturally occurring alpha-1 antitrypsin, as well as between Aralast and the other two products available to treat Alpha-1 in the United States (Prolastin and Zemaira), was that most of the protein in Aralast is missing one of the 394 amino acids that makes up the alpha-1 antitrypsin protein. The details of this difference in the last lysine amino acid are described in the accompanying article by Dr. Mark Brantly on page 7. However, also presented at the meeting was data suggesting that Prolastin and Zemaira also have a small amount of this altered protein in their products, but this has not been confirmed by an independent lab.

Further differences between the products were presented, including differences in carbohydrate side chains (sugar molecules that cling to the side of the amino acid backbone), and differences in the cysteine amino acids. The clinical consequences of these differences remain unknown. However, multiple labs agree that all of these products effectively inhibit human neutrophil elastase, the major destructive chemical in the lungs of Alpha-1 patients with emphysema.

Clinical consequences of these differences remain unknown.
An extensive discussion followed the scientific presentation. Some of the attendees expressed concerns about Aralast. There is a possibility that some unwanted functions of the predominant Aralast version of the alpha-1 antitrypsin protein are yet to be detected. In the following article by Dr. Brantly, some of the concerns are listed. One of the byproducts of speeding licensure of products for rare diseases by the FDA is that small numbers of Alphas are studied for a relatively short time to prove that the therapy works. Since the safety of a product usually requires a long period of time to establish, studies are always done after drug licensing to assure that safety of a new product is established.

The next step in the continuing story of the differences between the products will be the announcements of followup studies to assess long term safety. The story of differences between Alpha-1 products will not end here. The important role that experts in Alpha-1 can play is to assure that safety studies are well conducted and that the Alpha-1 Community is well informed about the results as they develop.

Multiple labs agree that all of these products effectively inhibit human neutrophil elastase, the major destructive chemical in the lungs of Alpha-1 patients with emphysema.

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**Summary of the Known Aralast Biochemical Difference from Normal AAT and Its Potential Implications**

*by Mark Brantly, M.D.*

*University of Florida College of Medicine*

**Editors Note:** I apologize in advance that this article has some biochemical jargon that some will find difficult to understand. However, for the scientists among us that want to know more about Alpha-1, I did not want to dilute the message either.

*Charlie Strange, M.D.*

**Background** Alpha-1 antitrypsin (AAT) is a 394 amino acid glycoprotein (protein with sugar side chains). A traditional way that AAT physical characteristics are determined is by studying this protein’s movement on very thin gels that allow for separation of glycoproteins by their charge. Typically, proteins have electrical charges between positive 3 and negative 3. At any given pH (acid environment) a protein will either be negatively charged, positively charged or have no net charge. Native (normal) AAT has no charge in the pH range of 4-5. The pH at which a protein has no net charge is called its isoelectric point. This is an important biochemical characteristic. The charge of proteins and glycoproteins often plays a major role in their function, bio-distribution and disposal in biological systems. AAT separates into its different isoforms based on the amount and type of sugars on the protein and modification of the protein after it is released from the liver cell.

Normal AAT, called MM (normal variants include M1M1, M1M2, M1M3, M2M2, M2M3 and M3M3) migrates in the middle of the gel centered at a pH of about 4.5 (figure 1).

Normal AAT typically has 5 bands representing AAT isoforms that may be identified on these gels. These isoforms are the 2, 4, 6, 7 and 8 bands (figure 1). Different variants of AAT (like ZZ) have different migration locations in an IEF gel corresponding to their specific isoelectric point. There are approximately 100 different variants of AAT that have been identified. They are named alphabetically from A to Z. Variants with isoelectric points nearest pH 4 are A, B, C etc. Variants with isoelectric points nearest pH 5 are V, X, Y and Z (figure 1).

(Continued on page 8)
AAT purified from a pool of human volunteers and used for augmentation therapy should be 99% MM (and mostly M;M) and have the typical migration pattern on IEF gels of MM (figures 1 & 2). All manufacturers of AAT studied to date, except Baxter (augmentation product: Aralast), have an MM pattern consistent with the pool of volunteers that have donated plasma for purification (figure 2).

More than 67% of all of the Aralast AAT protein is of a different migration pattern than normal pooled human AAT. This migration pattern is in the range of “E” variants. Normally, AAT deficient individuals have an M;Z migration pattern after augmentation with purified pooled human AAT.

Figure 1: Lanes with sample type, left, M standard bands, right, Z standard bands. Figure 2: Arrow A, lane of ZZ subject augmented with Aralast; Arrow B, lane of ZZ subject on Prolasin.

The University of Florida Genetics Laboratory discovered it while screening DNA Bank samples from blood submitted by AAT deficient individuals receiving Aralast augmentation therapy. This finding, after confirmation, was reported to the FDA, the Alpha-1 Foundation and each Aralast treated individual submitting a sample to the bank. The Temple University AAT laboratory identified a similar finding in subjects on Aralast and the results were reported to Baxter and the Alpha-1 Community.

Possible Implications of the Modification of Augmentation Products
It is possible that this modification has no significant health risks. Potential concerns which have not been thoroughly investigated include:
1) Altered half-life of drug (longer or shorter time in the blood stream).
2) Altered bio-distribution compared to normal AAT (different organ distribution and/or clearance mechanisms).
3) Increased antigenicity (ability of the protein to cause antibody formation) and secondary consequences of this antibody formation. (This is very unlikely since there are multiple amino acid changes which occur in AAT proteins. Blood and plasma treatments often have different forms of AAT which have, to date, not been found to cause the development of immunity to AAT).
4) Abnormal organ function due to abnormal bio-distribution or clearance of the modified AAT.

Conclusion
The AAT preparation Aralast, likely has been modified during the manufacturing process. It is unknown whether this modified preparation of AAT has clinical differences from the other currently available forms of AAT on the market.

Cause of the Aralast Isoelectric Point Difference
The cause of the migration/isoelectric point difference has been determined by a team of scientists at Baxter’s R&D labs in Vienna. The difference is caused by the loss of a single amino acid at the very end of the protein. The amino acid missing is a lysine, which is normally positively charged. When the positively charged amino acid is no longer present in the AAT protein, the net charge is more negative causing a shift in the migration of the protein on IEF gels. The loss of the last amino acid is caused by an enzyme(s) called a carboxypeptidase(s). Carboxypeptidases are a family of enzymes in very low concentration in human plasma that are important in some biological reactions.

How was this Difference Discovered?
This difference was discovered independently in two laboratories.
Development
by Angela McBride
Development Officer
Alpha-1 Foundation

Building Friends for a Cure continues attracting the support of Alphas nationwide

The Alpha-1 Foundation’s community friend-building campaign launched with many Alphas already committed to the cause. The campaign supports Alphas as they network with neighbors, friends, and local and regional media to build awareness and raise funds.

Alphas are playing a large role in raising revenue to support the mission and programs of the Alpha-1 Foundation. Alphas have committed to raise funds through an array of different activities including coupon books, golf tournaments, parties, garage sales and more.

Alphas interested in participating in the Building Friends for a Cure campaign can choose what type of commitment they want to make and how they would like to execute such commitment. As John W. Walsh, president and CEO of the Alpha-1 Foundation, eloquently says, “just imagine the cumulative fundraising power of each Alpha networking with just a handful of his or her friends and acquaintances. One Alpha asking 20 friends for a $50 contribution would raise $1,000.”

The Alpha-1 Foundation can help every step of the way. It has assembled a complete guide, offering detailed information and ideas for fundraisers, recruiting a committee to help, outlining a budget, and using resources available from the Foundation. For a free copy of “Building Friends for a Cure,” contact the Foundation’s Development Officer, Angela McBride, at (888)825-7421 ext. 233 or amcbride@alphacine.org.

Communications

Alpha-1 Foundation celebrates 10th Anniversary with a brand new look

With the advent of its 10th Anniversary, the Foundation’s brochures and other printed materials are being updated with new graphics and colors. To this end, three distinctive lines of brochures have been created:

- Educational Materials: The family of brochures that constitute the following resource materials: “What is Alpha-1?” “A Guide for the Recently Diagnosed Individual,” “A Guide for the Recently Diagnosed Carrier,” “Issues In End-Of-Life Care,” and “The Liver and Alpha-1 Antitrypsin Deficiency.” Educational grants were provided by AlphaNet, Centric Health Resources, and Telecris Biotherapeutics for many of these publications.
- Program Materials: This is the family of brochures that constitute the following publications: “Taking Part in Alpha-1 Research,” “University of Florida Alpha-1 Foundation DNA & Tissue Bank,” “The Alpha-1 Research Registry,” “The Alpha-1 Coded Testing (ACT) Study,” and “Family Linkage in the Alpha-1 Research Registry.”
- Outreach Materials: These materials include the Annual Report, “Alpha-1-To-One” magazine, and all general fundraising brochures. The purpose of these brochures is to raise funds to fulfill the Foundation’s mission.

Information and Education
by Linda Rodriguez,
Information & Referral Coordinator
and Laura Stuart Wall,
Health Education Coordinator
Alpha-1 Foundation

National Targeted Detection Program is increasing Alpha-1 awareness

Early this year, the Alpha-1 Foundation launched Phase II of its National Targeted Detection Program (NTDP) with a new emphasis on direct-to-consumer efforts. The program, implemented in Florida, which has the nation’s 4th largest COPD population, served as a test to determine whether the COPD population would be responsive to requesting information about Alpha-1 Antitrypsin Deficiency.

The Florida test supported the fact that direct-to-consumer efforts drive information requests. It showed 54% of all calls within a 30-day period to Information and Referral at the Alpha-1 Foundation were from Florida residents. This was an overwhelming increase in calls from Florida and in the total overall requests. An awareness campaign directed toward healthcare professionals was also implemented.

Based on the success of the Florida test, the Foundation launched similar initiatives in New York, New Jersey and Pennsylvania with the objective of confirming the Florida efforts. The results were as follows, in terms of physicians and respiratory therapists:

- The Foundation distributed e-mail messages to approximately 55,000 physicians with an interest in respiratory and/or liver functions. Another 17,000 messages were distributed to respiratory therapists in the tri-state area. Results from the e-mail distribution showed a 700% increase in visits to the www.shortofbreathgettested.org website compared to the previous month.

(Continued on page 10)
Advocacy and Public Policy

by Miriam O'Day
Senior Director of Public Policy
Alpha-1 Foundation

Ensuring that Pulmonary Rehabilitation will be provided to Medicare Beneficiaries

The treatment of chronic lung diseases such as Alpha-1 and Chronic Obstructive Pulmonary Disease (COPD) are frequently complicated, confusing and frustrating for patients, family members and those who care for them. Pulmonary rehabilitation combines education with therapeutic exercise and functional activities to help individuals understand and cope with the disease and function more comfortably and independently.

We continue to hear from individuals with Alpha-1 about the amazing improvements in lung health that pulmonary rehabilitation has provided. Learning to exercise regularly while respecting the body's health limitations is beneficial for all adults, not just those with pulmonary problems.

It is because pulmonary rehabilitation can have tremendous benefits for Alphas that the Alpha-1 Foundation commends Senator Mike Crapo (R-ID) and Senator Blanche Lincoln (D-AR) for introducing the "Pulmonary and Cardiac Rehabilitation Act of 2005 (S.1440)," designed to provide a national coverage policy ensuring that individuals are not denied or limited access. Often pulmonary and cardiac rehabilitation programs are services covered by Medicare under the "incidental to physician services" clause. However, S.1440 will end the debate between the Centers for Medicare and Medicaid Services (CMS), fiscal intermediaries and providers, by clearly defining pulmonary rehabilitation for Medicare recipients.

To advocate for Alpha-1 and the lung disease community, those interested may take action by asking senators from their states to co-sponsor S.1440.

Campaign to Preserve Medicaid

The Foundation was invited to participate in a special project with the National Health Council (NHC) as part of their ongoing Campaign to Preserve Medicaid. This special project is being conducted by the NHC in collaboration with the Georgetown University Health Policy Institute. Georgetown researchers created a Medicaid Beneficiary Questionnaire to measure the impact on chronic disease patients and illustrate personal stories that will elucidate the burden severe Medicaid cuts will have on current beneficiaries. The Georgetown report will be used in education and lobbying efforts with members of Congress and their staff. Thanks to the good work of the AlphaNet Coordinators who identified patients willing to participate, Alpha-1 will be featured in the study. The NHC will publicize the Georgetown report with a press conference on Capitol Hill featuring Alpha-1 Foundation President and CEO John W. Walsh and many of the chronic disease patients highlighted in the study.
Q. Is a regular exercise program helpful for Alpha-1 patients?

A. An attempt to maintain physical fitness is crucial for everyone who wishes to maintain a healthy, productive and longer life. Indeed, large population studies like the Framingham study have identified lack of physical exercise as a risk factor for cardiovascular disease and lack of physical fitness as a condition that can ultimately cause death. Besides these risks, inability to perform exercise, whether for pleasure or simple activities of daily living, is considerably debilitating and compromises many of the joys of life.

These facts are especially true for patients with chronic lung diseases including Alpha-1 Antitrypsin Deficiency (Alpha-1). When we become deconditioned or out-of-shape, several disadvantageous changes develop in our ability to perform exercise, including normal daily activities. Deconditioned muscles are weaker and when exercised tend to accumulate lactic acid earlier than if they were better conditioned. This lactic acid stimulates breathing and generates more carbon dioxide in the blood. The need for increased breathing places greater demands on the lungs, which can obviously be problematic for patients such as those with Alpha-1 who may already have compromised lung function due to emphysema. A good exercise program can reverse many of these problems, leading to reduced breathlessness, improved exercise capacity and better quality of life.

Exercise programs for patients with chronic lung diseases are usually provided by Pulmonary Rehabilitation Programs. These are typically hospital-based, outpatient programs offering supervised exercise training two or three times per week. The sessions should be customized to take account of the needs of the individual patient but also scientifically-based, utilizing a well-formulated exercise prescription. Each session should begin and end with a routine of stretching exercises to warm-up and cool-down. These exercises are important to avoid muscle injury during the more intense exercises to follow and also to improve flexibility, which is an important but often overlooked aspect of physical fitness. Thereafter, the goal should be to accumulate at least 30 minutes of moderate intensity exercise at each session (at least three times per week). Moderate intensity means a heart rate in the 100-120 beats per minute range, but this has to be carefully judged based on individual clinical assessment. Supplemental oxygen is helpful for many patients during these sessions since it allows them to achieve higher exercise intensity for longer periods and thus to derive more benefit.

Strengthening, or resistance, exercises are also important and provide for a balanced reconditioning program. Many would argue that muscle strength is equally as important as aerobic capacity when it comes to activities of daily living. Increased muscle strength, while not contributing to a higher aerobic capacity, does increase agility and help with joint stability. One surprising fact about resistance training is its beneficial effect on weight management. One pound of lean muscle, which is metabolically active 24 hours per day, burns as many calories in a week as going on a one-hour walk at three miles per hour. Thus, by building up lean body mass, or muscle, there will be a tendency to metabolize, or burn off fat, and this advantage lasts as long as the increased muscle mass is maintained.

Exercise programs provide a positive stimulus in the never-ending balance between physical fitness and disability. Clinical programs, which often last six or eight weeks, help reverse deconditioning and get patients back on the right track toward a higher level of physical ability. However, it does not end there. As we all know, the effort to maintain physical fitness needs to be continuous and maintenance exercise programs are just as important as intensive programs. Many hospital-based programs offer maintenance sessions on a nominal, self-pay basis. However, patients with less severe disease should become comfortable exercising on their own or with others on a regular basis. Joining a local health club is a reasonable option to consider.

The goal should be at least 30 minutes of moderate intensity exercise at least three times per week.
Coming Up...in 2006

Education Days, Events and Meetings

The following calendar features a partial list of events. Education Days are also planned for the following cities but dates have not yet been confirmed: Gainesville, FL; Nashville, TN; Milwaukee, WI; San Francisco, CA; Chicago, IL; Pittsburgh, PA; Boston, MA; Ann Arbor, MI; and Los Angeles, CA. For more current listings, check the website at www.alphaone.org.

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<tr>
<th>DATE</th>
<th>EVENT</th>
<th>LOCATION</th>
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<td>January 26-28</td>
<td>American Association for the Study of Liver Diseases (AASLD)/Alpha-1 Antitrypsin Deficiency And Other Liver Diseases Caused By Aggregated Proteins</td>
<td>Atlanta, GA</td>
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<td>March 4</td>
<td>Arizona COPD &amp; Alpha-1 Education Day</td>
<td>Tucson, AZ</td>
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<td>March 25</td>
<td>University of Texas Alpha-1 Education Day (Alpha-1 Foundation Clinical Resource Center)</td>
<td>Tyler, TX</td>
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<td>April (TBD)</td>
<td>San Francisco Alpha-1 Education Day</td>
<td>San Francisco, CA</td>
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<tr>
<td>June 23-25</td>
<td>Alpha-1 Association National Conference</td>
<td>San Diego, CA</td>
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The Alpha-1 Foundation, Alpha-1 Association and COPD Foundation extend their gratitude to the following organizations that are providing unrestricted educational grants for the 2006 COPD & Alpha-1 Education Day Series: AlphaNet, Boehringer-Ingelheim and Pfizer, Centric Health Resources, Talecris Biotherapeutics, ZLB Behring and Baxter Healthcare, a series exhibitor for the Alpha-1 Education Series.

*Commitments and dates are subject to change.

AAT Standards Workshop

The Alpha-1 Foundation organized an international scientific workshop, "Development of a Functional and Antigenic Alpha-1 Antitrypsin (AAT) Standard," on April 8, 2005. Support for this conference was provided by unrestricted educational grants from: AlphaNet, Amriva Pharmaceuticals, Inc., Baxter Bioscience, GTC Therapeutics, Grifols Biologicals, Grifols Biosciences, Kamada, Ltd., Octapharma Pharmazeutika Produktionsgmbh, Talecris Biotherapeutics, and ZLB Behring.

The 9th in a series of Gordon Snider Critical Issue Workshops, this meeting brought together scientists from academia, industry and pertinent regulatory agencies in the USA and Europe. The conference was Co-Chaired by Mark L. Brantly, M.D., University of Florida College of Medicine, Alpha-1 Research Program director, and N. Gerald McElvaney, M.D., F.R.C.P.I., F.R.C.P.C., Royal College of Surgeons, Dublin.

The goal of this workshop was to establish a consensus among experts on the development and implementation of a functional and antigenic AAT standard. This standard will be made available to all interested parties for the purpose of standardizing AAT characterization for augmentation therapies. This standardization will help to accelerate the development of therapies for alpha-1 antitrypsin deficient individuals and will promote a greater level of coordination among those working on the manufacture of AAT worldwide.

Jim Travis, PhD, a University of Georgia research professor, and Friedrich Kueppers, M.D., a Temple University professor and international leader in AAT biochemistry, genetics and medicine, were honored during the workshop for Excellence in AAT Research for their outstanding contributions.

Alpha-1 Foundation

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 Antitrypsin Deficiency (Alpha-1). The Foundation has invested more than $23 million to support Alpha-1 research and research-related projects, which includes funding grant awards to more than 45 academic and research institutions in North American and Europe.

AlphaNet

AlphaNet, Inc. is a unique disease management organization. Through its medical and operations staff, AlphaNet provides a wide range of integrated support services to individuals with Alpha-1 Antitrypsin Deficiency who require augmentation therapy, oversees and sponsors clinical trials involving Alpha-1 therapies, and makes available a comprehensive disease management and prevention program to improve the quality of life of those affected by Alpha-1.

Alpha-1 Association

The Alpha-1 Association is a member-based not-for-profit organization founded in 1991 to identify those affected by Alpha-1 Antitrypsin Deficiency and to improve the quality of their lives through support, education and advocacy. The Association has a network of over 60 volunteer-led support groups around the U.S.