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 Spring/Summer Edition of the Alpha-1 Foundation Research Registry Newsletter. This edition has a number of progress reports on new research initiatives. Among the many projects ongoing in the Alpha-1 community, the search for an accurate and timely measure of emphysema progression is among the most important.

One of the important factors in research is that we never want to waste any research money on studies that are already in progress somewhere else in the world. For that reason, an important Alpha-1 study is concluding this fall in Europe that will study the use of alpha-1 augmentation therapy (Prostastatin) for 2 years. This study is using computed tomography (CT) scans to look at lung density (how much emphysema is present) with or without augmentation therapy.

Since the study of CT lung density is very interesting for alpha-1 drug development and for the FDA, researchers in the United States also want to study the benefits of emphysema CT scans. Since the results of the European study are not available yet, a United States study will look at a different population of PiZZ Alpha-1 participants who have normal lung function.

Many of you know family members that were tested who have no lung symptoms but who are PiZZ. Technically, normal lung function is defined when one of the breathing tests called the FEV1 is > 80% predicted. Although the test may not be 100% of predicted, lung doctors must put a cutoff somewhere. Therefore, the number that is called normal is 80% predicted based on age, height, sex, and race.

Therefore, in this edition you will see the invitation to call one of the 8 Alpha-1 centers in the Rare Lung Disease Consortium that will be studying CT scans over 3 years in PiZZ individuals with normal (FEV1 >80% predicted) lung function.

On other fronts, the Registry continues its growth. The community looks forward to the day when larger studies in the United States will need additional research participants. So remember to change your address with the Registry when you move. We had more than 300 address changes with the last mailing. Why are you all moving so much?

As some of you remember, an invitation for 3 research studies was mailed in the winter. These invitations did not have a cover letter from me, but instead were signed by the individuals conducting research at other research institutions. These invitations were misinterpreted by a few of you to suggest that the Registry had released your names for the mailing. That has never occurred. All mailings including those 3 letters came from our office in Charleston. These researchers will never know you are a member of the Registry unless you tell them.

Thanks for all of the support you give our operation in the daily phone calls we receive. Encourage those Alphas around you to join the Alpha-1 Foundation Research Registry.

Sincerely,

Charlie Strange, M.D.
What's an empowered patient?
by Symma Funn, University of Florida Department of Anthropology, Gainesville, FL

What is patient empowerment?
MY MOTHER suffered from COPD for the last 25 years of her life. She never joined a patient support group, made few friends with her health condition, and suffered perhaps needlessly in her battle with advanced lung disease. I say needlessly because once I met Alphas, I began to understand how courageous, active and empowered a patient could get when they reached out to others with the same condition, understood more about the process of illness, and began to play a more active role in managing their own health.

I was so impressed by what I saw that I began to read up on patient empowerment. Most of the articles were in nursing journals and talked about what patient empowerment looked like in various disease communities. But no one had looked at patient empowerment in lung disease, much less among those diagnosed with Alpha-1 Antitrypsin Deficiency.

Why is it important to know?
I began to wonder if there was any benefit to becoming empowered. Would it improve a patient’s quality of life if they felt more in control? Would it actually improve their health? Before answering these questions, I realized first I had to define patient empowerment and find a way to measure it.

In the summer of 2006 I began a research project among individuals diagnosed with Alpha-1 Antitrypsin Deficiency (Alphas), as well as among the doctors, researchers, and nurses in the Alpha-1 research community who research or treat patients with Alpha-1. I wanted to identify what is involved in “patient empowerment” from those most involved with this issue. Like most anthropologists, my approach was to let the community, rather than myself, define the issue. I wanted to learn what the community thought “patient empowerment” might be.

The methods I used are standard in the field of anthropology and included meetings with patient focus groups, semi-structured interviews with doctors and nurses, and participant observation. Participant observation includes attending meetings, watching and listening, taking field notes and on occasion using a tape recorder to capture an individual’s exact words. The project was approved by the University of Florida Institutional Review Board and all participants, including the doctors and nurses, signed informed consent forms prior to our meetings.

The patient focus groups were meetings of 5-12 individuals, including both patients and family members. These meetings were held in four locations in the United States, chosen to make sure that different opinions and experiences would be included. I tried to ensure that both newly-diagnosed patients and those diagnosed for over 10 years were included, both lung and liver patients, and those awaiting or who had transplants. Children were not included.

The participants heard a brief presentation about some of the areas that have been identified as a part of patient empowerment (primarily in the nursing literature), but the focus of the session was a group discussion, where the group explored topics such as their experience of diagnosis, identity as an “Alpha”, education and awareness, disease management, cost of illness, family relations and their relation to doctors and nurses. We also discussed whether it is empowering for patients to participate in

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You may contact the Alpha-1 Foundation Research Registry staff by email, at registry@alphaone.org for additional assistance in locating resources related to AAT Deficiency research, to obtain information about current research activities, to participate in the Research Network or Registry, or to receive Foundation publications.
advocacy activities, community and national events, and if it makes any difference to participate in research.

Several themes show up over and over as universally important to Alphas. From the discussions, key areas that patients identified as being a part of “patient empowerment”:

- knowing enough about their own condition to manage episodes of illness (knowing which medicines to take or which therapies will help most)
- a good relationship and communication with either their doctor or nurse or respiratory therapist (ideally all three)
- supportive or understanding family members
- knowing where the best resources are for Alphas
- and most importantly, the opportunity to get together with other Alphas, or with health professionals expert in this field, to share experiences, feel supported and understood, and to learn from each other.

Most of those interviewed or who participated in the focus group sessions thought it was empowering to march on Washington or write to their legislator, to attend local support group meetings and national meetings, or participate in Alpha-1 events such as bike treks or holiday dinners. But most felt “activism” and “empowerment” are not the same thing.

Two final themes emerged in the patient focus groups:

- No power over costs – The only area where patients universally felt “un-empowered” was the cost of illness. There is unhappiness and dissatisfaction with the high cost of therapies and the patient’s lack of control over this.
- Trust – The final theme was what seems to be a high degree of trust between Alpha patients and their doctors and nurses. One reason may be the shortage of Alpha-1 experts. Once a patient finds a doctor or nurse who is expert about Alpha-1, they tend to stay in touch or at least have their primary physician stay in touch with the Alpha expert for guidance or treatment recommendations. Another reason, however, may be the extraordinary courage of most of the Alpha patients I’ve met. Those who seem the most “empowered” have accepted their condition and try to work with it to maximize their lives. The doctors and nurses I spoke with had tremendous respect for their Alpha patients and many trusted the patient to help manage their illness.

Semi-structured interviews were held with researchers, clinicians, nursing staff and organizational leaders in the Alpha community. The University of Florida IRB had approved a sample list of questions; however, these were open-ended interviews. They explored each participant’s background as a health care professional, the extent of their involvement with the Alpha-1 community, and which areas they believed may be involved in patient empowerment. Participants were encouraged to elaborate on any topic they felt was important or to offer information not covered by the questions.

Much agreement – In many areas, doctors and nurses agreed with the patients on what “patient empowerment” is. Most noted the importance of good communication with their patients as key, and how beneficial it is for a patient to become better educated. Many of the doctors and nurses also talked about the importance of information sharing between doctors and their patients. They mentioned how much good data on Alpha-1 and disease management is available on the Web and through patient organizations. Many doctors and nurses acknowledged that some patients know more than some of their doctors about Alpha-1.

Another area of agreement was the ability of patients to reach a stage where they can self-manage, to a certain extent, their condition by working closely with their doctors and nurses in making health-related decisions. A third area of agreement was that it is good for patients to participate in support groups, to get to know other Alphas and participate in research. Finally, doctors and nurses all noted the importance of family or caregiver support in coping with Alpha-1.

What I learned: Perhaps the one thing I did expect to find from the doctor and nurse interviews was how dedicated Alpha-1 experts are to this community. I knew before I began interviewing most of the participants, that this is a special group of doctors, researchers and nurses, many of whom have worked with Alphas for over 20 years.

What was unexpected but wonderful to discover was how many patients “felt blessed” to be a part of the Alpha community. Many seemed to care as much about curing this condition for future generations as they did about their own deteriorating health. This left me feeling as the doctors and nurses say they do, awed and humbled to be a part of this community and around such courageous and giving individuals.

Thanks and acknowledgements to every person who participated in this pilot project. I cannot thank you by name, but know how grateful I am for your input on this project. The health professionals gave up valuable time to participate in their interviews and were very open in their comments and observations. The patients were just fantastic to get to know, and they each helped me understand better what it means to be an “Alpha”. I begin to understand why this particular group of patients is as “empowered” as they are.
A Helping Hand for Parents of Alpha-1 Children

**Tip: Test the Parents First!**

by Laura Schwarz
Alpha-1 Research Registry Coordinator

I HAD THE OPPORTUNITY recently to speak with Mark Rabush and Melissa Seigman of Alpha-1 Kids about issues that Alpha-1 parents and their children face. Mark and Melissa know about these concerns firsthand as they are the parents of 2-year-old Evan, an SZ. Mark and Melissa are board members of Alpha-1 Kids and keep abreast of topics of interest to Alpha parents.

Many parents who are severely deficient and/or carriers say that their primary concern is the welfare of their children. Parents often question whether their children should be tested for Alpha-1 and at what age.

The Alpha-1 Coded Testing Study at the Medical University of South Carolina is approved to test children with parental consent. Because we can test does not always mean we should test.

One instance where testing should not be delayed is when the child could be showing symptoms of Alpha-1 liver disease.

When a parent phones the Alpha-1 Research Registry staff to request a test kit for a child, the coordinator asks the parents if they have already been diagnosed. Usually their response is that one parent with a background of Alpha-1 or Alpha-1 symptoms has been tested -- but the other has not. We urge biological parents to have testing performed before testing their children. Frequently it is not necessary to test a biological child or children. For example, if one biological parent is an Alpha with a ZZ genotype and the other biological parent is an MM genotype, it is not necessary to test the biological children because each child will be an MZ carrier for the deficiency. Other combinations of genotypes, for example, an MZ father and an MS mother, would result in a variety of genotype combinations. Ultimately, the decision on whether or not to test a child is up to the parents.

Parents should realize that the unpleasant task of pricking a baby or young child's finger with a lancet is not the only unpleasant result of testing. The potential labeling of a child as being "different" or "abnormal" because of testing could be an unnecessary psychological burden. Research from The American Thoracic Society explains that "the primary objection to predictive testing of children is that youngsters who learn they could or will incur a serious genetic condition later in life will experience devastating emotional damage." "Because children have a limited understanding of illness, they might come to view themselves as sick and damaged." One instance where testing should not be delayed is when the child could be showing symptoms of Alpha-1 liver disease, such as jaundiced eyes and skin, swelling of the liver or poor growth. It is the general recommendation that testing may prove beneficial if a biological parent is a ZZ or SZ, but testing of a biological child could be performed later in their adult years.

A parent's state of mind may be a major reason for early testing of a child. Mark and his wife were more comfortable knowing their son's diagnosis ahead of time so that they could "Alpha-proof" their son's environment. They wanted to be able to rid the house of cleaning agents and medications that could exacerbate their son's symptoms. For example, because they know that TYLENOL metabolizes in the liver, Mark and Melinda decided not to give their son TYLENOL. Since using cleaning products contained in aerosol cans may affect their son's breathing, they decided to buy products in non-aerosol cans. First on this list of choices should always be to limit exposure to second hand cigarette smoke and to encourage children to never smoke.

There are some negative consequences of testing. Since there is no proof that these medications and inhalants cause liver or lung disease in Alpha-1, the process of "Alpha-proofing" can cause unnecessary parental distress. Another major concern parents have is whether an Alpha-1 child will be denied life or health insurance when they carry a diagnosis of Alpha-1. Mark's recommendation to these parents is to "do their homework." He urges parents to obtain information from their physician but also to investigate further by calling the insurance company to make sure that the parents have the most current information, for example, that their current plan will cover the rare possibility of a liver transplant.

Parents should also read Alpha-1 Antitrypsin Deficiency Alphabet from A1 to ZZ, a children's book, to their children when they are old enough to understand their condition (from Alpha-1 Kids).

One project that Alpha-1 Kids is designing is a program for parents in crisis, for instance parents who are in the process of setting up a liver transplant for their child. Another project Mark and Melissa are developing is the creation of a standard procedure for pediatricians when a child presents with neonatal jaundice. Feel free to visit the Alpha-1 Kids website at www.alpha1kids.org or email them at mrabush@alpha1kids.org if you have any questions.

The Alpha-1 Research Registry invites severely deficient and carrier minors into the Research Registry with parental permission. These children will be required to sign up on their own as they transition across their 18th birthday.

*Figure 1 shows a current breakdown of ZZ's less than 18 years of age who have joined the Alpha-1 Foundation Research Registry.*
Ask the Alpha Doc

by Charlie Strange, MD

Q. Should Alpha-1 Augmentation therapy be used after lung transplantation?

A. The easy answer is that we do not know. However, there is much interest in exploring the possibility that Alpha-1 augmentation is effective in this setting.

Some would argue that it took on average 10-30 years of cigarette smoking for emphysema to develop in the first place; therefore, new lungs should not need additional Alpha-1 augmentation. In addition, medicines that are needed after transplantation are costly already and Alpha-1 augmentation therapy would add significantly to this cost. If augmentation therapy were important, then Alpha-1 transplants should have worse survival outcomes. Although the studies are not perfectly done, when transplantation outcomes are compared between Alpha-1 and other diseases, there appears to be no difference in survival. Therefore, a lung transplant should free an individual from ever having to use augmentation therapy again.

Proponents of augmentation therapy would suggest that lung transplants almost always have some degree of transplant rejection. Rejection is an inflammatory process in the small airways that might be blunted by Alpha-1 therapy. In addition, there is significant toll on the transplanted lung from infection. There is good emerging information that Alpha-1 is important in fighting infections of many causes including viruses, bacteria, and germs in the mycobacterial family such as tuberculosis. All of these infections also can cause transplant rejection, therefore using augmentation therapy makes good sense, particularly if a transplanted lung is failing.

The Alpha-1 Registry has enrolled 102 individuals with lung transplantation for Alpha-1. Although 12 individuals have died since 1996, 25 of the remaining 90 (28%) report augmentation therapy use and 72% have not used augmentation therapy since transplant. The decision to use Alpha-1 Augmentation therapy is often made between the transplant recipient, the transplant center, and the insurance company. Some insurance companies will deny payment for Alpha-1 use in this situation.

There continues to be Alpha-1 community and researcher interest in the question. Unfortunately, the optimal research study would take many years and would be costly. The sooner the studies can start, the sooner we will have answers.
THE ALPHA-1 FOUNDATION established a central storage facility for DNA and tissue donated by Alpha-1 Antitrypsin Deficient (AATD) individuals, their families and friends. Called The Alpha-1 DNA and Tissue Bank, this facility is housed at the University of Florida College of Medicine in Gainesville, under the direction of Dr. Mark Brantly. Since its inception more than six years ago, the Bank has been taking deposits of blood and tissues without getting bank withdrawals.

Currently, the DNA and Tissue Bank has the largest collection of Alpha-1 DNA in the world available for Alpha-1 research studies. The Bank has always invited researchers in the international community who are conducting studies on Alpha-1 and other related diseases to use these samples for meaningful research. Funding is provided through a grant from the Alpha-1 Foundation.

One of the major impediments in AATD research is the lack of availability of human tissue for investigators to study. Due to the rarity of the disease, many clinical centers have experienced difficulties in investigating AATD. The mission of the DNA and Tissue Bank is to remove these barriers to research by making available significant numbers of both AAT deficient and normal DNA to investigators.

Many people may not be aware that the DNA and Tissue Bank has collected lung samples, liver samples, and more than 1,500 blood samples to date. About 50% of these samples are from individuals severely deficient in AAT, (PiZZ, PiSZ, and rare genes) and 25% are from carriers of Alpha-1 (PiMZ and PiMS). Samples are accepted from families and friends, since comparisons between the Alpha-1 samples and non-Alpha-1 donations may improve future research.

As the DNA and Tissue Bank moves into the future, the investments made in deposits are now ready for withdrawal. The good news is that the Bank recently sent out its first samples of lung and liver tissue, requested by an investigator, for research. The interesting part of the Bank is that there is now enough DNA from the blood tubes many of us donated to supply 250 or more research projects.

Anyone can donate at any time by calling and talking to a coordinator in Florida. They will talk you through the process of filling out a consent form, obtaining a blood tube kit, and submitting it. This process is also a way for family members to find out their Alpha-1 genes. The results are mailed to you if desired when the blood is donated for the DNA bank. We encourage all Alphas to participate in this vital research conducted by the DNA and Tissue Bank. If you have not participated in this program would like more information about the Bank, please email a coordinator at alpha1lab@medicine.ufl.edu or call toll free, 1-866-284-2708.
Understanding COPD: Lessons from Alpha-1 Antitrypsin Deficiency

by Adam Wanner, M.D.

Editor’s Note: Dr. Wanner has accepted the position of Scientific Director of the Alpha-1 Foundation. We welcome him into that position and invite his comments on the future of Alpha-1 research in COPD.

Approximately six percent of the population has COPD, and COPD has become the fourth leading cause of death in the United States. Although the awareness of COPD as a global health problem is growing and although there has been a recent growth in COPD research, spawned by industry and to some extent government funding agencies, our understanding of how COPD develops remains fragmentary. Inhaled smoke, especially cigarette smoke, has been identified as the major cause of COPD, but it is not clear why only a minority of those exposed or exposing themselves to smoke develop clinical COPD. Genetic predisposition comes to mind as a possible explanation for this phenomenon, and the study of COPD genetics therefore is in full swing.

THE LUNG DISEASE of patients with Alpha-1 Antitrypsin Deficiency resembles COPD, including emphysema, chronic bronchitis and bronchiectasis. However, in contrast to COPD, the genetic defect and the resulting disease mechanisms that lead to the lung damage associated with Alpha-1 Antitrypsin Deficiency have been well characterized. Furthermore, strides are being made to discover additional gene mutations that seem to be needed for the full expression of the Alpha-1 Antitrypsin Deficiency phenotype. In this sense, alpha-1 antitrypsin research had it easier than generic COPD research, and this is exemplified by the impressive advances that have been made in our understanding of the biological and clinical consequences of the abnormal and deficient alpha-1 antitrypsin protein.

Indeed, the concept that an imbalance between proteases (enzymes that break down tissue) and antiproteases (proteins such as alpha-1 antitrypsin) can lead to COPD arose from the discovery of Alpha-1 Antitrypsin Deficiency and its association with emphysema. As this discovery was made in Europe, researchers in the US found that instilling proteases in to the lungs of animals cause emphysema in experimental animals, that human proteases are inhibited by alpha-1 antitrypsin, and that cigarette smoke suppresses alpha-1 antitrypsin’s anti-protease activity. Forty years later, the protease-antiprotease imbalance concept continues to serve as an important scientific basis for present-day research in Alpha-1 Antitrypsin Deficiency and COPD. Hasn’t the discovery of Alpha-1 Antitrypsin Deficiency initiated meaningful COPD research? Is it far fetched to think of Alpha-1 Antitrypsin Deficiency that affects a small segment of the population as a model disease for the study of COPD, a health problem for a large segment of the population?

One could argue that the protease-antiprotease principle has had its day in the scientific world and that no other links should be expected between Alpha-1 Antitrypsin Deficiency and COPD at large. New discoveries tend to refute this argument. For example, it has now been shown that the abnormal alpha-1 antitrypsin made by lung cells or reaching the lung through the blood circulation can cause inflammation in the lung that resembles the inflammation seen in COPD patients in general. Furthermore, alpha-1 antitrypsin seems to promote the survival of lung cells, thereby preventing emphysema. If the protease-antiprotease principle, which was fueled by the discovery of Alpha-1 Antitrypsin Deficiency, initiated decades of COPD research, why couldn’t other scientific observations derived from alpha-1 antitrypsin research continue to fertilize the study of COPD? An analogy can be drawn with cystic fibrosis, a genetic disorder in which an abnormal protein (cystic fibrosis transport regulator, CFTR) can explain how chronic lung disease develops in affected individuals. A recent study has shown that cigarette smoking inhibits CFTR in individuals who do not have cystic fibrosis, suggesting that CFTR could have a role in cigarette smoke-induced COPD.

Is it far fetched to think of Alpha-1 Antitrypsin Deficiency that affects a small segment of the population as a model disease for the study of COPD?

Continued on page 8
Broadening the alpha-1 antitrypsin research support base more likely than not would accelerate the progress toward a better understanding of COPD.

Thus, two genetic diseases characterized by obstructive lung disease have identified new mechanistic pathways that can be extrapolated to COPD at large.

I would therefore submit that from a scientific perspective, it is no longer appropriate or wise to consider Alpha-1 Antitrypsin Deficiency a boutique disease that is of little interest to investigators studying COPD, to COPD research funding agencies and ultimately to all patients that suffer from COPD. Broadening the alpha-1 antitrypsin research support base more likely than not would accelerate the progress toward a better understanding of COPD and the development of novel therapeutic and preventive interventions that will benefit not only patients with Alpha-1 Antitrypsin Deficiency but also the large segment of today’s population that suffer from COPD. The Alpha-1 Foundation is committed to educate agencies that support lung research and the pharmaceutical industry about the obvious links between alpha-1 antitrypsin research and general COPD research, with the goal to increase alpha-1 research funding. Wouldn’t it be a great accomplishment if focusing on alpha-1 research leads to a cure for all patients with COPD irrespective of whether or not they have Alpha-1 Antitrypsin Deficiency?

The Rare Lung Disease Consortium and Alpha-1

by Amic Gitter, RN
Medical University of South Carolina

The Rare Diseases Consortium is a novel initiative by the National Institute of Health in Bethesda, MD to jump-start research in rare diseases. The funding for this research endeavor was initiated indirectly because individuals like you with rare diseases suggested that the NIH was not doing enough to stimulate research on these diseases. There are currently 12 groups that were funded for the first round of initiatives. Thanks to Dr. Bruce Trapnell in Cincinnati, the Rare Lung Disease Consortium was formed and awarded a grant.

THE RARE LUNG DISEASE Consortium (RLDC) was awarded the grant because the research questions asked were important and because part of the grant was initiated to empower the patient community to take charge of their health.

There are 4 diseases involved in the consortium. These include Alpha-1, lymphangioleiomyomatosis (LAM), pulmonary alveolar proteiniosis (PAP), and childhood and familial idiopathic pulmonary fibrosis (IPF). Can you understand why everyone likes to use abbreviations for the diseases?

The first study on Alpha-1 to use the consortium will be a study of 60 individuals with normal lung function tests to see what the chest CT shows and to follow serial chest CT scans for 3 years. The best screening test for lung disease associated with Alpha-1 has been the forced expiratory volume in 1 second (FEV-1). This test is obtained on a spirometer, a machine in which you blow as forcefully as possible to figure out the amount of air that comes out in 1 second.

Unfortunately, there are some individuals with normal FEV-1 tests (defined as any value greater than 80% predicted) that still have Alpha-1 lung disease. Some rare individuals can have extensive emphysema (holes in the lung) with normal breathing tests.

Therefore, this study will define on high resolution computed tomography (HRCT or CT scan) how many persons have abnormal CT scans. If the CT scan progresses more than the FEV-1 does over three years, then the hope would be that the Food and Drug Administration would accept the CT scan to be the more sensitive measure to prove that new medicines work.

The rush to find new medicines for Alpha-1 that might be inhaled would then be helped along by having a sensitive measure for the effectiveness of these inhaled medications.

There is an invitation to the study in this version of the Registry Newsletter. Some of the inclusion criteria (ways to get into the study) and exclusion criteria (ways you would not qualify for the study) are technical and will need the assistance of your physician to determine. We will provide regular updates to the Alpha-1 community on the progress of the RLDC to keep you up to date on this important research.
Our Building Friends For a Cure Program is ready for action!

by Angela McBride
Alpha-1 Foundation, Development Director

EVER SINCE the Alpha-1 Foundation’s fundraising and publicity generating program, Building Friends for a Cure, Alphas, families and friends have responded to the need to continually raise awareness and funds for the Foundation.

I look back with pride and admiration for the many volunteers who heard our call and went out and made it happen: 2006 was a phenomenal year. Our volunteers organized a dinner cruise, a whale watch in Cape Cod, an art auction, golf tournaments, garage sales, a bowling tournament, dinner dances, Vegas nights -- not even to mention all the amazing walks and bike rides that our stellar Team Alpha-1 volunteers participated in. The list goes on and on!

The Foundation is committed to making the program work and provides the support and resources necessary, including a dedicated staff. We’re available to answer questions, mail updated educational materials on Alpha-1, provide over-the-phone training, and review letters and press releases.

There are many ways to get involved besides running a special event. A few of these:

**Commemorative Giving**

In Memoriam: To remember someone close to you by making a gift in their memory.

In Honor: To help in the fight against Alpha-1 by donating in honor of someone who has made a difference in your life.

**Commemorative Gift Packages** are available through the Foundation.

**Alpha-1 Wrist Bands**

We have a limited supply of these bands left. We have sold 15,000 to date and find they are a great awareness tool.

**Cure Alpha-1 Car Magnets**

We listened to our volunteers and launched our car magnet campaign. Support Alpha-1 research and promote awareness.

PS: You can separate the heart from the center of the magnet, put it on your refrigerator or a friend’s, and double your Alpha-1 awareness!

**Alpha-1 Scarf and Tie**

Give a gift that will help raise funds for research. We have an Alpha-1 Tie and a beautiful silk lady’s Alpha-1 Scarf, both available now — and both make great gifts all year long!

**Workplace Giving**

Many companies throughout the U.S. offer matching gift programs. Just ask your HR manager.

One may also choose to organize a

**Special Event.** The first rule is to determine what type of event; for example a themed dinner, walkathon, run or bike ride, garage sale or golf tournament. Pick what feels right for you, your community and your capabilities. Recruit a committee of people you can count on — family, friends and colleagues. Use the application form provided in the "Building Friends for a Cure" manual as a guide to organizing any event.

See FRIENDS page 10

Now battling Alpha-1:
From left, Frankie Otero, Edmio Ortiz and Tommy Torino entertained the crowd with a boxing exhibition that headlined the Celebration of Life fundraiser. Otero was formerly the top-ranked Junior Lightweight in the world, Ortiz, president of United in Miami, has been an amateur boxer since the 1980s, Torino was formerly a Junior Middleweight contender.

Alpha-1 Foundation board members Dr. Holly Miller, left, and Elaine Alfonzo joined the Celebration of Life festivities. Dr. Miller is vice president and chief medical information officer at University Hospitals of Ohio. Ms. Alfonzo is president of Fundacion Alfa-1 de Puerto Rico and a support group leader in Puerto Rico.
News from Capital Hill

Give Genetic Nondiscrimination Act a Boost

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

Update on Genetic Information Nondiscrimination Legislation

THE 110TH CONGRESS recently re-introduced the Genetic Information Nondiscrimination Act (H.R. 493). This Act, if enacted into law, would prohibit discrimination on the basis of genetic information with respect to health insurance and employment. H.R. 493, co-sponsored by Congresswoman Louise Slaughter (D-NY) and Congresswoman Judy Biggert (R-IL), was passed by the House of Representatives in April 2007 giving great hope that uniform federal protections against the misuse of genetic information may be finally enacted. In the absence of federal legislation, many states have implemented their own laws to shield individuals from insurance and employment discrimination. There should be a national policy to ensure that all Americans have equal protection.

In addition, the Senate has passed similar legislation under Senate Bill S.358, sponsored by Senator Olympia Snowe (R-ME) that will send this to conference between the House and Senate leadership.

This important legislation has languished for many years on Capitol Hill. We believe that this legislation is vital. We encourage each of you to follow the progress of this legislation in the various media and become involved.

Visit the U.S. Senate at: www.senate.gov to ensure Senate passage continues on its course.

Update on Pulmonary and Cardiac Rehabilitation Legislation. Senate Bill S.329 and House Bill H.R. 552

The treatment of chronic lung diseases such as Alpha-1 Antitrypsin Deficiency and COPD are frequently complicated, confusing and frustrating especially for patients, family members and for people caring for them. Pulmonary rehabilitation combines education, therapeutic exercise and functional activity to improve the lives of individuals coping with these diseases.

In an effort to ensure access to pulmonary and cardiac rehabilitation care, Senator Mike Crapo (R-ID) and Senator Blanche Lincoln (D-AR) have introduced legislation under Senate Act (S 329). Similarly, a house companion Bill H.R. 552 was introduced by Congressman John Lewis (D-GA) and Congressman Chip Pickering (R-MS).

For over 20 years organizations supporting pulmonary health have requested clear and consistent Medicare policy for pulmonary rehabilitation. Medicare statutes currently do not specifically provide reimbursement of pulmonary rehabilitation for beneficiaries.

Both the Senate Bill and House Bill 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.

The Alpha-1 Association and Alpha-1 Foundation urge you to take ACTION by contacting your Senators and Representatives requesting co-sponsorship of this important legislation.

Visit the House of Representatives at: www.house.gov to learn how to contact your Representative or visit www.senate.gov to learn how to contact your Senator. You may also call the Capital switchboard at 202-225-3121 to be directed to your legislator.
Panniculitis is an uncommon manifestation of Alpha-1 Antitrypsin Deficiency. This brief paper will discuss the definition of panniculitis, the variety of potential causes, current understanding of the mechanism of panniculitis, its signs and symptoms, and available experience with treatment.

Panniculitis is an inflammation of the panniculus, which is the fibro-fatty tissue layer that lies underneath the outermost or superficial layers of our skin. This layer of the skin resembles a honeycomb, with globules of fat separated by walls, or septae. In anatomic terms, panniculitis is categorized as either being septal (involving the walls separating the fatty sections of the panniculus) or lobular (affecting the fat globules or collections themselves).

Like most medical conditions, panniculitis can arise from many underlying causes. Alpha-1 Antitrypsin Deficiency is one of those causes. Among the other potential causes are a group of diseases known as connective tissue disease (which include conditions causing diffuse body inflammation, such as systemic lupus erythematosus and rheumatoid arthritis), underlying so-called lymphoproliferative diseases (like lymphoma), pancreatic disease, gout, kidney dysfunction, so-called atheroembolism (in which clots from blood vessels find their way to the fibro-fatty layer of the skin), and even adverse reactions to some drugs, including corticosteroids.

Panniculitis manifests as characteristically red nodular spots on the skin which may break down and ulcerate, causing an oily discharge. While these nodular blotches may occur anywhere on the body, common sites include the thighs and buttocks and areas subject to trauma. Conditions that may precipitate the development of such nodules include trauma (including rigorous exercise), intravenous injections, or cryosurgery on the skin (which is surgery involving freezing the skin). The lesions of panniculitis may go on to develop deep ulceration with tissue breakdown, called necrosis. Such necrotic nodules are usually painful to the touch.

Panniculitis is felt to be due to inflammation of the fibro-fatty layer of the skin, presumably mediated by unopposed protein breakdown. In Alpha-1-related panniculitis, the mechanism of panniculitis resembles that believed to cause the development of emphysema, namely the unopposed breakdown of tissue by the absence of alpha-1 antitrypsin, allowing proteases within the body to affect structures underlying the skin (in the case of panniculitis) or the support matrix of the lung (in the case of emphysema).

Panniculitis is an uncommon complication of Alpha-1 Antitrypsin Deficiency. It was first described in a patient in France in 1972 by Dr. Warter and colleagues. These physicians described a young woman with severe deficiency of alpha-1 antitrypsin who developed characteristic red nodular, painful skin ulcers. Since that original report, fewer than 50 cases of panniculitis in individuals with Alpha-1 Antitrypsin Deficiency have been reported in the medical literature, establishing that panniculitis is a very uncommon complication of Alpha-1 Antitrypsin Deficiency. For example, in the National Heart, Lung, and Blood Institute Registry of Individuals with Severe Deficiency of Alpha-1 Antitrypsin, only a single participant reported having panniculitis. In various reports specifically about panniculitis and Alpha-1 Antitrypsin Deficiency, only 28 patients had been described through 1997. Tallying all reported cases through 2003 shows a total of 44 individuals with panniculitis complicating Alpha-1 Antitrypsin Deficiency described in the medical literature. Importantly, panniculitis in Alpha-1 Antitrypsin Deficiency can accompany various phenotypes (or genetic types of Alpha-1 Antitrypsin Deficiency), some with severe deficiency of serum levels of alpha-1 antitrypsin (e.g., including Pi*ZZ and Pi*SNNull) and others with only mild deficiency (e.g., Pi*MZ and Pi*M5). In one series by Humbert and colleagues, of the 26 patients with panniculitis and Alpha-1 Antitrypsin Deficiency described, 62% were Pi*ZZ, 15% were Pi*M5, 8% were Pi*MZ, and 4% were Pi*SNNull; in the remaining 8%, the phenotype was not stated. The reported experience suggests that panniculitis occurs equally among men and women and that the mean age of onset is approximately 40 years old.

Various therapies have been tried and evaluated to treat panniculitis, including corticosteroids, antibiotics (including doxycycline and dapsone), full plasma exchange, and intravenous pooled human plasma alpha-1 antitrypsin (more popularly called augmentation therapy). Of these various treatments, augmentation therapy has been the most dramatically successful. Several reports describe resolution of panniculitis after as few as 3 doses of intravenous augmentation therapy. The dose of augmentation therapy for panniculitis is the same as that for established emphysema, 60 mg/kg once weekly.

In summary, panniculitis can be both an annoying and also potentially disabling complication of Alpha-1 Antitrypsin Deficiency. Panniculitis is thankfully very uncommon and is amenable to effective treatment with existing approaches for Alpha-1 Antitrypsin Deficiency, including augmentation therapy. Undoubtedly, the spectrum of treatment choices for panniculitis will grow along with ongoing research regarding optimal therapy of individuals with Alpha-1 Antitrypsin Deficiency and with the development of new treatment options.
# 2007 National Education Programs

**Education Days, Events and Meetings**

The following calendar features a partial list of events. For more current listings, check the website at [www.alphaone.org](http://www.alphaone.org).

For more information on attending or exhibiting at an education program, please contact: Marlene Erven at 1-800-521-3025 or email at mserven@alpha1.org

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<tr>
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<td>Co-Sponsors: Alpha-1 Association, Alpha-1 Foundation, St. Luke's-Roosevelt Hospital, Columbia University Medical Center of the New York Presbyterian Hospital</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 **2007 COPD & Alpha-1 Education Day Series**: AlphaNet, Centric Health Resources and Talecris Biotherapeutics. Series Exhibitors include Baxter Healthcare and CSL Behring.

*Commitments and dates are subject to change.

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**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 $28 million to support Alpha-1 research and research-related projects, which includes funding grant awards to more than 50 academic and research institutions in North American and Europe.

**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.

**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.

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