Letter from the Director

By Charlie Strange, MD
Professor of Pulmonary and Critical Care Medicine, Allergy and Clinical Immunology
Medical University of South Carolina

Dear Registry Members,

WELCOME to this edition of the Alpha-1 Foundation Research Registry Newsletter. Have you ever had the feeling that you've been busy all day but didn't get to finish the main project that you started first thing that morning? Sometimes it feels that way when we try to get the word out about all the research occurring in Alpha-1 Antitrypsin Deficiency (Alpha-1). Although we still don't have a cure, every step brings us closer.

In this edition of the Registry Newsletter, you will see reports on the survey that was mailed to all Registry members concerning severe and unusual infections. You will hear about the search for rare alpha-1 genes at the University of Florida. Please help the Alpha-1 Foundation as they have discussions about the Alpha-1 Coded Testing Study as it relates to the Genetic Information Nondiscrimination Act (GINA) now on Capitol Hill.

We are very pleased to highlight the University of Minnesota as the featured Clinical Resource Center in this edition. The focus on chronic obstructive pulmonary disease (COPD) in Minneapolis is strong and growing, as you will see. In addition to providing clinical care, pulmonary rehabilitation, and an internationally recognized transplant program, the University of Minnesota is committed to furthering COPD research while raising public awareness of this condition and others, including Alpha-1.

I am also excited to introduce Dawn McGee, one of two new staff members on the Alpha-1 team here at MUSC. As a certified genetic counselor, Dawn will staff the first Alpha-1 Antitrypsin Deficiency Genetic Counseling Call Center. This call center is funded by the Alpha-1 Association and is available for calls from the community about Alpha-1 genetics through a toll-free number.

In October, Rebecca McClure joined our staff as a Registry Coordinator. She is a very organized individual who tries to keep our priorities aligned with the mission of the Research Registry. The previous Registry Coordinator, Yonge Jones, has moved to Greenville, SC, as his surgeon wife took a wonderful job offer. We wish him well, and will still see him at future Alpha-1 Education Days.

Word in the wind is that some large Alpha-1 studies will likely begin in 2008. We want the Registry to be large enough to fill the studies quickly. Please invite your Alpha-1 friends to be members of the Registry in 2008. As always, we welcome your telephone calls and emails with suggestions for future research trials and studies.

Sincerely,

Charlie Strange, MD
Director, Alpha-1 Foundation
Research Registry
Do you have a

WHAT? You say you’ve never heard of a phenotype called M Heerlen Z?

Well, thanks to Mark Brantly, MD, and his laboratory team at the Alpha-1 Foundation DNA and Tissue Bank at the University of Florida, the second known family in America with this gene has been discovered. Elaine, a 72-year-old retired bank vice president in Swampscott, MA, is the somewhat relieved recipient of this special phenotype. Relieved: but only after many years of deteriorating lung function and frustrating misdiagnoses from physicians. We’ll tell you more about why Elaine was assigned this phenotype; but, first let’s go back 35 years to when she began having difficulty breathing.

At the time, she was a bank teller, after having taught kindergarten to emotionally disturbed children for 15 years. She wasn’t too concerned about her breathing problems until they steadily became more persistent. She saw a specialist who said she had adult onset asthma. The medications prescribed didn’t really help, so she went to another doctor who also told her she was asthmatic. Different medications were prescribed, which helped for a while. But eventually her breathing worsened to the point where she felt the shortness of breath was no better than before she started the asthma medications. By 1988, she had become vice president of the bank and had decided her breathing problem was something permanent and couldn’t be helped. She kept pushing herself, hoping her life would be as “normal” as possible. Needless to say, it didn’t work very well.

Elaine was hospitalized for pneumonia twice; still no Alpha-1 diagnosis. By age 68, her symptoms had worsened to the point that she had to retire. One evening not long after retiring, Elaine developed flu-like symptoms, without the fever. She had no appetite and could only breathe in an upright position. She sat up all night, feeling that she was surely going to die. When her husband found out she had sat up all night, he took her to the hospital. She said she would not be able to make it out the door, so he called 911. She insisted on taking a shower first—and now admits how foolish she was to spend precious time and energy getting clean for the ER. She was rushed to the hospital.

There she met Will Huang, MD, of North Shore Pulmonary Associates in Salem, MA. Finally, after all those years, Dr. Huang diagnosed Elaine with Alpha-1 when her blood test returned with a ZZ phenotype. He prescribed augmentation therapy, 24-hour oxygen, and pulmonary rehabilitation. Although Elaine’s lung capacity (FEV-1) was at about 50%, she felt better than she had in years.

Elaine encouraged her six children to get tested for Alpha-1. Some are reluctant to test, others are being tested, and her oldest child, Roberta, did test. Roberta, 51, is a mother of three. She is an artist, but paint fumes don’t bother her. There is no asthma in her family, and none of her children demonstrate any symptoms. Roberta’s test

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You may contact the Alpha-1 Foundation Research Registry staff by email at registry@alphafone.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.
Really Rare Gene?

returned with a negative (MM) genotype, which didn’t make sense, knowing her mother’s diagnosis. (During this time, the running joke was: “Are you sure she’s really yours?” Elaine’s reply: “Oh yes, I was there and I remember!”)

Elaine and the medical team knew Roberta had to be a carrier, and encouraged more testing. One of the most important tests in this particular situation is an Alpha-1 level. A level measures the total amount of alpha-1 protein in the blood. A very low level is seen in ZZ and Z Null individuals; an intermediate level is seen in carriers such as MZ individuals, and a normal level is seen when both genes are M. A blood level is best obtained from a tube of blood, though it can be estimated from a drop of blood on filter paper.

The second test that can be done on blood drawn in a blood tube is Protease Inhibitor Typing (also called phenotyping). A phenotyping test places blood proteins on a gel that looks like thick Saran wrap. When an electric current is applied, different proteins move farther than others, based on differences in the net positive or negative charge of the protein. The technique is called electrophoresis. By this test Elaine had been diagnosed with her ZZ phenotype, because only a single AAT protein was seen in the Z band. In other words, all of the protein present in the blood was Z protein. Similarly, when Roberta’s blood was tested this way, she was given an MM phenotype because only a single band was seen in the M region of the gel.

The third test is the one currently used by the blood spot cards placed in physician offices, and by the Alpha-1 Coded Testing Study (ACT), Talecris and Florida Targeted Detection study. This test uses a polymerase chain reaction or PCR test. This test can detect if one or two copies of the S or Z gene are seen. If two copies are seen, the patient would be diagnosed as a ZZ Alpha-1 deficient individual. When Elaine’s blood was tested using this technique, only one copy of the Z gene was seen. But her blood level was severely low, in the range of other ZZ individuals. This identified her as someone who has a gene that makes little or no alpha-1 — but not a Z gene. There are a variety of these genes that have been described; most are called Null genes. Very rarely, there are found genes that make AAT protein which can only be seen by phenotyping under special conditions not typically used.

When Roberta’s PCR test was performed, she was given a genotype of MM because neither a Z nor an S gene could be seen by the PCR primers. This result couldn’t be correct with her mother’s diagnosis of severe deficiency — implying that both genes are abnormal. Roberta then had a whole blood test and a measured alpha-1 level done by the DNA & Tissue Bank. Her level was intermediate range, but no S or Z proteins were seen. Therefore further testing was required — a fact easily missed if her family history weren’t known.

Although many different rare genes are known, many remain undiscovered. Elaine’s rare gene was next sequenced, a process where every building block of a gene is identified. If the gene sequence is determined to be unique, the gene can be submitted for an official name. Since we’ve run out of letters of the alphabet for newly-discovered genes, the names typically given are the names of the hometown in which the person was born. (For example, if Elaine’s gene were found to be a Null gene and she was born in Swampscott, MA, then Dr. Brantly could propose a new gene called Null Swampscott.)

But Elaine’s gene instead was found to be a very rare one (previously discovered) called M Heerlen Z. Her genotype is then called M Heerlen Z. The Heerlen gene migrates in the M region on electrophoresis, but makes very little protein. This explains why Elaine’s blood level is in the ZZ range and augmentation therapy is appropriate for her. It also explains why her daughter Roberta was misdiagnosed. Roberta is now known to have one M gene and one M Heerlen Z gene, so her blood level is in the intermediate range. Both of these diagnoses are different from the ZZ and MM diagnoses given them by screening tests — and demonstrate why blood levels are a valuable aide to diagnosis.

Elaine is now a strong Alpha-1 advocate. She delivers Alpha-1 literature to doctors and nursing students. She will always be grateful to Dr. Huang and feels he is one of the best pulmonary specialists around. And he’s always very appreciative when Elaine arrives in his office with new Alpha-1 information!
Q. When should someone with Alpha-1 Antitrypsin Deficiency and COPD consider lung transplantation?

A. LUNG TRANSPLANTATION is a potential lifesaver for many patients with advanced lung diseases, including emphysema from Alpha-1 Antitrypsin Deficiency. Since lung transplantation was introduced in 1981, over 16,000 lung and heart-lung transplants have been performed worldwide.

Unfortunately, lung transplantation still lags behind other solid organ transplants, such as kidney, liver and heart. For every 100 potential donors only 20-25 will have suitable lungs for transplantation. Therefore, although the number of lung transplants performed every year continues to increase to over 2000 a year, the number of potential recipients grows even faster. It has not been uncommon for some recipients to wait two to three years on a transplant list in an active center before a lung became available. Unfortunately, as the lists grew, so did the number of patients not surviving until lung transplantation. This increased waiting list led to a change in the way lung transplants are allocated as of May, 2005. Previously, the lung transplant list was based on a “first come, first served” basis with little or no adjustment for severity of disease. In 2005, the United Network of Organ Sharing (UNOS) implemented a grading system based on severity of disease. This score is based on a combination of: type of lung disease, lung function, amount of oxygen use, predicted survival and functional status. Now patients are able to advance on the list if their disease worsens.

The timing of referral is dependent on several factors. Mainly, it requires weighing the risks of transplantation and the potential survival after a lung transplant with the patient’s current severity of illness and quality of life. Most centers accept patients with severe COPD, such as lung functions (FEV1) less than 30% of their predicted values. Often the patients have severe exercise limitations and frequently are on oxygen. The age restrictions vary slightly between centers. At the University of Minnesota we accept patients up to the age of 65 to be placed on the list and they can remain on the list until they receive a transplant or develop contraindications to transplantation. Other factors, such as ability to follow a complex drug regimen, no other serious diseases and evidence of strong social support are required for a successful lung transplant.

The outcomes after lung transplantation need to be heavily considered when one is contemplating a transplant. Survival varies somewhat between centers with the combined international five-year survival for Alpha-1 patients after lung transplantation being about 50%. Those that are younger (less than 50) and receive two lungs at the time of transplant tend to have slightly longer survival times. About 56% of Alpha-1 patients receive two lungs. The decision for double versus single lung transplant varies between centers and often is based on organ availability, age of recipient, ability of the recipient to wait longer for a double lung and the severity of underlying emphysema.

One of the unknown questions is whether patients should receive augmentation therapy for Alpha-1 Antitrypsin Deficiency after lung transplantation. The use of augmentation therapy varies between centers and most Alpha-1 patients do not receive augmentation therapy. At the University of Minnesota, we do not routinely give replacement therapy. Our reasoning: The development of emphysema takes decades in those with Alpha-1. Since most patients are in their 5th to 6th decade of life, replacement therapy has not been initiated to prevent emphysema. However, recent laboratory and human studies have demonstrated a role of the alpha-1 protein in preventing infection and inflammation. These effects of alpha-1 augmentation may have implications for all transplant patients, not just those with Alpha-1 Antitrypsin Deficiency. Clinical trials studying augmentation after transplantation are needed to answer these questions.

<table>
<thead>
<tr>
<th>Number of Transplants in 2006</th>
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<tbody>
<tr>
<td>Lung = 1,405</td>
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<tr>
<td>Waiting List = 2,817*</td>
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<tr>
<td>Liver = 6,650</td>
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<tr>
<td>Waiting List = 16,946*</td>
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<tr>
<td>Kidney = 17,092</td>
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<tr>
<td>Waiting List = 70,870*</td>
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<td>Kidney/Pancreas = 924</td>
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<tr>
<td>Waiting List = 2,375*</td>
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<td>Heart = 2,192</td>
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<td>Waiting List = 2,847*</td>
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<tr>
<td>Heart/Lung = 31</td>
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<tr>
<td>Waiting List = 121*</td>
</tr>
<tr>
<td>Pancreas = 462</td>
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<tr>
<td>Waiting List = 1,733*</td>
</tr>
<tr>
<td>Intestine = 175</td>
</tr>
<tr>
<td>Waiting List = 229*</td>
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</tbody>
</table>

*As of April 2007

Overall, lung transplantation is a therapeutic option for those with Alpha-1 and severe lung disease. The combination of severe lung disease and poor quality of life are indicators to consider referral for lung transplantation. Those patients that are younger and receive a double lung transplant have better long-term survival; and the efficacy of using alpha-1 augmentation after transplantation has yet to be determined.
Featured CRC

Alpha-1/COPD Program at University of Minnesota

By Chris Wendt, MD
Associate Professor of Medicine, Fairview Medical Center
University of Minnesota

Diane Kacbel
Assistant Director, Center for Lung Science and Health
University of Minnesota, COPD Clinical Care

IT IS OUR PLEASURE to be featured in the Alpha-1 Foundation Registry Update. We want you to know about the University of Minnesota Alpha-1/COPD programs and invite you to consider the University of Minnesota for your Alpha-1 care.

Center for Lung Science and Health
To promote lung health and further enhance clinical care of patients with lung disease through interdisciplinary research, education and public outreach, the Center for Lung Science and Health was formed within the Medical School in 2007. Marshall Hertz, MD, director of our internationally-recognized lung transplant program, is also the Center Director. David Ingbar, MD, director of the Pulmonary, Allergy, Critical Care and Sleep Medicine Division, is the Executive Director. Dr. Ingbar is also the current president of the American Thoracic Society (ATS). Strong leadership for the Center’s COPD Program is provided by co-leaders: Dennis Niewoehner, MD, and John Connell, PhD, both prominent COPD researchers as well as leaders in the NIH COPD Clinical Research Network.

The Center’s official Scientific Kick-off was held in April, 2007. Guest speakers included Elizabeth Nabel, MD, Director of the National Institutes of Health (NIH) and James Kiley, MD, Director of the Lung Program within NHLBI/NIH. Dr. Kiley spoke about COPD, and the expert panel discussion on “What’s Needed in COPD Research?” included Dr. Kiley, university physicians and researchers involved in COPD studies, and a special guest, John Walsh, CEO and co-founder of the Alpha-1 Foundation.

University of Minnesota Fairview Hospital and Specialty Outpatient Clinic
The University of Minnesota Fairview Hospital is a large teaching hospital that provides comprehensive clinical care for patients with chronic lung disease. Affiliated hospitals also providing education and clinical experience for University of Minnesota pulmonary trainees include Hennepin County Medical Center, Regions Hospital, and the VA Medical Center. Additional recruitment is under way within the Division of Pulmonary, Critical Care, Allergy and Sleep Medicine at the University for faculty members with program and research interests focused on COPD.

University of Minnesota Fairview Pulmonary Outpatient Rehabilitation Program
Through education, exercise, nutritional counseling, breathing technique training, and psychosocial support, the Pulmonary Outpatient Rehabilitation Program helps patients with chronic lung disease improve understanding of their disease, control symptoms, and improve breathing, exercise capacity and quality of life. Patients may also participate in the program's pre- and post-lung transplant programs to help improve their outcomes.

Lung Transplant Program
Marshall Hertz, MD, Professor of Medicine, is Director of the Lung Transplant Program. Since its inception in 1986, we have performed more than 600 lung and heart-lung transplant procedures. Of these, more than 90 were performed in patients with Alpha-1 Antitrypsin Deficiency, and more than 200 were performed in patients with other forms of COPD. Our outcomes consistently exceed the seventy-adjusted “expected” survival rates (www.ustransplant.org). In addition, we maintain research programs that are focused on lung injury after lung transplantation (primary graft dysfunction) and on late deterioration of lung function (chronic rejection, bronchiolitis obliterans syndrome).

Continued on page 6
Liver Transplantation Program
John Lake, MD, division director for Gastroenterology, Hepatology and Nutrition, is also the Director of the Liver Transplant Program. He has recently served as Chair for the Liver and Intestine Committee for UNOS and as the Deputy Editor of the American Journal of Transplantation. Liver transplant was introduced at the University of Minnesota in 1964. Since then, University of Minnesota physicians have performed more than 700 adult liver transplants. Many of the liver transplants are done in combination with other organ transplants to treat rare diseases. In addition, more than 250 pediatric liver transplants have been performed here, with Alpha-1 being a leading cause for liver failure in childhood. Use of living donors and procedures in which segments of a single liver are transplanted into two recipients have earned the program a reputation for leadership in the field.

COPD Research
COPD Clinical Research Network (CCRN) of the National Institutes of Health (NIH)/National Heart, Lung and Blood Institute (NHLBI)
The NHLBI CCRN is a nationally-funded research network of 11 clinical centers involved in multi-center trials to improve the management of COPD. The University of Minnesota plays a central role in this network by providing key leadership for the CCRN. Dennis Niewoehner, MD, Professor of Medicine, chief of the Pulmonary Section at the VA Hospital, is an internationally-recognized leader in COPD and the CCRN Principal Investigator; John Connell, PhD, chair of the Department of Biostatistics in the School of Public Health, serves as the Principal Investigator for the CCRN Data Coordinating Center; and Chris Wendt, MD, is a Co-Investigator for the Data Coordinating Center. Patients continue to be recruited for clinical studies focused on limiting exacerbations of COPD.

FORTE
Dr. Connell also directed the Data Coordinating Center with Dr. Wendt as a Co-Investigator, for the Feasibility of Retinoic Acid Treatment Trial (FORTE). This nationwide, multi-center clinical, randomized control trial phase II trial studied the effects retinoic acid on the ability of the emphysematous lung to regenerate. Although regression of emphysema was not found, this trial advanced our knowledge of patient recruitment, biomarkers for COPD and quantitative CT scan analysis of emphysema.

Other Studies
The University of Minnesota has been the home of the Data Coordinating Center for the NIH Lung Health Study since 1986, with Dr. Connell serving as the Principal Investigator. Spanning 16 years with over 90 publications, the Lung Health Study has studied the long-term effects of smoking cessation and continued smoking on heart and lung illnesses in over 6,000 participants. At our VA center, Dr. Niewoehner is also the lead investigator in several multi-center trials for COPD. Kathryn Rice, MD, is the principal investigator of VA-sponsored studies to see if home treatment plans for COPD exacerbations improves outcomes. In addition to COPD clinical trials, Dr. Wendt is involved in translational research and is currently using state-of-the art methods to identify specific proteins or early biomarkers of lung transplant rejection and unique biomarkers for chronic lung disease such as COPD using samples from the Lung Health Study and FORTE trials.

COPD and Alpha-1 Community Education and Outreach
COPD/Alpha-1 Patient Education Days
The Center for Lung Science and Health provides COPD and Alpha-1 patient education days in partnership with the Alpha-1 Foundation and Alpha-1 Association. The most recent event was held May 12, 2007 at the University Radisson Hotel in Minneapolis. The invited speaker this year was Jeffrey Rubins, MD, from the Minneapolis VA Medical Center. While the education day was focused on lung disease, a special breakout session on liver disease in patients with Alpha-1 was conducted by John Lake, MD, Director of our Liver Transplant Program. Continuing Education Units were provided to nurses and respiratory therapists who attended.

COPD/Alpha-1 Awareness at Community Outreach Activities
The Center for Lung Science and Health is currently partnering with the NIH/NHLBI to help create COPD awareness through community education and outreach activities, including an annual patient education day for Alpha-1 and COPD. The Center also partners with the Alpha-1 Foundation to help create awareness of Alpha-1.

Recently, the Center participated in the university Academic Health Center’s annual education/outreach activity at the 2007 Minnesota State Fair by hosting a booth focused on lung health. The Chronic Lung Disease station included information on “What is COPD? Are you at risk? If you have COPD, there is one more test you may need to take.” The Alpha-1 Foundation’s informational brochures were provided. Consenting fair-goers also had the opportunity to have their lung function checked via free spirometry on-site by Ed Corazza, MS, CPFT, director of the Fairview Pulmonary Function Lab. Anyone participating in the free testing could immediately have their results interpreted by University of Minnesota pulmonologists, including Dr. Wendt, at the University of Minnesota Clinic via telemedicine. They were provided with a copy of their results and recommendations as to whether or not they should follow up with a physician/pulmonologist to be further evaluated. During a five-hour screening period, 73 individuals (about 70% more than 41 years old) had their lung function evaluated via spirometry and telemedicine. The pulmonologists recommended follow up and further evaluation to 17 out of the 73.

Summary
Our goal at the University of Minnesota is to provide comprehensive care to all those with COPD. Our mission is to improve care through new research. We hope you will consider our center for your healthcare needs. You may contact our Alpha-1 nurse coordinator, Julie Dunbar, for information or new appointments at 612-625-4427.
What is a Genetic Counselor?

By Dawn McGee, MS, CGC

I AM very often asked “What is a genetic counselor?”

There are many reasons that most people have never heard of this profession. The first is that it is a relatively new field. The term “genetic counseling” was introduced in 1947; however, it was not officially defined until 1975. The first graduate training program for genetic counseling was created in 1969 at Sarah Lawrence College, and in 1971 the first graduating class consisted of ten genetic counselors. Today, there are approximately 38 graduate training programs across the United States, Canada, the United Kingdom, and Australia. There were over 1,200 respondents of the most recent Professional Status Survey, illustrating that the field has grown dramatically in less than 40 years.

Another reason that genetic counseling is not well known: the field deals with genetic diseases. Genetic diseases are relatively rare and sometimes difficult to diagnose. Many people never have reason (or never know they have reason) to be referred to a genetic counselor. Those who have heard of genetic counseling are usually those that have met with a genetic counselor in the past.

Genetic information is very personal and, for most people, very private. Often people are not comfortable discussing their genetic information or family history of disease with friends or even other family members. Diseases in general are often not discussed even within families, due to fears of stigmatization and loss of employment or insurance. Therefore, anyone who met with a genetic counselor often did not share that information with others.

For all these reasons, the term “genetic counseling” is not well-known or understood. Genetic counselors are health professionals with master-level degrees and experience in medical genetics and counseling. I entered the field by obtaining my Master’s degree in Genetic Counseling after studying Biology and Psychology as an undergraduate. Genetic counselors work in a number of different settings, including prenatal, pediatrics, adult, cancer, research, education, and specialty clinics. Genetic counselors are constantly pushing the boundaries that define the career and creating new dimensions to the field.

Despite the different settings, genetic counselors generally work as members of a healthcare team. We bridge the gaps between researchers, clinical geneticists, social workers, and hospital administration. As defined on the website of the National Society of Genetic Counselors, we provide information to patients and families regarding inheritance, symptoms, management, testing, and treatments for genetic diseases. Genetic counselors obtain family histories and provide detailed risk assessments pertaining to the information provided by families. We help patients and families understand, make decisions, and cope with the genetic and psychological issues they may encounter.

We also provide psychosocial counseling. Patients not only need education and information about their specific disease, but they also need support in dealing with their emotional responses. We facilitate this through exploration of patients’ goals, culture, religion, resources, coping styles, and family dynamics.

Genetic counselors act as patient advocates by helping patients and families obtain the services they need. We provide education to patient communities and other healthcare professionals. We actively contribute to advancements in research in genetics and genetic counseling. Overall, genetic counselors are dedicated to providing support and education to families living with or at risk for genetic diseases.

The Alpha-1 Association has a Genetic Counseling Center located at the Medical University of South Carolina in Charleston, SC. The Counseling Center is available to patients, family members, caregivers, and healthcare professionals. The Counseling Center provides free, confidential counseling through its toll-free phone number, 1-800-785-3177. The Genetic Counseling Center can provide information about diagnosis and symptoms, answer questions, provide supportive counseling, and help individuals find additional support within the Alpha-1 community. This Counseling Center is specifically designed to provide expert services exclusively for the Alpha-1 community. It is accessible to everyone, regardless of geographic location, finances or insurance.
What Happens After Genetic Discrimination is Against the Law?

By Yance Jones

THE Genetic Information Nondiscrimination Act (GINA) of 2007 (HR 493) and (S 358) is a bill pending in Congress designed to protect individuals from discrimination by employers or insurance companies based upon the misuse of a person’s genetic information. Currently some states provide legal protection of a person’s genetic information. Not all states, though, provide protection and the language of the protection differs. GINA, if enacted into law, would provide universal legislation to protect citizens from misuse of their genetic information by employers. Potential misuse by an employer might include hiring, firing, or promotion based on genetic results. This proposed legislation would also prevent insurance companies from using genetic information to deny coverage to individuals. Many in the Alpha-1 community are interested in seeing this legislation signed into law.

Currently, the Alpha-1 Coded Testing Study (ACT) provides an opportunity for free, confidential testing to anyone wishing to learn their Alpha-1 genetic status using an “at home” finger-stick test kit. This study, based at the Medical University of South Carolina (MUSC) and funded by the Alpha-1 Foundation, has tested more than 7,000 individuals, many of whom have been found to be deficient for the alpha-1 protein. ACT provides genetic test results to a participant by mail, thereby assuring confidentiality to the extent that the US Mail service can deliver. The research component of the ACT study investigates the impact of genetic testing on important medical and social outcomes in life.

Participants in this study tell us they had testing performed without having to worry about the financial or social consequences from test results. However, the tests are expensive, more than $100 per test, and neither the Alpha-1 Foundation nor MUSC charge for the research study. If GINA is passed, participants in ACT could instead be tested through other confidential means such as their physician’s office, with the cost hopefully covered by health insurance.

Would anything be lost if most Alpha-1 testing was done in physician’s laboratories of choice? One thing lost might be ready access to Alpha-1 information that currently comes with testing results. The impact of having a genetic diagnosis established by persons who know about the disease is a goal of many other genetic communities. The impact of a genetic diagnosis is sometimes not known for years; the ACT study personnel are available for questions that arise long after the day of diagnosis. Access to the larger Alpha-1 community through invitations to contact the Registry, DNA and Tissue Bank, Alpha-1 Foundation and Association, and the Genetic Counseling Center might be lost.

Some of the lawyers in the Alpha-1 community suggest that GINA will need to be tested in the courts to determine if it affords the protection that all of us seek. Which side would win if someone with Alpha-1 began an expensive treatment and had insurance premiums rise the following year? Is this discrimination based on genes or dollars?

For now, the Alpha-1 Foundation and MUSC continue this study with continuing research about the risks and benefits of genetic testing. Should GINA pass, your opinion will count on whether the research goals of the study are sufficient to continue. Even in the post-GINA new age of genetic medicine – where we hope all genetic information is protected from misuse – there will be new challenges that affect our families and healthcare. We invite the Alpha-1 community to continue the dialogue with us and with Congress.

GINA is a bill pending in Congress designed to protect individuals from discrimination by employers or insurance companies based upon the misuse of a person’s genetic information.

Will GINA Eliminate Coded Testing?
Study seeks Alphas among 5,000 with COPD

By Dawn McGee, MS, CGC and Amie Gitter, RN, BSN

SOME 5,000 COPD patients will be tested to determine the prevalence of Alpha-1 Antitrypsin Deficiency (Alpha-1) in a study marking a major cooperative effort between the Alpha-1 Foundation and the American Association for Respiratory Care (AARC).

The principal investigator for the study is Robert A. Sandhaus, MD, PhD, of the Division of Pulmonary Medicine, National Jewish Medical and Research Center in Denver. Sandhaus is also the Clinical Director of the Alpha-1 Foundation.

The study will involve up to 20 sites. The study is an open, non-randomized, population-based research study of patients diagnosed with COPD (by the GOLD II-IV standard) that are identified by pulmonary function testing. In lay terms, the study will identify individuals with chronic obstructive pulmonary disease (COPD) in a breathing lab and test them for Alpha-1.

Many individuals with Alpha-1 Antitrypsin Deficiency do not understand what COPD is. Briefly, COPD is a lung disease that is defined by chronic (not completely correctable) problems with the flow of air through the small airways of the lung. This can occur from mucus as in chronic bronchitis, collapsible small airways when emphysema is present, or scars in the small airways. Many individuals with Alpha-1 have COPD, but not all patients with COPD have Alpha-1.

Because several small studies have suggested that about 3% of individuals with COPD have undiagnosed Alpha-1, the American Thoracic Society (ATS), European Respiratory Society (ERS), American College of Chest Physicians (ACCP), and the American Association for Respiratory Care (AARC) have recommended that all individuals that are symptomatic for COPD be tested for Alpha-1. This study involves respiratory therapists as the health professional to initiate testing for Alpha-1, because they have been enthusiastic about genetic testing for Alpha-1 and about ways to initiate the testing themselves.

The main objectives of this research study are threefold. The researchers aim to determine the detection rate of those severely deficient as well as carriers in a population of patients with COPD that are referred for pulmonary function testing. The second objective is to determine what pulmonary function parameters are associated with patients with COPD that are more likely to have Alpha-1. The last objective is to determine the age distribution within the patients that test positive for Alpha-1 and evaluate the pulmonary function parameters that are associated with age and Alpha-1.

The study will recruit 5,000 participants who meet the inclusion requirements. Individuals who are referred to a pulmonary function laboratory for pre- and post-bronchodilator spirometry with or without additional testing and have post-bronchodilator values of FEV1 <80% of predicted and FEV1/FVC <70% will be asked to participate in the study. Those who consent to participate will be given a brief questionnaire, then the finger-stick dried blood spot Alpha-1 genotype sample collection will be performed. Participants will be given an ID number to ensure their confidentiality.

The DNA analysis will be performed at the Alpha-1 Genetics Laboratory at the University of Florida. The written genotype results will be given to the test site and then disclosed to each participant by mail. Participants have the option to contact the Alpha-1 Association Genetic Counseling Center if they have questions or concerns regarding their participation or their results. This research study will allow for the detection of undiagnosed Alpha-1 Antitrypsin Deficiency in a population of patients with COPD as well as determine the frequency of Alpha-1 in this population. This study will also empower respiratory therapists to facilitate the diagnosis process.

The study is supported in part by an unrestricted charitable contribution from Talecris Biotherapeutics.

News from Capitol Hill

Gridlock Traps Alpha-1 Issues

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

AS 2007 came to a close, many issues facing the Alpha-1 community were at a standstill in Washington, DC. Congress rolled the most important provisions into an Omnibus Appropriations package, so there is not much news to report. The President continues to threaten veto of any bill that is presented to him that includes tax increases, even those he has supported in the past. This has led to more partisan gridlock among Congressional members, making legislation difficult.

We ended the year with many important agenda items open-ended. With 2008 being a Presidential election year, we will have a short "lame-duck" legislative cycle. In 2008, many bills that address the health of those with chronic disease and the need for a strong public health infrastructure may also remain undone. We will not give up, and in 2008 we will continue to focus on the need for federal legislation that ensures genetic nondiscrimination, as discussed in this month's article on the Genetic Information Nondiscrimination Act (GINA). We will fight for pulmonary rehabilitation to be a Medicare benefit and ensure that caps on oxygen equipment rental are not further reduced. We will keep on fighting for Medicare parity in all states and address regulatory issues like easing air travel for those who require supplemental oxygen. We will also be working on defining Alpha-1 as a special disorder whose waiting period should be waived for those seeking Social Security Disability Benefits.

As you can see, there are many unresolved issues facing the Alpha-1 community in 2008. We would love for you each of you to join our efforts and encourage you to follow these issues in the media and become involved. The Alpha-1 Association and Alpha-1 Foundation urge you to contact your Senators and Representatives and let them know that these issues are important to you and your loved ones. You may view the Public Policy section of the Alpha-1 Foundation website (under Alphas, Friends & Family) for action information, or 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 Capitol switchboard at 202-225-3121 to be directed to your legislator.
We're springing

By Angela McBride
Alpha-1 Foundation, Development Director

The Alpha-1 Foundation’s Building Friends for a Cure program will kick off our spring events just before St. Patrick’s Day with the “Half Shamrock Marathon 8K Race” March 15 in Virginia Beach, VA. Jennifer Clark is spearheading the event.

Jennifer was inspired to begin actively promoting Alpha-1 by watching the touching story of Alpha Len Geiger and Kevin and Kristi Shroyer on HBO’s “Real Sports with Bryant Gumbel” in November. The Shroyers made the brave and difficult decision to donate the lungs of their 14-year-old daughter, Korinne, five years ago. Geiger and the Shroyers have since become fast friends, regularly competing in 8K and half marathon races to raise awareness of Alpha-1 and organ donation.

Then in May, we really hit our stride.

May 2 is our annual Celebration of Life gala in Miami. Last year, we had our biggest fundraiser ever with our “Knockout Alpha-1” event, and this year we’ll do our best to top it.

On May 10, Lori Tartell and Joe Reidy spearhead the First NJ/NY George Washington Bridge Walkathon. The James P. Mara Center for Lung Disease at St. Luke’s-Roosevelt Hospital and other community partners will join together to raise awareness and funds to benefit the Alpha-1 Foundation.

May 16–18, Mary Pierce and Neva Maynor team up to participate in the West Virginia Bike Trek.

May 27 will be our Internet “Mother’s Day Campaign” to raise awareness.

Dennis Pollock and his support group, family and friends will hold their annual Alpha 8okes Silver Horn Golf Tournament” in Oklahoma City May 16.

Then on May 18, the Kushner Family Fund will hold its “Dinner with Emeril Lagasse” in Miami Beach, FL. Famed chef Lagasse is a good friend of John Kushner, who died of Alpha-1 liver disease. Barbara Kushner has organized the event in honor of her late husband.

Our “Weekend in Paradise,” an invitational fishing tournament and golf event, will be held May 30-June 1 in Key Largo, FL.

Frank Deford, HBO correspondent who did the “Real Sports” interview with the Shroyers and Geiger, will speak at the “Breath of Life Cocktail Reception” in Greenwich, CT, June 8. Ken and Bettina Irvine are the event’s organizers.

Not to be outdone by Mother’s Day, there will be an Internet “Father’s Day Campaign” on June 15.

Karen Erickson is organizing the “Breathe Easy Bike Ride” in Santa Inez, CA, on June 27-29.

The U.S. Transplant Games will be held in Pittsburg, PA, July 11-16. Every year the Foundation awards scholarships to the Games; this year we are especially seeking out newly-transplanted Alphas who have never before received a scholarship.

Sheila Favaza, Susan Binnall, and other Massachusetts support group members are organizing the annual Massachusetts Whale Watch July 26.

Then Sept. 12-14, one of the oldest Alpha-1 events of them all, the “Escape to the Cape” bike ride will be held on Cape Cod, organized by the large group known as the East Coast Alpha Friends & Family.

Lou Glenn and Jennifer Jacks are organizers of the “Lone Star Alphas Shoot for a Cure” third annual golf tournament in Flower Mound, TX, Oct. 6.

Christine Hannan will organize the “Second Annual Tri State Renaissance Faire” in Laughlin, NV, Nov. 14-16.

This summer for the first time, we will be having our Alpha-1 Necklace Campaign. All this is in addition to our ongoing Alpha-1 Awareness Wristbands and Alpha-1 Scarf, Tie and Car Magnet campaigns.

Repaired with a Smile - Mary Pierce of Team Alpha-1 repairs a bicycle tire at the 2007 Escape to the Cape ride and fundraiser held on Cape Cod. This year’s Escape to the Cape will be Sept. 12-14.
We had a year to remember in 2007:

Hap and Diane Eaton made a huge contribution with their 10,000-mile ride around the country on a tandem bicycle, winning stories on local newspapers and television stations along the way. The Eatons ended their muscle-powered trip with a celebration in St. Augustine, FL, Feb. 15.

The annual Fisherama tournament in the Florida Keys became an Alpha-1 awareness event in 2007, and raised $30,000 for the Foundation’s research and programs – even though tropical winds and tides actually kept the boats at dock! This has grown to the 2008 “Weekend in Paradise” and will continue to be an awareness and fundraiser for Alpha-1 through 2009.

And of course, there was our record-breaking “Knockout Alpha-1” fundraiser at the Celebration of Life.

Can we do even better this year? We’ll certainly try, with help from our Alpha-1 friends! So take action now and make a difference: It’s up to you!

The goal of the Alpha-1 Foundation’s Building Friends for a Cure Program is to build stronger links between the organization and the Alpha-1 community using social and health-related events to increase the community’s quality of life while raising funds for research.

For more information on any of these events, contact Yiomara Perry at 888-825-7421, Ext. 248 or yperry@alphaone.org

Does Alpha-1 Raise Risk of Unusual Infections?

By Frank Kirchhoff and Charlie Strange
Institute of Virology, University of Ulm, Germany, and the Medical University of South Carolina

IN THE SPRING of 2007, it was discovered that some parts of the alpha-1 protein are capable of fighting infections. The particular virus that was studied in the research laboratory in Germany was human immunodeficiency virus (HIV), the cause of AIDS. The entire molecule of alpha-1 and even fragments of the molecule were able to prevent HIV from replicating. Later this year, a patient from Europe was described that had a particularly rapid course with HIV infection and was found to be severely alpha-1 deficient.

From this European experience, a questionnaire was mailed to the Alpha-1 Foundation Research Registry on July 1, 2007. The questionnaire was short, but asked the important question of whether particularly severe or unusual infections had been diagnosed. Affected individuals were asked to call and tell us their stories. The registry received only 11 responses. Eight of these came from individuals with bronchiectasis.

Bronchiectasis is one of the manifestations of Alpha-1 associated with abnormal permanent dilation of the airways in the lung.

Bronchiectasis is one of the manifestations of Alpha-1 associated with abnormal permanent dilation of the airways in the lung. The large airways do not clear infections as well as normal lungs, predisposing individuals with bronchiectasis to repeated and sometimes severe infections. One of the infections that is seen with extra frequency in Alpha-1 is called mycobacterium avium complex (MAC). This germ is a distant cousin to tuberculosis; however, it is not contagious person-to-person. MAC can be difficult to treat and often requires many years of multiple drugs to control the infection. Individuals with bronchiectasis should receive cultures to see if MAC infection is present.

One infection was seen in a lung transplant recipient who had a difficult time treating a different virus called Epstein-Barr virus (EBV). Since it is sometimes difficult to control EBV even in persons without Alpha-1, the single report is not enough to lay blame to Alpha-1 Antitrypsin Deficiency for this infection.

One of the important functions of the Registry is to provide a rapid response network to help researchers know the importance of their research focus. Sometimes we make a difference and sometimes we don’t. In this case we would conclude that more work needs to be done to define and to how extent alpha-1 antitrypsin assists in control of infections.

We want to thank the Registry members who contacted us. More importantly, we want to thank all of you for being members of the Alpha-1 Foundation Research Registry.
# 2008 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](mailto:mserven@alpha1.org).

<table>
<thead>
<tr>
<th>DATE</th>
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<td>March 9, 2008</td>
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<td>March 29, 2008</td>
<td>Regional Support Group Meeting</td>
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<td>April 26, 2008</td>
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<td>October 18, 2008</td>
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<td>Pittsburgh, PA</td>
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The Alpha-1 National Education Series is co-sponsored with the Alpha-1 Foundation and is made possible by unrestricted educational grants from AlphaNet, Centric Health Resources, CSL Behring and Talecris Biotherapeutics. For information on attending or exhibiting at an education program, contact Marlene Erven at 1-800-521-3025 or email [mserven@alpha1.org](mailto:mserven@alpha1.org).

*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 nearly $31 million to support Alpha-1 Antitrypsin (AAT) research and programs in 60 institutions in North America 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.

The Registry Update is funded by unrestricted educational grants from CSL Behring and Talecris Biotherapeutics.