

Everyone can be in a study



Letter from
the Director

WELCOME to this edition of the Alpha-1 Foundation Registry Newsletter. This edition focuses on some of the new studies in the Alpha-1 community, with a particular interest in PIMZ carriers. As we all know, Alpha-1 is about the family. When some family members of different generations share genes, they also share disease risks. It is very important to remember that the Alpha-1 gene is not the disease. What happens after the gene lands in the family is usually the most important aspect of Alpha-1. The stories from all of you contribute to our knowledge in more ways than you know. Thank you for engaging with the researchers who work with the

Registry and ACT Study to advance the health of lungs and livers in the Alpha-1 community.

We also join in celebrating the recent merger of the Alpha-1 Association and the Alpha-1 Foundation. The staff at MUSC has been supported by both organizations. The Alpha-1 Genetic Counseling Center was an Alpha-1 Association endeavor and now is being continued by the Alpha-1 Foundation. The Alpha-1 Foundation Research Registry and Alpha Coded Testing Study continue to be Alpha-1 Foundation supported. Our programs will continue to be integrated with the mission of the Alpha-1 Foundation.

I would also like to thank Sara Wienke, our latest genetic counselor to transition to industry. Sara contributed an article to this newsletter and we wish her the best in her career move. We feel very fortunate to have Kimberly Brown, MS, accept the position of Genetic Counselor. Kim has previously worked with our lab on an Alpha-1 project from

her previous job in genetic counseling for MUSC Maternal and Fetal Medicine. She already has new ideas to enhance the position. The transition occurred at the Alpha-1 National Education Conference where Kim was available for one on one genetic counseling and did a great job.

We continue to have challenges to enrollment in some of the research studies in Alpha-1. I would like to personally thank all of you who have participated in past research. There is a research study for almost everyone in the Alpha-1 community. If you have not participated previously, please consider doing so. If you have participated, thank you. Your calls and emails to the MUSC staff are always welcome if we can help you or your family.

Sincerely,

Charlie Strange

Charlie Strange, MD,

Director, Alpha-1 Foundation
Research Registry and ACT Study

Why do some Alphas develop liver disease?

A 5-year study needs ZZ subjects to learn how liver disease develops

By Rosemary Nagy, RDN, LD, MBA
Saint Louis University



Saint Louis University and the University of California, San Diego, are currently enrolling participants in a study sponsored by the Alpha-1 Foundation to understand the natural history of liver disease in people with PiZZ Alpha-1 Antitrypsin Deficiency. (Only ZZ Alphas are eligible.)

Patients without any history or evidence of liver disease and patients with mild or moderate liver disease are invited to participate. This study is intended to build an understanding of Alpha-1 liver disease and provide essential information for designing treatments for liver disease. The study is urgently in need of ZZ Alphas to volunteer!

The study will be conducted at multiple centers, is expected to last up to five years, and will enroll approximately 120 subjects. At least one more site in the Eastern U.S. will be opening soon.

Why should you participate? The only way to develop new treatments and therapies for Alpha-1 liver disease is to study many people with the disease. Also, the testing involved may give you new information on your health.

“One benefit of this study for the patient is a very thorough liver checkup,” says Jeff Teckman, MD, the principal investigator. “The patient has a consultation with a nationally known liver specialist, they have a wide panel of blood tests and other evaluations (liver ultrasound, PFTs) and it is mostly paid for by the study. Our results are shared with the patient, and if they wish, their doctor. We have already had two participants find out about other health

issues from the testing in this study, which could be treated and have health improvement result.”

The study consists of an enrollment visit and four annual follow-up visits. If you are interested in volunteering, here's what is involved:

1. You will be asked to travel to one of the enrollment sites.
2. Your family history, medical history, current health, medical treatments, liver tissue, and blood (for clinical, genetic and research testing), are collected at certain times over the five-year period.
3. A liver biopsy and FibroScan testing (an ultrasound

technology) are performed at enrollment and again in year 5.

4. At each of the visits a liver specialist will examine you, and blood work will be performed to assess your liver health.

All research activities, including liver biopsy, laboratory testing and physical exams, are paid for by the study. You will be given a copy of your laboratory test results and liver biopsy findings to share with your personal physician.

To be eligible you must be at least 18 years of age, have a documented PiZZ phenotype or genotype, and be willing to be followed for 5 years. Some of the exclusions to participation include evidence of advanced liver disease, advanced lung disease (FEV1 < 40% predicted), previous organ transplantation, and evidence of chronic hepatitis B, hepatitis C, or HIV. If an initial review of your records determines you may be eligible for the study, you must have routine laboratory testing to determine if you can safely undergo a liver biopsy. The study will pay for these lab tests.

This study includes adults both with and without known liver disease. The investigators hope to learn what causes liver disease in some of the patients and how that

liver disease progresses. Researchers are wondering if new therapies can be developed to prevent or stop the progression of Alpha-1 associated liver disease. This is the first multi-center prospective natural history study of adults with Alpha-1 conducted in the United States.

Study subjects who live more than 50 miles from the sites will be reimbursed for their travel, up to a maximum of \$200 per visit.

For information on the St. Louis site, contact Jacki Cerkoski RN, BSN at **314-977-5239** or cerkoski@slu.edu

To speak with a coordinator at the San Diego site, contact Phirum Nguyen at **619-471-0774** or psnguyen@ucsd.edu.

You may also find additional study information at www.clinicaltrials.gov; search for study number **NCT02014415**.

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You may contact the Alpha-1 Foundation Research Registry staff by email, at alphaone@muscd.edu for additional assistance in locating resources related to Alpha-1 research, to obtain information about current research activities, to participate in the Research Network or Registry, or to receive Foundation publications.

Tell us what you want! We want to hear from you

The Research Registry wants you to tell us what you would like to read about in the next issue. Please express your interest and suggestions by emailing us at alphaone@muscd.edu. We also welcome your questions for the Alpha Doc or Genetic Counselor! We will do our best to answer them.

Tell us your Alpha-1 story

Do you have a unique, fascinating Alpha-1 experience to share? Please call me at 1-877-886-2383 or email me @ schwarzl@muscd.edu.

Thank you!
Laura Schwarz
ACT Study Coordinator

Alpha-1 testing for all: An Alpha shares her story



By **Laura Schwarz**
ACT Coordinator

Larnetta Jones of Dallas, TX, is an African-American woman with Alpha-1.

If you've looked around at Alpha-1 national conferences and education days, there does not appear to be a lot of racial diversity in the Alpha-1 community. Alpha-1 is a genetic disorder that is more common in some populations than others, especially those from northwestern Europe. Yet we also have concerns about preconceptions that may be leading to inadequate Alpha-1 testing for minority races.



For example, minorities with Alpha-1 symptoms may be less likely to be offered testing, due to false assumptions about the populations that can be affected. Further, some populations have been historically less likely to seek or receive equitable medical care or to participate in research.

The story of Larnetta Jones highlights these issues and emphasizes the meaningfulness of quality care and Registry participation for all.

Jones didn't know what to think when she saw the shocked look on her doctor's face. He held her lab results in front of him as he whispered, "Is your mother black?"

Jones answered, "Yes, why?"

"Well, is your father black?" he whispered again.

"Yes," she answered.

"You have a genetic disease called Alpha-1 Antitrypsin Deficiency (Alpha-1) but it's a white people's disease!"

Larnetta was equally surprised, but also relieved to finally have a name and a diagnosis for her condition. She is one of only a few African-Americans who have been diagnosed with Alpha-1.

Larnetta's story began in the summer of 1996 when she was only 20 years old. At the time she lived in Kansas City, MO.

One day she heard strange popping noises in her chest and then felt severe cramping and "pin sticks" in her

back. She was understandably terrified. She was alone but felt she needed immediate care. She drove herself to the emergency room at Truman Medical Center. The doctors told her that her left lung had collapsed and inserted a chest tube to re-inflate the lung. They reported a diagnosis of spontaneous pneumothorax with pneumonia and asthma.

Jones went home with an antibiotic, an inhaler and instructions to stop smoking.

Like many 20-year-olds, she did not follow the doctor's orders. She continued to smoke and she had five more lung collapses between 1997 and 1999, with continued episodes of "walking pneumonia."

After the first two collapses, she recognized the symptoms and knew what to do. She learned to keep herself from becoming overanxious. Her last collapsed lung occurred in November 1999 when she was pregnant. She went to St. Luke's Hospital, where she was considered high risk due to serious pulmonary issues during pregnancy. Her low weight also concerned her doctor, so he extended her stay. After over a month at St. Luke's, her baby, Cirr-Patrick Jones, arrived two months early by emergency C-section. After another month, both mother and son were discharged home.

Jones's job at this time was caring for an elderly woman in her neighborhood. This job included cleaning the



Larnetta and her son, Cirr-Patrick.

woman's house and, interestingly, she provided Jones with a mixture of vinegar and water as the only cleaning agent. Jones remained at this job for seven years while she attended school to become a certified nursing assistant.

Believing she had something other than asthma or bronchitis, she continued to see various doctors about her breathing and lung issues. In 2010, she went to see a pulmonologist who ordered some lab work including a thyroid test because of her weight loss, and an asbestos test because Jones spent a lot of time in the elderly woman's old home. Both tests results were negative.

This pulmonologist had also tested Jones to rule out Alpha-1 and this is when they were both taken aback to find that she had a "white people's disease." He explained the seriousness of having Alpha-1 and that her top priority upon leaving his office was to stop smoking. This time she followed her doctor's orders and quit.

She began augmentation therapy soon after. Her doctor provided her with a great deal of information, including the Family Awareness DVD and how to contact the Alpha-1 Foundation and obtain an ACT testing kit for confidential testing.

In June of 2011, Jones and Cirr-Patrick moved to Dallas, where she feels the air agrees with her.

Jones was tested through the ACT Study to clarify her genotype, and her result returned as ZNull. Null alleles are rare gene changes that are often not identified through first-line testing. We recommended that she order an additional test capable of detecting subtle DNA sequence changes through the Alpha-1 Foundation's DNA and Tissue Bank at the University of Florida.

She followed through on our suggestion. After she returned her informed consent and research questionnaire to the Tissue Bank, they sent her a test kit containing blood tubes and an overnight return envelope. She took the tubes into her physician's office for her blood to be drawn and returned them to the University of Florida in the express mailer.

Her DNA test revealed a rare null allele called QO Cincinnati. This result doesn't change her deficiency or treatment, but knowing the exact genetic change in the family may be beneficial for young Cirr-Patrick and other family members.

Jones has been on disability for the last two years and hopes to be added to a transplant list in the coming months. She plans to continue spreading the word about Alpha-1 and the importance of getting tested. She would love to see those who donate at her local plasma center receive more for their time and effort, "because they truly are lifesavers." She especially appreciates her infusion nurse and her AlphaNet coordinator, and speaks proudly of her son, who is now 14 and enjoys playing football and other sports with his friends.

Like many Alphas, Jones knows what it's like to live for years with unexplained illness and the relief that can come with finally receiving the right diagnosis. Sharing her story now helps other African-Americans and care providers recognize the importance of testing for uncommon, yet important, causes of disease.

Does inflammation harm Alphas who exercise? No!

Study surprise: Alphas with COPD who exercise have less inflammation than other COPD patients

By Deirdre Walker
Registry Coordinator



In 2009, the Alpha-1 Research Registry recruited members for a study that looked at muscle function. The muscles of people with COPD often get weak and lose muscle weight; how this happens is not known. One of the questions studied was whether muscle weakness in Alphas (people with Alpha-1 Antitrypsin Deficiency) who have COPD is different from muscle weakness in people with COPD who do not have Alpha-1.

Mark Olfert, MD, of West Virginia University, and Peter Wagner, MD, of the University of California, San Diego, examined the role of inflammation in skeletal muscle abnormalities. Specifically, they looked at circulation of inflammatory cytokines (small proteins associated with the body's response to inflammation) and the effect that augmentation therapy and exercise had on systemic inflammation in Alphas with COPD.

Participants were recruited based on their Alpha-1 genotype, their COPD history, and lung function. The study consisted of a 2-day visit that included pulmonary function testing, x-rays, exercise tests, blood tests and muscle biopsies. The muscle and blood samples were examined for markers of inflammation and blood vessel changes.

COPD has been linked to environmental irritants such as cigarette smoke, which cause acute and chronic (short and long-term) airway inflammation. One of the functions of alpha-1 antitrypsin protein (AAT) is to block the production of inflammatory cytokines in response to these irritants, protecting the lungs from inflammation caused by infection and inhaled irritants such as tobacco smoke.

It is believed that the loss or reduction of AAT in Alphas causes chronic systemic inflammation. Elevated levels of these inflammatory cytokines in the blood have been associated with COPD severity and exacerbations. Evidence suggests that in Alphas with the Z allele, cytokines may be increased. The study was intended to find out whether augmentation therapy influences systemic inflammation and muscle function.

Exercise is often recommended as part of a treatment plan for people with COPD. Exercise is an important factor in maintaining health, from boosting the immune system to improved effects on cardiovascular health. In recent years, researchers have learned that exercise also increases the body's pro-inflammatory cytokines. In healthy people (who have plenty of AAT), this increase is met with the body's own response of anti-inflammatory cytokines, offsetting any ill effects.

Could it be possible that exercise is harmful to patients with Alpha-1?

In response to that question, Dr. Olfert and his team examined the effects of exercise on Alphas both on and off augmentation therapy, as well as Alphas with and without COPD. Their aim was to look at the potential influence of augmentation therapy on biomarkers of systemic inflammation. They hypothesized that under both resting conditions and in response to exercise, the replacement of alpha-1 antitrypsin in people with COPD would result in lower levels of circulating inflammatory cytokines compared to those not on augmentation therapy. They also compared Alphas with COPD to usual COPD patients, as well as Alphas without evidence of obstructive airway disease.

Alphas who participated in this study were grouped on the basis of whether they had COPD; whether they had severe deficiency genes (ZZ or SZ); and whether they were on augmentation therapy. There were two control groups: usual COPD patients (non-Alphas), and healthy people. Each participant was studied over a 2-day period.

On the first day, participants consented to have their blood drawn for circulating AAT level, genotyping and a baseline concentration of cytokines in the serum. The first day also included pulmonary function testing (standard breathing tests), a whole-body x-ray scan to determine body fat percentage, and two separate exercise tests: a single-leg knee extensor exercise, and standard two-legged bicycle exercise. Have you ever ridden a bike with one leg? If you only ride with one leg, can you ride for twice as long?

Exercising one leg at a time allows patients with heart and lung problems to remain active while also receiving many of the same benefits as a full-body workout, such as running and cycling. This also gave researchers the ability to biopsy, or take a sample of tissue, from both the exercised muscle and the resting leg muscle. Blood was taken before, during and after exercise to determine if the levels of cytokines had been altered by the workout.

Circulating expression of some cytokines is altered between 4-8 hours after exercise, while other cytokine expression can be elevated anywhere from one to 24 hours after a workout. Researchers used this knowledge to determine that blood would be drawn 4 hours after exercise to examine the cytokine levels. They compared this to cytokines in the blood drawn on day 1 before exercise.

So is exercise more harmful than good for Alphas, or for people with COPD and chronic systemic inflammation? The answer appears to be no!

Exercise showed no effect on the levels of circulating cytokines. There was no evidence of exercise-induced inflammatory stress in either the Alphas or the non-Alpha COPD patients. The researchers did find that systemic

inflammation in the Alphas they studied was lower than in the non-Alpha COPD patients, but higher than the healthy controls. Alphas with COPD also had less inflammation than the non-alpha COPD patients – suggesting that they do not experience the same inflammatory cytokine response usually seen in patients with COPD. An unexpected finding of the study was that the group of Alphas that did not have lung dysfunction (they had normal breathing tests) tended to be more physically active throughout their lives.

Unfortunately, the study was not large enough to show whether augmentation therapy can reduce inflammation and improve muscle functioning during exercise.

The study was not designed to test the question whether regular physical activity might protect (or slow) the development of COPD in Alphas, but it raises several provocative questions for future research. For example, if exercise is protective for Alphas, how much and how often must one exercise?

A big thanks to all the research registry participants who helped to make this study possible. Stay tuned: there will be more opportunities in the future to participate in research studies aimed at trying to improve the lives of Alphas.



A patient performs a kick exercise with his left leg only, his right leg resting on a footstool. Mark Olfert, MD, in profile at far right, and Peter Wagner, MD, at center just behind the patient's pillow, are simultaneously drawing the patient's blood from artery and vein catheters for testing. The patient is breathing through tubes into the collection bags at left. Other lab workers are in the background.

Smoking makes risk of MZ lung disease 10 times higher

Study finds non-smoking carriers have normal risk of lung disease

By Kimberly Brown, MS, CGC

Director, Alpha-1 Foundation Genetic Counseling Program



Alphas are unique in many ways and being a carrier of Alpha-1 is a little less straightforward than being a carrier for most “recessive” diseases. Some questions about the significance of being an Alpha carrier are still being answered. Studying Alphas and carriers compared to the “normal” population continues to shed light on what being an Alpha carrier means.

In basic Mendelian genetics a “carrier” is a person who has two different versions of the same gene (called alleles), where one overrides the other and is the only one expressed. This describes recessive inheritance, where a recessive allele is not expressed at all when in the presence of a dominant allele. The recessive allele is carried silently and has no effect, so people often don’t know they’re carriers until after a family member is diagnosed or someone gets tested for another reason.

Recessive disease shows up only in people who have two copies of the recessive (abnormal) gene. Because we inherit one copy of each gene from our mother and the other copy from our father, a person is at risk to inherit a recessive disease only when both parents are carriers of, or affected with, the disease. For true recessive diseases, people might want to know their carrier status to find out if their children are at risk, but not for personal health reasons. When both parents are carriers for the same disease, the risk for each child to be affected is 1 in 4 (25%).

True to recessive fashion, severe classic Alpha-1 Antitrypsin Deficiency occurs when someone inherits two deficiency alleles (for example, ZZ, SZ, Znull). So the word “carrier” works well in Alpha-1 when discussing the risk for severe deficiency or a couple’s chance to have a severely affected child. The word carrier is less accurate from a biochemical standpoint, which is why there are still questions about what being MZ means. In Alpha-1, both alleles independently instruct protein production. This is where Alpha-1 is different from “recessive” diseases; the

term “co-dominant” is more appropriate in this case. This means that both alleles are expressed and the total amount and type of Alpha-1 protein produced depends on the combination of alleles a person has.

SERPINA1 is the name of the gene that tells our bodies how to make Alpha-1 protein. The normal *SERPINA1* allele will produce normal “M” protein. People with anything other than two M’s (MM) usually have lower levels of Alpha-1 protein in their blood. The Z protein gets trapped in the liver and fails to enter the bloodstream normally, while S protein is broken down faster than normal. People with one M and a second abnormal allele are called carriers. They usually have a level of Alpha-1 protein in blood plasma of about 60% of normal. ZZ Alphas are severely deficient, with about 10-20% of the normal amount of alpha-1 protein in plasma.

So Alpha-1 carriers have an intermediate amount of Alpha-1 protein in serum compared to normal MM and deficient ZZ Alphas. So, what are the effects of having an Alpha-1 level that is higher than a ZZ, but lower than normal? Research continues to clarify the risks for MZ carriers.

Kevin Malloy, a respiratory researcher in Ireland, recently led a study to examine risk for COPD in MZ carriers compared to people with normal MM genes. Malloy worked with both Irish colleagues and American colleagues at Brigham and Women’s Hospital in Boston. The findings emphasize the importance of gene-environmental interaction in the development of lung disease.

This study of 99 MM and 89 MZ individuals controlled for factors such as age and sex, and measured lung function by genotype and smoking status, both separately and combined. “Never smokers” were defined as people who smoked fewer than 20 packs of cigarettes or less than 12 oz. of tobacco in a lifetime, or less than one cigarette a day for a year. Spirometry was used to measure lung function and the presence or absence of COPD.

When the entire MZ group outcomes were compared to

MM outcomes, MZs had more airflow obstruction and about a 5-fold increased risk for COPD. But those numbers are deceptive: *MZ smokers were at about a 10-fold increased risk, while the risk for MZ never-smokers was not significantly worse than MM risk.*

This study demonstrates that while MZ carriers are at increased risk for lung disease, the risk is strongly influenced by exposure to cigarette smoke. It’s reassuring for carriers that MZ nonsmokers in this study were not at an increased risk for COPD.

The majority of lung and liver disease in humans occurs due to combinations of many genetic and environmental influences. Alpha-1 mutations are the single best-defined genetic factor, even though only a small percentage of people with lung or liver disease have Alpha-1. Understanding the risk conferred by your genes, as well as other risk factors, is important in order to take steps to improve or maintain your health. Identifying factors that contribute to disease risk will allow us to recommend more risk-reducing choices.

Because MZ carriers are more susceptible, if you are a carrier you should adamantly avoid smoking! If you do smoke, ask your doctor about resources to help you quit. The Z allele has been most thoroughly studied, but future

research may better clarify the significance of carrying the S and other rare alleles. Remember, smoking is an independent risk factor for COPD in people of all genotypes, and should always be avoided.

Families of Alphas are usually aware of augmentation therapy, which involves infusion of alpha-1 protein from purified plasma of healthy people into a person with Alpha-1. The goal is to achieve a protective level of alpha-1 protein in the blood circulation. A common question concerns who might benefit from therapy. The potential benefits and risks of any medical treatment should always be discussed with a specialist who knows your personal health history and situation.

Personal genomics such as gene variants are being studied in all areas of medicine. Belonging to the Registry is an important way to contribute to advances in Alpha-1 knowledge. We continue to make great progress in our understanding of Alpha-1. If you share these research findings with family members, you may encourage them to get tested and make healthy lifestyle choices or changes.

If you or your family have questions about genetics, personal testing options or results, call the Alpha-1 Foundation Genetic Counseling Program at **1-800-785-3177**.

Donating your tissue for Alpha-1 research

By Deirdre Walker

Registry Coordinator



The National Disease Research Interchange (NDRI) is a not-for-profit organization founded in 1980 to help researchers acquire resources needed to understand and cure disease. A core mission is to provide biosamples to researchers who work to discover new targeted treatments. One program, called the National Rare Disease Biospecimen Resource, has partnered with many rare disease organizations to acquire tissue samples from affected individuals for research purposes. So what does this mean for us?

It is hard to walk into a building and drop off a piece of liver or lung for research, yet these samples are critically needed to make advances. If you think about it, the only times these tissues are easily accessible are when we die or

have surgery such as an organ transplant. In order for liver or lung tissue to be helpful to researchers it must be meticulously processed very quickly after retrieval, so planning is key. To fill the need for these biosamples within the Alpha-1 community, the NDRI has made it simple to donate for those who are interested. All you have to do is make a phone call.

If you are scheduled for surgery or a transplant, you can donate your tissue to help Alpha-1 researchers by calling the NDRI at 1-877-221-NDRI (6374). There is no cost to you or your family. The NDRI will make all the arrangements and you will have helped supply resources that are urgently needed in the research community. After you consent and provide the information needed, NDRI representatives travel to pick up and distribute samples to medical centers across the country. The time to call is before your procedure!

Alphas can participate in this program by calling NDRI or by visiting their website at ndriresource.org and looking at their donor programs.

Registry members and their spouses react differently to communication

By Marisa Greenberg, MA
Pennsylvania State University

For the past two years, Rachel Smith, Associate Professor of Communication Arts and Sciences, along with a team of Pennsylvania State University researchers, has been investigating the communication and decision-making patterns of married couples. She surveyed couples through the Alpha-1 Research Registry, and their answers have provided insights into the way couples communicate and the influences between spouses.

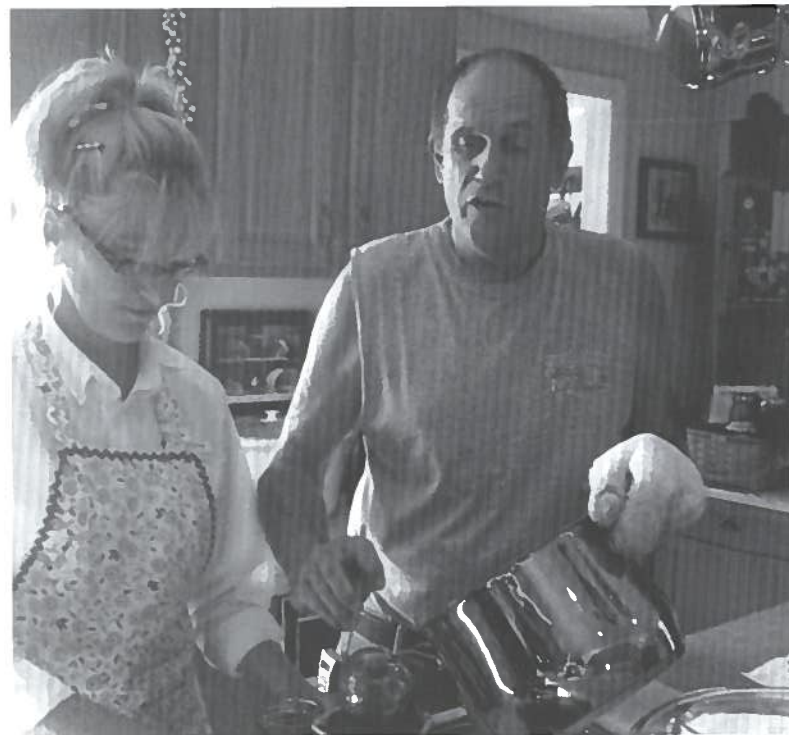
If adults are in committed relationships when one of them gets tested for Alpha-1, their partners or spouses also may be involved in discussing test results and deciding on future actions, including disclosing the discovery of a genetic condition to others.

For example, the Alpha-1 Foundation's website highlights how couples manage medical testing, interpret results for Alpha-1 Antitrypsin Deficiency (Alpha-1), and integrate this into other health conditions. The dynamics of a couple regarding beliefs and communication choices about an Alpha-1 diagnosis are crucial, but are not well understood.

Smith's work has allowed for the identification of five classes of married adults, based on their self-reported communication patterns with their spouses. These patterns range from spouses who talk frequently and want to talk more, to spouses who seldom talk and want to talk even less. Communication patterns of a couple may vary, and they influence decisions about disclosures to family, insurance companies, and physicians. Importantly, the opposite also seems to be true: perceptions of the testing experience, and possible risks such as insurance discrimination, predicted the pattern of communication that the spouses used.

The influences predicting spousal communication and perceived stress seem to differ between Registry members and their spouses. Registry members (Alphas and carriers) who reported talking more with their spouses about Alpha-1 reported no impact on their stress. But the spouses of these same Registry members reported increased stress if they had more discussions!

These findings indicate that genetic testing affects families in complex ways and offers some insight into these complexities.



Alpha-1 couple — Marian and Larry Hoffman preparing homemade jam for an Alpha-1 Foundation fundraiser. They've been working on fundraising for research ever since Larry was diagnosed.

Your genes: Are they your fate?

Don't believe it! Your own lifestyle can help you to stay healthy



Sara Wienke, MS, CGC
Former director, Genetic Counseling Program

Genetic determinism is the idea that our genes are our fate.

For some conditions, this may be true.

For example, people with the deltaF508 mutation (a mutation is a change in a gene, which can often lead to disease) in both copies of their CFTR gene will have cystic fibrosis, including lung disease and pancreatic insufficiency. (But even in those cases, changes in lifestyle and treatment can make a big difference. Better treatment has extended the lifespan of people with CF dramatically in recent decades.)

For more complex conditions like emphysema, there are many causes and one gene does not tell the whole story: while each gene does code for a protein in our cells, this gene works in concert with many other genes. Furthermore, our environment affects how our proteins respond.

Our entire body is made up of millions of cells that work together to function as one living being. The *SERPINA1* gene is the recipe or instruction manual that tells our cells how to make the alpha-1 antitrypsin protein.

Alpha-1 antitrypsin is important because it protects our lungs from damage caused by inflammation. Primarily made by our liver cells, it gets excreted into the blood where it travels to the lungs to protect the lung tissue. The normal version of the gene, the M, does just that. The Z version of the

gene does not.

Like a recipe gone wrong, the Z *allele* makes the alpha-1 antitrypsin protein in the wrong shape. Because of this, the Z versions of the alpha-1 protein can bind to each other in long chains or clumps called polymers. Only 5-15% of the Z protein will be released into the blood stream, where it continues to form polymers. Only a small fraction will actually be able to protect the lungs.

Everyone needs this lung protection. The PiZZ protein is actually enough protein for some people to get through life with normal lung function. Even people with PiMM (normal) genes have a background risk for COPD and liver disease. People of all genotypes who inhale cigarettes, large amounts of other particles or fumes are more likely to develop lung disease.

For people who already have COPD or emphysema, finding out that they are PiZZ may simply explain why they developed symptoms. It may even be a relief from self-blame for smoking or not knowing why they got sick.

For people without symptoms, discovering a deficiency genotype can help them to feel that there is something they can do to prevent or reduce illness by living a healthier lifestyle. Naturally, some may feel defeated by the discovery of genetic susceptibility. Yet Alpha-1 is a prime example of a condition where genes do not tell the whole story and early genetic detection can lead to improved outcomes.

Many people are now being tested at younger ages, before the onset of emphysema and potentially even before harmful lung exposures. Future articles will explore pre-symptomatic testing and the impact that can have on health outcomes and psychosocial adjustment.

Calendar 2014

Building Friends for a Cure Events

Feb. 27/ Ongoing	Hike for a Cure	Springer Mountain, GA to Mount Katahdin, ME	Karen Maidment km Maidment60@comcast.net
Oct. 11	Alpha-1 Fabulous 50s Dance for a Cure	Hyde Park, PA	Larry & Marian Hoffman alfalfaalphagroup@gmail.com
Oct. 26	River Walk for Alpha-1	Mishawaka, IN	Terri Nickerson canary.terry@live.com Tom Corron tcorron@live.com
Nov. 8	Step Forward for Alpha-1 Walk	Myrtle Beach, SC	Angela McBride amcbride@alpha1.org
Nov. 15	Step Forward for Alpha-1 Walk	Jupiter, FL	Lisa Kosak Lisa.kosak@gmail.com
Nov. 22	Italian Night	Clarkston MI	Jeannette Therrian jltherrian@live.com
Dec. 11	Las Vegas Rocks Alpha-1	Las Vegas, NV	Gus Straub kgstraub1@aol.com

Education Days

Nov. 1	St. Louis, MO
Dec. 13	Las Vegas, NV

Support Group Meetings

Oct. 2	Bakersfield, CA	O2 Seekers of Bakersfield	Oct. 27	Grand Island, NE	Central Nebraska Alphas
Oct. 4	Scottsdale, AZ	Alphazonies	Nov. 1	Scottsdale, AZ	Alphazonies
	Oak, PA	Alpha Opportunities		Hersey, PA	Southeast Keystone Alphas
Oct. 9	Needham, MA	Massachusetts Alphas	Nov. 8	North Myrtle Beach, SC	Myrtle Beach Regional SGM
Oct. 11	Colorado Springs, CO	Pikes Peak AlphaBeaters		Peoria, IL	Open Arms for A-1
	Gainesville, FL	Gainesville Alphas		Springfield, MO	Show-Me Alphas
	Nashville, TN	Music City Alphas	Nov. 11	Portland, OR	Alpha-1 PDX SG
Oct. 14	Portland, OR	Alpha-1 PDX SG	Nov. 15	Rockford, IL	Alphas of Northern Illinois
Oct. 15	Orlando, FL	Alpha Central of Florida		San Diego, CA	San Diego Alphas
Oct. 18	Richmond, VA	Central Virginia Alphas		Monroeville, PA	AlphaBurghers
	Houston, TX	Bayou City Alphas		Jupiter, FL	Alpha Gators
	New Britain, CT	Connecticut Nutmeggers			

Virtual Support Group Calls

Date	Group	Topic	Speaker
Oct. 21	Alpha-1 Kids	Infants to 5 Years: What to Expect?	Philip Rosenthal, MD
Oct. 28	Timely Topics/Pre & Post Transplant/Caregivers	Open Enrolment: Private Insurance and Medicare	Barbee Bennington
Dec. 16	Alpha-1 Kids	Liver Research Update	Jeffrey Teckman, MD

Directions for Dialing in: On the assigned day at 9 pm Eastern, dial this number: **1-800-920-7487**.

When prompted, enter the code: **9335 9985#**

For more information about events, contact us, 1-800-228-7321.

Alpha-1 Foundation

The Alpha-1 Foundation is committed to finding a cure for Alpha-1 Antitrypsin Deficiency and to improving the lives of people affected by Alpha-1 worldwide. The Foundation has invested more than \$50 million to support Alpha-1 Antitrypsin Deficiency research at 97 institutions in North America, Europe, the Middle East and Australia.

AlphaNet

AlphaNet, Inc. is a not-for profit organization that provides a comprehensive disease management and prevention program to improve the lives of people with Alpha-1 Antitrypsin Deficiency. AlphaNet also oversees and sponsors clinical trials involving Alpha-1 therapies.

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