The pathways to Alpha-1 Antitrypsin Deficiency (Alpha-1) testing are changing as genetic testing becomes more common and easy to access. More people are testing their genes through large panel tests. People diagnosed with Alpha-1 by one of these tests are usually healthier than the Alphas who have been diagnosed before. As our community grows, we look for ways to meet the needs of all Alphas and understand the full spectrum of Alpha-1. We encourage even healthy Alphas to get involved. Doing so can make a difference on the health of your family and on your own. Your involvement also empowers research and raises awareness.

While testing options grow, there are still COPD patients who have not been tested for Alpha-1. We share one success story of how to make Alpha-1 testing standard for people with COPD in a large healthcare system. Once diagnosed, Clinical Resource Centers (CRCs) provide top quality, guideline-based care for Alphas. If you have not visited a CRC, the Alpha-1 Foundation can help you do so. There are some 80 CRCs in the United States. Our featured CRC in this edition is Columbia University Medical Center (CUMC) in New York City.

We are looking forward to seeing you at the Alpha-1 Foundation’s 27th annual National Education Conference on June 29-July 1 in San Francisco. This is an excellent opportunity to learn more about Alpha-1, meet the specialists and connect with Alphas and families.

You are the most important part of the Alpha-1 research. We have asked several Alphas to share with you their experience of being in a study. If you have been in a study and would like to share your story, please email us at alphaone@musc.edu. As always, please contact us with any questions or concerns at 877-886-2383 or alphaone@musc.edu.

Sincerely,

Charlie Strange, MD,
Director, Alpha-1 Foundation
Research Registry and ACT Study
The Importance of Research

By Gwen Blanton
Research Coordinator

New treatments, new medications, and ultimately a cure, are what we strive for and work toward everyday as we conduct clinical research.

The road traveled to achieve these goals is usually long and winding with a few bumps along the way. Most people do not realize that the average timeline from beginning the first trial of a new treatment to getting FDA approval for clinical use is eight to 10 years. And that does not take into account all the previous years spent in the lab trying to get the formula just right and getting enough preliminary data to go forward. Researchers and clinicians have been conducting clinical studies dating all the way back to the 1700s. One of the biggest hurdles can be a shortage of individuals to volunteer to participate, especially in rare diseases.

Research participants make medical advancements possible. Without you, this would not happen. We always have new trials in the works and are always looking for new participants. Scientists and doctors are grateful to research participants, but what is it really like to be in a study? Why you? Several Alphas answered the call and answered our questions. With this registry newsletter we will begin a series of articles in where you, the participants, get to tell your stories and experiences (good and bad) about being in a study.

Helen Patnaude, Alpha from South Carolina

I signed up because I want to do whatever I can to help find a cure for this condition. Being diagnosed in 1987, a few months after losing my 30-year-old brother to AIAD, I felt I had been given a death sentence. Not much was known about Alpha-1 back then and I knew that needed to change.

I would tell people who are thinking of being in a study that not only are they helping with research, but they have an advantage of receiving treatment that may improve their condition.

The best part of being in a study was being able to see how I am doing by the tests I receive. The worst, for me, was my allergies interfering with my breathing tests.

Research is important to hopefully find a cure or a solution to help those affected to live a better life. Being a genetic condition, it is like a time bomb waiting to strike again. I don’t want my family or anyone’s family to be affected by this condition. By participating, I feel I am trying to help prevent someone from dying like my brother did. It is an advantage to me to be able to try treatments that may help me and others.
Belinda Williams, Alpha from North Carolina

I was first prompted to get involved in research not long after I was diagnosed. I wanted a better life for the next generation as I had small children at the time. My children are carriers of the disorder I have, but I wanted to be proactive for their sake and to hopefully one day see improvement in my own care.

My advice to others who may be considering research participation is: do your own research of the trial, weigh the pros and cons, and how it might benefit you or your loved ones. We, as patients, are the best advocate for our own care. If we don’t give our time, we can’t expect to see improvements in our own health.

I’ve participated in many research studies over the years and I have had more pros than cons. I have had a few cons along the way, but keep in mind, we get the best care we could possibly ever get from top notch doctors and medical staff. The staff becomes like family through a trial as we spend a lot of time together. I feel I receive the best possible care through a clinical trial. Even if I haven’t experienced the best outcome or the trial didn’t go as planned, I’ve never suffered lasting effects.

Also, as I get older, everything is checked out about my health, so if I felt something wasn’t just right, it would surely be uncovered during a study.

Clinical trials are of the utmost importance not only to ourselves, but for generations to come in the way of improved treatments, medical breakthroughs, and even a cure.

Calendar 2018

**Building Friends for a Cure Events**

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<tr>
<th>Date</th>
<th>Event Name</th>
<th>Location</th>
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<tr>
<td>Ongoing</td>
<td>Hiking for a Cure</td>
<td>Pacific Crest Trail</td>
<td><a href="http://facebook.com/hiking4acure">http://facebook.com/hiking4acure</a></td>
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<td>Aug. 4</td>
<td>Step Forward for Alpha-1</td>
<td>Denver, CO</td>
<td>Angela McBride <a href="mailto:amcbride@alpha1.org">amcbride@alpha1.org</a></td>
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<tr>
<td>Sept. 28-30</td>
<td>Escape to the Cape</td>
<td>Cape Cod, MA</td>
<td>Angela McBride, <a href="mailto:amcbride@alpha1.org">amcbride@alpha1.org</a></td>
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<td>Oct. 6</td>
<td>Step Forward for Alpha-1</td>
<td>Mishawaka, IN</td>
<td>Terry Nickerson &amp; Carla Ladig, <a href="mailto:cladig@alpha1.org">cladig@alpha1.org</a></td>
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<td>Oct. 13</td>
<td>50’s Friends for a Cure Dance</td>
<td>Shoemakersville, PA</td>
<td>Marian &amp; Larry Hoffman <a href="mailto:alfalfaalphagroup@gmail.com">alfalfaalphagroup@gmail.com</a></td>
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<td>November</td>
<td>Alpha-1 Awareness Virtual Walk</td>
<td>Nationwide</td>
<td>Angela McBride, <a href="mailto:amcbride@alpha1.org">amcbride@alpha1.org</a></td>
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For more information about Building Friends for a Cure, contact Angela McBride, (877) 228-7321, ext. 233 or amcbride@alpha1.org

**Education Days**

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<td>August 25</td>
<td>Omaha, NE</td>
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<td>Sept. 22</td>
<td>Detroit, MI</td>
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<td>Oct. 20</td>
<td>Seattle, WA</td>
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**National Education Conference**

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<tr>
<td>June 27-July 1</td>
<td>San Francisco, CA</td>
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For more information about Education Days or the National Conference, contact Kim Carballo, (877) 228-7321, ext. 323 or ycarballo@alpha1.org

For more information about upcoming events and support group meetings, please visit the calendar at alpha1.org or call us at (877) 228-7321.

**Notice:** Last Spring, Alpha-1 Genetic Counselor Kim Brown became Kimberly Foil after exchanging wedding vows with her husband, Mark Foil Jr. She looks forward to continuing to help Alphas in the years to come.
By Eryn Varano
Registry Coordinator

Columbia University Medical Center (CUMC) is situated on a 20-acre campus in Northern Manhattan, NY. CUMC shares its site and facilities with New York-Presbyterian Hospital and the New York State Psychiatric Institute.

Though the center has only recently received designation as an Alpha-1 Clinical Resource Center (CRC), the multidisciplinary practice has long focused on rare diseases of the lung, providing patients with comprehensive personal care and access to specialists. One of those specialists, Jeanine D’Armiento, MD, PhD, has a long history researching Alpha-1 Antitrypsin Deficiency (Alpha-1) and working and volunteering for the Alpha-1 Foundation.

She received both her MD and PhD in biochemistry and molecular biology at Rutgers University. After leaving Rutgers in 1992, she completed her Internal Medicine residency and Pulmonary fellowship at CUMC. She is now Director of the Center for Molecular Pulmonary Disease in Anesthesiology and Physiology and Cellular Biophysics, and Director for the Center for Lymphangioleiomyomatosis (LAM) and Rare Lung Diseases.

D’Armiento’s passion for research in lung injury and emphysema began in medical school and continued to evolve, leading to her interest in Alpha-1 — the only known form of hereditary emphysema. As a young investigator, she was awarded an Alpha-1 Foundation travel grant and was able to meet with the leaders of the Alpha-1 Foundation. This led to her regular attendance at the National Education Conference, and to the funding of her very first lung study. Today, she serves as Treasurer on the Alpha-1 Foundation’s Board of Directors, and last June, she received the Physician Appreciation Award for her volunteer service to the Foundation and her “many years of dedication to Alpha-1 patients.” Earlier this year she was honored with the Alpha-1 Foundation Shillelagh Award, at the 2018 Celtic Connection event.

Though D’Armiento’s research interests are broad, her primary focus for the past 20 years has been in understanding the mechanism of lung destruction in chronic obstructive pulmonary disease (COPD). She has focused on basic mechanisms in lung injury and repair, developing an understanding of the role of enzymes called matrix metalloproteinases that lead to tissue destruction during disease processes. She is now using her knowledge to test potential therapies in preclinical models, and is developing methods to identify biomarkers in emphysema.

D’Armiento is excited to build her Alpha-1 practice alongside her colleague, Monica Goldklang, MD. The two see patients together and are engaged in multiple clinical trials. They are presently conducting two Alpha-1 Foundation clinical trials led by Goldklang that they hope will help identify ongoing lung injury in Alpha-1 patients and potentially guide future treatment.

D’Armiento would like to thank all who are actively participating in Alpha-1 research. She stresses that it is due to your efforts and generous support that we have been able to make such progress, and it is because of you that we will continue to improve the lives of Alphas and ultimately, identify a cure for Alpha-1.

To schedule an appointment with D’Armiento or Goldklang at the Columbia University Medical Center CRC, call 212-305-3745 or email their clinical coordinator, Laura Fonseca, at lj2560@cumc.columbia.edu.
Gene Therapy Study Seeks ZZ and Znull Alphas

By Danielle Woodford
Research Coordinator

Big things are happening in Alpha-1 research. We are four months into the ADVANCE study. This is the first study in humans to test the safety and effectiveness of an investigational gene-therapy product intended to deliver a functional Alpha-1 gene to the liver.

Adverum Biotechnologies developed an experimental gene therapy product called ADVM-043 that uses recombinant adeno-associated virus (“AAV”) as a vehicle to carry the normal Alpha-1 gene into cells. This modified AAV is not like other viruses that, for example, cause the common cold. Recombinant AAV cannot multiply as its native genes have been replaced.

In ADVM-043, the viral genes have been replaced by a normal copy of the Alpha-1 gene as well as other genes to help Alpha-1 gene production. By adding the normal Alpha-1 gene, it is anticipated that once the experimental drug is administered to you, your body will produce therapeutic levels of the alpha-1 antitrypsin, which may slow the progression of your lung and/or liver disease.

The study design has multiple groups of patients receiving the medication by IV infusion. Each group receives a higher dose than the group before. We have filled cohort 1, and have treated the first patient in cohort 2.

Currently, University of Florida (Mark Brantly, MD) and Medical University of South Carolina (Charlie Strange, MD) are open for enrollment. Temple University in Philadelphia (Friedrich Kueppers, MD), University of Chicago (Kyle Hogarth, MD), and University of California, Los Angeles (Igor Barjaktarević, MD) are expected to be open in the near future. MUSC has screened many patients and has treated three so far. University of Florida is busy screening interested participants.

With a goal of 20, the study still needs participants and is still actively screening. There is a travel agency approved to facilitate travel, so it is easier than ever to visit a site. Participants must be ZZ or Znull. Patients may be eligible regardless of their need for augmentation therapy. The successful completion of this study will provide important data to determine whether to proceed to a phase 3 study.

Please visit https://clinicaltrials.gov/ct2/show/NCT02168686 or contact the Alpha-1 Research Registry for more information.

If you are interested in helping out the Alpha-1 community by volunteering for a research study, check out what is currently open and enrolling at www.alphaoneregistry.org.

If you would like your research experience to be featured in a future newsletter, please contact: alphaone@musc.edu.
Asthma and chronic obstructive pulmonary disease (COPD) are the two most common chronic lung diseases among patients with shortness of breath.

Some patients have features of both asthma and COPD. When a person has both conditions, it is referred to as Asthma-COPD overlap (ACO). ACO is increasingly recognized as a distinct diagnosis. It is important to correctly diagnose ACO because patients with ACO are more likely to have frequent exacerbations, more rapid lung function decline, poorer quality of life, and increased use of healthcare resources. Patients with ACO are also more likely to have other “comorbid” conditions than patients with either asthma or COPD alone.

The term “comorbid” is used to describe multiple chronic diseases that can occur together, when having one disease may increase the chance of having another. The interactions between comorbid diseases pose different problems than either condition alone. Comorbidities in chronic lung diseases are important and more research is needed to better understand them. Suchit Kumbhare, MBBS, Statistical and Research Analyst at Medical University of South Carolina (MUSC), performed new analyses to better understand comorbidities in patients with asthma, COPD, and ACO.

The study examined the demographics, smoking status, comorbid conditions, and hospitalization or emergency department (ED) visit among patients with chronic lung conditions. The data came from the 2012 Behavioral Risk Factor Surveillance System (BRFSS) conducted by the Center for Disease Control and Prevention (CDC), and included over 90,000 individuals, age 35 and over.

Results showed that ACO has a higher burden of comorbidities and more hospitalizations or emergency room visits than asthma or COPD alone. Patients with ACO were more likely to have a heart attack, coronary heart disease, stroke, cancer, arthritis, depression, kidney disease, and diabetes than those with COPD only. Patients with ACO were generally younger than those with COPD alone. People with ACO generally had higher BMIs, lower income levels, and less education than other groups of study participants. This study was published in the Annals of the American Thoracic Society and can be found at https://doi.org/10.1513/AnnalsATS.201508-554OC.

The key to improving outcomes and quality of life in these patients is to correctly identify and treat chronic lung conditions along with comorbidities. Most of the comorbid diseases found in this study can be detected and treated. Increased awareness is the first step. Physicians have increased responsibility to closely evaluate and examine patients who appear to have ACO. A patient may benefit from screening for depression and diabetes, discussion of cardiovascular risk factors, and testing of lipid panels, in addition to direct care for their lung disease. Future research will focus on the connections between comorbid conditions and ways to target comorbidities to improve people’s lives.
Building a Testing Program

By Laura Schwarz
ACT Coordinator

Kathie Burgess set a goal in high school to prove some people wrong. Growing up in orphanages and foster homes in the 1960’s came along with being told she was not college material.

When she was old enough she became a dedicated student. She began with nursing school, then a respiratory therapy (RT) program, followed by a Bachelor of Health Sciences at the Medical University of South Carolina (MUSC), a Master’s in Industrial Education at Clemson University, and a Master’s in Christian Ministry at North Greenville University.

Burgess had learned about Alpha-1 Antitrypsin Deficiency (Alpha-1) but never had any patients with the condition. When she found out that the Alpha-1 Foundation had an online course for RTs, she signed up. She continued her education at the 2014 South Carolina Society for Respiratory Care conference, where she learned that all COPD patients should be tested for Alpha-1 and how RTs can help. “I decided to pursue this initiative for our hospital, Bon Secours St. Francis,” said Burgess, who is an RT and the Clinical Education Coordinator there in Greenville, SC.

She approached the hospital leadership about Alpha-1 testing for the COPD population at Bon Secours St. Francis and was given the go ahead. She sought a physician champion for the detection program and Travis Greer, MD of Palmetto Pulmonary Associates agreed. Greer and Burgess worked with other clinicians in the practice and the institutional lab. They worked out a process for RTs to perform finger sticks and determined who would receive the lab results and coordinate follow-up.

Luckily, there was no problem getting test kits and financing the cost, as Alpha-1 industry partners (Grifols, Shire and CSL Behring) offered free Alpha-1 test kits to healthcare providers and performed the testing free of charge. A representative with one of these companies delivered the kits and educational brochures to the office for Burgess and her colleagues to use.

Alpha-1 testing at Bon Secours St. Francis was initiated in March 2015, just six months after Burgess set her mind to this goal. As of April 2018, some 2,852 people have been tested. Five are now on augmentation therapy while other Alphas are being closely monitored. Most COPD patients are appreciative of the test because it is free and provides important information for their healthcare and family members.

She commented, “I am grateful that Bon Secours St. Francis implemented this program and put the best interests of their patients first. The opportunity to provide the best care is why I continue working here after 30 years.” We applaud Burgess’ accomplishment of raising Alpha-1 awareness and detection. She has changed lives and demonstrates a model for standardizing Alpha-1 testing in large healthcare systems.

What’s next for her? She also serves as the Director of Hands of Kindness Children’s Ministry, a non-profit organization that helps orphans in Uganda. As she travels, she plans to find ways to raise Alpha-1 awareness worldwide.
Step forward

Importance of weight in Alpha-1

By Tatsiana Beiko, M.D.
MUSC Clinical Instructor

One of the common symptoms of Alpha-1 Antitrypsin Deficiency, especially for those whose lungs are affected, is shortness of breath. Individuals with worse lung function suffer from more breathlessness which can make exercise difficult.

Both shortness of breath and exercise intolerance can lead to a sedentary lifestyle. Without regular activity, exercise intolerance and breathing difficulties become even more pronounced.

In addition, these symptoms lead to undesired weight gain, which further impacts breathing and activity tolerance. Although all Alphas are encouraged to maintain healthy weight, guidelines lack specific recommendations. A research study, called STEP FORWARD, was undertaken to examine obesity in lung disease and interventions. The Alpha-1 Foundation is in the process of analyzing the results of the large 5-year interventional trial.

STEP FORWARD used nutritional guidance and education to move toward ideal body weight in over 500 Alphas. Similar but smaller studies have been published in individuals with non-Alpha-1 COPD, with promising results.

The spark of interest in obesity and lung disease stems from changing demographics of obesity worldwide. According to the data from World Health Organization, the prevalence of obesity around the globe had doubled in the past 30 years. In usual COPD, research had confirmed that obese individuals have worse health-related quality of life, more medication use, less response to medications and greater limitations in activity, regardless of degree of lung function impairment. Extra weight often plays more of a role in the level of breathlessness and functional limitations than lung function itself.

How do we measure obesity? The widely-accepted Body Mass Index (BMI) is used to rate body mass using a formula of weight and height. A BMI of 30 or greater indicates obesity; 25-29.9 is overweight; 18.5-24.9 is normal weight; and less than 15.8 is underweight. The downside of BMI is that it does not differentiate the muscle mass from fat mass and so other measurements are important to determine body composition.

Abdominal obesity (increased waist circumference) can be present in obesity, as well as overweight or even some normal weight individuals. Due to the proximity of the accumulated weight to the diaphragm, this can amplify the sensation of breathlessness. Prior research studies also suggest a link between obesity and Alpha-1 exacerbations.

Last summer, the participants of “STEP FORWARD” received an invitation to complete a short follow-up survey and were asked to measure their waist circumference, height and weight so the STEP FORWARD trial could include this important data on how they have done over time. We thankfully received responses from 65 individuals and are currently analyzing the data.

Most of the population in the United States struggle with their weight. Being overweight is most common, but being underweight carries risks too. It is always a good idea to review your weight with your healthcare provider. Discussion of dietary needs, safe exercise, and body composition can help combat abnormal weight. Even for those within a healthy BMI range, the discussion could prompt healthier lifestyle and assurance that the weight stays in the desired place for optimal health.