Rare Disease Registries

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Dr. Strange has been a consultant, grant recipient, or speakers bureau member for the Alpha-1 Association, Alpha-1 Foundation, Astra Zeneca, Baxter, NIH, Talecris Biotherapeutics, CSL Behring and Uptake Medical, Inc.
Orphan Diseases

• Disease for which <200,000 individuals are affected in the United States.
• Estimated to be >6500 orphan diseases.
• Orphan Drug Act of 1983 provided special pathways for FDA approval of drugs and devices that target orphan diseases.
• ?8% of the US population affected
• ?80% have a genetic basis
Alpha-1 Antitrypsin Deficiency (Alpha-1, AATD)

• Rare genetic disease affecting 65,000-100,000 individuals in the US
• Most important genetic predisposition to chronic obstructive pulmonary disease (COPD)
  – Smoking adds to risk
• Causes cirrhosis in infants and individuals over age 50
  – Obesity adds to risk
MUSC Programs in AATD

- Alpha-1 Foundation Research Registry
- Alpha Coded Testing Study
- Alpha-1 Association Genetic Counseling Program
- Multistate Referral Practice
- Pharmaceutical Clinical Trials
- NIH Clinical Trials
- International Collaborations in AATD
Cumulative Registry Enrollment
Alpha-1 Registry Participants
(N=2021)

Blue= 1 participant
Purple= 2 participants
Yellow= 3 participants
Red = 4 participants
AATD Clinical Presentation

Mean Age at first symptoms: 35 years
Mean Age at diagnosis: 41 years

Physicians Required To Make a Diagnosis:
- 1
- 2
- 3
- 4
- 5
- ≥6

Stoller, Clev Clinic J Med 1994; 61:461
LETTER FROM THE MEDICAL DIRECTOR By Robert (Sandy) Sandhaus, M.D., Ph.D.

THE LAST SEVERAL MONTHS HAVE BEEN EXCITING ONES AT THE ALPHA ONE FOUNDATION!
The big event was the second annual International Conference, Alpha₁-Antitrypsin Deficiency and Other Conformational Diseases. The conference was held at the Airlie Conference Center in Virginia this past June. It examined the newly recognized class of disorders collectively known as diseases of abnormal protein conformation.

Using Alpha₁-Antitrypsin Deficiency (Alpha-1) as the paradigm, researchers from a broad range of disciplines gathered to discuss their work and learn from each other. Many had never heard of Alpha-1 before. All agreed it was one of the most stimulating conferences they had ever attended.

This has become an especially important topic as companies attempt to bring new drugs to market to treat Alpha-1 and emphysema. Finding the most sensitive and reproducible test to detect disease and evaluate its progression will allow clinical trials to be completed with fewer subjects over a shorter period of time.

The Foundation also directs announcements of new research funding opportunities to the Centers so that those investigators with expertise in Alpha-1 research or clinical care can have access to funding opportunities to support their work. The percentage of applications funded has been increasing in recent years due to increased awareness and understanding of the disease.
From Chromosome to Protein

“Genetic Counseling Aids” 4th ed., Copyright 2002 by the Greenwood Genetic Center
Alpha Coded Testing (ACT) Study Questionnaire
Thank you for your interest in the ACT study. If you are interested in participating, please read the following 4 page consent form that will have an electronic signature at the end. Following the consent, a questionnaire must be answered completely. At completion of the consent and questionnaire, the Alpha-1 test kit will be mailed to you. If you have any questions about either the consent form or the questionnaire, please call us toll-free at 1-877-886-2383, or email us at alphaone@musc.edu.

Electronic Consent to Be A Research Subject  And HIPAA Authorization

Title: Alpha-1 Coded Testing Study
Principal Investigator: Charlie Strange, MD

If participants include those under 18 years of age: 1) The subject's parent or legal guardian will be present when the informed consent form is provided. 2) The subject will be able to participate only if the parent or legal guardian provides permission and the adolescent (age 12-17) provides his/her assent. 3) In statements below, the word "you" refers to your child or adolescent who is being asked to participate in the study.

A. PURPOSE AND BACKGROUND
You have been identified because of your interest in obtaining a blood test
AAT Genetics

- MM: 25%
- MZ: 50%
- ZZ: 25%
Alpha Coded Testing Trial

Consent

Fingerstick Blood Sample Mailed

Coded at MUSC

Assayed in Gainesville

Results Returned to MUSC

Results to Individual

Reasons for Testing
Perceived Risk/ Benefit Assessment
Anxiety/ Depression Queries
Family Impact

Questionnaire
Alpha Coded Testing (ACT) Study

Tests Ordered
14,953

Tests Returned
11,161 (74.6%)

PiMM= 5817
PiMS= 840
PiMZ=3817
PiMNull=45
PiSS=42
PiSZ=270
PiZNull=53
PiZZ=317

640 (5.7%)

Questionnaire 1
Benefit/Risk of Testing

Questionnaire 2
Quality of Life,
Family Functioning

Questionnaire 3
Smoking Intent
Childhood Testing

Questionnaire 4
Health Locus of Control
Secondhand Smoke and COPD

Questionnaire 5
Comorbidities of Alpha-1
Genetic Counselors

Genetic Counselors (GCs) are health professionals with a master's degree and experience in medical genetics and counseling. They augment your care, as the healthcare professional, by addressing the social impacts of Alpha-1 with patients, families and caregivers, and by providing you with advice and counsel regarding how to discuss the effect Alpha-1 may have on your patients.

GCs provide an additional resource for the healthcare professional. The expertise at the Alpha-1 Genetic Counseling Center may help you as a healthcare professional understand more about the genetic nature of Alpha-1, and the psychosocial and economic impacts on family members. Genetic counselors can also give you specific guidance on the risks and benefits of genetic testing.

The Alpha-1 Association Genetic Counseling Center is funded by grants provided by:

AlphaNet
Baxter
CSL Behring
Talecris Biotherapeutics

The Association is a non-profit membership organization dedicated to identifying those affected by Alpha-1, improving the quality of their lives through support, education, and advocacy, and encouraging participation in research.

Programs include:
- More than 75 support groups in the US
- A Peer Guide Program connects newly diagnosed individuals with others
- Free patient educational programs and conferences held throughout the US
- A website with e-education, community forums and a wealth of resources for Alphas and their families.

The Alpha-1 Foundation provides resources, educational brochures and information on testing and diagnosis for physicians and patients. It funds cutting-edge research to find treatments and a cure and supports worldwide detection.
Total New Calls to Date [668] by Category

- Family Member: 32%
- Untested: 8%
- Unknown: 8%
- Other Rare: 1%
- MM: 5%
- Carrier (MS, MZ, MNull): 20%
- Deficient (ZZ, ZNull, SZ, SS): 9%
- Health Professional: 17%
Conclusions

• Rare diseases need investigators.

• MUSC has the tools for an effective Rare Disease Registry infrastructure.

• Rare disease registries bring additional resources and patients to MUSC.

• Telemedicine has an opportunity to transform the rare disease experience for patients.