LETTER FROM THE DIRECTOR  By Charlie Strange, M.D., Medical University of South Carolina

MY FIRST YEAR AS DIRECTOR OF THE DATA COORDINATING CENTER OF THE
Alpha-1 Foundation's Research Registry has been a busy time. The infrastructure and
operations of the Registry are now fully established at Medical University of South Carolina.
We've hired staff, established a secure database, and formulated new recruitment strategies to
increase Registry enrollment. The protocol for the upcoming coded testing program, the
ACT pilot study, has been developed in conjunction with Mark Brantly, M.D., Director of
the Alpha-1 Program at the University of Florida.

We've seen a great deal of advances in the
field of Alpha-1 research in the past year, and the
establishment of important resources for the research com-
munity such as the Alpha-1 DNA and Tissue Bank at the University
of Florida. Many of the activities
described in this issue of Registry Update directly impact you as a
diagnosed Alpha, so the newslet-
ter is written specifically to keep
you in the community fully
informed. The Update is also our
primary means of letting you, the
Alpha-1 Community, understand
the types of research being
conducted in the field so we have
included in this issue a review of
the current Alpha-1 Foundation
sponsored projects. There are
descriptions of the various
scientific meetings, conferences,
workshops and patient education
days that have been held, and
articles that describe upcoming
projects such as the coded testing
trial. We have also included an
important review, by the
Foundation's Ethical, Legal and
Social Issues (ELSI) Working
Group, of the ethical issues
relating to linkage of family
members for research studies.

As always, we welcome your
comments, questions or sugges-
tions for topics you wish to see in
future issues. Please contact me at
the Medical University of South
Carolina if you have any com-
ments about the newsletter, or
wish to find out more about the
Alpha-1 Research Registry and
how enrollees in the Registry can
participate in research studies and
clinical trials. My email is
alphaone@musc.edu.
The Alpha-1 Coded Testing (ACT) Trial
By Charlie Strange, MD

The issues concerning ethics and discrimination associated with genetic testing are currently a sizzling topic in our society. With the Human Genome Project completed we can expect these topics to remain on the forefront of national healthcare debate. For many years the Alpha-1 Community has asked for a mechanism to obtain confidential testing for family members who may fear that the results of testing will be grounds for genetic discrimination in the form of higher insurance premiums or workplace discrimination. The Alpha Coded Testing Trial will attempt to address some of these important issues.

This new program established by the Alpha-1 Foundation will be headquartered at its Registry site in Charleston, South Carolina. The blood tests to obtain a diagnosis will be shipped to anyone who requests them, returned to Charleston, coded for anonymity, and transferred to the University of Florida for testing. The results will be sent to Charleston, decoded, and returned to the individual who may share them with anyone they have selected.

The project is being performed as a research trial that requires individuals to fill out two questionnaires, one before and one after tests return. The reasons for establishing this program as a research trial are twofold. The most important reason is that little is known about the feelings of individuals who receive a test result for a disease they may know little about. The questionnaires are designed to determine patient concerns that are independent of genetic discrimination.

The second reason to administer this project as a research trial is that the laws that assure confidentiality are strongest for research trials. Participation in the research trial requires a signed consent form that describes the research and the criteria for participation. These consent forms with signatures must stay on file in Charleston under lock and key. Research records like any test results from your doctor's office are always subject to subpoena by a court of law. However, the likelihood of a subpoena request is very much lower for confidential research than for other medical records. Furthermore, at the participant's request, the linkage between the consent form signature and the test result can be permanently broken after results have been received.

Prospective participants can dial toll free 1-877-886-2383 or send an email to alphaone@musc.edu to take part. The study requires little effort on the part of the participant. Depending on the current technology at the University of Florida, a tube or fingerstick blood test kit with instructions will be mailed along with a research questionnaire and consent form. Alpha-1 diagnostic information will be offered only when the participant returns the blood sample, consent form, and questionnaire completed in full to the Medical University of South Carolina (MUSC), and agrees to return a post-test questionnaire.

On the consent form, participants will be asked whether more questionnaires may be mailed over the next 5 years to determine the effects of the blood test on stress and family dynamics. Psychological risks of establishing an Alpha-1 diagnosis can include depression, anxiety and a state of fatalism. Social risks include changes in family dynamics, stress at home and at work, and the
possibility of discrimination. The results of research in these areas will be stronger when participants elect to continue participation and not immediately destroy the linkage to test results. Under the confidentiality provisions of this trial, only the ACT trial coordinator and director at Medical University of South Carolina will have access to these files.

The Research Registry is asking its members to present this opportunity to any family members who desire an Alpha-1 blood test. The Research Registry is conducting the trial and can be contacted Mon-Fri 8:30-5:00 for questions. We all believe early diagnosis makes a difference in this disease and encourage your family’s participation.

**Florida Screening and Detection Program**

*By Kyr Chesnut, Assistant Director of Alpha-1 Research Program*

BY now many of you have probably heard something about the Florida Statewide Screening and Detection Program. The State of Florida Department of Health awarded a grant to the Alpha-1 Foundation to establish the infrastructure to support a statewide screening and detection program. An estimated 780,000 Florida citizens are afflicted with chronic obstructive pulmonary disease (COPD). This planned screening has the potential to identify up to 15,000 patients in the State of Florida alone. The State of Florida legislature clearly understood how this program could improve the health of its own citizenry as well as serve as a prototype for a nationwide screening program. Why? Because there are tremendous benefits to early detection:

1. We can educate individuals about the importance of avoidance of tobacco smoke and other inhalants, and the need for vaccinations for influenza and pneumonia;

2. We can direct individuals to specialized care centers like the Clinical Resource Centers (CRCs), where they are knowledgeable about the need for early intervention in the treatment of pulmonary exacerbations;

3. Individuals can possibly initiate alpha-antitrypsin (AAT) augmentation therapy;

4. Individuals can gain access to clinical trials;

5. Individuals and their family members can have access to genetic counseling.

This program is a natural extension of the Alpha-1 Genetics program at the University of Florida that already provides one of the largest testing locations for Alpha-1 in the world. The program involves several modes of outreach including:

1. Targeted mailings to physicians most likely to treat lung and liver disease patients (especially those in the fields of pulmonology, hepatology/gastroenterology, asthma and allergy, internal medicine and general practice). These mailings include not only test kits, but also educational materials for the physician as well as the patients.

2. Coordinating visits to hospitals and clinics and scheduling conferences with groups of physicians throughout the state.

3. Enlisting the help of local medical societies, state and local lung associations, and other CRCs.

4. Increasing awareness about Alpha-1 by public advertisement to physicians and patients.

Hopefully, we can get more physicians and their patients asking one simple question, Could my COPD be Alpha-1? The test kits are mailed FREE-OF-CHARGE, the samples are processed and analyzed for phenotype and AAT levels at NO COST to the patient or referring physician. By the end of our first year, we will have screened approximately 2,500 COPD patients in the state of Florida. We eventually hope to screen up to 20,000 per year in the following years. It is a lofty goal, but a necessary one.
Alpha-1 DNA & Tissue Bank Established at the University of Florida
By Kye Chesnut, Assistant Director, Alpha-1 DNA and Tissue Bank

A major milestone to further Alpha-1 research was made with the establishment of an Alpha-1 DNA and Tissue Bank as part of the Alpha-1 Research Program at the University of Florida. The Bank was established by the Alpha-1 Foundation and made possible by a grant from Fundación Leopoldo Fernández Pujals which was instrumental in purchasing equipment and materials necessary to support this endeavor. All DNA and tissue is owned by the Alpha-1 Foundation with an independent DNA & Tissue Bank Advisory Committee provides oversight assuring that the Alpha-1 Community will retain these valuable assets.

The first "deposits" to the bank, approximately 140 DNA samples, was donated in a single day at the Patient Education Day in Gainesville, FL in early January, 2001. This Bank is now the single largest repository of disease-specific Alpha-1 serum and DNA in the world. This is a significant accomplishment and demonstrates the Alpha-1 Community's commitment to support critical research. It is important that this Bank continues to grow to fuel ongoing research. So, roll up your sleeves! Your contributions will allow researchers to perform studies that would otherwise be virtually impossible simply because of the limited number of Alphas identified and accessible to any one researcher. The benefits of these studies will be realized by the community and future generations. Representatives from the Bank will again gather DNA donations at the Patient Education Day in Phoenix, AZ in April, 2001. By participating, you become a part of the solution.

The Alpha-1 DNA and Tissue Bank and Research Registry are two keys to the same problem – limited resources for investigators committed to advancing our knowledge and to finding a cure for Alpha-1.
Patient Education Day
University of Florida, January 13, 2001
By Charlie Gregory

The first Alpha-1 Education Day presented by the Alpha-1 Alliance was held in January in conjunction with
the dedication of the Alpha-1 DNA and Tissue Bank located at the University of Florida, Gainesville. From a
patient perspective, this Alpha-1 Education day was well organized and the topics timely. Needs and issues of
lung or liver affected Alpha’s were addressed. The day was designed to be more than a glorified support group yet
less than a total conference. Morning presentations by Drs. Sandhaus, Gonzales-Peralta, Brantly and Flotte covered
topics on lung, liver, therapies and clinical trials, and gene therapy, respectively. The afternoon included updates
from the Alpha-1 Foundation and the Alpha-1 Association, plus presentations on basic science research, the Florida
Screening and Detection program and a wrap-up discussion led by Mary Pierce.

Throughout the day blood draws took place to help establish the Alpha-1 Foundation’s Alpha-1 DNA and Tissue
Bank as the largest bank of its type exclusively devoted to Alpha-1-Antitrypsin Deficiency. Over 100 samples were
collected on this first day of operation.

Plans are being made for other Alpha-1 Education Days around the country at Clinical Research Centers and other
locations where there are large populations of Alphas. Even though the “Patient Days” will be similar in format,
they are designed to be adapted to the needs of the participants and reflect resources available at the regional
Clinical Research Center where they are held. The Alpha-1 Education Days are the first of many events sponsored
by the Alpha-1 Alliance, a collaborative effort of the Alpha-1 Foundation and the Alpha-1 Association.

The Alpha-1 Alliance is a collaboration between the Alpha-1 Foundation, dedicated to improved treatments
and research for a cure of Alpha-1, and the Alpha-1 Association, a patient driven membership based advocacy
organization that provides education and support to individuals with Alpha-1 and their families.

Alpha-1 DNA & Tissue Bank Advisory Committee

The Alpha-1 Foundation has recently established an
Alpha-1 DNA, Tissue and Organ Bank at the
University of Florida under the direction of
Mark L. Brantly, M.D. To provide guidance and over-
sight to the overall goals and structure of the Tissue
Bank, the Foundation has created an advisory com-
mittee, which similar to the Research Registry Advisory
Committee and Medical And Scientific Advisory
Committee, will report directly to the Alpha-1
Foundation’s Board of Directors. This committee includes
experts both internal and external to the Alpha-1 Research
Network who are providing guidance at the inception of
the Tissue Bank and who will continue to provide
oversight as the functionality of the Tissue Bank grows.
The committee is chaired by Dr. James C. Hogg, a
leading pathologist at the University of British Columbia,
with over 20 years experience with tissue banks.

The Advisory Committee met for the first time on
March 16, 2001 in Denver, CO to review the contract
with the University of Florida and to begin to identify
areas that will require advice and guidance. Issues dis-
cussed at this first meeting included how samples will be
collected, what type of medical information should be
collected with the samples, how to maintain the highest
levels of confidentiality and security, how to ensure that
samples are processed in a manner that are scientifically
useful, what type of marketing plan is necessary to
promote this important resource, what type of FAQs to
post on the web about the Tissue Bank, and the
important issue of ownership of tissue.

Members of the Advisory Committee include the
following: James C. Hogg, M.D., University of British
Columbia, Chair; Mark L. Brantly, M.D., Director
of the Tissue Bank, Jeffrey Botkin, M.D., M.P.H.,
University of Utah School of Medicine, Stew Cogan,
Esq., Alpha-1 Foundation Board of Directors;
James M. Crawford, M.D., Ph.D., University of Florida
College of Medicine, Sally Everett, Esq., Alpha-1
Foundation Board of Directors, Len Geiger, a diagnosed
Alpha representing the Alpha lung community,
Frank D. Groves, M.D., M.P.H., F.C.A.P., Medical
University of South Carolina, Jon Merz, J.D., Ph.D.,
University of Pennsylvania, Center for Bioethics,
David Rodman, M.D., University of Colorado Health
Sciences Center, Center for Genetic Lung Disease,
Sharon Terry, M.A., PXE International, and Elena Halford,
a diagnosed Alpha representing the liver community.
Ethical, Legal, and Social Issues (ELSI) Working Group
Keeping Pace Scientifically and Ethically

By the Alpha-1 Foundation's Ethical, Legal, and Social (ELSI) Working Group:
Evan DeRienzo, Ph.D., (Chair), Nancye Baelew, Symma Finn, M.A., Jon Merz, J.D.,
Ph.D., Lynn Overson, R.N., M.N., A.N.P., Bob Senior, M.D., Richard Sharp, Ph.D.,
Jim Stocks, M.D., and Mark Yarborough, Ph.D.

Excellence in clinical research is a balance between the advancement of
scientific knowledge and adequate protection of the rights and welfare of
human subjects. Striking the appropriate balance is an art. Practicing this
art well has always been at the core of the Alpha-1 Foundation's efforts.

At the Foundation's beginning, the most pressing scientific and ethical bal-
ance was how to set up a Registry in a way that best protected participants' privacy and confidentiality. Another important goal was to create and
operate a Registry in a way that built the Alpha-1 Community’s and the
scientific community's trust in the integrity of the Registry operation and the
Foundation.

The Alpha-1 Research Registry has now been in operation five years. Over that time, the Research Registry has, we believe, established the
Foundation as a trusted member of both the Alpha-1 patient and scientific
communities. Over the same period of time there have been

breathing advances in genetic
science. The Foundation is committed to keeping pace, which means

continual reevaluation of its pro-
grams and processes. Concerning the Registry, the design that was

appropriate initially is being reconsidered and reevaluated so that it

can continue to be a cutting edge resource for the scientific

community yet maintain patient confidentiality.

Currently, considerations include: should the Registry move towards
family linkage? and, Should the Registry actively recruit asymptomatic
heterozygotes? There is no controversy among scientists that
evolving the Registry to be able to
identify family linkages would make it far more attractive and useful. But

that is only one half of the balancing

act. The other half is consideration

of the ethics of such a change and

how that will affect the Alpha-1

Community. That is, will the com-
xplexities posed by moving to a

Registry that can link family member
to family member be manageable in

a manner that will provide sufficient protection and confidentiality to

Alphas? And, will attempting to

manage and/or overcome these ethi-

cal complexities be worth the effort

in scientific payoff?

Within the Foundation, we have

begun a formal discussion of these

important issues. The Foundation's

Ethical, Legal, Social Issues (ELSI)

Working Group is presently debate-

ing the issue of family linkage, and

will be presenting the ELSI views to

the Foundation, shortly. As identified

so far, there is an important range of

ethical issues to take into account.

The most obvious are protection of

privacy and confidentiality. It is clear

that there are real threats to insura-
bility and employability from the

misuse of private genetic informa-
tion, Alpha-1 or otherwise. But these

are not the only potential harms

related to breaches of privacy and

confidentiality. Discrimination and

stigmatization can produce harms to
dignity, psychological well-being,

other aspects of economic status and

the development and maintenance of

social interactions. If it is agreed that

the Registry ought to pursue the

possibility of family linkage, mecha-
nisms to protect against such breach-
es will have to be very tight.

Processes are being developed to

provide family linkage. Materials,
such as consent forms, might include

a signature line that the first family

member enrolled in the Registry

would sign demonstrating his/her

willingness to be linked to any other

family member, if others in the

family subsequently join the

Registry. This is one way to balance

the pursuit of scientific knowledge

and the protection of the rights and

welfare of others.

The ELSI Working Group is also

concerned with the ethical complex-

ities posed by the stupendous suc-

cess of the Foundation, more broadly.

In addition to the Registry, we

now have a tissue bank, and a

protocol, stimulated by the Alpha-1

Community’s request for some type

of coded testing, to study the impli-
cations, both clinical and ethical, of
coded testing. But we must be cau-

tious with the expanded activities of

the Foundation. The more informa-

tion that we collect, the more vigi-

lant and coordinated we have to be

about setting up oversight. And not

just oversight of the individual

activities, but broad, overarching

oversight mechanisms that assure

that there is a coordinated approach
to finding just the right balance

between scientific progress and

protection of those for whom the
progress is being sought.

Relevant Readings: For related discussions of the ethical issues related to family members and genetics research, please see:

Botkin, J.R. (2001). Protecting the privacy of family members in survey and pedigree research. JAMA. 285(2):207-211. Please note that the author of this article, Jeffrey R. Botkin, MD, MPH, has just joined the AOF’s new Tissue Bank Oversight Committee.


CURRENTLY FUNDED RESEARCH

By Michael A. Aliberti, M.S.W., Grants Administrator, Alpha-1 Foundation

The Alpha-1 Foundation is currently funding 15 research projects. These include four awards from the Fernandez Liver Research Initiative: four Postdoctoral (also known as the Young Investigator) Fellowships; two awards in conjunction with the American Liver Foundation Innovative Seed Grants; four independent projects in the United States and an Alpha-1 Screening and Detection Study in Spain.

Fernández Liver Research Initiative Through the generous support of the Fundación Leopoldo Fernández Pujals, funding is provided for both basic science and clinical research of the liver disease associated with Alpha-1.

The two basic science awardees are David H. Perlmutter, MD, Pediatrics, Gastroenterology, and Nutrition, Washington University School of Medicine, St. Louis Children’s Hospital1 (Genomic Analysis of the Cellular Response in AAT Deficiency), and Richard N. Sifers, MD, Pathology, Baylor College of Medicine (Z Polymer Disposal as a Mediator of Heritable Liver Disease).

Dr. Perlmutter’s project is designed to determine how cells in the liver respond to retention of the mutant, AAT molecule, which forms into polymer chains in AAT Deficiency. Identifying the specific way the cells respond will provide essential information about the mechanisms of protection from liver disease and new strategies for prevention of liver disease. Dr. Sifers’s laboratory has shown that modification of specific cells in the liver produce a “degradation signal” that selectively eliminates polymers (chains) of AAT-variant PiZ. The specific enzyme that generates this essential modification is being added to cells as a means to accelerate the disposal process. Dr. Sifers’s lab is also characterizing a protein that supposedly recognizes the degradation signal; this knowledge will provide ways to successfully eliminate chains of misformed AAT thereby potentially relieving the liver of those cells that cause disease.

The clinical award recipients, each from the University of Florida are addressing aspects of treatment of Alpha-1: Mark L. Brantly, MD, Molecular Genetics and Microbiology, who is also Director of the Alpha-1 Research Program, along with co-Investigator Regino P. Gonzalez-Peralta, MD, Pediatrics, 4-Phenyl Butyrate

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1 Effective June 1, 2001, Dr. Perlmutter will be assuming the Vira I. Heinz Professor and Chairman of Pediatrics at the University of Pittsburgh School of Medicine. Scientific Director of Children’s Hospital of Pittsburgh/Rangos Research Center.
[4-PBA] Mediated Secretion Rescue in Alpha₁-Antitrypsin Deficient Individuals, and Terence R. Flotte, MD, Pediatrics & Molecular Genetics and Microbiology, Molecular Therapies for Alpha₁-Antitrypsin Liver Disease.

The first study is a dose escalation pilot study to test whether the substance 4-PBA will significantly increase secretion of protein and reduce the accumulation of Z-AAT and associated liver injury. Dr. Flotte's project has resulted in the development of vectors for delivery to the liver in conjunction with delivery of the normal AAT gene. This vector delivery to the liver has been optimized, demonstrating the method is feasible, safe, and can deliver normal genes that persist for more than one year in experimental animals. Other potential strategies for gene therapy of AAT-related liver disease are also being developed, including use of molecular chaperones that can guide the AAT out of the liver, and the use of DNA chip microarray techniques, which is being used to analyze molecular structure in an attempt to understand how AAT Deficiency disease progresses.

The Young Investigator Awards support postdoctoral research for studies in the basic science or clinical investigation of Alpha-1. The two initial Fellowships from 1999 are nearing the completion of their second year of funding: Alexei A. Guerassimov, MD, PhD, Department of Respiratory Medicine, McGill University, Quebec, Canada has been conducting a study on Animal model of Emphysema associated with Alpha-1 Deficiency. Shihong Song, PhD, Department of Pediatrics, University of Florida has been working on Adeno-Associated Virus [AAV] Vectors for Skeletal Muscle Mediated Gene Therapy for Alpha₁-Antitrypsin Deficiency Preclinical Study in Non-human Primates. Dr. Guerassimov has concluded that Alpha-1 significantly accelerates the emphysema from cigarette smoking over 30 percent sooner than in non-smoking animal models. These findings could add substantively to the understanding of the development of emphysema and the role of Alpha-1 in this process. Dr. Song has been able to show stable therapeutic levels of the AAT protein in a large animal model after injection of AAV vectors; results of this study has been accepted for publication by the journal Gene Therapy.

One of the Fellowship awards from 2000 was approved for transfer to Christopher M. Cabral, PhD, Department of Pathology, Baylor College of Medicine, effective January 17, 2001. Dr. Cabral has an exemplary record of training and accomplishments in Alpha-1 research. In one of his most recent articles in the Journal of Biological Chemistry, Dr. Cabral provided for the first time a description of how the quality control of PI Z AAT in hepatoma (liver) cells differs from what was previously observed in cell lines used for gene expression studies. Dr. Cabral will continue the study entitled Quality Control in the Secretory Pathway of Alpha₁-Antitrypsin originally awarded to Priya Choudhury, PhD. The other 2000 recipient is Jon Burrows, PhD, Department of Pediatrics, Washington University School of Medicine (Cellular Response to Intracellular Retention of Mutant Alpha₁-Antitrypsin Z).

ALF/AOF Innovative Seed Grants The joint research initiative with the American Liver Foundation was established to foster the development of imaginative research studies in Alpha-1 and/or directly related areas of scientific or clinical investigation. The Alpha-1 Foundation is pleased to announce two new Innovative Seed Grants for this year with applications due to the American Liver Foundation on or before May 25, 2001.

The recipients of the 2000 Innovative Seed Grants are Jeffrey H. Teckman, M.D., Gastroenterology, Washington University School of Medicine, Autophagy in the Physiology of Alpha₁-Antitrypsin Z, and Mark A. Zern, M.D., Internal Medicine and Director of the Transplant Research Institute, University of California, Davis, SV40
Vectors and Gene Therapy for Alpha₁-Antitrypsin Deficiency.

The study by Dr. Teckman seeks to understand how AAT-Z damages liver cells and how the liver responds to this damage. Human liver tissue, animal model tissue, and other experimental tissues are being examined to investigate possible methods to reduce or block cellular damage. Dr. Zern has developed the necessary transgenic mouse line that contains the abnormal human PiZ allele. This effort will allow him to determine the effectiveness of the gene therapy approach in an animal model before starting human studies. In addition, Dr. Zern has shown for the first time that normal AAT gene can be inoculated into human cells and, that the normal AAT protein can be secreted from the cells. This initial success is the first step in getting the protein into the blood stream when human studies are undertaken.

Investigator-Initiated Research In addition, a number of independent projects relating to AAT Deficiency were funded by the Alpha-1 Foundation during the past year. These include:

- **Alpha₁-Antitrypsin Deficiency Cost of Illness Model** - This study was conducted by C. Daniel Mullins, PhD, Pharmacoconomics, School of Pharmacy, Center on Drugs and Public Policy, at the University of Maryland, Baltimore. This research will determine the economic costs to society (i.e. burden of illness) associated with Alpha-1. The first phase of this study, begun in November 1998, has been summarized in a manuscript titled "The Direct Medical Costs of Alpha₁-Antitrypsin Deficiency" that was published in Chest, March 2001, Vol. 119, Issue 3: 745-52. The current grant award for phase 2 of the project will allow Dr. Mullins to fully analyze the responses from the self-administered supplemental questionnaire for individuals enrolled in the Alpha-1 Research Registry and to prepare more detailed, and perhaps more accurate, estimates of the medical costs of Alpha-1.

- **Milestones Project in Genetic Lung Disease** - This study has received 'bridge' funding from the Foundation to allow time to develop proposals to the NIH. The proposed project is a comprehensive multi-center study to examine decision-making for people diagnosed with either AAT Deficiency or Cystic Fibrosis. Mark Yarborough, Ph.D., Director of the Program in Health Care Ethics, Humanities and Law, University of Colorado Health Sciences Center (UCHSC), heads a study team that will focus on major decisions that patients face in three major life areas: 1) reproductive choices and/or diagnostic testing for family members; 2) lung transplantation; and, 3) advance care planning for the end-of-life. In addition to UCHSC the National Jewish Medical and Research Center in Denver, a number of the Alpha-1 Clinical Resource Centers have agreed to participate (University of Florida, St. Luke's/Roosevelt Hospital, Tufts University and Oregon Health Sciences University).

- **Protecting the Interests of Patients and the Public in the Commercial Biotechnology Marketplace** - Partial funding has been awarded to Jon F. Merz, J.D., Ph.D., M.B.A., Center for Bioethics, and co-Investigator David Magnus, PhD, Director of Graduate Studies, Center for Bioethics, at The University of Pennsylvania. Their project will examine the market for biotechnological intellectual property. This project seeks to view the contributions, goals, and motivations of market participants in genetic research through different models based on altruistic, financial, and moral concerns while developing optimal solutions to satisfying varied needs.

- **Phantom for Standardization of Lung Parenchymal Quantification** - Another grant has been awarded to Eric A. Hoffman, Ph.D., Radiology and Biomedical Engineering, University of Iowa College of Medicine, to develop a lung/chest phantom model that will be used to evaluate the differences among CT (computed tomographic) Scan equipment from various manufacturers. The development of the lung/chest phantom will provide the capability to uniformly evaluate the amount of emphysema and its distribution in patients. The result will also determine the design of the most appropriate scanning protocol(s) to utilize in an upcoming multi-center trials for individuals living with Alpha-1 specifically and Chronic Obstructive Pulmonary Disease.

- **Alpha-1 Screening & Detection Program in Spain** - An international award has been provided to Marc Miravitlles, MD, Fundación Catalana de Pneumología, Hospital General Vall d'Hebron, in Barcelona. See the following article for more information on the study.
Spanish Screening Program For Alpha\textsubscript{1}-Antitrypsin Deficiency

By Marc Miravitlles, M.D.
Consultant Chest Physician, Coordinator of the Spanish Registry of AAT Deficiency

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pain has traditionally been considered a country with a low prevalence of Alpha\textsubscript{1}-Antitrypsin (AAT) Deficiency. However, recent studies have demonstrated that approximately 3\% of the population is heterozygous for the Z allele; thus, considering a total population of around 40 million people, there should exist a number of severely deficient individuals, P\textsubscript{IZ}, close to 8,000.

Since 1993 there has been a Spanish Registry of AAT Deficiency; however, it only includes information on 305 deficient individuals. Therefore, AAT Deficiency is a largely undiagnosed condition in Spain, as in other European countries. Of interest, most of the registered individuals are index cases, smokers or former smokers and have poor lung function, which would indicate that physicians, particularly general practitioners, only consider a diagnosis of AAT Deficiency in patients with severe emphysema at a young age. This attitude must be changed, since the benefit patients can expect from any form of therapy, including quitting smoking and replacement therapy, decreases as disease severity progresses.

The Spanish Registry has a central laboratory with phenotyping and genotyping facilities, which receives samples from all over the country. This laboratory has identified and described two previously unknown deficient variants, called Ybarcelona and Mvall d’hebron, named after the city and hospital, respectively where they were first described. Both newly recognized polymorphisms were originated by point mutations in exon V and carriers of these deficient variants are at increased risk of pulmonary disease.

Providing support to such a large population is a challenge for a central laboratory. Samples must be sent from many miles away with the risk of being damaged in transit, furthermore, the shipping of biological samples is expensive. To overcome this problem, we developed techniques for measuring AAT concentrations, phenotyping and genotyping from dried blood spots on filter paper. This sampling method has multiple advantages: it is safe for the patient, easy to perform even in the physician’s surgery, and shipment can be made safely inside an envelope and sent by regular mail at low cost.

This technique should permit the implementation of a screening program in Spain aimed at identifying individuals with AAT Deficiency at an early stage of their pulmonary disease and gaining some insight into regional differences in prevalence of the deficiency around the country.

With the support of the Alpha-1 Foundation, the Spanish Registry is currently conducting such a screening program with a duration of one year. There will be a pilot phase in which 8 centers located in the area near the central laboratory will collect approximately 100 blood spots from patients with chronic obstructive pulmonary disease (COPD) and unknown AAT phenotype for one month. After the stability of the samples have been verified, collection of samples will be extended to seven different areas of Spain: Barcelona, Madrid, Asturias, Granada, Vigo, Cantabria and Biscay. The initial aim is to collect 1,000 samples from patients with COPD who have not been previously tested for AAT Deficiency.

This screening program is in accordance with WHO guidelines, which clearly emphasize the need for testing all COPD patients for the deficiency at least once in their lives. This aim is far from being accomplished in Spain, but with this initiative we attempt to facilitate the access to AAT testing for all COPD patients.

After this year of screening, results in terms of cost-effectiveness will be evaluated and, if positive, new strategies will be developed to increase awareness of the disease among general physicians who care for the largest number of COPD patients in Spain. There is still a long way to go, since recent epidemiological studies have shown that 9\% of the Spanish population between 40 and 70 years of age suffer from COPD, i.e. 1.2 million patients. Furthermore, only 22\% of these have been diagnosed and have received any kind of medical attention, including smoking cessation programs. Our current data also show that most of these 22\% of diagnosed COPD patients have never been tested for AAT deficiency. We hope that this initiative will permit AAT testing to be progressively extended as a routine test for patients with COPD.
Formula For Safety: Plasma Protein Therapies
By Linda L.S., Communications Director, Plasma Protein Therapeutics Association

As recently as the last meeting of the Blood Products Advisory Committee (BPAC) meeting in March, it was acknowledged by an FDA representative that today's supply of plasma protein therapeutics has never been safer. We believe this is with good reason.

There are many reasons for the high quality and safety of plasma therapeutics. Today, many more safeguards and quality standards have been put into place and new technologies have been discovered and implemented. It was stated at the BPAC meeting that since the introduction of these new virus inactivation and removal technologies, not one viral transmission has been reported. Simply stated, we're more advanced today than we ever have been.

Industry Initiatives The members of the Plasma Protein Therapeutics Association (PPTA) are committed to ensuring the safety of individuals who depend on plasma therapies and the quality of plasma protein therapeutics.

QSEAL One year ago, members of the Plasma Protein Therapeutics Association announced the development of a new program of voluntary standards that exceed those presently required by regulatory agencies. The program, called QSEAL, sets standards in several different areas and requires inspections performed by independent auditors at the manufacturing site. After successful completion of these inspections, companies become certified for a two-year period. The QSEAL standards are established for the following:

- **Viral Marker Standard** This standard ensures that collection centers collect plasma from low-risk populations. No donations will be accepted from any center that exceeds agreed limits for each or the combination of three viral markers – HIV, HCV and HBV.
- **Qualified Donor Standard** This standard eliminates the use of plasma from one-time donors. It requires that only plasma can be accepted for further processing when the donor has successfully passed at least two health history interviews and two panels of all required screening tests within a six-month period. If the donor does not come back within six months, then the first donation cannot be used for manufacturing purposes and the donor has to qualify again. Only if the donor returns and passes all tests will the plasma be used for the manufacture of medicinal products. Only then is the donor considered a Qualified Donor.
- **Inventory Hold** To further reduce risks in the manufacturing process, PPTA has introduced a standard that requires each plasma donation to be held in inventory for a minimum of 60 days. If in this period, post-donation information becomes available (such as infection of any kind), then all previous donations will be retrieved and destroyed before they enter the manufacturing process.
- **Nucleic Acid Amplification Testing (NAT)** PPTA members are committed to perform NAT testing on all incoming plasma for HCV, HIV and HBV. Space does not permit more details regarding all of the new standards being considered for the products PPTA members produce. However, one key initiative must be highlighted as well. This is an initiative that grew out of a partnership with consumer organizations. It was developed to take patient safety one step further – by assuring timely notification of product withdrawals and recalls.

Patient Notification System The Patient Notification System (PNS) is a free, confidential, 24-hour communication system providing information on plasma-derived and recombinant product withdrawals and recalls in the United States. Key consumer groups such as Alpha-1 Association and the Alpha-1 Foundation worked closely with a coalition of patient groups and PPTA members to design a system that ensures patient confidentiality and that functions effectively. For more information on the PNS or to register, visit www.patientnotificationsystem.org today.

The Alpha-1 Foundation has been one of the most energetic and responsive partners in the development of the Patient Notification System and in advocacy for standards regarding the safety and quality of plasma protein therapeutics. It is this commitment, vision and dedication of purpose that will ensure continued success in the years to come.

These safeguards from vein to vein through the plasma therapeutics network are the foundation for the members of the PPTA who are working to ensure the safety, quality and availability of plasma protein therapies worldwide.
FROM THE FOUNDATION MEDICAL DIRECTOR

Message From the Medical Director, Alpha-1 Foundation

By Robert (Sandy) Sandhaus, M.D., Ph.D.

My first year as Medical Director of the Alpha-1 Foundation has been exciting and productive. While we have accomplished much, there always seems to be more appearing in the INBOX than leaving the OUTBOX. I doubt that this feeling is unique in today's fast-paced world.

Researchers around the world are doing work today on Alpha-1 that would not be possible without the resources provided by the Foundation. Drugs and other therapies for Alpha-1 are being advanced today because of conferences and meetings organized by the Foundation. Patients are being identified and treated for Alpha-1 thanks to educational materials and detection methods developed and provided by the Foundation and supported by the ongoing push for awareness and detection both by the Foundation and the Alpha-1 Association.

The most important issue facing many Alphas today is Prolastin® drug supply. As a condition with only a single available specific therapy, Alpha-1 patients with lung disease must rely on the only supplier, Bayer, for production of this life-saving therapy. Right now, the demand has exceeded the supply and many patients are experiencing some interruptions in their shipments of Prolastin. It is important to note that, as the Medical and Scientific Advisory Committee of the Foundation has recently recom-

mended, Prolastin therapy is only one component of the treatment of the lung disease associated with Alpha-1.

Prolastin is a therapy designed to influence the long-term course of the disease. Short periods of time off Prolastin should not be considered harmful. (In the USA 1998 NHLBI sponsored Registry study, no significant difference was noted between those who were intermittently treated versus those always on augmentation therapy.) Overall therapy includes bronchodilators; early use of antibiotics; pulmonary rehabilitation; lifestyle changes, particularly smoking cessation; and flu and pneumonia vaccines.

Within this context, Prolastin plays an important but not exclusive role in patient care.

The Alpha-1 community awaits the appearance of additional intravenous products that may help meet the demand of the growing numbers of identified Alpha-1 patients. At the same time, the Foundation is working to facilitate the development of new products and alternate delivery methods for the treatment of Alpha inhaled alpha-1-antitrypsin (AAT) has the potential to deliver plasma-derived product more efficiently to the lungs than IV and may therefore make it possible to treat more patients. In addition, inhaled AAT derived from other than blood plasma (recombinant sources) may provide a virtually unlimited amount of drug to the community. Newer agents, such as elastase inhibitors in pill form, are in the early stages of development.

Combined with the exciting work in the treatment of liver disease and the progress in gene therapy, these advances make the future for therapy of Alpha-1 bright indeed.

Finally, I must mention how sad it has been to lose so many Alphas to their disease this past year. In this age of instant and constant communication our small circle of friends becomes ever larger. We touch and are touched by so many more people. Both good and bad news moves with the speed of light. Therefore, although I don't believe that there are more Alphas dying now than before, we all know more Alphas personally, and we learn about their progress or failures in "real time." This only emphasizes the critical fact that the race for the cure of Alpha-1 must accelerate before it can be won - in the name of those whose lives have been lost to the disease!

If you have suggestions, comments, or questions, please don't hesitate to contact me directly at rasandhaus@alphone.org or by telephone at 888 825-7421 ext. 226.
FAQ's - Questions raised by patients

By Sandy Sandhaus, M.D., Ph.D., Medical Director, Alpha-1 Foundation/AlphaNet

Q: I had my pulmonary function tested and my FEV₁ is only 37% of predicted. Does this mean that I have lost 63% of my lung function? Does it mean that 63% of my lungs have been destroyed by emphysema?

A: The two most common lung function tests that people hear about are the Forced Vital Capacity (FVC) and the Forced Expiratory Volume in One Second (FEV₁). These two measurements are included in what is called spirometry, the type of lung function testing that can be done with a small, relatively inexpensive machine in a doctor's office or screening facility. The FVC is the volume of air you can exhale from your lungs from top to bottom after breathing in to the top of your breath and blowing out all your air as fast and hard as you can (keep going . . . keep going . . . keep going!) The FEV₁ measures how much of that top-to-bottom breath was expelled during the very first second of the breath. People with normal lungs can get 70% to 90% of their breath out during that first second. If there is any resistance to the normal flow of air out of the lung, the time it takes to get that air out is prolonged, and the FEV₁ goes down.

There are a lot of things that can make the FEV₁ lower, in addition to the emphysema of Alpha-1. Spasm of the airway muscles (asthma) can cause increased resistance to airflow, as can mucus in the airways. If someone has small lungs, which can be due to disease (scarring in the lung or interstitial lung disease), chest wall deformities (such as scoliosis or curvature of the spine), or due to an unusual chest wall size, then the FEV₁ would be lowered and the value could be below the predicted normal value. These would not necessarily mean that your lungs had lost a specific amount of function based on the FEV₁ measurement.

Also confusing is the fact that the measurement of FEV₁ is very effort-dependent. In other words, the value can change a great deal depending on the effort put in during the testing. If you were tired that day or your respiratory muscles were not up to full strength, the FEV₁ would be down.

If all of this information wasn't complicated enough, there is the problem that the FEV₁ measurement isn't necessarily a measure of lung function, especially in emphysema. An Alpha-1 patient can have significant emphysema on their x-rays and more sophisticated lung function measurements, but have a normal FEV₁. Similarly, the FEV₁ can be quite low with only mild emphysema. It is thought that the change in FEV₁ is most directly related to the loss of elastic fibers holding the airways open. This "tethering" by the elastic fibers keeps the airways from collapsing as you force air out of the lungs during exhalation.

So, the simple answer is "No," the percent predicted FEV₁ does not tell you how much emphysema you have or how much lung you have lost. Still, this measurement, with all its complexities, is one of the best simple tests we have to tell whether someone with obstructive lung disease is becoming worse, stable, or improving. Done in a consistent manner, on different visits, it can provide a gauge to evaluate how someone is doing over time.
Featured Clinical Resource Center: The James P. Mara Center For Lung Disease
Written by Lon Trottier and Gerard M. Turino, M.D., Director
The James P. Mara Center for Lung Disease at St. Luke’s Roosevelt Hospital Center in New York City was dedicated in December, 1998 and was founded by the generosity of Judith and Russell Carson. Judith Carson’s brother, James P. Mara, died at forty years of age from pulmonary emphysema related to Alpha-1-Antitrypsin (AAT) Deficiency. From the outset, the focus of the Mara Center has been to alleviate suffering and advance our knowledge in the diseases of asthma and emphysema, with a special interest in emphysema related to AAT Deficiency. Prior to the formation of the Mara Center, Drs. Gerard M. Turino and Edward Eden directed a Center for AAT Deficiency, which was part of the National Heart, Lung, and Blood Institute Registry for this disease. The Mara Center continues to participate in the Registry for pulmonary patients under the auspices of the Alpha-1 Foundation.

The James P. Mara Center for Lung Disease encompasses a multi-faceted effort to enhance the clinical care and research of these diseases at St. Luke’s Roosevelt Hospital Center and its affiliated Beth Israel Medical Center. Funds of the Mara Center are used to initiate and continue programs related to the basic mechanism of disease and clinical investigations in asthma and emphysema. In this regard, the Mara Center coordinates facilities in emergency medicine, pediatrics, internal medicine, surgery and respiratory therapy to enhance the quality of care delivered.

The Mara Center is directed by Dr. Gerard M. Turino, John H. Keating, Sr., Professor of Medicine, Columbia University College of Physicians and Surgeons and Attending Physician at St. Luke’s Roosevelt Hospital Center. Dr. Edward Eden directs the Pulmonary Rehabilitation Program for patients with chronic obstructive pulmonary disease (COPD) for the Mara Center. Drs. Lawrence Scharer and Mary O’Sullivan co-direct the Asthma Program at St. Luke’s Roosevelt Hospital Center. A Smoking Cessation Program has been initiated by Dr. Mary O’Sullivan at the St. Luke’s site and maintains an effective program with a difficult problem.

Several programs of research are ongoing at the Mara Center. Dr. Gabriella Grunig is conducting research regarding the characteristics of the inflammatory reactions associated with asthma using methods of molecular genetics. Dr. Jerome O. Cantor is conducting biochemical studies on the pulmonary structure to determine which parts are involved in pulmonary injury caused by neutrophil and macrophage proteases. A particular focus of his research is the role of hyaluronan aerosol in preventing lung degradation caused by proteases and thereby, preventing the development of emphysema in animal models and possibly in man. Dr. Jayar Bahattacharya directs the Laboratory of Lung Vascular Biology, which studies cellular and chemical factors, which control the exchange of fluid, protein and electrolytes in the lung.
In addition to these laboratory investigations, clinical studies of aerosolized alpha_1-antitrypsin are underway. Other clinical studies concern the safety and delivery characteristics of aerosolized insulin and the effectiveness of new therapies for chronic obstructive pulmonary disease.

A major clinical effort is being devoted to the early diagnosis of pulmonary emphysema among the smoking population in New York City. This program is combined with a computer tomography screening program for lung tumors in the smokers. This effort has evolved from the recognition that early diagnosis of emphysema offers the prospect of limiting progression of the disease over the patient's lifetime.

To enhance patient care, the Mara Center, through its facilities, maintains a Pulmonary Rehabilitation Program as well as patient education programs for asthma and chronic obstructive pulmonary disease and a patient support group through the concept of a "Wellness" Program.

As a result of collaboration with the Community Outreach Department of St. Luke's Roosevelt Hospital Center and Beth Israel Medical Center, the Mara Center conducts community awareness programs for lung disease throughout the New York area. These programs include lectures, meetings and health fairs.

Presently, approximately sixty percent of all hospital admissions in New York City are accompanied by breathing disorders. It is anticipated that environmental agents may result in a significant increase in lung disease in the future. The programs of the Mara Center are dedicated to overcoming the human suffering from lung disease through the better understanding of the mechanisms of lung disease as well as more effective therapies. For more information about the James P. Mara Center for Lung Disease, please call the center at (212) 523-5471.
CRITICAL ISSUES WORKSHOPS

Alpha-1 Foundation Critical Issues Workshop No. 3
Computed Tomography (CT)
Chairmen: James C. Hogg, M.D. and John D. Newell, Jr., M.D.
February 2-3, 2001, Coral Gables, Florida
By Symma Fann, Alpha-1 Foundation

Background: Computed tomography (CT) has been proposed as a technique for quantifying the severity of emphysema in chronic obstructive pulmonary disease (COPD) of usual type and due to Alpha$_1$-Antitrypsin (AAT) Deficiency. One advantage of using CT technology in research studies is the reduction in patient sampling size. A recent CT study in 56 subjects with AAT-COPD showed significant results. This is in contrast to calculations based on annual decline of FEV(1) that would require 550 patients to show a 50% reduction of annual decline.

But there are problems with the current technologies that need to be worked out before CT could be considered an optimal diagnostic tool in COPD and AAT Deficiency. For example, CT is currently performed using equipment made by a number of different manufacturers. It is not clear whether the digitized data from different manufacturers can be merged into a single program for analysis. Such merging is essential for multi-center trials that will be organized for the
study of treatment effects in a rare disease such as AAT deficiency. Other issues include determination of the most sensitive methodology for detecting changes over time in emphysema severity, whether it is important to measure regional distribution of emphysema as well as tissue density, and how to reduce the radiation dosage and still obtain a clear diagnostic image.

Workshop Goals: A workshop was organized that included radiologists, physicists, engineers, computer scientists and pulmonologists from academia and industry to explore these questions. The workshop goals were:

- To Summarize Existing Data
- To Standardize Methodologies
- To Design a Multi-Center Trial Using CT as a Diagnostic Tool for Emphysema Associated with COPD & AAT Deficiency

The participants also included representatives of government whose input proved invaluable during roundtable discussions of CT methodologies, quality control, radiation dosage, analysis methods, and how best to standardize the different equipment currently in use. Thanks in large part to the leadership of the workshop chairs and the quality and clarity of the presentations by leading experts in pulmonary CT imaging, the participants achieved consensus on these important topics. Other positive outcomes of the workshop included the preliminary design of a multi-center trial, the purchase of a chest phantom to begin standardization of the different equipment used by various centers, and the production of a scientific summary of the workshop that has been submitted for publication to the American Journal of Respiratory & Critical Care Medicine.

A-1 Foundation Critical Issues Workshop No. 4
Lung Inflammatory Factors as Markers of Lung Destruction in AAT Deficient Individuals
Chairmen: Mark L. Brantly, M.D. and Manuel G. Cosio, M.D.
February 16, 2001, Bethesda, Maryland
By Symma Finn, A-1 Foundation

Background In Alpha 1-Antitrypsin (AAT) Deficiency-related lung disease, the intensity of tissue inflammation is related to the extent of tissue injury and destruction. Therefore, it is reasonable to hypothesize that concentrations of inflammatory factors in the lungs increase the risk of lung destruction. Even more important to Alpha patients, scientists hypothesize that since lung inflammation precedes lung destruction, decreasing the concentration of lung inflammatory factors will result in a decrease in lung destruction. What may also be true is that a reduction in lung inflammatory factors could also be used to determine the effectiveness of drugs proposed to reduce lung destruction.

The A-1 Foundation organized the fourth in its Critical Issue Workshop Series to explore inflammatory factors as potential markers in clinical trials. This has the potential to shorten the length of trials and bring therapies to the market sooner. The workshop included researchers and clinicians, as well as government and industry representatives, all with a research focus or related interest in pulmonary inflammatory processes and the development of therapeutic approaches to address the inflammation and lung destruction associated with AAT Deficiency. The workshop was structured to promote consensus building among the participating scientists by highlighting the commonality of their ultimate goal – to provide effective therapies at an earlier stage in the pathogenesis of AAT Deficiency.
**Workshop Goals:** The goal of the workshop was to determine if there is sufficient scientific evidence to support the hypotheses listed above. The ultimate goal is to promote the use of lung inflammatory markers as clinical trial outcome variables in the study of drugs meant to decrease the progression of lung destruction. This is not intended to substitute inflammatory markers for other endpoints, but to add them to the repertoire of possible clinical endpoints.

The workshop covered the current scientific evidence for the role of inflammatory markers in promoting lung destruction, the currently available approaches for evaluating lung inflammation and destruction, and the feasibility of using markers of lung inflammation in the evaluation of therapies designed to prevent or reverse lung destruction. Some factors in favor of utilizing inflammatory markers include the ease of measurement of these factors and the ability to define normal ranges for these factors (providing a standard for comparison). Some of the negative factors include the overall complexity of the inflammatory process, the lack of understanding of the day-to-day variation in these measurements (variability), and the inability at present to define what constitutes significant improvement in these measurements. In addition, specific data was identified which would be useful in establishing inflammatory markers, including the variable progression of AAT Deficiency among patients and the choice of markers that correlate with the course of disease.

**Outcomes:** One of the more important outcomes of this workshop was the recognition and identification of gaps in the scientific understanding of inflammatory processes. Although the process by which lung inflammation leads to lung destruction has not been established in all its complexity, workshop participants did agree that lung...
inflammation leads to lung destruction. Other areas of agreement included:

- Lung destruction is the result of both chronic and acute inflammation,
- Markers of inflammation can be measured in bronchoalveolar lavage fluid (BAL), sputum, and breath condensate. Among those markers of particular interest are cells (including measures of apoptosis), cytokines and chemokines, neutrophil defensins, and measures of elastin degradation
- It may be better to consider a combination of inflammatory factors rather than pick one outcome variable.

Although the workshop did not conclude with the identification of a specific inflammatory marker for use in clinical trials, a great deal of progress was made to establish the feasibility and importance of utilizing markers that can be recognized at an earlier stage in the progression of AAT Deficiency. The end result of these efforts will greatly benefit the Alpha-1 Community by attempting to address lung inflammation before it progresses to lung destruction. The Foundation wishes to thank Dr. Brantly, in particular, for his ongoing efforts to promote research of this critical issue.

**UPCOMING MEETINGS AND CONFERENCES**

May 19, 2001: Alpha-1 Forum at the American Thoracic Society

The Alpha-1 Foundation will be hosting its 4th Annual Alpha-1 Forum during the American Thoracic Society’s Annual Meeting. Since Alpha-1-related abstracts are often presented in a variety of different sessions, this forum gives pulmonary researchers and clinicians the opportunity to review Alpha-1 research in one coordinated session. Each year, since 1998, the Foundation has therefore brought together experts and young investigators in the field of Alpha-1. Presentations at the forum will also include a review and update of the Alpha-1 Research Network’s activities during the past year, and the status and direction of current research on Alpha-1. The forum will be held Saturday May 19th from 6:00 to 9:00 pm in the Golden Gate Hall A1, B2 level, San Francisco Marriott.

June 19-22, 2001

3rd International Scientific Conference on Alpha-1: The Challenge of A Genetic Condition

The Foundation has organized the third international scientific conference on Alpha-1 for June 19-22, 2001 at Airlie Conference Center, Warrenton, VA. The purpose of the conference is to stimulate a multi-disciplinary understanding of the psychosocial and medical challenges of inheriting a genetic condition.

The conference includes presentation of the Eriksson Award for Scientific Excellence in AAT Deficiency Research and announcement of the Alpha-1 Foundation’s research awards for 2001. This year the Eriksson Award is being presented to Magne Fagerhol, M.D., one of the early pioneers in AAT research and person most responsible for the naming of the earliest identified phenotypes. Dr. Fagerhol will join us from Sweden to accept this recognition of his contributions to the field, and to share with us some of the history and background of the initial genetic discoveries in AAT Deficiency.

*An image of inflammatory cells in the lung with AAT Deficiency*  
*Image provided by Costa NG et al. Am Rev Respir Dis 1986; 133:120-131*
ALPHA-1 EDUCATION DAYS

May 5, 2001
University of North Carolina at Chapel Hill
James F. Donohue, M.D.
Chapel Hill, NC
Contact: Janie Mascarella, R.N. (919) 966-2531

August 18, 2001
Dartmouth Hitchcock Medical Center
Lebanon, NH
Contact: Vicki Cameron, (888) 526-9077, ext. 427

September, 2001 (date to be announced)
California Pacific Medical Center
Kaiser Medical Center, Oakland, CA
Contact: Bobbie Stafford, (510) 267-4221

October (date to be announced)
The Cleveland Clinic Foundation
The Jean Bennett Conference on Alpha-1
James K. Stoller, M.D.
Cleveland, Ohio
Contact: Dan Laskowski (216) 444-3702

October 8, 2001
Oregon Health Sciences University
Alan F. Barker, M.D.
Portland, OR 97201
Contact: Lynne Oveson, R.N., M.N., A.N.P.
(503) 494-7680

Alpha-1 Education Days are sponsored by the Alpha-1 Alliance, a collaboration between the Alpha-1 Foundation, dedicated to improved treatments and research for a cure of Alpha-1, and the Alpha-1 Association, a patient driven membership based advocacy organization that provides education and support to individuals with Alpha-1 and their families.

Alpha-1 Foundation:
For information about the Alpha-1 Foundation activities and sponsored research please check their web site at www.alphaone.org or by calling their toll free number at 888-825-7421. You may also contact the Alpha-1 Foundation Research staff by e-mail at sfinn@alphaone.org for additional assistance in locating resources related to AAT Deficiency research, obtaining information about current research initiatives, participating in the Research Network or Registry, or to receive Foundation publications.

Alpha 1 Association:
Information and educational resources related to Alpha-1-Antitrypsin Deficiency can also be obtained from the Alpha 1 Association, 8120 Penn Avenue South, Suite 549, Minneapolis, MN 55431-1326, by calling their toll free number 800-521-3025; or by checking their web site at www.alpha1.org.

The Registry Update is funded by a restricted educational grant from the Bayer Corporation.

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