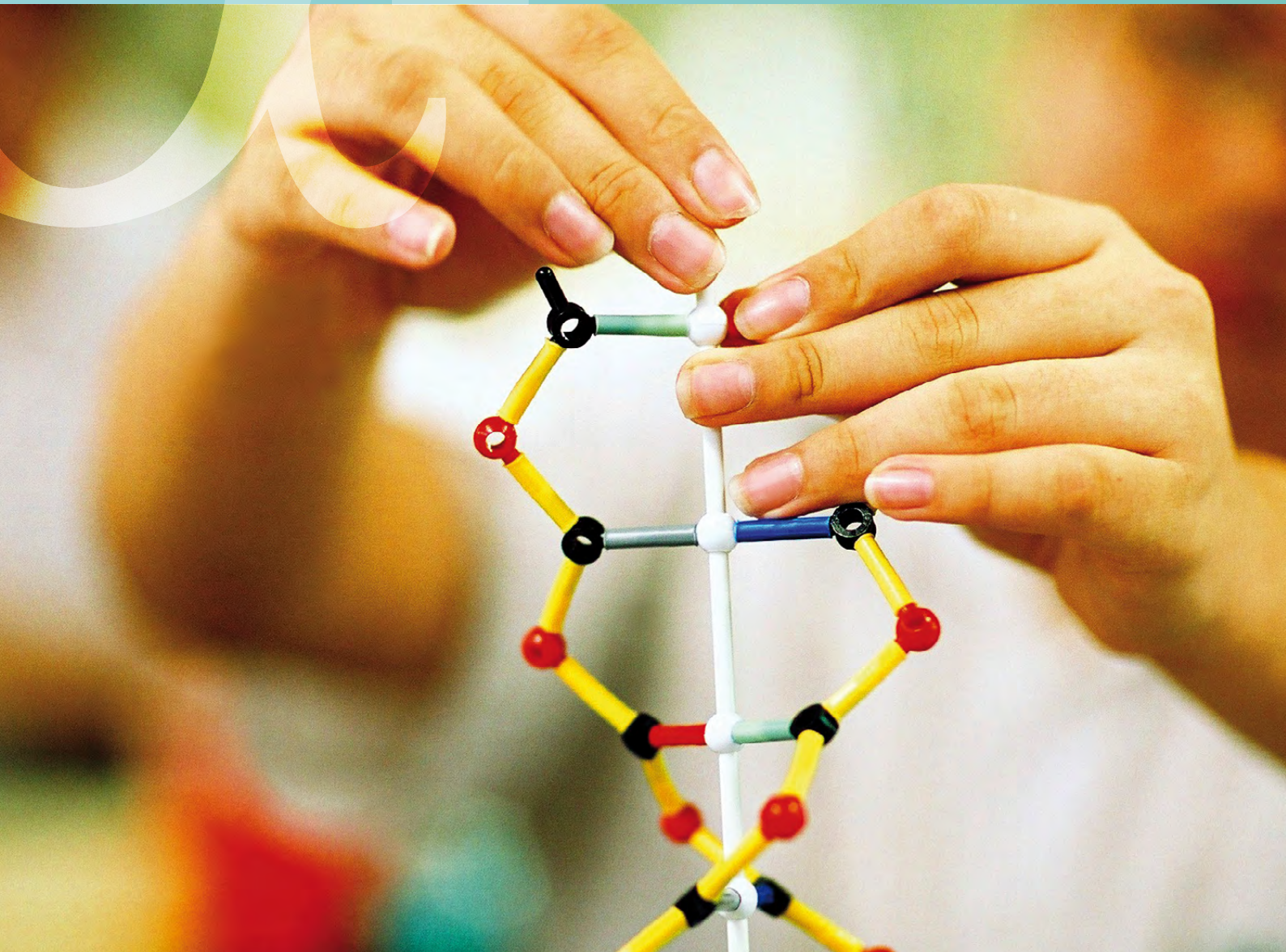


Alpha
one

ANNUAL REPORT 2006

Alpha



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Summary

The Alpha One Foundation was established in 2001 to promote research into and awareness of Alpha-1 Antitrypsin Deficiency (Alpha-1), to improve diagnosis and treatment and to improve life expectancy and lifestyle of people with the condition.

All patients are entitled to know the full extent of their condition. They are also entitled to receive the best available therapies; medical, physical and social that is appropriate to their condition.







The last two years have been the most productive in our organizations brief history. We have, through our alliances, moved the Alpha-1 issue ahead aggressively. Our progression of the Targeted Detection Screening Programming into regional Hospitals throughout the country, implementation of the Alpha-1 Registry and research in new therapeutic interventions has expanded the Foundations role within the public health arena.

These gains come from a strategic alliance with advisory communities, organizational memberships, Healthcare professionals, pharmaceutical companies, universities and foundations.

The Alpha One Foundation aims to fulfil its responsibilities to all Alpha-1 patients whether diagnosed or undiagnosed. This is the objective to do through our Alpha One Specialist centre based at Beaumont Hospital. It is our objective to detect and treat as many people with Alpha-1 in Ireland as possible.

Alpha One Foundation Programmes

The Foundation has had continuous growth, and has developed a solid infrastructure to promote research and the development of new therapies for those diagnosed with Alpha-1.

-  Targeted Detection Screening Programme
-  Alpha-1 Registry
-  Scientific meetings, conferences and workshops
-  Clinical Resource Centres
-  Replacement Therapy Clinical Trial
-  Genetic Modifiers of Alpha-1 Antitrypsin Deficiency Study

Alpha One Strategic Partnership

These past two years, the Alpha One Foundation has successfully established an unprecedented number of strategic partnerships with voluntary health agencies, government agencies and other organizations and has jointly funded grants.

ADVISORY COMMITTEES

- α Irish Asthma Society
- α Alpha-1 Foundation (US)
- α Alpha-1 Association (Italy)
- α Alpha-1 association (Spain)
- α Plasma and Protein Therapeutics Association
- α EURODIS: European Platform for Rare Diseases
- α RCSI Education and Research Centre Beaumont Hospital
- α EMEA: European Medicines Agency
- α ITS: Irish Thoracic Society
- α ANAIL: Irish Respiratory Nurses Association
- α European Alpha-1 Detection Consortium

ORGANIZATIONAL MEMBERSHIPS

- α AIR: Alpha-1 International Registry
- α ALFA Europe
- α Medical Research Charities Group (MRCG)
- α Alpha One International Network
- α Irish Donor Network
- α Pro Health lobby of the Smoking Ban
- α IPOSSI: Irish platform for Patients Organisations , Science and Industry

Targeted Detection Programme

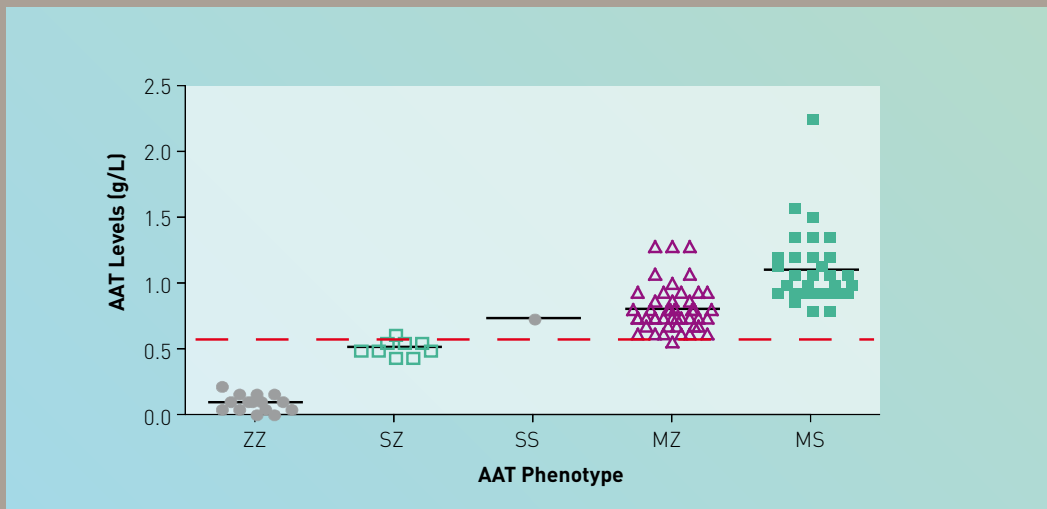
The objective of the project is to screen for Alpha-1 Antitrypsin deficiency in a population with chronic obstructive pulmonary disease (COPD) and poorly controlled non-responsive asthmatics.

Alpha-1 Antitrypsin deficiency is an under diagnosed condition. It is estimated that there are approximately 1200 individuals with Alpha-1 Antitrypsin deficiency in Ireland but as yet less than 5% have been identified. The World Health Organization has recommended screening of individuals with chronic obstructive pulmonary disease for Alpha-1 Antitrypsin deficiency. The Alpha One Foundation has developed a simple test kit for the early detection of the gene that identifies both individuals and carriers of Alpha-1. Using a lancet similar to that used by diabetics, physicians obtain a small blood sample on the collection card. There is also a simple questionnaire. Information brochures on Alpha-1 and a stamped addressed envelope are also supplied. This is sent to a diagnosis laboratory based in the Alpha One centre in Beaumont Hospital. The testing kit and test is free of charge to all.

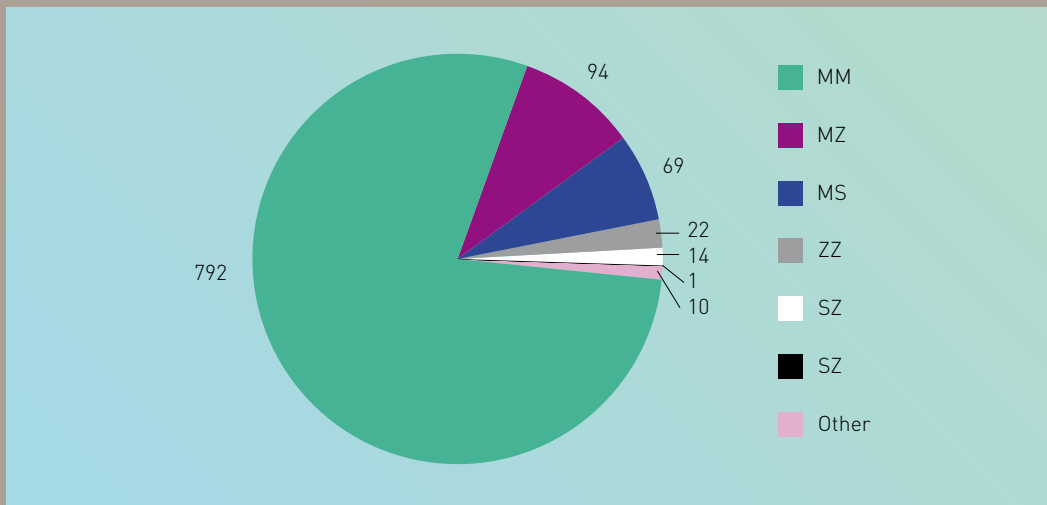
This dried blood spot method utilizes specially treated filter paper. Dried blood spot specimens have been assessed as a method for serum alpha-1 antitrypsin screening. The nephelometric method used to quantify Alpha-1 Antitrypsin from dried blood spots is both sensitive and specific with a detection limit of 0.284mg per dl, corresponding to a serum

concentration of 13mg per dl according to regression curve. The correlation coefficient between dried blood spot Alpha-1 Antitrypsin levels versus serum samples is excellent and the samples can be sent by regular mail to a central laboratory, rendering screening for alpha-1 antitrypsin deficiency both convenient and cheap. This methodology was first employed by the Spanish Registry of patients with alpha-1 antitrypsin deficiency, which now includes information on thousands of patients.

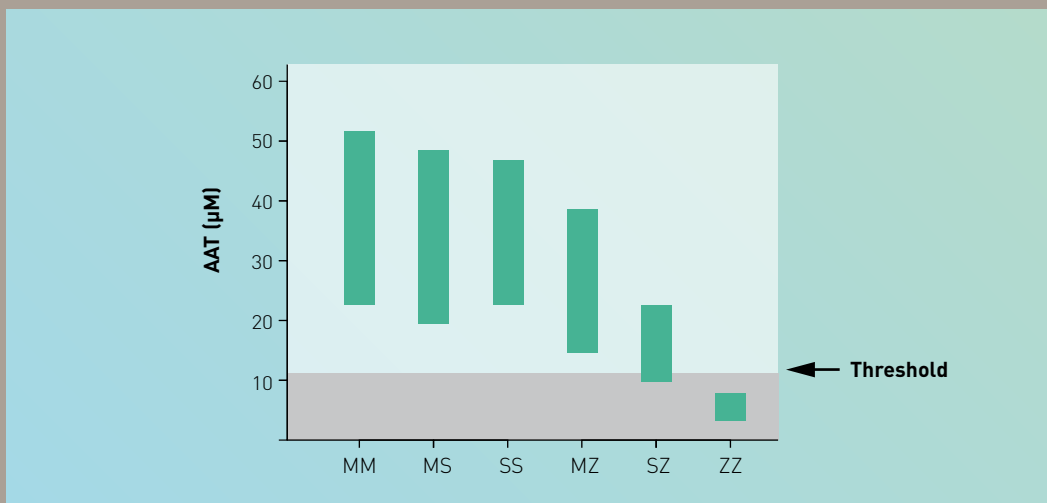
Approximately 80% of patients attending respiratory outpatient clinics suffer from chronic obstructive pulmonary disease (COPD). The likely frequency of alpha-1 antitrypsin deficiency is similar to that of cystic fibrosis. There are more than 1200 people with cystic fibrosis in the Republic of Ireland. It is therefore estimated that alpha-1 antitrypsin is relatively common in Ireland. In addition it is estimated that 2-3% of individuals with COPD actually have underlying alpha-1 antitrypsin deficiency. This screening programme evaluates individuals with obstructive pulmonary disease in an outpatient setting and will detect significant numbers of individuals with alpha-1 antitrypsin deficiency.



Plot of AAT levels (g/L) versus phenotype in Irish patients identified to date. AAT serum concentrations below the threshold of 0.572g/L correspond to deficient phenotypes. May 2006

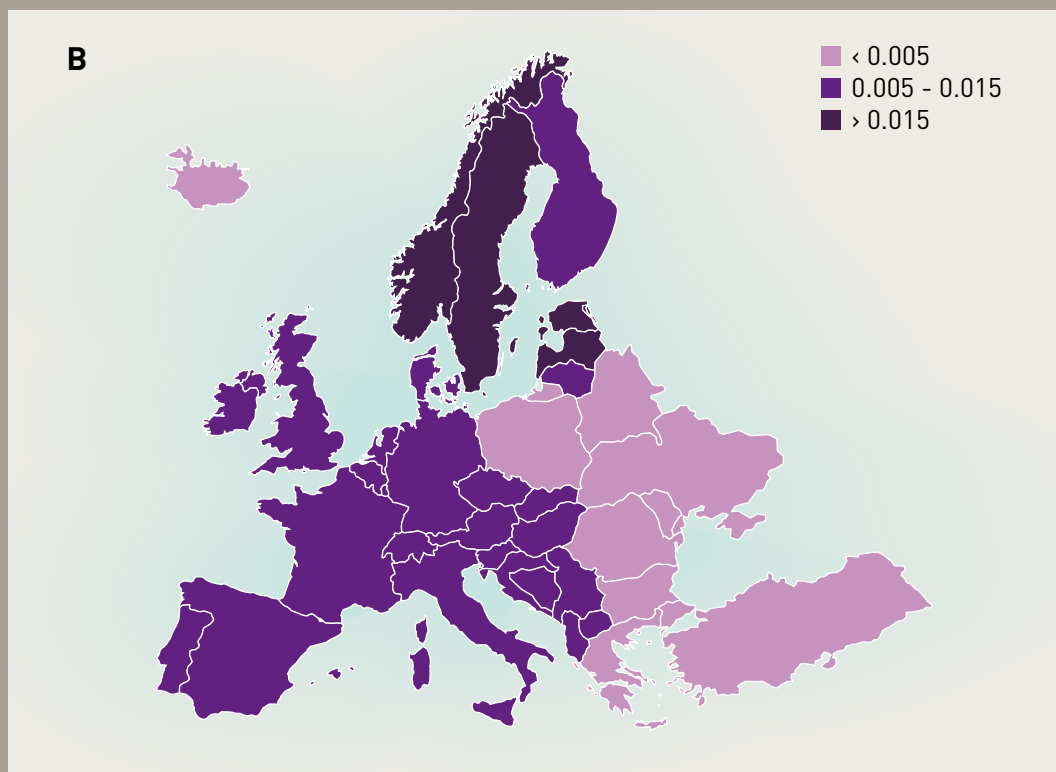
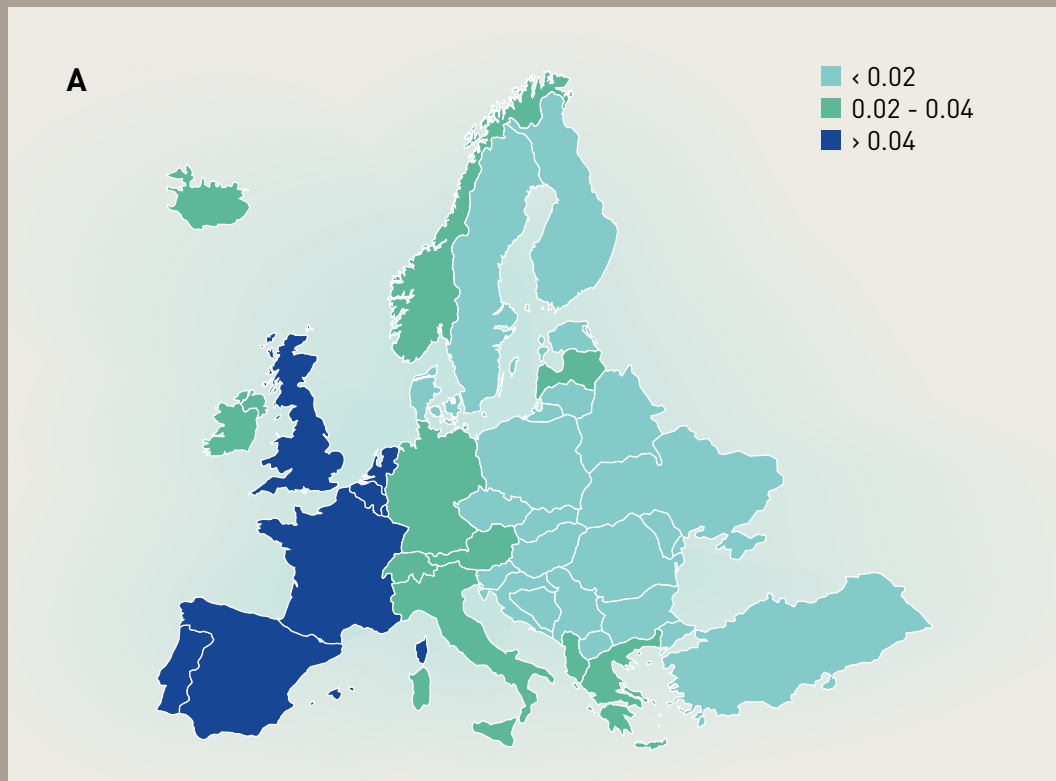


Distribution of AAT phenotypes detected in Irish TDP, May 2006



Relationship between levels of AAT and phenotype. AAT serum concentrations below the putative protective threshold of 11µM are associated with an increased risk of lung disease

Frequencies of (A) S and (B) Z genes in Europe. Luisetti, M et al. Thorax 2004; 59:164-169



Alpha-1 Participating Centres

The programme is two years old. To date we have tested 1,400 individuals in Beaumont and other hospitals. We use a combination of venous blood collection and the dried blood spot method (involving a simple finger prick), from which we can determine phenotype and genotype (confined to Z and S alleles). The results of the tests are as follows: 792 MM, 22 ZZ, 94 MZ, 69 MS, 14 SZ, 1 SS, and 10 rarer phenotypes. These figures are from May 2006.

During the year we have visited and received support from the major teaching hospitals, who have all signed up to the programme. During the visits we presented to respiratory teams the aims of the programme which were very well received. We also attended the Irish Thoracic Society conference in Galway where we had Alpha-1 information booths which proved very popular with nurses and clinicians alike.

To date we have signed up with the following Hospitals and respiratory clinicians.

- α Tallaght Hospital, Dr Stephen Lane
- α Beaumont Hospital, Prof Gerry McElvaney
- α Mater Hospital, Dr Sean Gain
- α St James's Hospital, Dr Finbarr O'Connell
- α Drogheda Hospital, Dr John Kiely
- α Dundalk Hospital, Dr John Kiely
- α Mullingar Hospital, Dr Aidan O'Brien
- α Peamount Hospital, Dr Stephen Lane
- α Crumlin Children's Hospital, Dr Billy Bourke
- α National Children's Hospital, Dr Peter Greally
- α St Michael's Hospital, Dr Tim Mc Donald

The following smaller centres have sent samples and/or expressed keen interest:

- α Rialto Clinic, Prof Luke Clancy
- α Cavan General Hospital, Dr James Hayes
- α Naas Hospital, Dr Joan Power
- α U.H. Cork, Dr Cathal Bredin
- α Limerick Regional Hospital, Dr Eithne Mulloy
- α H. H. Galway, Dr J. J. Gilmartin
- α Sligo Hospital, Dr Eamon MacSearaigh
- α Letterkenny Hospital, Dr Vera Keating
- α Blanchardstown Hospital

The following centres are earmarked for early visits:

- α Wexford Hospital
- α Waterford Hospital

Information packs and some test kits have been sent to individual General Practitioners and local colleges of general practice. We have obtained ethics approval in most hospitals, with two submission pending.

Our Research Nurse attends clinics in the hospitals to take samples, to train personnel and to kick start the programme in each. We plan to continue this successful initiative in the future.

We attend many nurse meeting and general meetings to increase the profile of the disease and the detection programme.

Since the beginning of year 2006 there has been a noticeable increase in receipt of samples averaging 20 per month and increasing, indicating that the message is getting through to doctors and nurses. We predict 1,500 individuals will be tested over the next twelve months.

Since the criminalisation of genetic discrimination in Ireland on 31st December 2005 we predict an increase in family testing in the future. Details can be obtained on our website, www.alpha1.ie, which is being updated on an ongoing basis.

Our plan in the future is to employ a full time dedicated technician which will lead to increased efficiencies and we estimate there should be a decrease in the time taken to return results from 2/3 weeks to not more than 10 days. This will also allow for improvement of genotyping techniques facilitating the use of real time PCR technology. The technician will also be tasked with records and analysis reporting. It would enable us to improve techniques in measuring AAT levels, utilising nephelometric methods.



Study Participation Consent Form

To participate in the screening programme a signed consent form is required. A fully informed consent should be obtained prior

to screening by the nurse or doctor you are attending.

CONSENT FORM



You have been asked to take part in a study to screen for Alpha 1 Antitrypsin Deficiency. It is important that you understand several principles which apply to all people who take part in this study.

1. Taking part is entirely voluntary and you will not be paid.
2. Personal benefit may not result from this study but knowledge will be gained that may benefit yourself and others. People with alpha-1 antitrypsin deficiency have an increased susceptibility to infection and therefore have been shown to benefit from vaccination, both against pneumococcus and influenza. In addition, it has been shown beyond all doubt that people with alpha-1 antitrypsin deficiency should avoid cigarette smoking either actively or passively. Furthermore, aggressive treatment of infections is recommended for individuals with alpha-1 antitrypsin deficiency.
3. You may withdraw from the study at any time and withdrawal from the study has no bearing whatsoever on the medical care that you will receive.

I _____ voluntarily agree to participate in a research project conducted by McElvaney, Beaumont Hospital. The research being carried out is a screening programme for Alpha-1 Antitrypsin Deficiency. I understand that I will have a small blood sample taken. This specimen will be evaluated to identify whether levels of alpha-1 antitrypsin in my blood are low. If this is the case I understand that a further blood test will be taken to confirm that I have alpha-1 antitrypsin deficiency. Following a positive diagnosis I understand that this test can be extended to my family. I acknowledge the procedure has been explained to me and I can withdraw from participation at any time. I have been assured that the results will be for research purposes only and will be kept completely confidential.

Signature _____ Date _____

Signature of Principal Investigator or nominee _____ Date _____

You may be attending the Respiratory Out-patients Department in Beaumont Hospital with symptoms suggesting that you have difficulty getting air in and out of your lungs. The common causes of these symptoms include asthma, which is a narrowing of the airways usually due to an allergic type reaction, damage to the lung caused by cigarette smoking, and damage to the lung caused by infections particularly early in life. Occasionally, individuals may inherit certain genes which predispose them to narrowing of the airways and difficulty in getting air in and out of the lungs.

The commonest form of this genetic disorder is called Alpha-1 Antitrypsin Deficiency. Alpha-1 Antitrypsin is a protein produced in the liver. Normally it travels from the liver into the blood stream and from there goes to the lung where it protects the lung against damage. In alpha-1 antitrypsin deficiency, the alpha-1 antitrypsin is abnormal and is retained in the liver. Because it does not get into the blood stream, it cannot protect the lung as well as it should. In these circumstances, people with alpha-1 antitrypsin deficiency are more prone to early and severe lung damage, resulting in difficulty getting air in and out of the lungs.

This condition is relatively common in Ireland. It is thought to be as common as Cystic Fibrosis. Unfortunately, to date, we have only identified approximately 80 people in Ireland with this condition, where we think there are as many as 1200.

We are asking you to let us take a small sample of blood, which we will put on a piece of paper and will then measure the levels of alpha-1 antitrypsin on that piece of paper. If the levels on that piece of paper are low, we may then ask you to give us some more blood for testing, this will involve just one further blood test. This test will either definitely prove whether you have alpha-1 antitrypsin deficiency or not.

There is a specific treatment available for alpha-1 antitrypsin deficiency which is not recommended for other types of lung destruction. In essence this type of treatment involves administration of alpha-1 antitrypsin purified from normal plasma and given to individuals with alpha-1 antitrypsin deficiency, or administration of a synthetic form of alpha-1 antitrypsin to replace the deficiency. However this particular treatment is still in its experimental stages. Finally, if proven to have alpha-1 antitrypsin deficiency, your family will be invited to undergo the same screening process as this is a hereditary disorder. All results of these tests are confidential.

If you have any questions with regard to taking part in this study, please contact the principal investigators:

Professor Noel McElvaney, Dept of Respiratory Medicine, Beaumont Hospital, Dublin 9, Tel (01) 809 3764 / (01) 809 3000

Kitty O'Connor, Clinical Research Nurse, Alpha-1 Foundation, Tel (01) 809 3871

Alpha-1 Genetic Testing Insurance Implications

An issue that has recently raised a lot of concern to families affected by alpha-1 antitrypsin deficiency is insurance implications. As stated in our recent information letter (below) to patients genetic discrimination is illegal in Ireland from December 2006.



RE: ALPHA-1 GENETIC TESTING INSURANCE IMPLICATIONS

Dear Friends,

At our Patient Information Day on October 7th concern was expressed about the effect testing family members for Alpha-1 would have on insurance and mortgage possibilities. Since then I have done some research into the matter and have been in contact with the Insurance Ombudsman, IFSRA (the regulatory body for the industry) and the Insurance Information Office. I have received some good and clarified information.

Firstly: Under part 4, section 2 of the Disability Act 2005, it will be illegal to use (process) the results of genetic testing for Insurance, Life Assurance or Mortgage purposes.

This also applies in the case of: Employment, Health Insurance and Occupational Pension.

In other words, **genetic discrimination will be illegal in Ireland from December 31st 2005.**

What will be considered when a person is looking for a pension etc will be the usual criteria:

- Health history (symptomatic)
- Smoking status
- Usual family history questions

It was emphasised that although the approach may vary from company to company, they are very competitive and are interested in individuals and as long as we tell it as it is there should be no great problems.

Although genetic discrimination does not seem to have been generally applied there was always the fear that it would. Now that fear is removed and that is good news for us all. I plan to arrange an Insurance Information slot for our next patient conference.

I trust that this information will put minds at rest.

Yours sincerely,
Larry Warren, Chief Executive

Blood Spot Testing Kits and Information

A0063518

S&S® 903™ Lot # W-011

A0063518

S&S® IsoCode Lot # 6047102

A0063518

A0063518

<p>Race:</p> <p><input type="radio"/> White <input type="radio"/> Asian/Pacific Is.</p> <p><input type="radio"/> Black <input type="radio"/> Hispanic</p> <p><input type="radio"/> Am. Ind. <input type="radio"/> Other</p>	<p>Smoking History:</p> <p><input type="radio"/> Never <input type="radio"/> Current</p> <p><input type="radio"/> Past ___ Packs/day for ___ years</p>
<p>Lung Disease History: <input type="radio"/> None <input type="radio"/> Asthma <input type="radio"/> Bronchitis</p> <p><input type="radio"/> Emphysema <input type="radio"/> Shortness of Breath <input type="radio"/> Bronchiectasis</p> <p><input type="radio"/> Allergies <input type="radio"/> Alpha-1 Antitrypsin Deficiency</p>	
<p>Liver Disease History:</p> <p><input type="radio"/> None</p> <p><input type="radio"/> Cirrhosis</p> <p><input type="radio"/> Jaundice (yellowing skin/eyes)</p> <p><input type="radio"/> Hepatitis</p> <p><input type="radio"/> Liver Transplant</p>	<p>Medication:</p> <p><input type="radio"/> Alpha-1 Antitrypsin augmentation therapy</p> <p><input type="radio"/> Tamoxifen</p> <p><input type="radio"/> Danazol</p> <p><input type="radio"/> Birth Control</p> <p><input type="radio"/> Oral Steroids</p>
<p>Alpha-1 Antitrypsin Deficiency family history?</p> <p>If Yes, <input type="radio"/> Mother <input type="radio"/> Other maternal family member</p> <p><input type="radio"/> Father <input type="radio"/> Other paternal family member</p> <p><input type="radio"/> Sibling</p>	
<p>Patient received the brochure "What is Alpha-1 Antitrypsin Deficiency (Alpha-1)? Should I be tested?"</p> <p><input type="radio"/> Yes <input type="radio"/> No</p>	

ALPHA-1 FOUNDATION
Alpha-1 Targeted Screening & Detection Program

UNIVERSITY OF FLORIDA
Alpha-1 Antitrypsin Genetics Lab
Mark Brantly, M.D., Director
UF College of Medicine

This is for screening evaluation to identify Alpha-1 Antitrypsin Deficient individuals. As with most laboratory tests with substantial treatment implications, confirmation of the diagnosis of Alpha-1 Antitrypsin Deficiency should be done by repeat evaluation.

REFER TO INSTRUCTIONS ON BACK

A0063518

Today's Date: _____

Gender: Male Female Birth Date: _____

Patient's Name: _____

Street Address: _____

City: _____ State: _____ Zip Code: _____

Telephone #: _____

Physician's Name: (Results sent to Physician's address) _____

Street Address: _____

City: _____ State: _____ Zip Code: _____

Telephone #: _____

Fax #: _____

ALPHA-1 *screening*

Six Easy Steps to Test for Alpha-1 Antitrypsin Deficiency (total time to complete is about 5 minutes)

- 1 Please read all instructions before removing the contents!**
Contents (enough testing cards and collection materials for 5 patients):
 - Business reply envelopes
 - Dried Blood Spot collection cards with supply bag that includes: lancets, alcohol wipes, sterile gauze packs and bandages
- 2 Please have your patient review "What is Alpha-1? Should I be Tested?" card before proceeding with this FREE screening**
- 3 Prepare a clean, flat surface on which to collect the blood sample**
- 4 Prepare the collection card for use**
Using latex gloves, remove collection card from bag and lay out on a clean, hard surface. Please do not allow anyone except the patient to touch the circles on the cards since DNA contamination may occur and invalidate the test results. Fill in the provider's name and address. Assume that all the information on the card has been completely filled out.
- 5 Obtain the blood sample by finger stick**
Wash the patient's hand thoroughly and dry.
Remove lancet from sterile bag, being careful not to press red trigger.

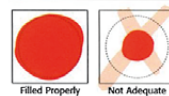
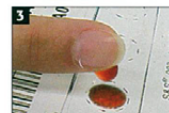


With an alcohol wipe, clean tip of finger (refer to photo #1) and allow to air dry, approximately 12-15 seconds. Do not blow on finger. Hold the patient's hand palm up. Place lancet, with trigger on top,

against fingertip and quickly and firmly depress the trigger button (refer to photo #2)



When blood begins to flow, touch drops of blood to the card in order to completely fill two or more circles on each row of circles. Do not press the finger into card. After the first drop is applied, gentle pressure can be applied to the base of the finger and massaged toward the tip of the finger (refer to photo #3 for examples of properly filled collection circles). After all circles have been properly filled, use the sterile gauze to stop the blood flow and then apply the bandage. Tricks to increase blood flow from finger sticks include warming the hand with warmed cloth and assuring that the hand is well below the patient's heart.



It is very important to allow time for the samples to completely air dry at room temperature before placing back in the envelope for shipping. Use slot inside box to hold card for drying. DO NOT REFRIGERATE!

- 6 Sample Shipment**
After the card is completely dry, place the card into the pre-addressed, postage paid Tyvek business reply envelope provided and send to the AAT Lab as soon as possible. Results from this FREE screening will be sent to the health care provider's address via mail in 2-3 weeks.



If you have any questions, comments, or need more kits please contact us at:
University of Florida • Alpha-1 Antitrypsin Genetics Research • P.O. Box 100225 • 1600 S.W. Archer Rd. • Gainesville, FL 32610
Phone: TOLL FREE 1-866-284-2708 • Fax: 352-846-3748 • EMAIL: Alpha1lab@medicine.ufl.edu

Reports

FEV1% PREDICTED

The pulmonary function tests that are recorded in the screening programme are 'Forced Expiratory Volume in 1 second' and 'Forced Vital Capacity'. Both these tests are indications of the condition of lung functioning. The table below

contains the FEV1 % predicted averages for the each phenotype divided into MM, MZ, ZZ, SZ, SS and other. These figures are comprised from information that was available at the time of screening.

FEV1 VS PHENOTYPE REPORT		
Phenotype	# Patients	Average FEV1%
MM	679	61.35
MZ	96	75.63
ZZ	21	52.22
SZ	17	95.5
SS	1	61
MS	54	51.2
Other	3	56

SMOKING HISTORY

Smoking history is a vital component in assessing lung disease. In our table below we divide smoking history into current, past and never and compare these numbers which are divided into phenotype categories. This gives

us an indication into lung disease within the smoking population tested. These figures are comprised from information that was available at the time of screening.

SMOKING HISTORY REPORT			
	CURRENT (n=132)	NEVER (n=708)	PAST (n=239)
Phenotype	# Patients	# Patients	# Patients
MM	84	444	151
MZ	16	66	14
ZZ	3	12	6
SZ	-	16	1
SS	-	1	-
MS	2	41	11
Other	-	2	1

CONSULTANT RESULTS

Individual consultant reports on the number of patients tested, gender and phenotype are available. The following report summarizes consultants' participation in the targeted

detection screening programme for alpha-1 antitrypsin deficiency, throughout the country.

CONSULTANT TO PATIENT REPORT

Consultant	# Patients	# Male	# Female	MM	MZ	ZZ	SZ	SS	MS	Other
Dr Luke Clancy	1	1	0	0	0	0	0	0	0	0
Dr Richard Costello	16	7	9	11	1	0	1	0	0	0
Dr Sean Gaine	1	1	0	1	0	0	0	0	0	0
Dr Peter Greally	2	0	2	0	2	0	0	0	0	0
Dr John Kiely	44	25	19	32	4	0	0	0	0	0
Dr Stephen Lane (Peamount)	17	7	10	13	1	0	0	0	0	0
Dr Stephen Lane (Tallaght)	17	6	11	10	1	1	0	0	1	0
Dr Pat Manning	1	1	0	0	0	0	0	0	0	0
Prof Noel G McElvaney	314	141	173	188	32	16	8	1	26	1
Dr Aidan O'Brien	64	24	40	45	1	2	0	0	0	0
Dr Finbarr O'Connell	13	8	5	0	0	0	0	0	0	0
Professor Shane O'Neill	171	70	101	129	7	0	1	0	6	1

ANTITRYPSIN REPORT

All data reported by Dr Tomas Carroll and Olwen Floyd

Patient ID	Patient	Gender	DOB	MRN	Consultant	Hospital	Date Sample Taken	Phenotype	Phenotype Level	Phenotype Percent
XXX	Jane Doe	F	xx/xx/xxxx	XXXXXX	Prof Noel G McElvaney	Beaumont Hospital	xx/xx/xxxx	ZZ	0.11	7

Research

We take a very broad view of research including: Basic science, translational science, clinical trials, psychosocial studies, dietetics, establishing standards and detection programmes. In fact, a study of anything that might affect the health of Alpha-1 patients would be seen by us as health research.

Current research projects include:

1. National Targeted Detection Programme for Alpha-1 Antitrypsin Deficiency.
2. Participating in an international collaborative study to establish the first WHO International Standard for Alpha-1 Antitrypsin (AAT or alpha-1 proteinase inhibitor). The study is being organised by the National Institute for Biological Standards and Controls (NIBSC), the primary WHO International Laboratory for Biological Standards, in collaboration with the Food and Drug Administration (FDA) and the Centre for Biologics Evaluation and Research (CBER).
3. Development of a Smoking Cessation initiative, involving the use of the mnemonic SMOKER.
4. Basic scientific research projects into the mechanisms underlying Alpha-1 antitrypsin deficiency, including ER stress responses activated by Z alpha-1 antitrypsin, caspase activation associated with Z alpha-1 antitrypsin, mucin expression in the lungs of alpha-1 deficient individuals, gene therapy for alpha-1 antitrypsin deficiency using RNA interference.

Q: What are the current policy objectives with respect to health research in Ireland?

We agree with the combined approach of both SFI and HRB policies as a national movement. We are happy to work with them and also MRCG and IPPOSI to develop a programme of translational research. We are of the opinion that there may be too much emphasis on basic science, which is not providing much in the way of therapies for patients.

Q: What are the current policy objectives with respect to the exploitation of health research in Ireland? Where has Ireland found success so far?

Smoking cessation programmes, alcohol treatment programmes and health and safety in the workplace are of great benefit and should be developed. We regard the smoking ban as a very positive initiative, which is already bearing fruit. The "Genetic Discrimination" element of the Disability Act 2005 is also of benefit both to patients and researchers.

Q: What are the major barriers with respect to exploiting research findings to the maximum effect?

Lack of interest by statutory bodies to date together with lack of funding by these bodies. This is slowly improving. There is also a lack of interest in and understanding of the various scientific findings by the populace in general. There is a lack of awareness of scientific research and the educational promotion of science must be increased. They are not being sold to industry or investors.

Q: What changes should be made to national policy to make it more effective in this area?

Awareness strategies need to be developed. Medical/scientific jargon does not help in awareness or dissemination programmes. Basic English is as important as basic science to communicate research and its findings.

STRATEGY

Q: What is the national strategy for health research?

We consider the document, Making Knowledge Work for Health: A Strategy for Health Research to be the national strategy and commend its many good ideas including the emphasis on translational research and its recognition of the usefulness of a partnership between health agencies, colleges, research charities and industry.

α What is our organization's strategy for health research?

Our major concern for the future is to attract and develop translational research into Alpha-1 Antitrypsin Deficiency. We will continue with our Targeted Detection Programme. We will continue with the existing research programme as set out above and strive to develop other similar programmes. Health research is central to our work.

FUNDING

α What are the three priorities with respect to the funding of health research?

1. Emphasis on Translational research
2. Public awareness
3. Value for money

α What are the alternative sources of funding?

- Industry where appropriate but with a "health warning".
- Charitable funders nationally and internationally.
- International statutory bodies, e.g. NIH, patient group charities.

None of these should take the place of a properly developed national research funding statutory bodies or in any way let the State abdicate from its responsibilities.

INFRASTRUCTURE AND FACILITIES

α What are our views on the current infrastructures in place to support health research and its exploitation?

We are satisfied with the work being done by HRB and SFI. However, we are not so sure about the exploitation of the results of the medical/health research to date. Again, things are improving.

α What should be done in terms of

- **Organisation structures?**
Optimise and rationalise existing structures and institutes
- **Education/training and IPR arrangements in universities?**
Again, we would stress the development of and education towards translational research.

- **Developing career structures that will recognise the value of researchers and make health research a more attractive profession?**

Researchers should be seen as an integral part of hospital and college staffs and not as an adjunct. As pillars of their institutions they need to be recognised with pay and promotion incentives.

RESEARCH PERFORMANCE AND OUTPUTS

α What are the immediate opportunities for Ireland? For our organisation?

The opportunities to both are huge. Ireland can be an EU leader in health research. We can achieve a high place in the international league just as we have done in the Information and Communications Technology sector. The Alpha One Foundation is a world leader in Alpha-1 research and is recognised as such by the WHO. We currently hold the Chair of AlfaEurope and Alpha International Network. This is not unusual for Irish Charities.

α What are the immediate and longer-term threats?

Other countries may overtake us if we are not very proactive. Duplication of resources. Not keeping up to speed with international movements and developments. Not giving value for money. Lack of development of effective therapeutic treatments. "Stigmas" attached to various conditions.

EMPLOYMENT TERMS AND CONDITIONS

α How would you modify current employment terms and conditions to enable better exploitation of health research?

We see it as an essential part of any hospital's or college's progress that they recognise the worth and work of their researchers and develop a career and wage structure with an element of incrementality and permanency.

REGULATORY ENVIRONMENT

α How effective is the existing legislation?

We are satisfied with it as it operates. We have no wish that people will be treated with untested therapies.

European Alpha-1 Detection Consortium Meeting Outcomes 2005

The European Alpha-1 Detection Consortium was held in May 2005. This was established to discuss standards and guidelines between the European countries testing for Alpha-1 antitrypsin deficiency.

At the last meeting the main topics were: 'Optimizing Laboratory Protocols', 'Improve Identification' and 'Increase Awareness'.

The feedback from the individual countries attending the meeting was as follows:

OPTIMIZING LABORATORY PROTOCOL

General Consideration: Alpha 1-reference lab/each country/region

- Each country should establish its own reference lab optimally connected with a national registry

Standards

- Implement ATS/ERS Guidelines
- The minimum requirements for a reference laboratory are assessment of quantitative serum levels assay and identification of the most frequent deficient variants

Exchange between labs

- Exchange samples with rare alleles, to improve know-how
- Develop expert laboratories for training and modeling to implement new techniques and improve standardization
- Amy McGrath will distribute actual techniques from the LAP I meeting

Quality control

- Establish external quality control program on an individual basis
- Blinded sample sent to centralized lab for control checks (Maurizio Luisetti)

New techniques

- The "Point of care Testing", introduced by Niamh O'Luanaigh, was discussed and considered as a potential useful tool for screening of special situations

Particular Country

Ireland

- Implementation of methods for detection of genotypes
- Exchange protocols with other labs
- Standards for common alleles

IMPROVE IDENTIFICATION

General Consideration: Defining a reference lab for Alpha 1 for each country/region optimally connected to a national registry

- Follow ATS/ERS recommendations and define the exceptions from these recommendations, taking into account the national setting i.e. gene frequency, smoking habits, availability of augmentation therapy
- Link to COPD and consider possible occupational diseases and DMP (Alpha 1 exclusions integrated in the guidelines)
- Role of Alpha Kit

Particular Country

Belgium

- National COPD Day with respiratory function test and possible capillary level testing

Germany

- Increase awareness by sending Alpha Kits to all chest physicians
- Implement disease management program
- Increase awareness of ATS/ERS recommendations

Ireland

- Increase awareness of ATS/ERS recommendations
- Alpha Kits sent to chest physicians and GPs in Dublin area, website information
- Expanding TDP to cover more regions nationwide

Italy

- Distribute Alpha Kits i.e. educational mailings and increase database of physicians
- Disseminate ATS/ERS guidelines
- Attend National Lung Conference in Oct and host an open house to discuss ATS/ERS guidelines, demonstrate Alpha Kits and discuss new projects
- The aim of the planned neonatal project is mainly under an epidemiology point of view but will increase identification of Alpha 1 deficient individual

Portugal

- Establish national registry
- Screening of COPD patients
- Increase awareness of chest physicians and general public
- Increase awareness of the general public about the causes of Alpha 1 from occupational exposure

Spain

- Implement IDDEA program
- Increase awareness of GPs and distribute Alpha Kit
- Develop and evaluate IDDEA program

INCREASE AWARENESS**General Consideration: Specialists (pulmonologist and pediatricians)**

- Translation of ATS/ERS guidelines (each physician in this group would have the summary translated)
- Post ATS/ERS guidelines summary on the website available as a PDF for downloading

General practitioners

- Provide physicians with a kit which includes educational materials such as CD-ROMs, bookmarks, and brochures with summary of the ATS/ERS guidelines

Patients

- Increase awareness of the patient organizations
- Create patient organizations for support and education

General public

- National COPD Day
- Figure head/famous person to promote Alpha 1/COPD DAY/ campaigns
- National Breath Day
- Journalist Award-Award given to a journalist who creates the most Alpha 1 awareness

Politicians

- Increase awareness of Alpha 1 by developing contacts with politicians

Particular Country**Belgium**

- Increase awareness of Alpha 1 among specialists and GPs
- Create new opinion leader group

Germany

- Increase awareness among lung specialists and pediatricians: Alpha kits, scientific symposia at German Society and ERS for 2006

Ireland

- Will have a booth at the Irish Thoracic Society to distribute Alpha Kits, demonstrate testing

Italy

- Increase awareness of "National Breath Day" among patients in others countries. Lung function demonstration, distribute educational materials

Portugal

- National COPD Day for patients and medical staff: possible free rapid test, lung function test
- Increase awareness among the general public

Spain

- Increase awareness among GPs, politicians, and specialists
- Patient organization is very active and trying to join with other national organizations-lung transplantation, etc.

AGENDA FOR NEXT MEETING

- Review LAP I plan
- Develop standards or procedures for new labs
- AIR to be invited to receive educational grant from Bayer/Telecris to sponsor this meeting
- Expert labs have to be defined as training models for new laboratories to train staff (new techniques, standardization)
- Alpha 1 guidelines developed from ATS/ERS guidelines-meeting supported by Telecris/Bayer
- Organize dissemination of standards
- Algorithms for different scenarios (Step 1, Step 2, Step 3)
- Publish procedures in journal sponsored by AIR and supported by Bayer HealthCare

Patient Information

Alpha 1 Deficiency Clinical Trial: Study is being conducted in Beaumont Hospital by Professor McElvaney and team. Study will be starting in early 2006 and each patient will participate for two years.

Study involves weekly administration on intravenous alpha 1. This is a straightforward procedure which can be done in the Hospital or your own home. It takes 15 minutes and will be administered always by a member of the study team.

Study being conducted in order to assess the impact of the drug on the progression of emphysema in patients. It is hoped that the study will show benefit to patients and also help evaluate further the effectiveness of the treatment for patients.

Patients will only need to come to Beaumont every 3 months. Study visits will include short CT scan of your chest, physical examination, pulmonary function test, blood/urine tests, checking of blood pressure/weight/temperature etc. and asking questions about your health. Visits would take approx. 1-2 hours each.

Patients must be between 18-60 in order to take part and also be no longer smoking. Patients will be individually assessed by the team to ensure they are suitable. All procedures and tests and subsequent results will be explained to you throughout the study. You will be able to contact us at all times if you have any problems/queries. The study is voluntary meaning you are free to withdraw at anytime you may wish.

Your safety and wellbeing are of the most importance to us. Patients who are too unwell will not be allowed to participate and any abnormality detected during your visits/tests will be discussed with you and appropriate treatment given if necessary.

The trial is a placebo controlled double blind study which means patients are split into two groups. One half on the treatment and the other

half off the treatment. This is very common in research as it helps us to scientifically and accurately assess the drug properly by splitting the patients into two groups. One on the drug and one off and then you can compare how they do over the course of the study. Neither you nor we have any control over what group you are put in. It is important you understand and are aware of this before deciding to participate.

The advantages of the study are access to tests and expert evaluation and continuous monitoring. Taking a drug which may improve your condition. Participating in a study to help evaluate further a drug which may be beneficial to patients with emphysema in the future.

We will be contacting patients over the coming months and also discussing the study in clinics with patients. We will be providing patients with more detailed information in due course.

If you are interested and would like to discuss further please contact the study coordinator David Farrell on 8093864 or 086 0695526.

Thank you.

There are nine patients on this study at present and recruitment continues with six more starting the screening phase of the trial over the next few weeks.

Patient Meetings & Support Groups



PROGRAMME

6pm, Wednesday, 29th March 2006
Alpha One Suite, RCSI Building, Beaumont Hospital, Dublin 9

Introduction: Kitty O'Connor

Replacement Therapy Research Trial: Prof Noel G McElvaney

Genetic Testing and Insurance Implications: Larry Warren

Patient Support: Joe Clinton

Open Discussion

Our annual patient information evening was held in the Alpha One Suite in Beaumont Hospital. The meeting was attended by approximately 20 patients and family members. The main topic of discussion was the Replacement Therapy Clinical Trial. Prof N.G. McElvaney discussed the background and purpose of the study, what happens if patients enrol in the study, possible side effects of the treatment, the possible disadvantages and risks that can occur from taking part and the possible benefits from taking part.

Other issues raised were in relation to genetic discrimination and insurance implications. The new legislation and its effect on families wishing to be screened, was discussed in detail. We hope to have more information and a representative from a government insurance body at our next meeting in October 2006.

Patient support groups were heard and the views of family members expressed. A plan to establish a group via e-mail or meeting was proposed. Members of this support group will attend our meeting in October to discuss any issues.

Registry

The Alpha One Registry has now over 80 members, which includes carriers and alpha-1 deficient patients. The foundation started the Registry in 2004 as a core programme to promote new research initiatives, promote the development of improved treatments, and find a cure for Alpha-1 Antitrypsin Deficiency. The Registry is located in the Alpha-1 Suite in Royal College of Surgeons building, Beaumont Hospital under the direction of Prof N.G. McElvaney.

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At present the limiting factor for data entry is the rate at which Consent forms are signed. These are available from the Alpha-1 Foundation, situated at the Alpha-1 Suite. Once signed, the initial entry process involves registration, diagnosis and one annual assessment. The annual assessment is a retrospective record of data over the previous 12 months). At present the vast majority of Alpha-1 patients entered have registration and diagnosis completed.

The ideal situation is that all Alpha-1 patients are entered on the registry and that all of their registration and diagnosis are up to date. When this is achieved we will then look at entering their annual assessments.

WHAT IS THE REGISTRY?

The Alpha-1 Registry is a confidential database, involving individuals diagnosed with Alpha-1 Antitrypsin Deficiency (Alpha-1) and individuals identified as Alpha-1 carriers. The information

in the database will include details of alpha-1 levels and genotype (The genotype is a description of the variation in the sequence of a particular gene), general health, as well as how Alpha-1 affects patients' livelihoods.

The Registry was established in 2005 by the Alpha One Foundation to improve our understanding of Alpha-1 condition, promote the development and improve treatments and provide a cure for Alpha-1.

WHO IS ELIGIBLE TO ENROL IN THE REGISTRY?

Individuals of all ages who are diagnosed with Alpha-1 Antitrypsin Deficiency and individuals identified as carriers of Alpha-1 Antitrypsin Deficiency are encouraged to enrol in the Registry.

Alpha-1 Antitrypsin Deficiency is a genetic condition. In individuals with Alpha-1, the AAT protein is not released from the liver into the blood stream. This creates a deficiency of AAT throughout the body. Some people with AAT Deficiency are not affected, while others develop liver or lung problems such as cirrhosis and emphysema.

HOW TO ENROL IN THE REGISTRY?

Patients' physician will approach them and explain the benefits and aims of the registry. The main aim is to gather as much information as possible on how alpha-1 affects individuals

with the deficiency. This will improve our understanding of the condition and help in delivery of therapies.

To enrol patients need to sign a consent form. Then the relevant alpha-1 information recorded in their medical hospital chart will be entered into the registry. A consistent annual assessment update will also be made. Participation in the Registry is Voluntary. Refusal to participate in the Registry will involve no penalty or loss of benefits to which they are entitled. Everyone is entitled to receive a copy of his or her signed Consent Form.

WHO WILL HAVE ACCESS TO MY NAME?

HOW CONFIDENTIAL IS THIS DATABASE?

Personal and medical information will go directly to the Registry Database at the Alpha-1 Foundation, Beaumont Hospital Dublin, which is under the academic supervision of the Royal College of Surgeons in Ireland.

The database will be encrypted. This means that it will not be understandable to anyone who enters the site unless they have access to an encryption key. The individuals who will have access are Prof N.G. McElvaney, Respiratory Consultant Kitty O'Connor, Clinical Nurse Specialist, Dr Tomas Carroll, Scientist. The database is kept under tight security at all times. This means that it is password protected. Only the Registry Director and Coordinators have access to a member's personal information.

RIGHT TO WITHDRAW FROM THE REGISTRY

Anyone enrolled in the Registry has the right to ask any questions concerning the Registry at any time.

An enrollee will be informed by your doctor of any significant new information pertaining to your condition that arises from information contained in the Registry.

Patients have the right to withdraw from the Registry at any time.

If someone would like their information removed from the Registry, they will be given copies of the information that is removed from the Registry and assured that the information has been taken from the Registry.

If you have any questions or queries regarding the Alpha-1 Registry please contact: **Kitty O'Connor**, Clinical Research Nurse, Alpha-1 Suite Beaumont Hospital, Tel (01) 809 3871 or www.alpha1@rcsi.ie or Principle Investigators: **Prof Noel McElvaney**, **Prof Shane O'Neill** or **Dr Richard Costello** in the Department of Respiratory Medicine, Beaumont Hospital, Beaumont Hospital, Dublin 9 Tel (01) 809 3764 / 809 3000

Conclusion

The Department of Health and Children has published a "National Health Information Strategy". It contains many clear objectives to "promote, protect, restore and maintain the health of individuals and the population." The Alpha One Foundation has closely aligned its objectives of the health information strategy.

The healthcare sector is moving rapidly into the field of "knowledge management". This may be described as the use of computer technology to organise facts and data, bring together all sources of information into one system; and then interrogate it for relationships that superficially may not seem to exist. This knowledge management technique is being used to bring down costs in healthcare and increase efficiency in health systems. The same technology can be applied to all health conditions. In this case, efficiencies naturally result because more orderly information is at the disposal of the doctor when he/she makes a crucial treatment decision.

No analysis is complete without a detailed and exhaustive look at the past. Technology allows us to do this task almost instantly. This will enable us to see why patients respond to treatments. This clinical history will assist us to predict the future response to treatments. This computer system organises this clinical history, and compares outcomes which helps us assess patients and provide best standard practice treatments for the patient.

With a system like the Alpha One Registry, we can simultaneously look at a history, while building and testing hypotheses for improved care. As the bank of historical data grows, so too does the power of observation of any present population. The testing of a change in therapy can take place within a short time span.

In order to speed up enrolment and add subsequent annual assessments, further resources /staff is required. This can be satisfied by an addition of one data entry person.

Further interrogation of the database should be the territory of extra resources.

A publication (2002) on Disease Registers from the UK recommended that the physical location for a research register should be in an academic environment, with statistical and epidemiological expertise available, where all potential users feel they have equal access and where those with legitimate scientific interests feel on an equal footing. As the Alpha One Foundation is located in The Royal College of Surgeons Building, Beaumont Hospital we fulfil the recommended location for the registry. We hope the following will be considered by the Department of Health and Children.

- Permanent commitment to the Registry.
- Support for an increase in staff when needed.

On the 10th April 2006 Ms Mary Harney, T.D., Tanaiste and Minister for Health and Children visited the Alpha One Suite in the RCSI Building Beaumont Hospital. The visit consisted of a presentation from Prof N.G. McElvaney on Alpha-1 Antitrypsin Deficiency research within RCSI at present and for the future. Dr Tomas Carroll presented research from the Targeted Detection Programme, since its commencement in 2003. Ms Harney also visited the site and met with alpha-1 patients, researchers and hospital personal.

In November 2005 the Alpha One Foundation was also visited by US Ambassador James C Kenny, promoting our strong links with the Alpha-1 Foundation in the US.

Alpha One Foundation was established to promote research into Alpha 1, to improve its diagnosis and treatment and to improve the life expectancy and lifestyle of people with this condition.