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Alpha-1 antitrypsin (AAT) is an antiprotease produced chiefly by the liver. Alpha-1 antitrypsin deficiency (AATD) is a genetic disorder characterised by low serum levels of AAT and is associated with lung and liver disease. In May 2004 a national targeted detection programme for alpha-1 antitrypsin deficiency was established in Beaumont Hospital. Funded directly by the Department of Health, the programme provides free testing to patients with chronic obstructive pulmonary disease (COPD), non-responsive asthma, cryptogenic liver disease and to relatives of AATD patients. A range of methods are used to diagnose AATD including phenotyping by isoelectric focussing and genotyping by RT-PCR. Upon diagnosis the Alpha-1 Foundation also provides a range of ancillary services to patients including counselling, expert advice, information packs and leaflets, and opportunities to enrol in clinical trials and to join the Alpha-1 patient support group.

AATD is under-diagnosed with prolonged delays in diagnosis common. In addition, the majority of AATD individuals with emphysema are misdiagnosed as COPD patients. A recent US study showed it takes an average 5.6 years from the time symptoms first appear to accurate diagnosis. Increased awareness and understanding of AATD is therefore vital to prevent the continuing under-diagnosis of this condition. To this end, we have launched a national registry of AATD patients and a website (www.alpha1.ie) providing a resource for doctors, patients, and the general public. All patients diagnosed through our targeted detection programme are offered a variety of services including counselling, expert advice, information packs/leaflets, and opportunities to enrol in clinical trials and to join the Alpha-1 patient support group. Based on studies in other European countries it is estimated that 1,200 Irish citizens have AATD and up to 200,000 Irish citizens are carriers, yet only 110 individuals with AATD have been identified in Ireland to date. A research project recently undertaken in our laboratory screened 1,000 anonymised DNA samples provided by the Trinity College Biobank for the presence of the S and Z mutations. This investigation of a sample Irish population revealed a gene frequency of 0.05 for the S mutation and 0.02 for the Z mutation, which is higher than anticipated based on studies in other European populations.
WHO (World Health Organisation) guidelines advocate targeted detection programmes for AATD in patients with COPD, non-responsive asthma or cryptogenic liver disease. In May 2004, a national targeted detection programme for AATD was launched by the Alpha-1 Foundation in Beaumont Hospital. The programme employs a full time clinical research nurse who attends respiratory outpatient clinics where patients are targeted for screening. AATD can be diagnosed from a venous sample drawn during a blood test, or alternatively a finger-prick test can be used to collect a dried blood spot (DBS) sample on specially treated filter paper for DNA isolation. When a venous sample is obtained serum can be isolated from blood and used in two different assays. The first assay measures circulating levels of AAT by radial immunodiffusion (RID). The second assay, performed on serum isolated from a venous sample, is phenotyping by isoelectric focussing (IEF). IEF separates molecules according to differences in their charge, with each molecule migrating to a point in a pH gradient where it has no net charge (Figure 1). The various phenotypes are identified by comparison with reference standards (for example MM, SZ, ZZ). Standard protein electrophoresis is not precise enough for an accurate analysis of the various forms of AAT so isoelectric focussing must be performed to correctly diagnose patients. It is also worth considering that determination of AAT levels alone is insufficient evidence of AAT deficiency. AAT is an acute-phase protein and consequently levels can sometimes be falsely elevated. Therefore, determination of the quantitative level of AAT must be combined with phenotypic or genotypic analysis.

In addition, our laboratory is participating in a pilot UK NEQAS (National External Quality Assessment Service) Alpha-1 Antitrypsin Phenotyping scheme since July 2007. Every three months the scheme provides us with two serum samples for inclusion in our screening programme and so far we have achieved 100% compliance with NEQAS. In the last year a DNA genotyping system has been developed which can detect the two mutations (S and Z) responsible for almost 98% of all cases of AATD. After a short questionnaire is filled out for each patient, a lancet is used to obtain a small blood sample which is collected on specially treated filter paper. DNA isolated from this paper is then used to genotype the patient by RT-PCR (Real-Time Polymerase Chain Reaction), using primers and probes specific to each mutation. The major advantage of implementing the genotyping method is that the ease of sample collection and storage has allowed for self-testing in the home, and the finger-prick kit test is particularly useful for family screening.

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>AAT Level (g/L)</th>
<th>What Does It Mean?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>MM Normal range 1.0-2.2g/L</td>
<td>Does not carry any altered AAT genes and will not develop disease</td>
</tr>
<tr>
<td>Carrier</td>
<td>MZ/MS/MI 0.616-1.51g/L</td>
<td>Mild to moderate AAT deficiency – carries an altered AAT gene and may develop disease</td>
</tr>
<tr>
<td>AAT Deficiency</td>
<td>ZZ/SZ/SS 0.084-0.661g/L</td>
<td>Moderate to severe AAT deficiency – carries two altered AAT genes and will develop disease</td>
</tr>
</tbody>
</table>

Table 1: Explanation of the various AAT phenotypes and their clinical consequences
Information brochures on AATD and a stamped addressed envelope are supplied with each kit and the completed kit can be sent directly to the diagnostic laboratory in the RCSI Education & Research Centre at Beaumont Hospital.

2,500 individuals with COPD, asthma or asymptomatic first-degree relatives of known AATD individuals have been screened since the inception of the screening programme over four years ago. A total of 102 AATD individuals have been identified including 57 ZZ, 35 SZ, and 10 SS. Over 500 AATD carriers were detected including 308 MZ, 182 MS and 11 rare MI phenotypes. The percentage of deficiency alleles (>20%) detected has been quite high and the S variant, more prevalent in the Iberian Peninsula, has been detected with an unusually high frequency. Several rare phenotypes were also identified and further analysis will reveal whether these phenotypes predispose individuals to lung or liver disease.

In summary, AATD is more prevalent in Ireland than previously thought, even allowing for the targeted, symptomatic population investigated in this programme. The advantages of early and accurate diagnosis of AATD are manifold and include (1) closer observation and management of affected individuals, especially regarding pulmonary and liver health, (2) family member testing, at least some of whom may have lung or liver complications, (3) aggressive smoking cessation efforts, which have been associated with lower rates of smoking among AAT-deficient individuals, and (4) consideration of occupational hazards and environment as exposures to some occupational dusts and vapors can accelerate pulmonary decline. Once identified, AATD patients have the opportunity to enroll in clinical trials currently taking place in Beaumont Hospital, such as the AAT augmentation therapy clinical trial for ZZ individuals, and the MZ family study which is attempting to fully clarify the risk of COPD in MZ individuals. To conclude, the importance of an early diagnosis of AATD cannot be over-emphasised as the resulting appropriate medical follow-up and lifestyle changes can help prevent or at least postpone the development of AATD-related lung and liver disease.

Further information can be obtained from:
Kitty O’Connor, Clinical Research Nurse, The Alpha-1 Foundation,
RCSI Education & Research Centre, Beaumont Hospital, Dublin 9.
* catoconnor@rcsi.ie (01 8093871).

http://www.health-data.info/v2/default.asp
Leads to a site called Health Data. It aims to be an information service whose ‘ethos...is the pooling of information and resources, and the provision of a simple practical web-based tool for the exchange of information and knowledge.’ It is a collaborative enterprise of health-related organisations in Ireland. Registered users are encouraged to submit information on project based activities and research led projects. Currently there are 11 member organisations participating. The site is searchable and information includes initiatives on health promotion, quality and safety in healthcare and community development.

An initiative of the ACB, the Royal College of Pathologists and the Foundation for Genomics and Population Health this booklet is aimed at alerting the public to the dangers of testing in the healthy population. The booklet, entitled Making Sense of Testing, highlights the lack of regulation of new test introduction and the possible dangers of ‘high street testing’. The authors call for a national system to evaluate diagnostic tests and a publicly accessible database to provide evidence of test performance and usefulness. They emphasise that tests are but one aspect of a diagnosis.

Thanks to Olwyn Lanigan for highlighting these sites.
‘Labs are Vital™’

The ‘Labs are Vital™’ initiative was launched in the US by Abbott Diagnostics Division in 2006. Its objectives are to:

- Highlight the value of the laboratory professional, both within the healthcare system and to the general public
- Address the issues that laboratories face today, from workforce changes to reimbursement strategies and laboratory utilisation
- Serve as a community for laboratory professionals to exchange ideas and suggestions, working as a catalyst for positive change
- Promote careers in laboratory science among students in Ireland.

It was launched in Dublin on the 29th April at Biomedica.

‘Labs are Vital™’ is dedicated to creating greater awareness and appreciation of the importance of laboratory professionals in Ireland’s healthcare system. Every day, laboratory professionals provide critical information that saves lives and helps control the costs of care in our hospitals. It is estimated that 60 – 70 per cent of health care decisions are influenced by laboratory run tests.

Since its launch in the United States by Abbott in 2006, ‘Labs are Vital™’ is successfully promoting the valuable work of laboratory scientists in the United States, the United Kingdom, the Netherlands and now in Ireland, where Abbott employs more than 3,400 people across seven manufacturing sites, including the Diagnostic Plants at Sligo and Longford.

Laboratory professionals working in Ireland make a very significant contribution to our health care system. From early diagnosis, to effective treatment, to maintaining affordable costs – all rely on the continued vitality of our clinical laboratories. ‘Labs are Vital™’ is an important initiative which will help promote better understanding of the work of laboratories and will also facilitate peer-to-peer engagement on issues affecting the profession. Both the Association of Clinical Biochemists in Ireland and the Academy of Medical Laboratory Science fully support this initiative. Internationally more than 30 associations have aligned with ‘Labs are Vital™’, including the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC).

“‘Labs are Vital™’ is a programme whose success is driven by the active involvement of laboratory professionals and their professional organisations. It embraces new media including social networking sites such as facebook.com, to create awareness of their work and the exciting career opportunities which exist in the profession. It also supports the professions in promoting their work within the wider health care system. We are delighted with the enthusiastic response from the professional bodies and we look forward to seeing ‘Labs are Vital™’ grow from strength to strength in Ireland”, said Dolores Quinn, Marketing and Communications Manager, Abbott Diagnostics.

Visit the ‘Labs are Vital™’ website www.labsarevital.com to learn how to become involved and to get regular updates.
This meeting, to honour Dr Helen Grimes on the occasion of her retirement as Consultant Biochemist, was a great success and the numbers that attended gave credit to the high regard in which she is held. The location was the Ardilaun Hotel in Galway and a varied and exciting programme had been organised by Dr Maria Fitzgibbon and Galway Hospital staff and by Dr Ophelia Blake of the ACBI. Many companies from the diagnostic industry had sponsored the meeting: Roche, Abbott, Cruinn / Siemens, Randox, Medicon, BD, and Radiometer for which we were very grateful. In spite of the awful weather conditions, approximately 80 delegates and speakers arrived at the hotel from all over the country as well as from the UK.

Maria introduced the meeting and spoke briefly on Helen’s career and she thanked Ann Mannion, Chief Medical Scientist, from Galway University Hospital for her help in organising the meeting. Dr Damien Griffin, Consultant Chemical Pathologist at Galway, chaired the first session. The first speaker was Professor Ian Young from Belfast. He spoke about lipids and atherosclerosis and presented some cases from his clinic. He mentioned the challenges in treatment strategies in which decreasing LDL- or increasing HDL – cholesterol was the aim. He concluded by saying that intensive management was now normal and that increasing HDL-cholesterol should be an aim but that this would require new treatment strategies. The discussion following centred on the use of statins in liver disease.

Dr Marcia Bell, Consultant Endocrinologist at Galway University Hospital spoke on the management of thyroid cancer. She described the investigations of a typical patient who presents at her clinic with thyroid swelling and she mentioned the poor prognostic indicators and described some recent cases. She also discussed the role of TSH measurements in investigating recurrence and the technical problems of measuring Thyroglobulin in the presence of antibodies in the patient’s serum.

Maria Fitzgibbon chaired the second session of the morning and introduced Professor Marie Cassidy, State Pathologist who spoke on the effect of media on forensic investigations, what she called “the CSI effect”. She gave an entertaining and informative description of the different ways in which her work and that of the courts are affected by what is reported in the media. She said that changes in science have had little impact on her work except for developments in DNA analysis. She mentioned that her role was to act on behalf of the Coroner and to provide impartial advice or an opinion based on the scientific facts, however she pointed out that if the facts were to change then this would also affect any opinion based on them.

The last speaker before lunch was Professor Bill Fraser from Liverpool who spoke about metabolic bone disease, in particular osteoporosis, Paget’s disease and Vitamin D. He mentioned the treatment options for osteoporosis including bisphosphonates and PTH. He discussed the use of bisphosphonate therapy in Paget’s disease and that its main effect (as seen in the PRISM study) was to reduce enzyme activity without any great effect on fractures. Professor Fraser then discussed Vitamin D and its measurement.

A superb lunch was provided by the hotel.

Rowly Reece of St Vincent’s University Hospital chaired the first afternoon session. The first speaker was Dr Amar Agha, Consultant Endocrinologist, Beaumont Hospital. He spoke about pituitary dysfunction after traumatic brain injury. He described the various types of hypopituitarism that could occur and how they may be seen early or late after injury. He mentioned the importance of hormone replacement especially the possibility that Growth Hormone deficiency may be a cause of long-term poor quality of life. A lively discussion occurred after his presentation on the use of Growth Hormone replacement.

The next speaker was Mr James Binchy, Consultant Emergency Physician at Galway University Hospital. He described some cases in which drug overdose was suspected.
and their management; resuscitation and support did not depend on results of drug analysis; sedation and body cooling were important management strategies. He described how cocaine could cause platelet aggregation but that thrombolysis was usually only necessary in older patients with chronic use.

The next speaker was Dr Ian Watson, President of the ACB from Liverpool. He gave an entertaining review of famous musicians who had died young due to drug overdoses. He finished with an amazing musical montage and his talk proved a pleasant respite from the strictly scientific content of the programme.

The last session was chaired by Mr Jimmy Newell, Laboratory Manager at Galway University Hospital. He introduced our honoured guest, Dr Helen Grimes who gave a presentation titled “Memories and Prophecies of a Clinical Biochemist” in which she discussed the changes she had seen over her career from the introduction of quality control in the 1960’s to the forthcoming Pathology Review. Her final remarks included the phrase “United we stand, Divided we fall”.

The day was rounded off by a champagne reception and fine dinner in the Ardilaun Hotel. Pre-dinner speeches from colleagues from Galway University Hospital and the Biochemistry profession praised Helen’s contribution to biochemistry. After a delicious meal, delegates, friends and family of Helen remained chatting until the early hours of the morning. It was a fitting tribute to Helen and she will be very much missed by her colleagues in Clinical Biochemistry.

Some pics from the meeting
Report from ACB (NI) / ACBI meeting
11th April 2008, Radisson SAS Hotel, Belfast.

By Ruth O’Kelly on behalf of the ACBI Scientific Committee

The annual Belfast meeting was once again a great success. There was a very good turnout with approximately 80 delegates of which over a quarter came from the Republic region. The meeting was helped by company sponsorship particularly from Roche as well as from Abbott Diagnostics, Analab, Cruinn Diagnostics, Medico Ireland, Siemens and Vector Scientific.

The meeting was opened by Dr Maurice O’Kane, chairperson, ACB (NI) who thanked the sponsors and introduced the chairperson of the morning session – Ms Margaret McDonnell, Belfast City Hospital. The first speaker was Dr Ignacio Ansotegui who spoke comprehensively on the role of the laboratory in the diagnosis of allergic conditions. He described the different definitions of allergy – whether IgE or non IgE-mediated. The goal is to identify the allergen to allow immuno-modulation if possible or avoidance. Problems in diagnosis are caused by the fact that different proteins share common epitopes. New techniques include protein micro-arrays and flow cytometry. The latter can detect activation of basophils by the monitoring the changes in surface markers whether or not IgE-mediated.

Margaret then introduced Ms Orla Maguire of St Vincent’s University Hospital, Dublin. Orla spoke on a new controversial marker IMA (ischaemia modified albumin). She gave an excellent description of the pathogenesis of Acute Coronary Syndrome (ACS) and suggested how albumin may be modified in such events. She then described her evaluation of the Cobalt binding assay for the measurement of IMA. She mentioned the limitations she found including bias between methods and dilution problems but found the assay to have good precision. The use of EDTA as a calibrant was also discussed. Orla also described a study she had undertaken on Emergency Department (ED) patients but had difficulty in categorising patients due to the different cut-offs and reference ranges available so could not at this time recommend the test as a “rule–out” for ACS in the ED.

The last speaker before lunch was Liz McLean from Belfast City Hospital who excellently described the problems of testing for Drug Abuse. She described how drug testing was now undertaken almost everywhere but that the users often did not understand the significance of either positive or negative results. She gave examples of misinterpretation of results and described a survey she had done on the inserts that come with point of care kits. Although they all suggested confirmation of results by GCMS, they tended not to mention common interferences or undetected metabolites. She also mentioned other sample types such as saliva and hair.

A delicious lunch was provided in the hotel thanks to company sponsorship, without which these meetings would not be such a success.

After lunch the afternoon session was chaired by Dr Mark Lynch, ACB (NI) Meetings Secretary, Altnagelvin Hospital. The first speaker was Jonathan Berg from Birmingham City Hospital. Jonathan gave an entertaining introduction to harmonisation before describing his own efforts at pathology harmonisation in the UK. Using funding for “Action Learning Sets” initiatives he organised meetings at which pathology staff looked at areas that GPs in particular wanted reform. These areas included reference ranges, policies for phoning results, test names and endocrine protocols. Agreement was reached on many issues particularly on reference ranges and it is hoped to implement these soon.

The next speaker was Dr Paul Collinson from St George’s Hospital, London who spoke entertainingly but informatively on the new definition of Myocardial Infarction. He described how the latest definitions now include imaging criteria but that at the moment Troponin was still the most important marker, provided it was used in the appropriate clinical situation. The main problems with troponin assays are that they are not precise enough in the reference range. However new sensitive methods are being developed.

The final speaker was Professor Anthony Bjourson from the University of Ulster. He discussed the control of metastatic invasion in cancer using work from one of his PhD students. This was a fascinating insight into cutting edge research. Techniques included gene chips to detect up and down regulation. He also discussed the role of interferon and how it may not be a suitable treatment in some form of metastasis.

Following a drink in the hotel bar, delegates headed for home after another successful Belfast meeting.


Agency for Healthcare Research and Quality
http://www.ahrq.gov/

Wide ranging American site much of it specific to the US. Under the ‘Clinical Information’ heading, however, reports published on evidence-based practice, outcomes and effectiveness, technology assessment and clinical practice guidelines can be found. Many of these are relevant to laboratories everywhere.

ChemIDplus Lite

Enter a name of a chemical into its search engine and you will get a wealth of information searchable under various database headings. Find out how toxic and dangerous some compounds, for example sodium azide, can be.

Open Directory—Health—Endocrine Disorders
http://www.dmoz.org/Health/Conditions_and_Diseases/Endocrine_Disorders/

The Open Directory is the largest human-edited directory of the web. The subheading of Health/Conditions and Diseases has over 15,000 links including 732 for endocrine disorders.
The venue for this year’s ACBI Conference is the SAS Radisson Royal Hotel, a new hotel opened in 2008, located at the crossroads between Golden Lane and Chancery Lane, Dublin 8. 5-10 minutes walk from Stephen’s Green, Grafton Street, O’Connell Street and Henry Street, 12 km from Dublin Airport and 3 km from Dublin Port. The hotel has extensive facilities, both conference and leisure. The 7th floor bar has panoramic views of Dublin and there is a rooftop terrace.

The hotel has 60 underground car parking spaces which are available to all guests. The entrance to the car park is via Ship Street Great. All guests who use the car park will incur the following charges: €2.90 per hour; €10 per 24 hours (overnight resident guests); €10 per 12 hours (meeting, conference or event guests: 7.00am –7.00pm); €20 per 24 hours (non-resident guests).
Annual conference
The Association of Clinical Biochemists in Ireland

Friday 17 and Saturday 18 October 2008
Radisson SAS Hotel
Dublin city centre

Conference topics

Impact of changing ethnic populations on clinical biochemistry
A public health perspective on the changing ethnic population in Ireland - Dr Margaret Fitzgerald
Socioeconomic differences in markers of cardiovascular risk in Greater Glasgow - Dr Kevin Deans
Clinical laboratory services for a multiethnic population - Ms Janet Smith

Heart Disease, from failure to rescue
Heart failure - a medical perspective - Dr Niall Mahon
BNP and the heart - Dr Michael Penney
Advanced lung disease and lung transplantation - Prof Jim Egan
Measuring immunosuppressive drugs - is there any point? - Prof David W Holt

Biochemistry for the elderly
Caring for the older person in Ireland - an overview - Dr Dermot Power
Aspects of biochemistry tests in the elderly - Ms Margaret McDonnell
Management of the older person - case histories - Dr Bláithín MacMahon
One foot in the...Laboratory - Dr John Doran

On the front line - Biochemistry for the emergency department
Clinical biochemistry - an emergency physicians viewpoint - Mr Patrick Plunkett
Clinical biochemistry tests in A & E - what tests and knowledge is required? - Dr Danielle Freedman

Registration forms can be downloaded from:
www.acbi.ie or www.acbroi.org.uk
or by contacting the
ACBI 2008 Registration Coordinator, Georgia Gallagher,
59 Iveragh Road, Whitehall, Dublin 9, Ireland.
Telephone: +353 87 9089128       Fax: +353 1 684 9996
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not a leap of faith

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