



Welcome
to
ACBI 2009

16 - 17 October 2009

**The Proceedings of the 32nd Conference
of the
Association of Clinical Biochemists in Ireland**

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Golden Lane, Dublin 8, Ireland

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From the President of ACBI



Welcome to ACBI 2009, our 32nd Annual Conference, set once again in the historic centre of Dublin city.

As ever, we have an interesting programme addressing various aspects of our field of clinical biochemistry. We begin with a session on the challenging topics of the management, leadership and configuration of our service for the future, as the pressures intensify to maintain quality in the face of increasing demand for services and contracting resources.

Later, we turn our attention to the endocrine functions of the kidney. On Saturday morning, we will consider biochemical aspects of undernutrition and overnutrition. In the afternoon, we launch the latest in the ACBI guidelines series, which deals with the biochemistry of body fluids other than blood and urine. This is followed by presentations on ascites and on pleural fluid.

Throughout the two days there are opportunities to view the scientific poster presentations, and on Saturday afternoon the annual award of the Geraldine Roberts medal for the best poster will take place.

At the end of the Friday afternoon session, there will be a presentation from Labs Are Vital (Ireland) to outline current activities.

Over the years, our conference has benefitted from the generous and committed support of our corporate colleagues in the diagnostics industry, and once again they have rallied to the cause, and we thank them sincerely for this. I also want to recognise the generosity of the speakers, who kindly accepted the invitation to present at our meeting – we appreciate the time and effort that this entails. I thank those who have presented their work at the poster sessions, another important element of the meeting. On behalf of the Association, I acknowledge the great work of the organising committee from the Mater Hospital, chaired by Dr. Marguerite MacMahon.

With all of this in place, the remaining vital elements for a successful conference are the participating delegates. I welcome you all, and I know that you will engage enthusiastically in the proceedings. I look forward to the debate and discussions, both the light-hearted and the serious, the solemn moments and the irreverent. I am certain that we will leave with knowledge refreshed and spirits renewed.

Dr Alan Balfe

President, ACBI

Continuing education

The Royal College

ACBI 2009 has been approved for CPD by the Royal College of Pathologists (RCPATH).

Clinical Biochemists and medical staff in career grade posts who are enrolled with the Royal College of Pathologists for CPD purposes and attend the meeting will be entitled to receive CPD credits.

CPD: Maximum 9 credits for the two day meeting

In order to receive these credits, a participant must sign the RCPATH attendance register for each day or session attended and is issued with a certificate of attendance by the meeting organiser.

Academy of Medical Laboratory Sciences

ACBI 2009 has been approved by the Academy of Medical Laboratory Sciences (AMLS) for the award of CPEP points. Ten CPEP points will be awarded for each day attended or 20 CPEP points for the full two day conference.

In order to receive these points, an AMLS member must sign the AMLS attendance register for each day or session attended and be issued with a certificate of attendance by the conference organiser.

Evaluation of ACBI 2009

All conference participants are requested to complete the conference evaluation form provided and return it to the Conference Registration Desk. ACBI evaluates the quality and educational benefits of its meetings in order to maintain a tradition of high educational standard. This process also assists in the planning of future meetings.

ACBI 2009 conference team



Committee from left to right Kieran Halton, Rachel Cullen, Peadar McGing, Marguerite MacMahon, Mark Kilbane.

Registration coordinator Siobhan Lyons

Concept & design John Wiles

Welcome to ACBI 2009

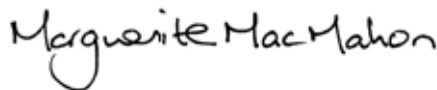
It gives me great pleasure on behalf of the organising committee to welcome you to ACBI 2009, the 32nd annual conference of the Association of Clinical Biochemists in Ireland. A warm welcome to our invited speakers, guests, delegates, ACBI and ACB colleagues, and all attending the conference. A particular word of welcome to our corporate sponsors, their generous support is vital to ensuring the continued success of the ACBI's annual scientific and social meeting. The ACBI members in the Mater University Hospital have again been entrusted with the responsibility of organising the conference.

The scientific programme includes lectures on the role of biochemistry in a number of topical areas, ranging from the importance of laboratory medicine and nutrition to endocrinology and nephrology. There will also be discussion on the area of managing resources and planning for the future of Clinical Biochemistry.

The ACBI will launch the next in its Guidelines series on Fluid Biochemistry on Saturday afternoon and we will also receive an update on Labs are Vital over the past year. We hope you find the lectures, cases and poster presentations stimulating and contributing to a memorable meeting.

As part of our social programme we have organised two contrasting evening events. On Friday evening we will be at the famous Hugh Lane Gallery a fitting venue in 2009, as October marks the centenary of the birth of the artist Francis Bacon. A private tour of the gallery collection, including the artist's studio, has been arranged. The gala dinner will be held in the historic Dining Hall of Trinity College on Saturday evening.

Finally, on behalf of the organising committee, we wish to thank all our colleagues in the Biochemistry Department of the Mater Hospital whose understanding over the last year has made the task of organising this event possible.

A handwritten signature in black ink that reads "Marguerite MacMahon". The script is cursive and fluid, with the first name and last name clearly distinguishable.

Dr Marguerite MacMahon (Chairperson)



Programme - 16 October 2009

8.45 Registration

9.45 ACBI President's address - Dr Alan Balfe

10.00 Keynote address - Ms Mary Harney TD, Minister for Health and Children

Session 1 Biochemistry for the future - managing resources

Chairperson - Dr Sean Cunningham, St Vincent's University Hospital, Dublin

As we face into a period of undoubted change and reconfiguration in the Irish clinical laboratory service, this opening session will highlight many of the issues pertinent to such reconfiguration. Following the opening lecture some of the evolving issues affecting accreditation in this country will be addressed. The need for clinical leadership has been stressed in recent reviews in both Ireland and the UK, as has the importance of pathology networks, both formal and informal.



10.30 Medical laboratory accreditation to ISO 15189

Ms Marie O'Mahony, Irish National Accreditation Board (INAB), Wilton Park House, Dublin

11.00 Tea & coffee and poster presentation viewing

11.30 Clinical leadership and the future of laboratory medicine

Prof Chris Price, University of Oxford, Dalingworth, Cirencester, England

12.10 Pathology networks – Whether or whither?

Mr Gilbert Wieringa, Royal Bolton Hospital, Department of Clinical Chemistry, Farnworth, Bolton, England

12.50 Lunch





Programme - 16 October 2009

Session 2 Endocrinology and nephrology

Chairperson - Dr Thomas Smith, St Vincent's University Hospital, Dublin

While its primary function is excretion of waste products, the kidney has two other major functions - maintenance of extra-cellular fluid volume and composition, and hormone production. This session will address these latter two functions, focussing on the reciprocal interactions between the kidney and hormones, with particular emphasis on hormone-mediated hypertension, vitamin D, and renal disease as a cause of endocrine-related disease.

**14.15 Endocrine consequences of renal disease**

Dr Denise Sadlier, Department of Renal Medicine, Mater Misericordiae University Hospital, Dublin

14.50 Aldosterone mediated hypertension

Prof John Connell, BHF Glasgow Cardiovascular Research Centre, University of Glasgow, Scotland

15.25 Tea & coffee and poster presentation viewing

Authors of posters 1-14 in attendance

15.50 Analysis of vitamin D using LC-MS/MS and the challenges it poses to the laboratory

Mr Brian Keevil, Department of Biochemistry, Wythenshawe Hospital, Manchester, England

16.25 Clinical case presentations & discussion

Ms Mary Stapleton, Cork University Hospital, Cork

Dr Maria Fitzgibbon, Mater Misericordiae University Hospital, Dublin

17.00 Labs are vital**17.15 ACBI AGM (members only)****19.00 An evening at the Hugh Lane Art Gallery, Dublin**



Programme - 17 October 2009

Session 3 Laboratory medicine and nutrition

Chairperson - Dr Maria Fitzgibbon, Mater Misericordiae University Hospital, Dublin

Nutrition is essential for life and fully balanced nutrition is vital for optimal health. Imbalance in nutrition is both a cause and a consequence of ill health. This session will review the role of the laboratory in this aspect of health-care, from micro- to macro-nutrients, from routine to specialist biochemical testing, and from long established simple tests to the latest genetic information.



9.30 Dietary fats, inflammation and insulin resistance - insights from nutrigenomic approaches

Prof Helen Roche, Conway Institute of Biomolecular & Biomedical Research, University College Dublin, Belfield, Dublin

10.10 The role of the laboratory in malnutrition and malnubesity

Dr Ruth Ayling, Department of Clinical Biochemistry, Derriford Hospital, Plymouth, England

10.50 Tea & coffee and poster presentation viewing
Authors of posters 15-26 in attendance

11.20 Iron metabolism in hereditary haemochromatosis

Prof John Crowe, Centre for Liver Disease, Mater Misericordiae University Hospital, Dublin

12.00 Micronutrient assessment in acute inflammation

Dr Denis O'Reilly, Department of Clinical Biochemistry, Glasgow Royal Infirmary, Castle Street, Glasgow, Scotland

12.40 Lunch



Programme - 17 October 2009

Session 4 Fluid biochemistry

Chairperson - Dr Damian Griffin, Galway University Hospital

Measurement of biochemical parameters in fluids other than blood and urine can make a critical difference in the differential diagnosis of patients, yet it is an area that presents much difficulty for clinicians and laboratory scientists alike. This session will see the launch of a new set of guidelines from the ACBI on fluid biochemistry. Critical appraisals of the use of biochemical tests in pleural and peritoneal fluids will be presented during this session, from the points of view of the user and of the provider.



14.00 Launch of the ACBI guidelines on fluid biochemistry

Dr Peadar McGing, Chairman, ACBI Scientific Committee

14.15 The clinical relevance of ascites

Dr Barry Kelleher, Department of Gastroenterology, Mater Misericordiae University Hospital, Dublin

15.00 Testing the waters - what should we measure in pleural fluid?

Ms Ruth Lapworth, Department of Clinical Biochemistry, William Harvey Hospital, Ashford, Kent, England

15.45 Presentation of the Geraldine Roberts medal by the President of the ACBI

16.00 Close of conference

Dr Marguerite MacMahon, Chair of the organising committee, Mater Misericordiae University Hospital, Dublin

19.00 Reception and conference dinner

The Dining Hall, Trinity College, Dublin



Keynote address



Ms Mary Harney TD
Minister for Health and Children

Mary Harney was appointed as Minister for Health and Children in September 2004, and reappointed following the 2007 General Election. Previously, she was Tánaiste and Minister for Enterprise, Trade and Employment from 1997 to 2002 and was re-appointed in June 2002, making history as the first woman to hold the title of Tánaiste and also to serve a second successive term. She served as leader of the Progressive Democrats Party from 1993 to 2006.

She was Minister of State at the Department of Environment with special responsibility for Environmental Protection 1989-1992. She was first elected to the Dáil in 1981 as a Fianna Fáil candidate.

Mary Harey was a founder member of the Progressive Democrats with Desmond O'Malley in 1985. In entering political life as a Senate nominee of then Taoiseach, Jack Lynch in August 1977, she became the youngest ever member of the Seanad. She had been a candidate in the 1977 general election in Dublin South-East, and was eventually elected to the Dail in 1981. She was a member of Dublin County Council (1979-1991) and Vice Chairperson of County Dublin Vocational Educational Committee (1985).

Biochemistry for the future - managing resources

As we face into a period of undoubted change and reconfiguration in the Irish clinical laboratory service, this opening session will highlight many of the issues pertinent to such reconfiguration. Following the opening lecture some of the evolving issues affecting accreditation in this country will be addressed. The need for clinical leadership has been stressed in recent reviews in both Ireland and the UK, as has the importance of pathology networks, both formal and informal.

Chair

Dr Sean Cunningham

Sean Cunningham is Head of the Clinical Biochemistry Department and the Director of Endocrine and Metabolism Laboratories at St Vincent's University Hospital Dublin. He is a member of the Consultative Group on Point of Care Testing, the Joint Working Group on Irish Laboratory Accreditation and a National Standards Authority of Ireland expert nominee to ISO/CEN TC212. Sean is a member of the International Scientific Committee of EuroMedlab 2009. His current interests include biochemical markers of myocardial injury, BNP, lipids and cardiovascular risk factors, adrenal function, Point of Care Testing and accreditation.

Speakers

Ms Marie O'Mahony

Marie O'Mahony is the Quality Manager with The Irish National Accreditation Board. She is responsible for monitoring INAB's quality management systems and processes to ensure compliance with the international standard ISO 17011 and with relevant European and International requirements placed on INAB to maintain its international recognition. Marie also manages a portfolio of applicant and accredited medical laboratories, and manages INAB's GLP (Good Laboratory Practice) Compliance monitoring programme. Marie is the INAB representative on the EA (European Co-operation on Accreditation) MAC (multilateral recognition agreement Council) and the INAB representative on the EU and OECD GLP expert groups. Prior to joining INAB Marie gained worked in the pharmaceutical and medical device sectors. She has a BSc from UCD in Chemistry and Maths, and an MBA from Trinity College Dublin.

Prof Christopher Price

Christopher Price PhD, FRCPATH, FRSC, FACB, is Visiting Professor in Clinical Biochemistry at the University of Oxford, and Clinical Director of the Cumbria and Lancashire Pathology Commissioning Network. Previous appointments have included Vice President of Outcomes Research for the Diagnostics Division of Bayer HealthCare, and before that Professor of Clinical Biochemistry at the St Bartholomews and Royal London School of Medicine and Dentistry, and Director of Laboratory Medicine at the Barts and London NHS Trust. His interests are mainly in areas of point-of-care testing, evidence-based laboratory medicine, commissioning of services and clinical leadership.

Mr Gilbert Wieringa

In 1999 Gilbert became head of a newly established clinical biochemistry service at Christie Hospital. In 2004/05 he was seconded to Greater Manchester Strategic Health Authority leading on three Department of Health-sponsored pilots one of which involved point of care testing by high street pharmacists for management of people with diabetes and coronary heart disease. Over 2005/06 he directed the establishment in Manchester of a primary care led pathology network. In 2007 he was seconded to the Chief Scientific Officer of the Department of Health developing prescribing roles for healthcare scientists, raising the profile of healthcare science's contribution to more effective healthcare delivery and supporting a West Midlands-based workforce modernisation project. In 2008 he was appointed consultant biochemist at Royal Bolton leading on the delivery of the North West region's Down's syndrome screening services, establishment of molecular diagnostics services and further pursuit of pharmacy-clinical biochemistry partnerships.

Medical laboratory accreditation to ISO 15189

Ms Marie O'Mahony
Quality Manager
The Irish National
Accreditation Board
Dublin

The presentation addresses medical laboratory accreditation to the international standard for medical laboratories ISO 15189 ("Medical laboratories – particular requirements for quality and competence") and the role of INAB in accreditation to this standard. By way of background some information is presented on INAB in Ireland, the European accreditation structure and the role of the European Body EA (European Co-operation on Accreditation) both in Europe and on an international level, and on the new EU regulation 765/2008.

The Irish National Accreditation Board was established in 1985 and is a division of Forfas, the national policy advisory body for enterprise and science. INAB is the national body with responsibility for accreditation of laboratories, inspection bodies and certification bodies.

There are currently 150 accredited organisations in the INAB programme.

INAB's co-operation with other accreditation bodies in Europe and globally through Multilateral Recognition Agreements (MLAs) means that certificates issued by INAB accredited organisations are recognised internationally. The European framework for accreditation is EA - the European Co-operation on Accreditation. It is a network of nationally recognised accreditation bodies. The purpose of EA is to give Europe an effective accreditation infrastructure and to operate a sound, robust reliable peer evaluation process. EA operates through a series of specialist committees. In relation to medical testing there is an EA Laboratory Medicine Working Group.

To further strengthen the role of accreditation in Europe and to use accreditation as a basis for notification a new EU Regulation 765/2008 was introduced in 2008. It recognises EA as the European accreditation infrastructure. At a national level this regulation requires the appointment of a single national accreditation body. The Regulation becomes effective from 1st January 2010. It will require laboratories, inspection bodies or certification bodies seeking accreditation to apply to the national accreditation body.

The ISO15189 medical laboratory standard was developed to address additional issues not sufficiently addressed in ISO 17025 "General requirements for the competence of testing and calibration". INAB Accreditation to ISO 15189 is a peer review process to verify technical competence for a defined scope of accreditation. INAB currently has a register of 70 qualified specialist assessors/experts that hired on a contract basis to perform assessments.

Clinical leadership and the future of laboratory medicine

Prof Christopher Price
Visiting Professor in
Clinical Biochemistry
Department of
Clinical Biochemistry
University of Oxford
Oxford
England

Laboratory medicine has been in a constant state of evolution since the first observation was made on urine (probably the first example of a 'test') to assist in the diagnosis of a disease. The number of tests has grown, and continues to grow at an inexorable rate, whilst the analytical performance, as well as approaches to test delivery, have improved immensely. Today tests are used for a wide variety of reasons to address different clinical needs including screening, ruling in or ruling out a diagnosis, guiding selection and optimisation of therapies, and assessing compliance and prognosis. Despite this record of scientific advancement we are faced with increasing claims that there is inappropriate use of tests, poor quality of evidence for the use of tests, failure to make use of tests results, and an increasing cost of services - offering poor value for money.

Several reviews of laboratory medicine services have pointed to an absence of clinical leadership and business management in the delivery of the services. One might therefore argue that laboratory medicine is reaching a watershed where greater leadership is required, and it has been argued in line with the reviews that both translational and transactional leadership is required. The former equates to direction and is about identifying the context, establishing the vision (or specifically the clinical need), setting the standards and ensuring it happens, whilst the latter equates to management and is about ensuring efficient delivery against those standards. The emphasis on clinical leadership is to stress that laboratory medicine is a key part of, and operates within, the clinical team responsible for the care of the patient.

Clinical leadership should therefore focus on meeting the challenges identified above, improving the quality of evidence for use tests, ensuring that test results are used appropriately, delivering improved health outcomes.

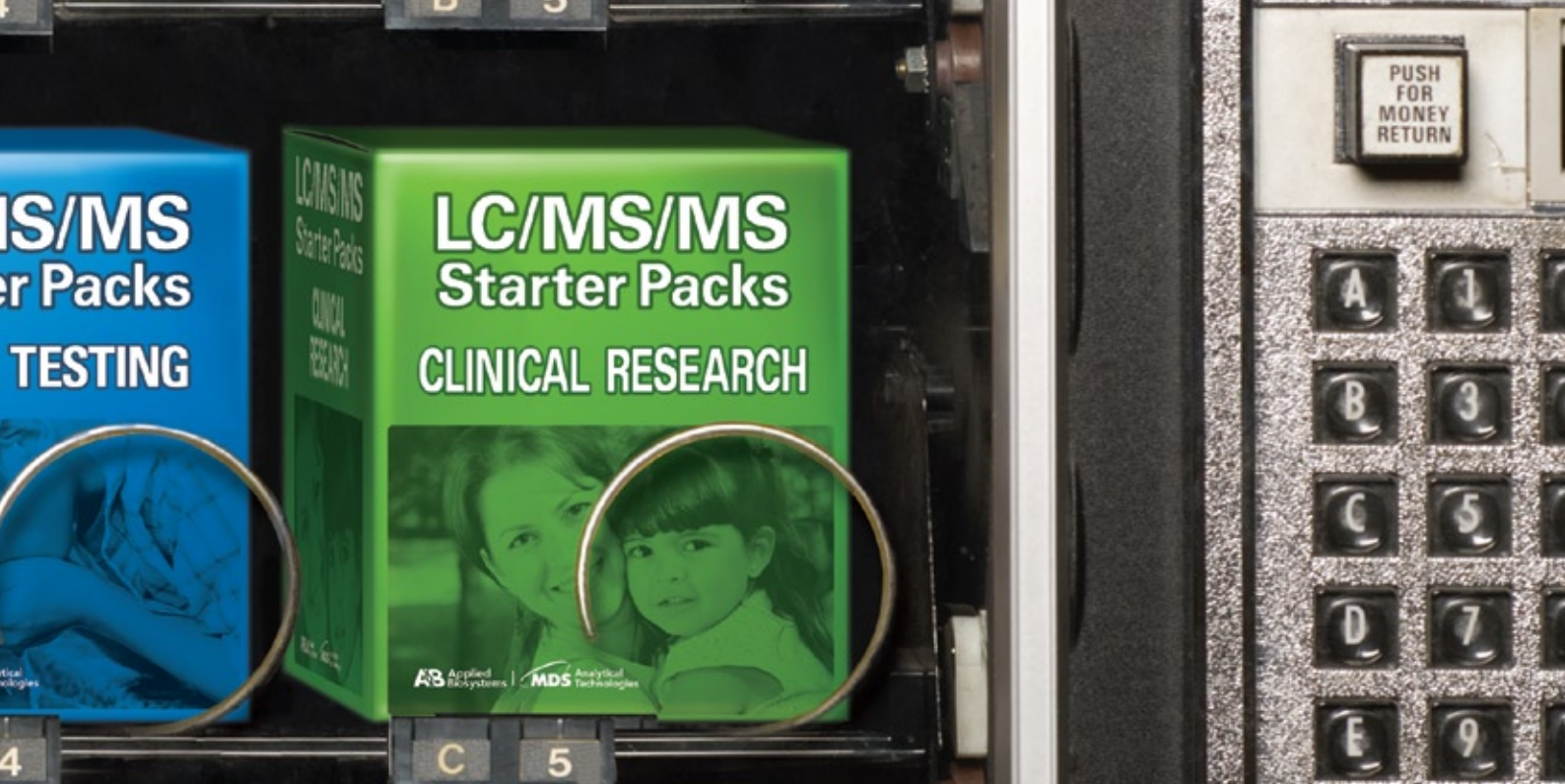
Pathology networks – whether or whither?

Mr Gilbert Wieringa
Consultant Biochemist
Royal Bolton Hospital
NHS Foundation Trust
Bolton
England

Network: “A system, *etc* (sic), of co-operating individuals”
(Collins Concise English Dictionary).

By inference networking is everywhere – within laboratories, across disciplines, between hospitals, amongst organisations. The shift from informal networking to a formal network is perhaps best justified if better services can emerge. Local drivers might include the need for greater cost efficiencies, enhanced effectiveness, improved quality, workforce recruitment and retention issues. Local circumstances eg personalities, geography, leadership issues, secondary care (foundation) trust status, primary care influence, strategic health authority agendas are perhaps the greater influence on the required shape and structure of a network – informal, federated or managed. Drawing on examples in England from Path Links, the West Midlands, Greater Manchester and Cumbria/ Lancashire, this talk argues that understanding how best to respond to local drivers and circumstances determine whether a network can be successful and sustained.

What of the future? Demarcations between primary care, secondary care and independent sector providers, emerging roles for strategic health authorities in services regulation in turn may dictate the shape and structure of networks that can emerge within conurbations. As such further change in policy is likely to determine the relevance and opportunity for already established and newly emerging networks. This talk concludes by considering what may be new developments in healthcare delivery policy in England and the possible impact on networking.



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Endocrinology and nephrology

While its primary function is excretion of waste products, the kidney has two other major functions - maintenance of extra-cellular fluid volume and composition, and hormone production. This session will address these latter two functions, focussing on the reciprocal interactions between the kidney and hormones, with particular emphasis on hormone-mediated hypertension, vitamin D, and renal disease as a cause of endocrine-related disease.

Chair

Dr Thomas Smith

Tom Smith is Principal Clinical Biochemist in the Endocrine Laboratory at St Vincent's University Hospital Dublin where he directs the provision of a specialist Endocrine laboratory service. Prior to his current appointment, Tom worked in the Mater Hospital, St James's Hospital and also Trinity College Dublin. Tom has previously served on the ACB Republic of Ireland Region Committee as Treasurer and more recently Chairman. He is currently a member of both the IEQAS steering committee and the HbA1c review group. Special research interests include the aetiology, and clinical consequences of macroprolactin together with novel markers of diabetes.

Speakers

Dr Denise Sadlier

Denise Sadlier graduated from University College Dublin in 1996. She entered the Specialist Registrar Training programme in Nephrology & General Internal Medicine in 1999 and subsequently completed a Harvard Fellowship in Nephrology and Renal Transplantation working in both Brigham and Women's Hospital and Massachusetts General Hospital in Boston, USA. In 2005, she was awarded a PhD for research into the molecular pathogenesis of renal fibrosis. She returned to Dublin in 2007 as Consultant Nephrologist and Senior Lecturer in Medicine at University College Dublin where her areas of interest clinically include cardio-renal syndrome, electrolyte disorders and glomerular disease. In addition, she continues to pursue an active research programme in diabetic nephropathy and renal fibrosis.

Prof John Connell

John Connell graduated in medicine from Glasgow in 1977. After initial training in endocrinology, he was appointed as a Clinical Scientist to the MRC Blood Pressure Unit, Western infirmary, Glasgow in 1983. He held an MRC Travelling Fellowship in the Howard Florey Institute for Experimental Physiology and Medicine, working on the regulation of steroid hydroxylase genes. He was appointed Senior MRC Clinical Scientist and Honorary Consultant Physician in 1987, Professor of Medicine in 1993 and joined the University of Glasgow as Professor of Endocrinology in 1995. He leads (with Dr Eleanor Davies) the MRC Blood Pressure Group, based in the BHF Glasgow Cardiovascular Research Centre. The work of the group focuses on the regulation of synthesis of aldosterone, and on the associations between aldosterone and cardiovascular disease. Their studies have described the association between variation in the genes encoding aldosterone synthase (CYP11B2) and 11 β -hydroxylase (CYP11B1) and hypertension. He is a lead Principal Investigator on the MRC Bright Study on "the genetics of hypertension" and collaborates closely with research groups in the UK (Birmingham, Newcastle, London and Edinburgh) and also in the USA (Dallas, Augusta) and in Europe (Paris, Padua).

Mr Brian Keevil

Brian Keevil is a Consultant Clinical Scientist and has worked at the University Hospital of South Manchester for 25 years. His main area of research has been in the development of LC-MS/MS methods for therapeutic drugs and steroids. He is a fellow of the Royal College of Pathologists and has over 80 published papers.

Endocrine consequences of renal disease

<p>Dr Denise Sadlier Consultant Nephrologist Department of Renal Medicine Mater Misericordiae University Hospital Dublin</p>	<p>The kidney has a number of important endocrine functions that help maintain normal homeostasis. The endocrine functions of the kidneys encompass bone metabolism, electrolyte balance, blood pressure control and iron metabolism. While many consider each of these functions individually, here the basic physiology of the main endocrine functions of the kidney will be reviewed followed by a discussion of how these endocrine pathways impact on common clinical conditions such as hypertension, diabetes mellitus and chronic kidney disease.</p>
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Aldosterone mediated hypertension

Prof John Connell
Professor of
Endocrinology
MRC Blood Pressure
Group
University of Glasgow
Scotland

Aldosterone has widespread effects on cardiovascular homeostasis. Around 10% of hypertensive subjects have evidence of Primary Aldosteronism, although less than half these subjects have an autonomous adenoma. We have shown, in previous studies, that aldosterone levels are heritable, as are levels of cortisol and precursor steroid hormones of aldosterone and cortisol. We have shown that this is explained, at least in part, by variation at the genes encoding aldosterone synthase (CYP11B2) and 11-beta hydroxylase (CYP11B1). We have shown, furthermore, that this is likely to be accounted for by variation in 5' untranslated regions that control gene expression. Thus, key polymorphisms in 11-hydroxylase are associated with reduced expression levels in adrenal tissue which is translated into inefficient hydroxylation in vivo. The same polymorphisms are associated with hypertension in large population studies.

These data have led us to hypothesise that common genetic variations in the CYP11B1/CYP11B2 locus are associated with reduced efficiency of 11-hydroxylation that is compensated for by activation of the hypothalamic/pituitary/adrenal axis. Over a long period of time this will lead to adrenal cortex hyperplasia and, in susceptible subjects, aldosterone-related hypertension.

Analysis of vitamin D using LC-MS/MS and the challenges it poses to the laboratory

Mr Brian Keevil
Consultant Clinical
Scientist
Department of
Biochemistry
Wythenshawe Hospital
Manchester
England

The analysis of vitamin D presents several challenges to the laboratory. It is a hydrophobic compound, it exists in two main forms (25OHD2 and 25OHD3), it binds tightly to vitamin D binding protein (also albumin & lipids), other metabolites may be present in serum, and because of its lipophilic nature it is vulnerable to matrix effects in any Protein Binding Assay and also in LC/MS assays.

Solubility of these analytes is not an issue in serum but this property is important to remember when preparing solutions from dried material and in particular the subsequent dilutions and reconstitution steps when preparing the serum samples. Approximately 85% of 25OHD is bound tightly to the vitamin D binding protein, with the rest bound to serum albumin and lipids. Very little is bioavailable and efficient release of the analytes from the proteins is required to enable us to quantify them effectively.

Structurally, 25OHD2 differs from 25OHD3 by an extra methyl group on carbon-24 and a double bond in the side chain between carbons-22 and -23. Mass spectrometers can distinguish between the two forms easily because they have different molecular weights. 1-OHD, the 3-epimer of 25OHD3 and a cholesterol metabolite 7-ketocholesterol (major dietary oxysterol, same MW as 25OHD3) have been identified as potential interferences in LC-MS/MS. Only the 3-epimer of 25OHD3 co-elutes with the analytes causing interference, therefore routine protocols we have now are not suitable for paediatric samples and extended chromatography conditions will be required.

All assays are vulnerable to matrix effects, 25OHD assay particularly, due to the hydrophobic nature of the compound. Matrix effects are apparent in mass spectrometry by the ion enhancement or ion suppression of the analyte of interest. The obvious matrix effects arise from the patient serum that will vary from subject to subject. We must also consider contaminants from blood collection devices and labware used in sample preparation. We can reduce the interferences during sample pre-treatment by performing solid-phase or liquid liquid extraction on the protein precipitated serum sample. The need to improve sample pre-treatment puts increasing time and manpower constraints on the laboratory, particularly with a large workload, and some form of automation may be necessary. Various approaches to the automation of the assay will be discussed. Calibration of the assay has also been a problem with a wide variation of results shown on proficiency testing schemes even for the LC-MS/MS group. This has been compounded by the lack of a suitable reference material against which to calibrate vitamin D assays.

Recent studies have shown that harmonisation of results can be achieved by using a common calibrator and confirms that calibration is the single most important cause of interlaboratory variability. Hopefully, the introduction of a new reference material from NIST should finally resolve some of these issues.

Clinical case presentation & discussion

Ms Mary Stapleton
Principal Biochemist
Cork University
Hospital
Cork

Case presentation 1

Dr Maria Fitzgibbon
Consultant Biochemist
Mater Misericordiae
University Hospital
Dublin

Case presentation 2

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- Through *Labs Are Vital*, Abbott Diagnostics has developed a key opportunity for laboratory professionals. You can guide its growth and development by recruiting laboratorians to be active participants, and by promoting local activities that support the mission of *Labs Are Vital*.



Labs are Vital - 2009 update

Dr Maria Fitzgibbon
Consultant Biochemist
Mater Misericordiae
University Hospital
Dublin

Since its ACBI Conference launch in 2008, Labs Are Vital has continued to gather momentum in Ireland.

Labs Are Vital is a global initiative established to raise the profile of laboratory medicine, both within the healthcare system and to the general public. In Ireland, the programme is run jointly between the Association of Clinical Biochemists in Ireland, the Academy of Medical Laboratory Science, the Irish Medical Devices Association and Abbott Diagnostics.

To coincide with UK National Pathology Week (2-8 November 2009), Labs Are Vital is encouraging Irish laboratories to organise events that promote the role of their laboratory. These could range from poster displays in hospital foyers to photography competitions and open days. A letter was recently sent to laboratory managers asking them to host events and a resource toolkit is provided for free via the Irish Labs Are Vital website.

This dedicated site was launched over the summer. Visit www.labsarevital.com and select Ireland from the world map to access news and useful information and to download free materials such as posters, presentations, photos. Please also take the opportunity to register your support for Labs Are Vital.

2009 has also seen Labs Are Vital and the European Federation of Clinical Chemistry launch an Award for Excellence in Outcomes Research in Laboratory Medicine. This new award programme, with a 15,000 Euro prize, will recognise the clinical lab or laboratory professional in Europe whose published work best demonstrates improved clinical and/or economic outcomes through the utilisation of in vitro diagnostic tests. For full details, visit www.labsarevital.com

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Laboratory medicine and nutrition

Nutrition is essential for life and fully balanced nutrition is vital for optimal health. Imbalance in nutrition is both a cause and a consequence of ill health. This session will review the role of the laboratory in this aspect of health-care, from micro- to macro-nutrients, from routine to specialist biochemical testing, and from long established simple tests to the latest genetic information.

Chair

Dr Maria Fitzgibbon

Maria Fitzgibbon is Consultant Clinical Biochemist at the Mater University and Cappagh Hospitals, Dublin. Previous to this she was Lead Consultant in Clinical Biochemistry at Barts and the Royal London. She is a graduate of University College Dublin (BSc Hons), Trinity College Dublin (MSc) and the Royal College of Surgeons in Ireland, where she completed a PhD on the metabolic and immune response to brain injury. She is a fellow of the Royal College of Pathologists (UK) and has worked in clinical biochemistry, trauma and was Associate Director of Trinity College Institute of Neuroscience. Her specialist interests are the development and translation of biomarkers in trauma, sepsis and in acute and chronic disease.

Speakers

Prof Helen Roche

Helen Roche was recently appointed Associate Professor of Nutrigenomics at the Conway Institute, UCD, Ireland. She is also a SFI Principal Investigator within the context of Molecular Nutrition. Prior to that as Wellcome Trust Fellow & Senior Lecturer in Molecular Nutrition at TCD, Dr Roche established the first Nutrigenomics research group in Ireland, at the Institute of Molecular Medicine in TCD.

Nutrigenomics uses state-of-the-art 'omics' technologies to gain a greater understanding of the molecular effects of nutrition on health. This approach is very innovative and at the cutting edge of translational nutrition research.

Dr Ruth Ayling

Dr Ruth Ayling PhD, FRCP, FRCPath is a Consultant Chemical Pathologist at Derriford Hospital, Plymouth and Head of the Peninsula Deanery School of Pathology. She qualified from Guy's Hospital and trained in Chemical Pathology at King's College Hospital London. Ruth has many years experience of working as part of a multidisciplinary nutrition team and has clinical and research interests in nutrition support and gastroenterology. She is co-author of the ACB book 'Nutrition & Laboratory Medicine'.

Prof John Crowe

John Crowe is Consultant Gastroenterologist and Hepatologist at the Liver Centre, Mater Misericordiae University Hospital and Newman Professor, University College Dublin. He was formerly a lecturer at King's College London. His research interests include: Molecular biology of iron metabolism and hereditary haemochromatosis, molecular basis to treatment response and viral clearance in chronic hepatitis C virus infection, and neurocognitive function in chronic hepatitis C.

Dr Denis O'Reilly

Denis O'Reilly graduated from University College Cork and trained in clinical biochemistry in Birmingham and Bristol. He is currently a consultant in clinical biochemistry at Glasgow Royal Infirmary and director of the Scottish Trace Element and Micronutrient Reference Laboratory. His research interests include the usefulness and effects of inflammation on the clinical applications of diagnostic tests.



Dietary fats, inflammation and insulin resistance - insights from nutrigenomic approaches

Prof Helen Roche
Professor of
Nutrigenomics
Conway Institute
UCD
Ireland

The Metabolic Syndrome (Met Syn) is a very common condition that often precedes T2DM and is associated with a greater risk of CVD. It is characterized by abdominal obesity, insulin resistance, dyslipidaemia and hypertension. There is always a concomitant sub-acute pro-inflammatory state which impedes insulin signalling. Obesity is characterised by the infiltration of macrophages into adipose tissue, a key organ which probably explains the sub-acute pro-inflammatory state associated with insulin resistance. Our group have addressed this interaction between adipose tissue, inflammation and insulin sensitivity from a number of perspectives.

This presentation will focus on the interaction between dietary fat composition, insulin sensitivity and inflammatory stressors. Data drawn from a combination of cell culture, animal models and human intervention studies; which determined the effects of a pro-inflammatory genotype and/or anti-inflammatory nutrients, within the context of insulin resistance will be explored.



The role of the laboratory in malnutrition and malnubesity

Dr Ruth Ayling
Consultant Chemical
Pathologist
Department of
Clinical Biochemistry
Derriford Hospital
Plymouth
England

Malnutrition is associated with clinical complications which lead to increased morbidity and mortality and it is now recognised that nutritional care is an essential part of the management of both acute and chronic disease. A number of common laboratory tests are performed as part of nutritional monitoring – for example measurement of reduction in cholesterol in response to dietary advice. However, the laboratory has a specific role in the monitoring of nutritional support to ensure such treatment is supplied appropriately and that complications such as the refeeding syndrome are detected and managed.

Obesity is an increasing public health problem. Many obese patients consume a highly refined energy-dense diet which is low in micronutrients (“malnubesity”). It has been postulated that the resulting hyponutrient deficiency contributes to perturbed metabolism of macro-nutrients and that this may underlie some of the complications associated with obesity .

Bariatric surgery has been shown to be an effective treatment of morbid obesity. Micronutrient deficiency after surgery is a major concern but there is evidence to show poor micronutrient status in obese individuals prior to treatment secondary to suboptimal dietary choices. The laboratory therefore has a role in biochemical monitoring of this group of patients with more intensive testing being required after surgical treatment.

Nutrigenomics offers the potential to individualise nutritional therapy by providing understanding of individual differences in response to dietary patterns and providing a basis for development of safe and effective nutritional therapies for specific sub-populations of patients. In the not too distant future the laboratory may have a role in monitoring individualised nutritional therapy for malnutrition and malnubesity.



Iron metabolism in hereditary haemochromatosis

Prof John Crowe
Consultant
Gastroenterologist
Liver Centre
Mater Misericordiae
University Hospital
&
Newman Professor
University College
Dublin

Iron is an essential mineral for life, playing a vital role in cellular ATP formation and oxygen transport by haemoglobin. Iron excess is toxic and deficiency results in anaemia. Although elegant mechanisms exist for tight regulation of iron levels and maintenance of homeostasis, there is no dedicated process to facilitate its excretion. The liver is the main storage site for iron, and therefore the organ most affected by iron excess.

Several exciting recent discoveries have been made in the field of iron metabolism, not least the discovery of hepcidin, a peptide hormone produced by the liver which inhibits iron absorption, and which is considered to be the central regulator of iron homeostasis. Disordered hepcidin synthesis is thought to underlie several common diseases, including Hereditary Haemochromatosis (HH) and the anaemia of chronic disease. Through its interaction with the cellular iron exporter ferroportin, hepcidin regulates both dietary iron absorption and iron release from macrophages. Intense research has revealed that hepcidin production may be induced by iron, endoplasmic reticular (ER) stress, and inflammation (through IL-6), and inhibited by oxidative stress (from alcohol or hepatitis C virus), hypoxia and the serine protease TMPRSS-6.

These discoveries have returned the spotlight to Hereditary Haemochromatosis, which is the most common inherited metabolic disorder in Ireland, as a platform to advance understanding of iron metabolism. HH typically results from the C282Y mutation of the HFE gene. The mutated HFE gene fails to form an iron sensing complex and as a result the production of hepcidin is deficient and systemic iron overload ensues. The phenotype is highly variable and the reasons why this is so have not been defined. When it occurs, hepatic iron accumulation leads to fibrosis, cirrhosis and hepatocellular carcinoma.

Our current research attempts to unravel the pathogenesis of this disorder, through transcriptomic analysis and hepatoma cell line models.



Micronutrient assessment in acute inflammation

Dr Denis O'Reilly
Consultant in Clinical
Biochemistry
Glasgow Royal
Infirmary
Scotland

The classical features of localised inflammation are – pain, redness, swelling, heat and loss of function. These are accompanied by clinical systemic effects such as asthenia, anorexia and hypodipsia, and biochemical effects such as a decrease in the serum albumin concentration and increases in the concentrations of fibrinogen and CRP.

Micronutrients are by definition essential for health and recovery from injury. Thus the assessment of micronutrient status is a common problem especially in metabolically active patients during severe inflammatory episodes.

The concentrations in plasma of many micronutrients are also affected. The zinc, selenium and vitamin concentrations decrease while copper increases. The time course and magnitude of these changes is variable for different micronutrients. Some of these changes can be partially explained, and corrected for, by taking into account changes in the concentration of their respective transport proteins.

In practice this has not proven to be entirely satisfactory. Some micronutrients such as zinc are actively secreted into serous fluids. There is also an increase in the dispersion of the “reference range”, which we find to be related to the severity of the inflammatory response. We have recently examined erythrocyte micronutrient concentrations during the evolution of the inflammatory response.

This approach appears to have the potential to overcome the problem¹. We have recently issued guidance from our laboratory on the limitations of using plasma micronutrient measurements to assess the micronutrient status of patients with systemic inflammatory conditions. The data and rationale behind this guidance will be presented.

1. Oakes EJC, Lyon TDB, Duncan A, Gray A, Talwar D, O'Reilly DStJ. Acute inflammatory response does not affect erythrocyte concentrations of copper, zinc and selenium. Clin Nutr 2008; 27: 115-120.

Fluid biochemistry

Measurement of biochemical parameters in fluids other than blood and urine can make a critical difference in the differential diagnosis of patients, yet it is an area that presents much difficulty for clinicians and laboratory scientists alike. This session will see the launch of a new set of guidelines from the ACBI on fluid biochemistry. Critical appraisals of the use of biochemical tests in pleural and peritoneal fluids will be presented during this session, from the points of view of the user and of the provider.

Chair

Dr Damian Griffin

Damian Griffin graduated from UCC medical school in 1989. He trained in Chemical Pathology in St. James's Hospital and Southampton University Hospital Trust. Over that period he completed an MSc in Computer Science at TCD for his work on Distributed Decision Support Systems and an MD on the Genetics of Renal Stone Disease in Southampton University Hospital. In 2003 he took up a consultant post in Swansea and in 2006 his present position as Consultant Chemical Pathologist in Galway University Hospitals. His special interests include medical informatics and lipid metabolism.

Speakers

Dr Barry Kelleher

Barry Kelleher is a Consultant Gastroenterologist and Hepatologist at the Mater Misericordiae University Hospital, Dublin. He graduated in 1995 from UCD and completed Specialist Training in Dublin prior to advanced fellowships in both Interventional Endoscopy and Hepatology at Harvard's Beth Israel Deaconess Medical Center, Boston. He became a consultant in Boston in 2005 and returned to take up his post in the Mater at the end of 2006.

Ms Ruth Lapworth

Ruth Lapworth is a Consultant Clinical Scientist and the Clinical Director of Pathology in East Kent Hospitals University NHS Foundation Trust, England. She has a wide experience of clinical biochemistry having worked in a number of district general and teaching hospitals.

Her interest in the biochemical analysis of pleural fluids developed after undertaking an audit of testing practice in laboratories in the South Thames region. She has collaborated with Dr Anne Tarn to produce recommendations on pleural fluid testing and is currently working on recommendations for the analysis of ascitic fluid.

ACBI guidelines on fluid biochemistry

Dr Peadar McGing
Chairman
ACBI
Scientific Committee

Analysis of body fluids, other than blood and urine, provides a valuable interpretative tool in the diagnosis and monitoring of disease. This latest volume in the series of guidelines commissioned and produced by the Scientific Committee of the Association of Clinical Biochemists in Ireland (ACBI) deals with the analyses of body fluids covering physiology and pathology, analytical issues, interpretation of results and limitations of testing. A small selection of the information covered in the guideline booklet is included here for illustrative purposes.

Most fluids are ultra-filtrates of blood that have undergone processing by the relevant tissues while some are produced by active transport. Fluids such as Cerebral Spinal Fluid (CSF) are present in the healthy population while fluids such as pleural fluid are usually only seen in noticeable quantities in disease.

Biochemical analysis of fluids produced in excess (e.g. pleural and peritoneal fluids), can be a valuable aid in the differential diagnosis of disease, or it may be useful for diagnosis of disease organs associated with the fluid (such as with CSF and semen).

The fluids most commonly analysed are CSF, pleural and peritoneal (ascitic) fluids, and sweat (which should only be analysed in specialist centres). Of these, CSF is the most commonly measured with 24-hour availability for biochemistry (particularly glucose and protein, \pm spectrometry) and haematology/microbiology (cell count and cell culture).

Biochemical analysis is very important in the investigation of the causes of excess pleural or peritoneal fluids. A definitively low or a high fluid total protein will usually differentiate between transudate (<25 g/L) and exudate (>35 g/L) respectively. For intermediate protein concentrations, Light's criteria (using serum and fluid LDH and protein) is the most commonly used tool. pH may be important in determining if drainage is needed for purulent pleural fluids. Albumin gradient between serum and ascitic fluid is also a very useful diagnostic tool.

The guidelines also address the issue of pre-analytical factors such as taking the required samples (e.g. concomitant serum sample for Light's criteria), the correct containers (e.g. air-free 'blood gas' syringe for pH), and the correct preservative (e.g. for glucose). A section entitled Analytical Issues is included in the chapter for each of the fluids, and a summary table is also included at the start of the booklet.

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The clinical relevance of ascites

Dr Barry Kelleher
Consultant
Gastroenterologist
Mater Misericordiae
University Hospital
Dublin

Chronic liver disease results in liver fibrosis and ultimately cirrhosis. In the UK between 1992 and 2001 there has been a 45% increase in the incidence of cirrhosis. In Ireland we can only estimate similar disease burden. Once decompensation occurs the only real viable treatment is liver transplantation. Patients in the diagnostic phase of their liver disease and also in the management phase of decompensation have a large requirement for diagnostic laboratory tests which are crucial to effective patient management.

There is a broad differential diagnosis in patients with elevated Liver Function Tests and understanding what laboratory investigations are useful in narrowing this differential is vital. An outline of these investigations will be delivered along with the central role of laboratory diagnostics in the management of patients with advanced liver failure.

Testing the waters : what should we measure in pleural fluid?

Ms Ruth Lapworth
Consultant Clinical
Scientist
Department of
Clinical Biochemistry
William Harvey
Hospital
Ashford, Kent
England

Pleural effusions are a common medical problem. Light's criteria¹ have been used to classify pleural fluids as either an exudate or transudate. Subsequent modification of these criteria and their use in less well defined populations has resulted in lower diagnostic accuracy than originally reported². The publication of guidelines by the British Thoracic Society (BTS) in 2003³ rekindled interest in this area.

A structured approach to the investigation of a unilateral pleural effusion of unknown cause can be helpful if a transudative effusion has been excluded from the patient's history, clinical examination and chest x-ray.

The most useful laboratory investigations are cytology and measurement of pleural fluid total protein concentration. It is important before any biochemical testing is undertaken to record the appearance of the fluid and to determine its suitability for analysis after centrifugation. A pleural fluid total protein concentration greater than 35g/L is consistent with an exudative effusion whereas a concentration less than 25g/L suggests the fluid is a transudate.

Measurement of pleural fluid lactate dehydrogenase (LD) is only indicated in those samples with an equivocal total protein concentration (i.e. 25 – 35g/L).

Other biochemical tests should be restricted to answer specific clinical questions such as:

- pH – does this parapneumonic effusion need draining?
- Amylase – is pancreatitis the cause of this effusion?
- Creatinine – is it urine?
- Triglyceride – is it a chylothorax?

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Poster Presentations

- 1** Urine protein electrophoresis: Comparison of agarose gel and capillary zone electrophoretic techniques
Anne-Marie Curtin in co-operation with Dr. Liam Casserly, Renal and Haematology-Oncology Out Patients Departments of the Mid-Western Regional Hospital, Limerick
Department of Clinical Chemistry, Mid-Western Regional Hospital, Limerick
- 2** A study of cocaine detection in post mortem samples in Ireland
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The Toxicology Laboratory, Department of Chemical Pathology, Beaumont Hospital, Dublin 9
- 3** HPLC-tandem mass spectrometry method for analysis of serum 25-hydroxyvitamin D3 and D2 in a large public hospital biochemistry laboratory
Healy MJ¹, Cox G¹, Walsh JB², Casey MC², Crowley VEF¹
¹Biochemistry Department, Central Pathology, St. James's Hospital, Dublin 8
²Mercer's Institute for Research on Ageing, St. James's Hospital Dublin 8
- 4** Prevalence of vitamin D insufficiency: A review of one year's assay results in St. James's Hospital
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¹Biochemistry Department, Central Pathology, St. James's Hospital, Dublin 8
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- 5** 'Less than' results for albumin are inadequate in SAAG calculation for differential diagnosis of patients with ascites
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¹Biochemistry Department, Mater Misericordiae University Hospital, Dublin 7
²Biochemistry Department, Cork Institute of Technology, Cork
- 6** A case of symptomatic hypocalcaemia in Autoimmune PolyEndocrinopathy Candidiasis Ectodermal Dystrophy Syndrome (APECEDS)
Reilly C, Neylon O, Costigan C, Brady J
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- 7** The value of metabolic markers in diagnosis of Vitamin B12 deficiency
Deverell D¹, Fitzsimons PE¹, Macken A², Crushell E², Mc Mahon C³, Mayne PD¹
¹Biochemistry Department and ²National Centre for Inherited Metabolic Disorders, Children's University Hospital, Temple Street, Dublin
³Department of Haematology, Our Lady's Children's Hospital, Crumlin, Dublin
- 8** Critical evaluation of four creatinine assays with a view to the clinical interpretation of creatinine and eGFR on a diabetic cohort
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Biochemistry Department, Mid Western Regional Hospital, Limerick

- 9** Comparison of bromocresol green- and bromocresol purple- measured albumin methods in renal disease and the merits of introducing an interconversion formula
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- 12** Determination of an ion exchange chromatography method for the measurement of plasma tryptophan in patients with Glutaric Aciduria Type I
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¹Department of Cardiology, Royal Victoria hospital, Belfast
²SpR Public Health Medicine, Belfast
- 14** Screening for classical Galactosaemia in the Republic of Ireland
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- 20** Inherent MCP-1 suppression in C282Y hereditary haemochromatosis links disordered iron
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¹Centre for Liver Disease, Mater Misericordiae University Hospital, Dublin
²Department of Histopathology, Mater Misericordiae University Hospital, Dublin
- 21** Elevated hepatic transferrin expression in hepatic iron overload is specific to hereditary
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- 22** Development and validation of a genotyping assay for the S65C mutation in the HFE gene
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¹Department of Clinical Biochemistry, Galway University Hospitals, Galway
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- 24** Prevalence of the HFE S65C mutation and correlation with iron status in Irish patients investigated
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Street, Dublin 7

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Urine protein electrophoresis: Comparison of agarose gel and capillary zone electrophoretic techniques

Anne-Marie Curtin in co-operation with Dr. Liam Casserly, Renal and Haematology-Oncology Out Patients Departments of the Mid-Western Regional Hospital, Limerick
Department of Clinical Chemistry, Mid-Western Regional Hospital, Limerick

Background Proteinuria, the excess excretion of protein in the urine, is a clinical finding in a variety of conditions such as renal disease and neoplastic disorders e.g. Multiple Myeloma. Consequently, electrophoretic investigation of proteinuria type is a valuable and widely utilised non-invasive diagnostic tool.

Aim The aim of this study was to examine various agarose gel and capillary zone electrophoretic techniques in order to establish a method choice for the separation of urinary protein.

Methods Comparisons were made based on protein fractions detected and monoclonal (M) peak quantifications. An examination of a capillary zone electrophoresis (CZE) based method for the identification of monoclonal components such as Bence Jones Protein (BJP) was also carried out. Random urine samples ($n = 88$) (U. Prot. > 0.15 g/L) underwent analysis by four electrophoretic techniques: Neat urine high resolution (HR) gel electrophoresis, Concentrated urine HR gel electrophoresis, $\beta 1\beta 2$ agarose gel electrophoresis and CZE. All samples also underwent a BJP immunofixation screen (gold standard) and a CZE immunosubtraction screen.

Results Statistical evaluations, using the laboratory's existing method of $\beta 1\beta 2$ agarose gel electrophoresis as the standard for comparison, showed best agreement with neat urine HR gel electrophoresis ($\kappa = 0.655$). The least association was noted with CZE ($\kappa = 0.450$). While very similar monoclonal peak quantification values were noted with all three agarose gel based methods (medians 41.75 %, 41.2 % and 46.6 %), the greatest difference was seen with the CZE technique (median 29.3 %). BJP immunofixation screening revealed a total of 21 urines containing M components, 16 of which were evident on CZE and $\beta 1\beta 2$ gel electrophoresis, 17 were detectable on HR Neat electrophoresis and 18 were detectable on HR concentrated electrophoresis.

Conclusions It appears, based on these findings, that neat urine HR gel electrophoresis followed by BJP immunofixation of any suspected monoclonal components is the most reliable and practical technique of those examined for the investigation of proteinuria.

A study of cocaine detection in post mortem samples in Ireland

McBrierty D, O'Neil N, Collier G

The Toxicology Laboratory, Department of Chemical Pathology, Beaumont Hospital, Dublin 9

Introduction The National Advisory Committee on Drugs (NACD) in 2007 published a report on the use of cocaine in Ireland and stated that cocaine use is highest in the 15-34 age group, is more common in males than females and is largely centred in urban areas. The National Health and Lifestyle Surveys (SLAN) indicate that cocaine use has increased since 1998. In addition there has been a significant increase in deaths by poisoning where cocaine alone or in conjunction with other drugs was implicated.

Objectives To establish the population profile that had cocaine alone or in conjunction with other drugs detected at post mortem examination and to determine if our findings reflected that of the NACD report. Also to assess if there was a marked increase in the detection of cocaine in post mortem samples since 1998.

Methods All post mortem cases presented to the toxicology laboratory in the years 1998 and 2008 were examined. The age and sex of all cases who screened positive for cocaine and other drugs at the time of death was determined.

Results In 1998, 1,274 post mortem cases were referred to Beaumont for toxicology studies and of these 611 (48%) were screened for drugs of abuse. In 2008 we received 1,817 cases and 1,396 (77%) were screened for drugs of abuse. In 1998, five cases tested positive for cocaine, whereas in 2008 eighty three cases tested positive. This represents approximately a 7 fold increase over a ten year period. The average ages of the deceased who tested positive for cocaine were 29 and 30 years in 1998 and 2008, respectively. In 1998 all of the deceased were male and in 2008, 88 % were male.

In addition 100 % (1998) and 98% (2008) screened positive for other drugs in conjunction with cocaine.

Conclusion This study found that cocaine was detected mainly in the post mortem samples from young males, the majority of whom had other drugs in their system at the time of death and that there has been a marked increase in detection of cocaine in post mortem samples since 1998.

HPLC-tandem mass spectrometry method for analysis of serum 25-hydroxyvitamin D3 and D2 in a large public hospital biochemistry laboratory

Healy MJ¹, Cox G¹, Walsh JB², Casey MC², Crowley VEF¹

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Introduction Measurement of 25-hydroxyvitamin D3 and D2 (25-OH D3 and D2) is essential for investigating vitamin D status. 25-OH D3 is derived from the action of UV light on skin while 25-OH D2 is found in food or supplements. Immunoassays for vitamin D cannot resolve these metabolites. This has implications for assessing efficacy and monitoring compliance of supplementation with 25-OH D2 in patients with suboptimal vitamin D concentrations.

Method We describe here a liquid chromatography–tandem mass spectrometry (LC-MS/MS) method for quantitation of 25-OH D3 and 25-OH D2. The LC-MS/MS system consists of an Shimadzu HPLC (UFLC XR) interfaced to an Applied Biosystems API 4000 triple quadrupole mass spectrometer. Sample preparation involves addition of precipitation reagent to serum, control or calibrator. Deuterated 25-OHD3 is added as internal standard (IS). Vials are vortexed, incubated at -4°C for 10 minutes and centrifuged. Aliquots are placed into the HPLC autosampler. A trap column concentrates and cleans the sample. A six-port-valve connects the trap column to a C18-reverse phase analytical column where chromatographic separation takes place. Mass spectrometric detection occurs using atmospheric pressure chemical ionisation and multiple reaction monitoring. Total run time per sample is 5 minutes.

Results The method is linear to 625 nmol/l. The lower limit of quantitation is 5.4 nmol/l for 25-OHD3 and 3.6 nmol/l for 25-OHD2. Recovery of 25-OH D3/D2 from serum is 91% and 98% respectively. Intra-assay precision for the two metabolites ranged from 3.4-4.1% and interassay precision ranged from 4.4-6.1%. Comparison of 183 samples previously assayed on our Diasorin Liaison immunoanalyser showed good correlation ($r=0.92$) and a difference plot gave a mean difference of +3.3 (1.17 - 5.44) in favour of the mass spectrometer.

Conclusion The LC-MS/MS method is accurate, sensitive and cost-effective, allows for the resolution of 25-OH D3 and D2, and is suitable for routine use in a hospital laboratory.

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Prevalence of vitamin D insufficiency: A review of one year's assay results in St. James's Hospital

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Introduction The classical role for vitamin D is as an essential component of bone health. More recently vitamin D has been associated with several other pathologies including diabetes, hypertension, multiple sclerosis and many forms of cancer. Adequate vitamin D is also important for normal muscle function.

Epidemiological evidence has shown that vitamin D inadequacy is widespread. Our aim was to review vitamin D concentrations measured in St. James's Hospital over a one year period by assaying 25-hydroxyvitamin D (25OHD), the major circulating form of vitamin D.

Method In 2008 a total of 5208 samples were assayed for 25OHD in our laboratory. Assays were performed on a Liaison immunochemiluminescence platform. In total 24 external agencies and, within St. James's Hospital, 62 wards requested the measurement.

Results The mean patient age was 61.7 (± 2.3 ; SE) with an age range of 1-99 years. Females made up 74% of the total. 72% of requests were for patients in the 50 to 89 age group. The therapeutic cut-offs for 25OHD used in St. James's are >80 nmol/l replete; 25-80 nmol/l insufficient; <25 nmol/l deficient. 88% of patients were in the insufficient range with 45% having values <40 nmol/l. 5% were vitamin D deficient. Looking at different age groups; patients <20 yrs had the highest mean 25OHD 51.0 nmol/l (± 2.5 ; SE-females) and 53.0 nmol/l (± 2.1 ; SE-males). Means for age groups <30 yrs, <50 yrs, <70 yrs, < 90 yrs, were similar (42.6, 42.1, 50.0, 46.9 nmol/l-females) and (43.1, 37.7, 44.3, 40.2 nmol/l-males). There was a weak but significant negative correlation between parathyroid hormone and 25OHD ($r = -0.2$, $p < 0.0001$). Seasonally overall mean 25OHD peaked July-September at 53.9 nmol/l and troughed January-March at 41.6 nmol/l ($p < 0.0002$).

Conclusion It is evident from these figures that vitamin D insufficiency is highly prevalent in this population sample. What implications this may have from a public health perspective remains to be defined.

'Less than' results for albumin are inadequate in SAAG calculation for differential diagnosis of patients with ascites

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Introduction The concept of diluting samples that are beyond the upper level of assay linearity to give accurate results of clinical value is a concept familiar to Biochemistry labs. However, it is rare for us to attempt to give accurate numerical values below the measurable range. We were approached by a hepatologist for help with albumin quantitation for use in calculation of the Serum:Ascites Albumin Gradient (SAAG), an important diagnostic tool in patients with ascites.

Materials and methods SAAG was calculated as serum albumin minus ascitic fluid albumin (both g/L). An SAAG less than 11g/L strongly indicates ascites due to portal hypertension. Albumin was measured by BCP method on the Beckman DxC800.

Results Dilution studies showed that albumin could be accurately measured on a neat sample down to 9g/L (10g/L quoted in Beckman literature). Investigation of SAAG calculation showed that on occasion serum albumin was between 9 and 18g/L – this means that any report of fluid albumin as less than 9g/L was meaningless. For example if serum albumin was 17g/L and the true albumin level in the ascitic fluid was 8g/L the SAAG would be <11 whereas if the true albumin was 4g/L then the SAAG would be >11 and diagnosis would be different.

Selected fluid samples with albumin of 20g/L or less were diluted to give expected values of 2 to 8g/L. These samples were then mixed 1:1 with appropriate QC and re-assayed. Values obtained on samples diluted into the range of 2 to 8g/L were within 1g/L of the estimated result. This shows that it is valid to use 'dilution' with QC samples to accurately measure albumin levels below the measuring range.

Conclusion Albumin levels in ascitic fluid samples with levels below the measurable range can be determined on mixing with QC material and appropriate post-assay calculation. This should be done where serum albumin is in the range 11 to 20g/L approx due to the diagnostic value of the calculated SAAG.

A case of symptomatic hypocalcaemia in Autoimmune PolyEndocrinopathy Candidiasis Ectodermal Dystrophy Syndrome (APCEDS)

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- Introduction** A number of presentations characterise the rare (1: 130,000) Autoimmune PolyEndocrinopathy Candidiasis Ectodermal Dystrophy (APECED); chronic mucocutaneous candidiasis, hypoparathyroidism and adrenocortical failure. APECED is a recessively inherited disease due to a faulty AIRE gene which produces a protein preventing the immune system attacking its own tissues.
- Clinical presentation** Patient A initially presented to the Children's University Hospital Temple St (CUH) with lethargy, weakness and seizures in 1999 with a calcium of 1.20 mmol/l (2.15 – 2.65) and a PTH of 10 ng/l (20 – 60), thus she was hypoparathyroid and hypocalcaemic. Subsequently she was also found to be homozygous for the AIRE gene. She transferred from CUH to Our Lady's Children's Hospital, Crumlin (OLCHC) in 2002.
- Lab findings** Late in 2008 patient A was admitted to OLCHC symptomatic for hypocalcaemia with diarrhoea (due to fungal oesophagitis), cramps in the legs and carpopaedal spasms. At this time she had a positive Chvostek test, and the following plasma results:
Ca 1.53 mmol/l (2.15 – 2.65), Alb 40g/l (36 – 50),
PTH <1.2 ng/l (11 – 35) and Vit D 22.3µg /l (8.0 – 60).
- Treatment** Medication, at this point was calcium 20 mmol qds, 1 alpha 4µg od and recombinant PTH 20µg bd sc. An intravenous (IV) calcium infusion for 1 week was sufficient to maintain the plasma calcium between 1.80 – 2.20 mmol/l with values above 1.65 mmol/l improving symptoms. Diarrhoea returned 3 weeks later (due to autoimmune enteropathy) followed by hypocalcaemia again requiring another *iv* calcium infusion of max dose 54 mmol/d for 7 days. Patient A was given *im* stoss therapy vitamin D 300,000 units and her one-alpha was increased to 20µg bd leading to her calcium levels steadily improving to between 1.85 – 2.00 mmol/l.
- Conclusion** Patient A is currently asymptomatic with a Ca level of approximately 1.67 mmol/l (2.15 – 2.65). She is currently taking high dose oral calcium and megadose 1 alpha.

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The value of metabolic markers in diagnosis of Vitamin B12 deficiency

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- A Clinical presentation** A 4mth old boy (youngest of 5 siblings) presented to his G.P. with pallor. Initial investigations showed profound anaemia, thrombocytopenia and leucocytopenia. On admission to CUH an abdominal ultrasound showed mild hepatosplenomegaly and lymphadenopathy. Myocardial dysfunction and papulosquamous rash also noted. An initial diagnosis of leukaemia was suspected. Following full haematology, dermatology, cardiology and infectious disease workup a metabolic consult was then sought. Our metabolic laboratory investigations included amino acids, acylcarnitines and urinary organic acids.
- Laboratory findings** Abnormal results included elevated urinary methylmalonic acid (MMA) = 2582 mmol/mmol cr. (0 – 8), propionylcarnitine (C3) = 5 mmol /L (0.17 – 2.32), total homocysteine (tHcy) = 247 mmol /L (<18) and low methionine = 8 mmol/L (5-77). Free homocystine (usually non detectable) was found in plasma and urine. Vit B12 was <150 pmol/L (293 -1210).
- Diagnosis** Differential diagnosis included Methylmalonic Aciduria, B12 deficient diet in exclusively breastfed infant, Transcobalamin II defect, Intracellular combined cobalamin defect. Maternal clinical history revealed a history of hypothyroidism and an episode of severe anaemia 15yrs previously. Current blood film did not reveal anaemia nor macrocytosis, Mother was found to have slightly elevated MMA, homocysteine and C3 reflecting tissue Vit B12 deficiency, while serum Vit B12 level was low normal. Maternal intrinsic antibodies were positive. Baby was diagnosed with profound early Vit B12 deficiency secondary to maternal subclinical pernicious anaemia. Baby's intrinsic factor antibodies were negative.
- Outcome** Baby was treated with Vit B12 injections and an excellent response achieved. MMA, tHcy and C3 normalised. One month later haematological changes resolved, rash disappeared, cardiac function improved and development was normal.
- Conclusion** This case highlights the importance of MMA and tHcy as diagnostic indicators of profound and subtle Vit B12 deficiency. It should raise the awareness of the possible consequences of exclusively breastfeeding infants by mothers with subclinical Vit B12 deficiency, caused by either poor dietary sources (e.g.vegan) or undiagnosed pernicious anaemia.

Critical evaluation of four creatinine assays with a view to the clinical interpretation of creatinine and eGFR on a diabetic cohort

Doupé A

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Background With the recent introduction of the reporting of estimated glomerular filtration rate (eGFR), professional bodies have recommended that all creatinine methods should be traceable to a reference method based on isotopes dilution mass spectrometry (IDMS). This modification should remove bias between methods and requires the use of a revised Modification of Diet in Renal Disease equation (MDRD) with a 6% change in calculation factor from a value of 186 to 175.

Aims The aim of this study was to evaluate four different methods for the determination of serum creatinine. A cohort of diabetic patients was selected to determine if there was any clinical implication in assessing CKD staging in this population depending on which method was utilised.

Methods Validation performance tests were used to evaluate each method. Three of these methods were enzymatic and the fourth was the Modified Jaffè method.

A paediatric cohort was selected to assess the performance of these methods at the low end of the analytical range.

Diabetic nephropathy causes renal failure in diabetics and it is crucial that a valid eGFR from a reliable creatinine result is available to assess renal function. Serum creatinine was estimated across these methods on a diabetic cohort. The eGFR was then estimated from the creatinine obtained from each method. The results were evaluated to determine if there was any clinical variation present depending on the method used. Clinical variation was analysed by the classification of CKD staging using the eGFR obtained from each of the methods.

Conclusions The proportional positive bias associated with the Modified Jaffè method caused the eGFR obtained from this method to be lower and thus a greater proportion of this diabetic population fell into stages 1, 2 and 3 of CKD. Conversely the negative proportional bias associated with the enzymatic methods lead to a higher eGFR value and hence significantly fewer patients fell into stages 1, 2 and 3 of CKD.



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Comparison of bromocresol green- and bromocresol purple- measured albumin methods in renal disease and the merits of introducing an interconversion formula

Doupé A

Biochemistry Department, Mid Western Regional Hospital, Limerick

Background Albumin has been shown to be predictive of survival and hospitalisation both in dialysis and renal transplant patients. It is predominantly two automated dye-binding techniques that measure this analyte, namely Bromocresol Purple (BCP) which is in use in this Biochemistry Dept in Limerick Regional Hospital and Bromocresol Green (BCG) which is used in the laboratory at St Johns Hospital Limerick. Systematic differences between the two methods have long been recognised and since albumin from renal patients would be analysed at both of these sites it was essential that a comparative study on albumin estimation was investigated with the possibility of introducing a conversion formula when data from the two laboratories were being combined.

Method A user defined Bromocresol Green Albumin method from Randox was set up in the Limerick Biochemistry laboratory on the Beckman Coulter DxC.

Initial comparative studies involved the use of three different cohorts of patients which included patients who attended AE, GP surgeries and Pre Dialysis patients. Each of these cohorts had 24 patients. Albumin using both methods was then measured on these three cohorts. Then 65 Pre Dialysis samples were analysed by Limerick's BCP method and St. Johns BCG method.

Results As expected there was a difference between the two methods. For the initial three cohort study the difference (g/L) was 2.6 for GP patients, 6.4 for AE patients, and 7.0 for Pre Dialysis patients; The 65 pre dialysis samples analysed in the two laboratories had a mean difference of 5.5.

Data from the Pre Dialysis cohort was then divided randomly into a derivation set and a validation set and the intraclass correlation coefficient (ICC) was used to express agreement between the calculated and measured BCG.

Conclusion The interconversion formula extrapolated from this study may be helpful when data derived from the two methods is being combined or compared

Adjusted and ionised calcium in the critical care setting

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Introduction We are concerned at the use of mathematical adjustments of serum calcium for variations in albumin concentration even in settings where ionised calcium measurements are available.

Objective This study examined the relationship between adjusted serum calcium and whole blood ionised calcium in patients in the ICU and in seriously ill patients presenting to the A&E.

Method 496 ICU and 505 A&E patient arterial blood samples were analysed for ionised calcium and pH. Total serum calcium and albumin were measured in a corresponding serum sample for each patient. Adjusted calcium values were calculated as: $\text{adjusted calcium} = \text{total calcium} + 0.02 \times (40 - \text{Albumin})$.

Results A positive correlation was observed for total and ionised calcium in the ICU and A&E patients ($r = 0.62$ and 0.63 respectively). A weaker correlation was observed between adjusted calcium and ionised calcium in the same patients ($r = 0.57$ and $r = 0.55$ respectively). 98% of ICU patients had serum albumin levels below the reference range while 85% had total serum calcium below the reference range.

Adjusted calcium results for the ICU patients showed that 7 % were hypocalcaemic while ionised calcium results showed that 61% of patients were in this category. Surprisingly, adjusted calcium results placed 14% of the ICU patients in the hypercalcaemia category.

Adjusted serum calcium placed 11% of the seriously ill A&E patients in the hypocalcaemic category whereas ionised calcium results showed 38% of these patients should be in this category.

Conclusion Adjustment of serum calcium yielded misleading results for ICU and A&E patients when compared to ionised calcium. It underestimated the percentage A&E and ICU patients with hypocalcaemia while overestimating the number of ICU patients with hypercalcaemia. Adjusted calcium results should not be reported for ICU and A&E patients. Ionised calcium measurement should be available to all critical care areas of the hospital.

The development of a partial general unknown screen for drugs by GC/MS in Beaumont Hospital

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Introduction The number of pharmaceutically active compounds in the world is so large and ever growing, that the exact number is not known. However in contrast, the number of these compounds which can be detected by immunoassay has not changed significantly in the last 20 years, and represents only a very small percentage of the total number of these compounds.

All indicators point to an increase in the incidences of abuse of Over-the-Counter and prescription drugs such as Opioids, Selective Serotonin Reuptake Inhibitors, Serotonin Norepinephrine Reuptake Inhibitors and Nonsteroidal anti-inflammatory drugs, none of which could be detected by our routine screen. The detection of such drugs could aid the clinician in the management of patients who present at the Emergency Department with unexplained toxicity.

Aim To develop and offer to our users a wider and more appropriate toxicology service at Beaumont Hospital.

Method Urine samples spiked with isotopic internal standard were cleaned by Solid Phase Extraction (Isolute HXC) and derivitised using BSFTA & TMCS. The derivitised sample extracts were then analysed by GC/MS (Agilent 6890/5973N) using a Retention Time Locked method, containing an in house Screener Database of 80 compounds.

Results The assay was validated to confirm cocaine ingestion to meet the requirements of all guidelines, and to qualitatively confirm the presence of the 80 compounds currently in the Screener Database.

Conclusion This method can tentatively detect over 300,000 other compounds which, upon demand can be confirmed retrospectively, and in so doing expand the drug panel even further. It is envisaged that analysis will be performed weekly, but in exceptional situations a turnaround of 4 hours is possible.

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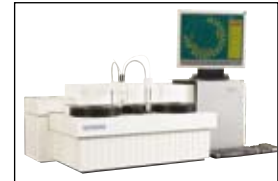
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Determination of an ion exchange chromatography method for the measurement of plasma tryptophan in patients with Glutaric Aciduria Type I

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Background Glutaric Aciduria Type-I (GA-1) is an autosomal recessive inborn error of metabolism, it is caused by a deficiency of the mitochondrial enzyme glutaryl-CoA dehydrogenase (GCDH). This enzyme plays a key role in the catabolic pathway of lysine, hydroxylysine and tryptophan. GA1 is a preventable cause of brain damage in childhood and diagnosis of this disorder before the brain has suffered injury is essential to outcome. Diet therapy is the only treatment currently available for this disorder and patients on low protein diets need to be monitored closely so that their nutritional status can be determined. The GA1 diet is low in protein and both lysine free and tryptophan reduced. Lysine levels are regularly measured for GA1 patients attending Children's University Hospital(CUH) , however tryptophan measurement has not been available to date.

Aim This study aims to develop an ion exchange chromatography method for the quantitative measurement of tryptophan levels in the plasma of patients with GA1.

Method The method was developed on the Amino Tac Amino Acid Analyser (Jeol), which uses ion exchange chromatography with ninhydrin detection.

Results The method was validated by determining precision, sensitivity, linearity and recovery. A reference range was established using apparently healthy patients (non-GA1) who were age-matched with the GA1 patient group. Samples from GA1 patients attending CUH were then analysed using the newly validated method to determine if their tryptophan levels were within the acceptable reference range.

Conclusion A successful method was established for the measurement of plasma tryptophan in the metabolic laboratory. GA1 patient samples were analysed using this method and their plasma tryptophan levels were found not to be statistically different from the non-GA1 paediatric group.

An audit assessing the establishment and utility of NT-proBNP analysis in support of community heart failure services

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¹Department of Cardiology, Royal Victoria hospital, Belfast
²SpR Public Health Medicine, Belfast

Introduction NT-proBNP is a test for suspected heart failure. The problem with introducing a new test lies in establishing appropriate funding and usage. This is particularly relevant for NT-proBNP which has wide clinical application and relevance. The aim of this study was to assess the introduction of NT-proBNP analysis with respect to use of limited resources and appropriateness of requesting using on-going education and audit.

Methods Audit forms were collected from April 2007 to December 2007 from primary and secondary care. NT-proBNP was measured by immunoassay on the Roche Modular analyser. Clinicians completed an audit form with each NT-proBNP request. This requested information regarding past medical history, symptoms, ECG findings, alternative causes of symptoms, and current medication. Clinicians were asked to comment on how NT-proBNP results affected patient management.

Results In total, 1045 forms were collected. Of these, 24% had results <125 ng/L, which rules out heart failure as a cause of symptoms. 57% of results were above age/sex matched reference intervals, indicating possible cardiac dysfunction, and 59% of these were markedly raised, indicating a degree of heart failure. 77% patients had relevant past medical history, and 65% had possible alternative causes for their symptoms, such as chronic obstructive pulmonary disease (20%). 93% of requests recorded relevant symptoms, and of the 52% of patients who had an ECG, 62% recorded an abnormality. Main reasons for NT-proBNP requests were diagnosis (29%), treatment (22%) and echocardiography referral (21%). Data from primary care showed that following circulation of guidance notes from the laboratory, NT-proBNP analysis increased 165%, with 85% of practices using the test.

Conclusion NT-proBNP analysis has application in a growing spectrum of clinical areas with the risk that demand will outstrip a limited budget. We feel our measured introduction of NT-proBNP accompanied by education and audit has successfully optimised test requesting and clinical utility.

Screening for classical Galactosaemia in the Republic of Ireland

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Introduction Classical Galactosaemia, due to a deficiency of galactose-1-phosphate uridyltransferase (GALT), results in the accumulation of galactose and galactose-1-phosphate.

Screening for Classical Galactosaemia has been part of the Irish National Newborn Screening Programme since 1972. The overall incidence in Ireland is 1 in 19 500 births, comprising an incidence of 1 in 32 000 in the general population and 1 in 480 in Irish Travellers.

The method in use, based on Guthrie's Bacterial Inhibition assay (BIA), measures free galactose and is carried out in combination with a qualitative Beutler assay for Galactose-1-phosphate uridyltransferase.

Aim The aim of this study was to select and implement an enhanced screening strategy by assessing methods for measuring Total Galactose (TGAL) and Galactose-1-phosphate uridyltransferase (GALT) and to establish cut offs to ensure no increase in the false positive rate. Ethical approval was granted.

Methods Two commercially available methods for each of TGAL and GALT and an in-house semi quantitative fluorometric Beutler assay were evaluated using 1000 randomly selected, anonymised blood spots from routine newborn screening samples and samples from known galactosaemia patients. DNA analysis was performed on 800 samples for Q188R (allele frequency 89% in the general population; 100% in Irish Travellers) and N314D (incidence of Duarte variant 1 in 650 in the general population).

Results There was poor correlation between the Bio-Rad and PerkinElmer GALT assays. GALT assay performance characteristics were spread across a range with total variation (% CV) of 7.7% (Bio-Rad) and 25.3% (PerkinElmer). With a 99% cut-off for the Bio-Rad TGAL assay of 560 $\mu\text{mol/L}$ no sample had a GALT activity below the 99th percentile by any method. No compound heterozygote for Q188R and N314D has been identified.

Conclusion Based on the analytical performance, assay characteristics and experimental design criteria, Bio-Rad TGAL with subsequent in-house semi quantitative Beutler assay was selected as the screening strategy of choice.

Narrowband UVB phototherapy increases serum 25(OH) vitamin D in Psoriasis patients

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Aims Narrowband UVB (NB-UVB) phototherapy is a widely used treatment of chronic plaque psoriasis. Enhanced cutaneous synthesis of 1,25(OH)₂D by keratinocytes which increases serum 25-hydroxyvitamin D (25(OH)D), may partly account for the therapeutic effect of UV radiation in psoriasis. We assessed the UV mediated increase in serum 25(OH)D in psoriasis patients treated with NB-UVB during wintertime compared to a matched control group of patients with psoriasis. We also examined determinants of vitamin D status in psoriasis patients before phototherapy.

Methods Serum 25(OH)D was measured at baseline, after 12 exposures (or at 4 weeks for controls) and at the endpoint of treatment.

Results Serum 25(OH)D increased significantly ($p < 0.0001$) from median (range) of 58(22-115) nmol/L at baseline to 106(72-194) nmol/L after 12 exposures and 126(79-279) nmol/L at the end of treatment. Serum 25(OH)D was unchanged in the control group. Number of exposures of NB-UVB ($r = 0.609$; $p = 0.0005$) and cumulative UVB dose ($r = 0.465$; $p = 0.011$) both correlated with the change in serum 25(OH)D in the treatment group.

At baseline, 10 patients in the treatment group (34%) and 20 patients in the control group (69%) had insufficient 25(OH)D levels, namely serum 25(OH)D < 50 nmol/L. At the end of the study, all patients in the treatment group were vitamin D sufficient but 75% of the control group were vitamin D insufficient. In a multiple regression model, prior phototherapy was the sole predictor of baseline serum 25(OH)D ($r^2 = 0.13$; $p = 0.006$), the number of exposures to NB-UVB was the sole predictor of change in serum 25(OH)D ($r^2 = 0.38$; $p = 0.001$).

Conclusions NB-UVB effectively increases serum 25(OH)D while clearing psoriasis; the level of increase correlated with number of exposures of treatment. Up to 75% of Irish patients with psoriasis are vitamin D insufficient during wintertime, which was rectified by NB-UVB, highlighting the need for seasonal supplementation in the population.

Comparison of spot protein:creatinine ratio and 24 hour urinary protein for the identification of significant proteinuria in pregnancy

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Background Pre-eclampsia is a syndrome that affects about 5% of all pregnancies. It is defined by two imperfect measures of end organ involvement, hypertension and proteinuria. The International Society for the Study of Hypertension in Pregnancy defines significant proteinuria as $\geq 300\text{mg}/24\text{hours}$. A recent systematic review concluded that, the spot protein:creatinine ratio (PCR) is a reasonable "rule out" test for the detection of proteinuria in hypertensive pregnancy, but because of the variability in laboratory methods used to measure urinary protein, performance of the PCR would have to be validated in each individual laboratory and diagnostic criteria established.

Aim The aim of this study was to assess the usefulness of PCR as a reasonable "rule out" test for the detection of proteinuria, in hypertensive pregnancy using two distinct method types routinely used for protein measurement, Turbidimetric e.g. Audit Diagnostics Benzethonium chloride and dye binding e.g. Olympus Diagnostics Pyrogallol-Red Molybdate.

Methods 24 hour urine collections were obtained from 65 hypertensive pregnant women. A spot urine sample was taken either before or after the 24 hour urine collection. Urine total protein was measured by both methods on the Olympus AU400 analyzer. Urinary creatinine was also measured on the Olympus AU400 using the Olympus Diagnostics Jaffe creatinine method.

Results At $300\text{mg}/24\text{hours}$ the PCR to "rule out" proteinuria of $\geq 300\text{mg}/24\text{hr}$ was calculated as $<27\text{mg}/\text{mmol}$ for the Audit Diagnostics Benzethonium Chloride method. (Sensitivity 84%, Specificity 94%, LR+12.9, LR-0.17)

At $300\text{mg}/24\text{hours}$ the PCR to "rule out" proteinuria of $\geq 300\text{mg}/24\text{hr}$ was calculated as $24.7\text{mg}/\text{mmol}$ for the Olympus Pyrogallol-Red urinary protein method.

(Sensitivity 84%, Specificity 94%, LR+13.9, LR-0.17.)

Conclusions PCR could be used to rule out clinically significant proteinuria in Pre-eclampsia.

In terms of diagnostic accuracy both methods performed equally well but when the PCR to "rule out" proteinuria of $\geq 300\text{mg}/24\text{hr}$ was calculated the PCR values differed by $2.3\text{mg}/\text{mmol}$.



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.....Proteins
.....Hunic acid
.....Chlorogenic acid
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.....Aliphatic acids
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.....Minerals
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Post mortem ethanol levels in Ireland

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Introduction The Global Burden of Disease Study found that alcohol was the third most detrimental risk factor for ill health and premature death. The Strategic Task Force on alcohol report stated that Ireland has the second highest per capita consumption of alcohol in Europe with Irish men drinking more than women and experiencing greater adverse consequences. In addition to this, alcohol related mortality has increased over the last decade in Ireland.

Objectives To establish the prevalence of ethanol in post mortem samples in males and females over a certain period of time and to assess if the prevalence has changed in ten years.

Methods Toxicological analysis of blood samples from autopsies included the measurement of ethanol levels. Post mortem reports from July-December 1998 and 2008 were examined and ethanol levels, age and sex of the deceased was determined

Results A total of 1,480 post mortem results were examined for this study. In the 1998 period, toxicology analysis was carried out on 466 males and 156 females (3:1 ratio). Of these samples, 47% of male and 32% of female results were positive for alcohol. In 2008, 591 males and 267 females had toxicological analysis (2:1 ratio) and 30% of male and 25% of female results were positive for alcohol. The median level for alcohol was 111mg% (1998) and 98mg% (2008) in females. The median level for ethanol was 140mg% (1998) and 118mg% (2008) in males. The median age of females in this study was 58 in 1998 and 67 in 2008, however the average age was lower in males; 50 years old in 1998 and 58 in 2008.

Discussion This study showed that the actual prevalence of ethanol detection was lower in both sexes in 2008 compared to 1998. In addition we found that the alcohol levels were higher in males than females at the time of death. Also the requests for toxicology analysis had increased in males by 27% but more significantly in females by 71%.

Survey of point of care services in the Republic of Ireland

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O'Gorman P, O'Shea P
POCT Consultative Group Sub-committee (ACBI, AMLS)

A survey of POCT services was carried out following the launch of the new "Guidelines for Safe and Effective Management and Use of Point of Care Testing" by the POCT Consultative Group representing the ACBI, AMLS, IMB and RCPI Faculty of Pathology.

Aim The aim of this survey was to provide a snapshot of current services, to compare these services with those of the UK, and to provide a baseline for a further audit to evaluate the effectiveness of the new Guidelines.

Method A questionnaire was devised based on a similar questionnaire distributed by WEQAS in the UK; Irish distribution was achieved through IEQAS. The questionnaires covered accreditation status, existence of POCT committees and Quality Management Systems and staff resources. 55 institutions received at least one questionnaire.

Results 27 hospital laboratories replied (49%); 33% of the laboratories were accredited, 56% had a POCT policy and 44% had a QMS in place. There were 15 designated POCT co-ordinators but all except one had other duties. Laboratories provided POCT support as follows: Training (70%), Health and Safety (67%) and Maintaining documentation (56%). Most support was for blood gases and glucose analysis. Compared with UK results, Ireland gave similar support for blood gases, less for glucose and much less for urinalysis. In both UK and Ireland there was poor IT support. Comments from respondents predominately related to lack of resources such as POCT co-ordinator, no link staff on wards and lack of IT connectivity.

Conclusions Compared to the UK, Ireland fared badly in relation to the availability of POCT policies and QMS. Resources for POCT were considered very scarce. Support for blood gas analysers was good, but poor for other parameters, and connectivity to LIS was limited. The majority of the respondents (21/27) were not happy with the service they supported.

Motivate Project: an innovative weight management program developed to help patients manage their weight, improve their health and enhance their quality of life

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The Motivate Program makes use of behavioural principles to promote change in patient's health related behaviours. The program will primarily focus on patient's eating and activity patterns to improve physical and psychological well being. Primary evaluation will focus on cost-effectiveness; however the service will also be evaluated on the basis of its impact on quantifiable psychosocial, clinical, biochemical, and prognostic indicators.

The project began in 2009 and is scheduled to conclude in 2011. The program is conducted over a 6 month period; face to face contacts are on a bi-weekly basis. Telephone support and individual intervention are offered as necessary. For the first 3 months intervention is a combination of diet/behaviour modification and regular exercise. From months 4 - 6 more intensive behavioural interventions, as well as weight loss medications, are available for patients with limited weight loss. The main problem however with all treatments for obesity is a slow return to baseline weight after treatment intervention ends.

The Motivate Program offers two methods of long term support, either long term via a patient led support group and / or short term via telephone. The intervention is delivered by a multidisciplinary team that includes the support of medical staff. At baseline all patients have at least one obesity related co-morbidity. Initial results: (n = 15) after 3 months intervention, 87% of patients attended the required number of sessions.

For all patients weight change is -3.4kg (3%) increasing to - 4 kg for fully compliant patients. 62 % of the group have Type 2 diabetes. As a group, diabetic patients have reduced their insulin usage by 30 %.

In conclusion the Motivate Program is an evidence-based program and initial finding suggest this is a clinically effective approach to weight management in patient refractory to conventional interventions.

Inherent MCP-1 suppression in C282Y hereditary haemochromatosis links disordered iron metabolism and an altered immune response

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Introduction Hereditary Haemochromatosis (HH) is the commonest inherited disorder in Ireland, typically due to the C282Y mutation of the HFE gene. Production of hepcidin, the main regulator of iron homeostasis, is defective, leading to hepatic iron overload, fibrosis and cirrhosis. Several studies have also shown an attenuated immune response in HH.

Method To elucidate the genetic mechanisms underlying this disease, liver tissue from 10 untreated HH patients and 4 controls (negative for HFE mutations) were analysed using the human Ironchip   microarray. Of genes differentially expressed, Monocyte Chemoattractant Protein-1 (MCP-1) was of particular interest. MCP-1 is a prolific inflammatory chemokine, recruiting monocytes and T lymphocytes to areas of tissue injury and has been implicated in hepatic fibrogenesis through hepatic stellate cell activation. Furthermore, a previous report demonstrated reduced serum MCP-1 levels in C282Y homozygotes compared to wild-type controls.

Aim The aim of this study was to examine hepatic MCP-1 and hepcidin expression in untreated C282Y HH. Gene microarray findings were validated by QRT-PCR on 25 untreated male C282Y homozygotes with evidence of iron overload; mean age 48yrs, ferritin 1569ug/l; median transferrin saturation 89%, hepatocellular iron staining 3+ and fibrosis grade 1(out of 4). Controls consisted of male donor transplant livers (n=4). Both MCP-1 and hepcidin mRNA transcription were significantly lower in the HH cohort when compared to controls ($p<0.002$ and $p<0.015$ respectively). Furthermore, MCP-1 expression correlated significantly with that of hepcidin ($p<0.004$). Immunohistochemistry revealed weaker hepatic MCP-1 staining in the HH cohort compared to control liver tissue.

Conclusion The finding that suppression of hepatic MCP-1 transcription occurs in C282Y HH despite the presence of hepatic fibrosis and significant iron-loading, agrees with a previous report of reduced serum MCP-1 levels in HH. This suppression correlates significantly with diminished hepcidin expression. Taken together, this data suggests an inherent and inappropriate reduction of both MCP-1 and hepcidin in C282Y HH, further interlinking the disordered iron homeostasis and altered immune response described in this disease.

Elevated hepatic transferrin expression in hepatic iron overload is specific to hereditary haemochromatosis

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Abstract Hereditary Haemochromatosis (HH) is a disorder of iron metabolism caused by the C282Y mutation in the HFE gene in >90% cases. A deficiency of hepcidin, the key negative regulator of iron absorption, results in systemic iron overload. Transferrin (Tf) is the primary iron transport plasma protein, produced mainly by the liver. The Tf gene is induced by iron deficiency and suppressed by iron overload. Low serum Tf levels are a feature of HH, presumed due to down-regulation of the Tf gene by hepatic iron. Contrary to this, we recently reported a surprising elevation of hepatic Tf expression in iron-loaded C282Y HH males.

Method To assess this further, we examined hepatic Tf and hepcidin expression in a cohort of patients without HH but with secondary hepatic iron deposition, and compared results to 22 HH males (mean hepatocellular iron-staining grade 3+/4+) and 10 male controls (negative for HFE mutations). The secondary hepatic siderosis cohort consisted of 20 male patients identified to have hepatic iron deposition at liver histology (mean hepatocellular iron-staining grade 1+/4+), 10 with alcoholic liver disease (ALD) and 10 with chronic viral hepatitis.

Results QRT-PCR demonstrated a significant elevation of hepatic Tf mRNA expression in HH compared to ALD, chronic viral hepatitis and controls ($p < 0.001$), with concomitant suppression of hepatic hepcidin expression in the same group ($p = 0.003$). A significant negative correlation between transferrin and hepcidin expression was observed ($r = -0.38$, $p = 0.01$).

Conclusion Despite significant differences in baseline iron parameters between groups analysed, this study suggests that hepatic iron accumulation is associated with an appropriate reduction in Tf gene expression in cases of secondary hepatic siderosis, while a contrasting upregulation occurs in C282Y HH. This upregulation correlates with a suppression of hepcidin, which underlies HH, suggesting an important interaction exists between these two genes within this common disorder of iron metabolism.

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Development and validation of a genotyping assay for the S65C mutation in the HFE gene (Hereditary Haemochromatosis)

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Introduction Hereditary haemochromatosis due to mutations in the HFE gene is the most common inherited disease of European populations. In Ireland, about 92% of patients with hereditary haemochromatosis are homozygous for a point mutation, C282Y, in the HFE gene. A further 7% of cases are compound heterozygotes for two point mutations in this gene, C282Y and H63D. The remaining 1% of cases do not have these genotypes. Another point mutation in the HFE gene, S65C, has been described. Some reports suggest that S65C may be associated with a milder haemochromatosis phenotype.

Aims To develop and validate a genotyping assay for the HFE S65C mutation.

Methods Two alternative methods were set up, using DNA amplification by the polymerase chain reaction, and restriction fragment length polymorphism analysis. The S65C mutation abolishes a Hinf I restriction site in the DNA sequence. For method A, the amplicon from our H63D assay, which spans the S65C polymorphic site, was used. Method B was a published S65C assay. For validation, human DNA samples from the UKNEQAS HFE scheme with known S65C genotype were analysed. Selected samples, identified as SS, SC and CC in the assay, were analysed by DNA sequencing.

Results Both assays yielded the expected length of PCR amplicon and Hinf I digest fragments, and correctly identified 4 samples with known genotype SS and 4 samples with known genotype SC. Method A was judged to be more robust than method B, because the amplicon in method A contains an additional Hinf I restriction site separate from the S65C polymorphic site, and this serves as an internal control for the digest, independent of the S65C genotype. DNA sequencing of samples confirmed the genotypes.

Conclusions A robust S65C assay was developed and validated on DNA samples from human subjects.

Case report: factitious hypoglycaemia

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Aim To report a case of factitious hypoglycaemia and illustrate the properties of human insulin immunoassays.

Methods We describe the clinical presentation and laboratory findings.

Results A 40 year old female was admitted to hospital with a three week history of vomiting and nausea. Twelve months previously the patient underwent gastric banding. Prior to surgery her BMI was 41kg/m², weight 106kg and she was a Type 2 Diabetic treated with insulin and metformin. On admission the patient weighed 74.2kg and no longer required insulin or metformin.

After admission the gastric banding was adjusted to its most open position and the vomiting and nausea resolved.

Point of care glucose monitoring indicated that the patient had episodes of hypoglycaemia. These were confirmed by laboratory measurement of glucose and Whipple's triad. To prevent these hypoglycaemic episodes, the patient was placed on two-hourly feeds. Seventy two hours continuous glucose monitoring (CGM) did not record any hypoglycaemic episodes. After removal of the CGM the hypoglycaemic episodes recurred.

Initial investigations could not explain the cause of the episodes of hypoglycaemia. On four occasions, concomitant with confirmed hypoglycaemia, measurements of insulin and c-peptide (both Roche E Module) in our laboratory presented inexplicable data.

A sulphonylurea screen on a hypoglycaemic serum sample was negative.

Measurement of insulin and c-peptide by other methods produced data consistent with administration of exogenous insulin. After informing the patient of these results there were no further episodes of hypoglycaemia

There are a number of methods for measurement of human insulin. An understanding of the properties of the insulin immunoassays in routine use contributes to the evaluation of suspected factitious hypoglycaemia.

Prevalence of the HFE S65C mutation and correlation with iron status in Irish patients investigated for possible hereditary haemochromatosis

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Introduction Haemochromatosis associated with point mutations in the HFE gene is the commonest inherited disease of European populations. Most patients with HFE-related haemochromatosis are homozygous for the C282Y mutation or compound heterozygous for both the C282Y and H63D mutations. S65C is a much less prevalent mutation in the HFE gene. There are conflicting reports that S65C is associated with haemochromatosis, either independently or combined with a C282Y or H63D mutation, or conversely, that there is no such association. This question has not been investigated in an Irish population.

Aim To determine (i) the S65C allele frequency, and (ii) whether this mutation is associated with iron overload, in an Irish patient cohort investigated for possible haemochromatosis.

Methods A cohort of 654 patients investigated for possible haemochromatosis was studied. HFE genotypes were determined using DNA amplification and RFLP analysis for the C282Y, H63D and S65C mutations. Serum iron concentration and unsaturated iron-binding capacity were determined using FerroZine dye-binding methods on the Hitachi Modular analyser (Roche Diagnostics). Serum ferritin concentration was determined by sandwich-immunoassay on the Beckman Coulter Access analyser. Correlations between genotype and iron indices were determined using the Wilcoxon / Kruskal-Wallis non-parametric test.

Results One patient was homozygous and 24 were heterozygous for S65C. The S65C allele frequency in the patient group was 2%. No significant difference was found between the iron status of patients with one S65C mutation compared to those with no HFE mutation. There was no significant difference between the iron status of compound heterozygotes with one S65C mutation and one C282Y mutation, or one S65C mutation and one H63D mutation, compared to simple heterozygotes with only one mutation (either S65C, C282Y or H63D).

Conclusion The S65C allele frequency in the patient group is similar to that reported for the general population in the west of Ireland. There was no association between the S65C mutation and iron status in the patients studied.

Development of a method for comprehensive BCHE genotyping and report of a novel silent mutation in BCHE causing suxamethonium sensitivity in an Irish patient

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Background Human Butyrylcholinesterase (BCHE, serum, plasma or pseudocholinesterase) is responsible for the hydrolysis of succinylcholine (Suxamethonium), a short acting muscle relaxant used in anaesthetic practice. Mutations in the BCHE gene can inhibit enzyme activity and this can have serious adverse effects, in particular causing post-operative apnoea, so called suxamethonium sensitivity. A number of different genetic variants in BCHE have been identified, including atypical (A), fluoride resistant (F) and Kalow (K) variants, all of which can differentially decrease BCHE activity. Biochemical phenotyping methods have now been superseded by DNA-based genotyping methods and the current genotyping methods are primarily based on PCR-RFLP or multiplex reactions. While these specifically detect known BCHE variants such as A, F and K, in some instances a loss of function silent (S) mutation may be responsible for suxamethonium sensitivity but will not be detected using current genotyping methods.

Method A method for mutation scanning of the coding region (Exons 2, 3 and 4) of BCHE was developed in the Biochemistry Department, St James's Hospital to provide a more comprehensive diagnostic insight into underlying BCHE genotypes causing low plasma cholinesterase activity. This assay uses PCR amplification and direct nucleotide sequencing of amplicons and was validated using DNA from patients with known BCHE genotypes. As part of the diagnostic application of this method a novel silent splice site mutation c.1518-1G>T was identified in a 71-year old female patient who presented with severe apnoea post ECT. The patient was admitted to ICU with a markedly low plasma cholinesterase level of 1157 U/L (Reference range:5320– 12960 U/L). She subsequently recovered and her full genotype revealed compound heterozygosity for the (A) variant c. Asp70Gly and the S variant c.1518-1G>T, as well heterozygosity for the K variant.

Conclusion In conclusion we report the first S mutation causing suxamethonium sensitivity in a patient admitted to an Irish hospital. A method for establishing a comprehensive BCHE genotype has been established and is a routinely available service.

HCG and its subunits - assay specificities and clinical utility in oncology

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Introduction Human chorionic gonadotropin (hCG) is a glycoprotein composed of alpha and beta subunits, joined non covalently. Common hCG-related molecules in serum samples include regular hCG, hyperglycosylated hCG, nicked hCG, hCG missing the beta subunit C-terminal extension, free alpha subunit, free beta subunit, free beta subunit missing the C-terminal extension, hyperglycosylated free beta subunit and nicked free beta subunit. The same molecules plus beta core fragment are present in urine samples. While hyperglycosylated and regular hCG predominate in pregnancy samples, any one of these multiple hCG related molecules may be the principal source of immunoreactivity in gestational trophoblastic disease, gestational trophoblastic neoplasm, choriocarcinoma and placental tumour cases as well as in testicular (seminoma) and germ cell tumour (non seminomatous). As such it is critical to appropriately detect all of these isoforms in the management of these diseases. Only 2 tests, the DPC Immulite & UK RIA (used at Charing Cross hospital) detect all of these hCG related molecules.

Study aims To measure hCG concentrations in 23 male patients (45 samples) with known hCG producing testicular tumors using the Siemens Centaur Total hCG assay and compare concentrations with the Immulite hCG assay to help determine the optimal assay for clinical use.

To measure hCG concentrations in 50 male patients who underwent treatment for a previous tumour to test the security of the baseline measurement using both assays.

To investigate, using the Immulite Free beta hCG assay, whether the Total to free beta hCG ratio provides any additional information in diagnosis in each disease state over Total hCG.

Results In 42/45 samples tested, hCG concentrations were 1-3 times higher using the Immulite assay compared to the Siemens Centaur reflecting the Immulite assay's ability to pick up circulating nicked forms of beta hCG.

No difference was detected between assays on hCG negative samples from patients with a history of testicular cancer. This confirmed the security of the Centaur assay at the clinically important baseline level and suggests that this group do not produce nicked hCG. The ratio of total to free beta hCG did not provide any additional information in the group selected as no significant levels of Free Beta hCG were detected in the 45 patients with known hCG producing tumours.

Conclusions The difference in concentration between the Immulite and Centaur hCG assays reflects the Immulite assays ability to pick up circulating nicked forms of beta hCG. No difference between assays was observed in hCG negative samples from patients with a history of testicular cancer, thus confirming the security of the Centaur assay at the clinically important baseline level, suggesting that this group do not produce nicked hCG.

Use of the Immulite assay over the Centaur may be important in cases where a significant proportion of hCG is suspected to be nicked in origin

